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Oral, Poster, and Video Session Abstracts

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October 12-16, 2019
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These abstracts of research studies, published as submitted by the authors, are presented in the ASRM 2019 Congress sessions and are published in the order of their presentation. Abstracts of plenary lectures, symposia and interactive sessions are not included.
OBJECTIVE: Depression and antidepressant medication use is prevalent in women of reproductive age. Evidence is conflicting regarding antidepressant exposure and miscarriage risk. Therefore, using prospective data on pregnancy and loss from a cohort of women in the Effects of Aspirin in Gestation and Reproduction Trial, we assessed the association between pre-conception-measured antidepressant exposure and time to pregnancy, pregnancy loss, and live birth.

DESIGN: Prospective cohort study of 1228 women with proven fecundity and 1-2 prior pregnancy losses, attempting natural conception while participating in a randomized controlled trial of pre-conception-initiated low-dose aspirin.

MATERIALS AND METHODS: Fluoxetine, sertraline, escitalopram, citalopram, trazodone, nefazodone, etoperidone, and tricyclic antidepressants and related compounds were measured in urine from enrollment and at each conception cycle and pregnancy visit (weeks 4 and 8) via a biochip competitive chemiluminescent immunoassay (Randox Toxicology). Any antidepressant medication use was also assessed via self-report. Cox proportional hazard regression models estimated fecundability odds ratios; log-binomial models estimated pregnancy loss and live birth incidence. Models adjusted for age, body mass index, education level, employment, smoking, alcohol use, marijuana use, and opioid use.

RESULTS: Of 1218 women, 183 (15%) had positive detection of antidepressant compounds prior to conception (at enrollment or at the last cycle prior to conception). Antidepressant exposure prior to conception was associated with lower fecundability (FOR: 0.77, 95% CI: 0.61, 0.99) though overall all live birth incidence was similar (48% in exposed vs. 56% in non-exposed women: RR: 0.91, 95% CI: 0.77, 1.08). Among 785 hCG pregnancies, there was no association between pre-conception exposure and pregnancy loss (25% loss in exposed, 24% in non-exposed; RR: 1.04; 95% CI: 0.73, 1.50), and antidepressant exposure at 4 and 8 weeks’ gestation also yielded a null finding. Sensitivity analyses including additional women in the positive exposure category based on self-reported antidepressant use yielded similar findings for all outcomes of interest.

CONCLUSIONS: Antidepressant medications may lengthen time to pregnancy without impacting live birth rates, and importantly, did not increase risk of pregnancy loss. Given the close prospective follow-up of early pregnancy and loss incidence, including antidepressant exposure assessment both prior to and during early pregnancy, these data help alleviate concerns for miscarriage with use of this important class of medications.

SUPPORT: Intramural Research Program, DIPHR, NICHD, NIH.

O-2 Monday, October 14, 2019 11:00 AM

EFFECTS OF FOLIC ACID AND ZINC SUPPLEMENTATION IN MEN ON SEMEN QUALITY AND LIVE BIRTH AMONG COUPLES UNDERGOING INFERTILITY TREATMENT: FINDINGS FROM THE FASZT RANDOMIZED TRIAL.

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OBJECTIVE: Folic acid and zinc are thought to improve semen quality parameters. We conducted a randomized trial to determine the effect of daily folic acid and zinc supplementation on semen quality and live birth.

DESIGN: The Folic Acid and Zinc Supplementation Trial (FASZT) was a multi-center, double-blind, block-randomized, placebo-controlled trial.

MATERIALS AND METHODS: Men ≥18 years old who with partners were planning infertility treatment were block randomized by site and planned infertility treatment strata (IVF, non-IVF at a study site, and non-IVF at an outside clinic) to receive either 5 mg folic acid and 30 mg elemental zinc or placebo for 6 months during infertility treatment. The primary outcomes were live birth and semen quality parameters, analyzed by intention to treat.

RESULTS: Between June 3, 2013, and December 30, 2017, 2370 men were recruited and randomized (1185 active, 1185 placebo). Daily supplementation was not associated with live birth (active 399 [34%], placebo 408 [34%], risk difference -0.76, 95% CI: -4.58, 3.06) or with sperm concentration, motility, morphology, or total motile sperm count. Supplementation was associated with increased DNA fragmentation (risk difference 2.5, 95% CI 0.6, 4.4). No effects on pregnancy rate, pregnancy loss, gestational age at delivery, embryo parameters, or other adverse neonatal outcomes were observed, except that preterm birth was higher with supplementation (risk difference 1.94, 95% CI: 0.24, 3.64). Gastrointestinal symptoms were also more common with supplementation.

CONCLUSIONS: Use of folic acid and zinc supplementation by men did not improve semen quality and increased DNA fragmentation and gastrointestinal problems. The increase in preterm birth warrants further investigation. The wide-spread impression that supplements will at least ‘do no harm’ may be unfounded. The lack of efficacy and potential risks of folic acid and zinc supplementation can now be communicated to couples seeking infertility treatment.

SUPPORT: Intramural Research Program of the Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health.
MATERIALS AND METHODS: Participating women underwent both HyFoSy and HSG, in randomized order, by a physician unaware of the result of the first test (NTR 4744). In case of discordant results for HyFoSy/HSG, women were randomly allocated to either a management strategy based on HSG or women underwent both HSG and HyFoSy. Assessment of tubal patency was performed using the ExEm FOAM number 837001504). ZonMw funded the whole project. IQ Medical Ventures a randomized controlled trial. BMC women's health. 2018;18(1):64.

Study protocol for nography (HyFoSy) a cost-effective alternative for hysterosalpingography in assessing tubal patency in subfertile women? Study protocol for one year follow-up.

RESULTS: Between June 2015 and January 2019, a total of 1164 women were scheduled to undergo HSG and HyFoSy. At moment of writing, data on 97% was available. 2.3% of the women did not undergo any tests, 5.0% had HSG only and 0.6% had HyFoSy only. From the women who had both tests, 2.9% had an inconclusive HSG and 8.5% had an inconclusive HyFoSy (RR 2.3, 95%CI 1.6-3.2). In 0.8%, both tests were inconclusive. Among the women with two tests completed, 85% had concordant results (94.7% patent tubes, 3% with unilateral occlusion, 0.9% with bilateral occlusion, 1.4% with other findings). The mean pain score on the 1−10 VAS-scale was 5.4 (95%CI 5.2-5.6) for HSG compared to 3.0 (95%CI 2.9-3.2) for HyFoSy (p-value<0.001). Pain score of HyFoSy was not affected by the order of the tests (p=0.34).

Of the 136 eligible women with discordant results, 108 women gave consent to be randomly allocated to management based on HSG (n=53) or HyFoSy (n=55). At moment of writing, data on the primary outcome were available in 58.5% of the HSG group versus in 54.6% of the HyFoSy group.

Ongoing pregnancy occurred in 30.2% of the women allocated to management based on HSG, and in 27.3% of the women allocated to HyFoSy (RR 1.1, 95% CI 0.6-2.1). By October 2019, 90% of women will have complete one year follow-up.

CONCLUSIONS: HyFoSy and HSG have a concordance of 85%, with HyFoSy experienced as significantly less painful and without the need of radiation exposure. In case of a discordant result, management based on the results of HyFoSy or based on the results of HSG lead to similar pregnancy outcomes.


SUPPORT: The FOAMY study is an investigator initiated study, funded by ZonMw, a Dutch organization for Health Research and Development (project number 837001504). ZonMw funded the whole project. IQ Medical Ventures provided the ExEm FOAM® kits free of charge. The funders had no role in study design, collection, analysis and interpretation of the data.

O-5 Monday, October 14, 2019 11:45 AM

BEETROOT, WATERMELON AND GINGER JUICE SUPPLEMENTATION MAY INCREASE THE CLINICAL OUTCOMES OF INTRACYTOPLASMIC SPERM INJECTION CYCLES. Gabriela Halpern, MSc,a Amanda Souza Setti, MSc,b Daniela Paes de Almeida Ferreira Braga, PhD,b Assumpito Iaconelli, Jr., MD,c Edison Borges, Jr., PhDd Fertility Medical Group, Sao Paulo, Brazil;e Fertility Medical Group / Sapientiae Institute, Sao Paulo, Brazil.

OBJECTIVE: The endometrium is a highly dynamic tissue that undergoes cyclic cellular proliferation, differentiation, and immune cell trafficking in response to circulating ovariian-derived steroids. The goal for the present study was to prove the hypothesis that beetroot, watermelon and ginger juice supplementation would improve the endometrial receptivity and clinical outcomes of intracytoplasmic sperm injection (ICSII) cycles.

MATERIALS AND METHODS: This study enrolled 296 female patients undergoing ICSI cycles from Jan/2017 to Jan/2018, in a private university–affiliated IVF center. The sample size calculation suggested that 265 cycles would be enough to demonstrate a 20% effect with 90% power and 5% significance level considering as primary outcome clinical pregnancy rate. Female patients were randomized in a 1:3 ratio to either Control (n=74) or Supplementation Group (n=222). All patients received nutritional orientation before the beginning of the treatment. Participants in the Supplementation Group were instructed to intake a daily dose of homemade juice, prepared with fresh beetroot, watermelon and ginger, from the day of embryo transfer until the day of pregnancy test, while patients in Control Group did not follow the juice protocol. Generalized Linear Models, adjusted for potential confounders (female age, body mass index - BMI, endometrial thickness upon embryo transfer, and number of transferred embryos), followed by Bonferroni post hoc test for the comparison of means between groups, were used to investigate the impact of juice supplementation on the clinical outcomes of ICSI.

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OBJECTIVE: Frequent marijuana use has been associated with poor sperm quality. The aim of this study was to evaluate the association between male marijuana use and adverse pregnancy outcomes. We evaluated the association between male marijuana use and spontaneous abortion (SAB).

DESIGN: Prospective randomized study.

MATERIALS AND METHODS: This study uses data from 1,413 couples enrolled in Pregnancy Study Online (PRESTO), a North American pre-conception cohort study of pregnancy planners. At baseline (preconception), male and female partners completed questionnaires, demographics, medical history, and lifestyle/behavioral factors, including marijuana use frequency. Women completed bimonthly follow-up surveys for up to 12-months or until conception. Data on SAB were ascertained from follow-up questionnaires completed in early pregnancy (<12 weeks gestation) and late pregnancy (~32 weeks gestation). Additional data were reported on the first positive pregnancy test date, due date, and gestational weeks at loss. Frequency of male marijuana use in the previous 2 months was ascertained at baseline and categorized as follows: no use, <1 time/week, or ≥1 time/week. Cox proportional hazards regression models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI) for the association between male baseline marijuana use frequency and SAB. The timescale was gestational weeks from date of first pregnancy detection. We controlled for age at baseline (male and female), household income, education, race/ethnicity, smoking status, environmental tobacco exposure, alcohol intake, caffeine intake, sugar-sweetened beverage intake, body mass index, exercise, multivitamin use, sleep duration, hours of work per week, history of sexually transmitted infections, depression/anxiety, and frequency of female baseline marijuana use. Additional models controlled for reproductive history, including having impregnated a partner previously, parity (female), history of pregnancy loss (female), and family history of SAB (female).

RESULTS: Among the 1,413 couples followed, 1,164 (82.4%) men reported no marijuana use, 132 (9.3%) reported using marijuana <1 time/week, and 117 (8.3%) reported using marijuana ≥1 time/week in the 2 months before baseline. During follow-up, 266 (18.8%) SABs were reported. Compared with no male marijuana use, adjusted HRs for male marijuana use <1 time/week and ≥1 time/week were 1.07 (95% CI: 0.65-1.77) and 2.04 (95% CI: 1.28-3.24), respectively. The association (≥1 time/week vs. none) persisted after adjusting for reproductive history (HR=2.05, 95% CI: 1.29-3.26), and was slightly stronger after restricting to couples where the female partner did not use marijuana (HR=2.19, 95% CI: 1.26-3.80).

CONCLUSIONS: Couples with male partners who used marijuana ≥1 time per week during preconception had a greater risk of SAB compared with no male marijuana use. Little association was found for men who used marijuana <1 time per week. Possible mechanisms include an adverse effect of frequent marijuana use on sperm quality.
PHASE 3 TRIAL RESULTS: Efficacy and Safety of Elagolix in a Subset of Women with Uterine Fibroids and Adenomyosis.

OBJECTIVE: Adenomyosis is a benign lesion within the myometrium associated with heavy menstrual bleeding (HMB) and dysmenorrhea, and commonly co-exists with uterine fibroids (UF). Adenomyosis is also present in 15-57% of hysterectomy specimens with leiomyoma (Genc M, et al, 2015; Taran FA, et al, 2010). This analysis evaluated the efficacy and safety of elagolix, an oral, gonadotropin-releasing hormone receptor antagonist, with add-back therapy in a subset of women with UF, HMB, and co-existing adenomyosis.

DESIGN: Data were pooled from two 6-month, randomized, double-blind, placebo-controlled phase 3 studies, Elaris UF-1 and UF-2. Premenopausal women (18-51 years) with ultrasound-confirmed diagnosis of UF and HMB (>80mL menstrual blood loss [MBL]/cycle) were randomized 1:1:2 to placebo, elagolix 300mg twice daily (BID), or elagolix 300mg BID with 1mg estradiol/0.5mg norethindrone acetate (E2/NETA) once daily.

MATERIALS AND METHODS: This subset analysis was conducted in women with HFMB associated with UF and co-existing adenomyosis diagnosed by ultrasound and/or MRI at baseline (BL). The primary endpoint was the proportion of women with <80mL MBL during the final month and ≥50% reduction from BL to the final month. MBL, and the diagnosis of HFMB was assessed with the alkaline hematin method. Adverse events (AEs) were monitored.

RESULTS: Of 790 women treated, 16% had ultrasound and/or MRI diagnosis of adenomyosis at BL. Pooled data demonstrated that the proportion of responders for the primary endpoint was significantly greater (P<0.001) for elagolix+E2/NETA [76.8% (95% CI, 65.8, 87.8)] compared to placebo [72.1% (95% CI, 64.5, 80.0)] at BL, and elagolix+E2/NETA significantly reduced MBL compared to placebo, elagolix 300mg BID, or elagolix 300mg BID with 1mg estradiol/0.5mg norethindrone acetate (E2/NETA) once daily.

CONCLUSIONS: In women with HFMB associated with UF and co-existing adenomyosis, elagolix+E2/NETA significantly reduced MBL versus placebo similar to the all-subject group. AE reports in this group were similar to the all-subject group. These data suggest that further studies investigating the effect of elagolix in women with HFMB associated with UF and adenomyosis may be warranted.

ART LAB: BASIC

O-7 Monday, October 14, 2019 10:45 AM

IMPLEMENTATION OF AN ELECTRONIC WHITEBOARD FOR QUALITY MANAGEMENT IN THE IN VITRO FERTILIZATION LABORATORY. Philip A. Romanski, MD, a Ann M. Thomas, PhD, a Jay Patel, MS, a Dan Zhang, MD, PhD, a Catherine Racowsky, PhD a Brigham & Women’s Hospital and Harvard Medical School, Boston, MA; b Brigham & Women’s Hospital, Boston, MA.

OBJECTIVE: In 2014, we implemented an electronic whiteboard as a quality management tool to assist our embryologists to ensure their adherence to established standards for performing time-sensitive procedures (1). We aimed to test the hypothesis that use of an electronic whiteboard in the IVF laboratory increases the likelihood that critical evaluation procedures are performed within optimum pre-set time ranges.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Retrievals in our IVF clinic between 6/30/12 and 5/31/18 were included. The pre-electronic whiteboard time-period was 6/1/12 to 4/5/14, during which embryologists strived to adhere to the set optimum evaluation times but without a formal guide. The post-electronic whiteboard time-period was 3/1/15 to 5/31/18. The 13 months after the electronic whiteboard was introduced (4/6/14-2/28/15) were defined as a transition period and were excluded. Optimum pre-set time ranges were 16-18 hours post-insemination or ICSI (HPI) for the pronuclei (PN) check, 65-67 HPI for day 3 evaluations and 114-117 HPI for day 5 evaluations. Log binomial models estimated the risk ratio (RR, 95% confidence interval [CI]) of evaluations occurring within the optimum time ranges. Models were adjusted a priori for ICSI.

RESULTS: A total of 44,957 oocytes from 6,302 retrievals met inclusion criteria, of which 44.4% underwent ICSI. There were 16,434 oocytes from 2,703 retrievals pre-electronic whiteboard and 28,523 oocytes from 3,599 retrievals post-electronic whiteboard. The proportion of oocytes evaluated at the PN check within the optimum time range was statistically significantly increased after implementation of the electronic whiteboard (89.2% vs 80.8%, RR 1.11 [95% CI 1.10 – 1.12]). The proportion of day 3 and day 5 checks that occurred within the optimum time ranges were also statistically significantly increased after implementation of the electronic whiteboard (day 3: 73.3% vs 57.2%, RR 1.75 [95% CI 1.54 – 1.99]) and (day 5: 74.1% vs 58.8%, RR 1.26 [95% CI 1.24 – 1.29]).

CONCLUSIONS: Our findings indicate that use of an electronic whiteboard that posts optimum time ranges for performing critical IVF laboratory procedures tightens the actual evaluation times towards these ranges. Such improved standardization may lead to positive downstream effects on quality assurance analyses and embryo transfer and embryo cryopreservation management decisions. Future studies will investigate whether use of an electronic whiteboard in the IVF laboratory improves overall clinical care.


SUPPORT: None.

O-8 Monday, October 14, 2019 11:00 AM

THE CLINICAL RESULTS OF PIEZO-ICSI COMPARED TO CONVENTIONAL-ICSI: A SIBLING-OOCYTE STUDY. Noriyuki Okuyama, M.Sc.,a Ryuichiro Obata, Ph.D.,a Nao Oka, M.Sc.,b Nobuya Aono, Ph.D.,b Masayoshi Hashimoto, M.D., Ph.D.,c Kento Kyoni, M.D., Ph.D.,c Kyono ART Clinic Takawan, Tokyo, Japan; d3-13-1, takanawa, Minato-ku, Tokyo, Japan.

OBJECTIVE: Clinically, conventional ICSI (CI) is a common, widely-used method, while there are few reports with respect to Piezo ICSI (PI). PI is effective in degeneration rate and fertilization rate (Kimura, Y & Yana- moshi, R, 1995). It is known that degeneration rate and survival rate of oocytes are lower after CI; however, degeneration rate improved markedly using PI. PI is an effective technique for cases with fragile oocytes. It has been reported that the survival rate is similarly improved in human oocytes (Hiraoka, K & Kimamura, S, 2015). However, most of the studies reporting on PI are retrospective studies. Here, we prospectively compared the degeneration rates, fertilization rates and embryo development of PI and CI in a sibling study.

DESIGN: This is a prospective randomized controlled single-center study, using sibling oocytes, conducted from August 2018 to March 2019. Written informed consent was obtained from all patients involved in this study.

MATERIALS AND METHODS: This sibling oocyte study comprised 26 cycles in 26 cases. CI was performed in 149 mature oocytes. CI consists of mechanical penetration of the zona pellucida, breaking the oocyte membrane by aspiration of cytoplasm. PI was performed in 162 mature oocytes. PI consists of reducing the oocyte zona pellucida by the focused acoustic pulse. PI is effective in degeneration rate and fertilization rate (Kimura, Y & Yana- moshi, R, 1995). It is known that degeneration rate and survival rate of oocytes are lower after CI; however, degeneration rate improved markedly using PI. PI is an effective technique for cases with fragile oocytes. It has been reported that the survival rate is similarly improved in human oocytes (Hiraoka, K & Kimamura, S, 2015). However, most of the studies reporting on PI are retrospective studies. Here, we prospectively compared the degeneration rates, fertilization rates and embryo development of PI and CI in a sibling study.

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RESULTS: This is a prospective randomized controlled single-center study, using sibling oocytes, conducted from August 2018 to March 2019. Written informed consent was obtained from all patients involved in this study.

CONCLUSIONS: In conclusion, the present study has demonstrated there was no significant difference in the clinical results of piezo-ICSI and conventional-ICSI. However, this may be attributable to the limited number of cases with fragile oocytes, etc. In our experience, PI is safer and easier to learn and...
perform in clinical work in a shorter period, especially for beginners. Further studies are necessary.

**O-10 Monday, October 14, 2019 11:30 AM**

**PROPORTION OF PATIENTS DETECTED WITH SUBCLINICAL HYPOTHYROIDISM IS INDEPENDENT OF TIME OF BLOOD DRAW.** Christine Briton-Jones, PhD, HCLD,a Jenna Friedenthal, MD, b Sydney Chang, MD, b Taraneh Gharib Nazem, MD,a Dmitry Gounko, MA,a Joseph A. Lee, BA,a Alan B. Copperman, MD d Reproductive Medicine Associates of New York, New York, New York; ¥Icahn School of Medicine at Mount Sinai, New York, NY.

**OBJECTIVE:** There are differences in clinical opinion regarding the benefit of treating subclinical hypothyroidism in infertile patients. However, for patients with a thyroid stimulating hormone (TSH) serum level > 2.5mIU/L it is recommended to continue monitoring or administer levothyroxine to reduce TSH serum levels <2.5mIU/L (ASRM guideline document 2015). TSH levels in adults, have a predictable circadian rhythm, with the highest levels produced between 2am and 4am; while the lowest levels occur between 4pm and 8pm. Whether there is a misdiagnosis of subclinical hypothyroidism and underlying normal circadian rhythm due to testing afternoon blood draw is a current clinical concern. Only one study has showed the potential for this misdiagnosis, albeit the study included a small sample size. [1] The aim of this study was to identify any differences in the mean TSH levels obtained from morning compared to afternoon blood draws in patients seeking infertility treatment.

**DESIGN:** Retrospective cohort analysis

**MATERIALS AND METHODS:** This study examined patients having routine TSH levels tested for either cycle day 3 evaluations or as part of a new patient consultation from January 2018 and March 2019. Serum TSH concentrations were obtained via electrochemiluminescence immunoassay Elecsys for use on Cobas e601(Roche) Detection range of 0.005 – 100 mIU/L. Chi Square analysis was used to determine statistical significance with p<0.05 considered significant.

**RESULTS:** Of the 8345 patients who had routine TSH testing performed, 5028 were drawn in the morning and 3287 were drawn in the afternoon. There was no significant difference in the mean (± SD) TSH levels, 2.104±0.34 (4.30) for am blood draws and 2.104±0.26 (4.31) for pm blood draws. There was also no differences in the in the percentage of TSH results showing >2.5mIU/L in morning 25% compared to afternoon blood draw groups 26%.

**CONCLUSIONS:** This study showed no shift in the mean or in percentage of patients with elevated TSH levels in the morning compared to afternoon blood draw group. This data shows that afternoon blood draws are just as likely to detect elevated TSH levels as blood samples drawn in the morning. The strength of this study is its ability to define risks of misdiagnosis of sub-clinical hypothyroidism due to potential underlying changes in TSH levels for the different times of blood draw using binomial sorting of patient data in a diverse population of patients seeking ART treatment. This study highlights how TSH fluctuations that may occur throughout the day are clinically insignificant and even with ultra-sensitive immunoassays not, detectable in a population of patients undergoing reproductive treatment.


**SUPPORT:** None.

**O-11 Monday, October 14, 2019 11:45 AM**

**PRELIMINARY RESULTS FROM THE FIRST REGISTERED PILOT TRIAL WITH MATERNAL SPINDLE TRANSFER TO OVERCOME INFERTILITY.** Nuno Costa-Borges, PhD,a Eros Nikitos, MSc,a Katharina Spath, PhD,a Degan Wells, PhD,a Klaus Rink, PhD,a Yannis Vasilopoulos, MD,a Ioannis Zervamanolakis, MD,b Dimitriopoulos Konstantinos, MD,a Polyzos Panagiotis, MD,a Stylianos Grigorakis, MD, FRCOG,b George Kontopoulos, MD,b Konstantinos Kostaras, MD, PhD,a Panagiotis S. Psathas, MD,a Gloria Calderon, PhD Embryotools, Barcelona, Spain; ¥Institute of Life, Athens, Greece; ¥IVI RMA, Oxford, United Kingdom; ¥Institute of Life, Athens, Greece.

**OBJECTIVE:** In assisted reproductive technologies (ART), implantation rate is limited by the number of embryos available for transfer. The maintenance of a sufficient number of embryos to achieve a pregnancy is one of the main challenges faced in the treatment of infertility. Embryos transferred during ART cycles show a wide variability in terms of blastomere size and morphology. These differences have been associated with implantation rate and clinical outcome of ART. A recent study showed a significant increase in implantation rates after the transfer of equal embryos [1]. The use of uniform size blastocyst transfers in ART has been linked with better clinical results [2]. However, uniform size transfer is associated with low pregnancy rates [2]. The equal embryo transfer is not feasible in many situations due to the low number of embryos available in ART cycles. Thus, the establishment of a less invasive and objective criterion to select embryos for transfer would represent a valuable addition to ART protocols.

**MATERIALS AND METHODS:** In this study, we used a novel morphokinetic algorithm (Geri-Assess) to select embryos for transfer. A database of 1,370 embryos (N = 284 patients) at IVIRMA Valencia clinic was used. All embryos were normally fertilized embryos cultured up to day 5/6. Embryos were selected based on the automatic morphokinetic algorithm Geri-Assess 2.0 software (GA2), including filtration of events falling outside the pre-defined time-ranges, as is done in the full Geri-Assess system. Both morphokinetic manual and automated annotations went through an embryo selection algorithm developed by Basile et al. (2015) considering the morphokinetic parameters t3, ec2 (t3-t2) and t5. Embryos were graded and the accuracy in the prediction was assessed between both groups of patients undergoing reproductive treatment.

**RESULTS:** High accordance was found between IVI and GA2 embryo grading through Basile’s algorithm. Out of the 1,370 embryos, 1,045 were utilized as transferral or vitrified, showing no statistically significant differences between both groups in all grades: A+, A, A+, B+, C+, C, D+ and D; except for No Grade (p < 0.05). More ungraded embryos were found in the automated group, as Geri-Assess 2.0 is designed to eliminate events falling outside of pre-defined time-ranges, as is done in the full Geri-Assess system. All morphokinetic manual and automated annotations went through an embryo selection algorithm developed by Basile et al. (2015) considering the morphokinetic parameters t3, ec2 (t3-t2) and t5. Embryos were graded and the accuracy in the prediction was assessed between both groups of patients undergoing reproductive treatment.

**CONCLUSIONS:** The results of this study support the use of automated systems for embryo morphokinetic annotations. This non-invasive and objective tool standardizes the annotating process avoiding inter- and intra-grader variability, in addition to facilitating the routine clinical practice. The establishment of automation would need a gradual transition controlled by lab professionals, as yet chaotic embryos or artifacts in the well hinders its performance.
OBJECTIVE: Oocyte cytoplasmic dysfunction is a major contributor to impaired embryo development. Since maternal spindle transfer (MST) allows replacement of the entire cytoplasm of a poor quality oocyte, it holds a great promise to enhance oocyte quality. Our previous studies using mice and human oocytes donors for research have shown the technical feasibility of MST to overcome embryo development arrest. This registered pilot trial represents the next step forward in the validation of MST as a potential methodology for addressing certain infertility problems, some of which are refractory to current clinical strategies.

MATERIALS AND METHODS: Meiotic spindles from patients’ oocytes were isolated under polarized light microscopy within minimal amounts of cytoplasm. Spindles were transferred to previously enucleated donor oocytes, inseminated by ICSI and cultured in a time-lapse incubator. Blastocysts of good morphology were biopsied and screened for aneuploidy. Additionally, mitochondrial DNA (mtDNA) copy number levels were assessed. Euploid embryos were transferred and DNA samples were obtained either from amniotic fluid or at birth, to confirm the origin of the mitochondrial and nuclear genomes.

RESULTS: 2,960kg. Analysis of DNA fingerprints from biopsied cells, amniotic fluid and samples collected after birth (blood, urine, saliva, cord blood, placenta) confirmed the parentage of the child and the origin of the donated mtDNA. The second pregnancy is currently at 14 weeks of gestation (51cm and 2,960kg).

CONCLUSIONS: These results indicate that MST-derived embryos are able to implant and sustain a healthy pregnancy to term. Given the difficult reproductive history of the patients, this initial data is encouraging. However, carefully controlled trials will be required to determine whether MST is truly beneficial in the context of assisted reproductive treatment.

SUPPORT: Institutional funding.
O-14 Monday, October 14, 2019 11:00 AM

SEX DIFFERENCES IN BIRTH OUTCOMES FOR MASSACHUSETTS INFANTS FOLLOWING ART

ART: Sunah S. Hwang, MD MPH,a Dmitry Dzhakhvany, MD MPH,b Daksha Gopal, MPH,c Howard Cabral, PhD, MPH,c Hafsatou Diop, MD, MPH,c Judy E. Stern, PhD,c* University of Colorado School of Medicine, Aurora, CO;cAffiliation not provided;cBoston University, Boston, MA;bMDPH, Boston, MA; bDartmouth-Hitchcock, Lebanon, OR.

OBJECTIVE: Sex differences in infant and adult health outcomes have been demonstrated. While prior studies have shown adverse birth outcomes for infants conceived by assisted reproductive technology (ART), data on whether outcomes differ by infant sex are lacking. Our objective in this study was to determine the presence and magnitude of sex differences in neonatal health outcomes among infants conceived by ART.

DESIGN: Retrospective observational cohort analysis of singletons born in Massachusetts between July 1, 2004 and December 31, 2013 who were conceived by ART.

MATERIALS AND METHODS: We linked the Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS), a clinical database of treatment information on all ART cycles and the Pregnancy to Early Life Longitudinal (PELL) data system, which links birth certificates to hospital discharge records for mothers and infants in Massachusetts. The analysis was limited to singleton, live births to women ≥ 18 years, conceived by ART. Birth outcomes for ART deliveries were compared between male and female infants using chi-square tests. Health outcomes were obtained from PELL. Multivariable logistic regression was used to model the potential association between infant sex and adverse health outcomes, controlling for maternal age, race/ethnicity, education, insurance, chronic and gestational diabetes, hypotension, parity, and gestational age (results displayed as adjusted odds ratio; 95% confidence interval).

RESULTS: A total of 16,034 singleton live births conceived by ART were included: 7,737 female and 8,297 male. In the adjusted analysis, compared to female infants, male infants had greater odds of being preterm (1.19; 1.07-1.32), having birth defects (1.31; 1.05-1.63), experiencing respiratory (1.37; 1.24-1.51) and neurologic (1.29; 1.09-1.53) conditions, and prolonged hospital stay (1.25; 1.09-1.43). Despite the higher odds of preterm birth, male infants had lower odds of being low birthweight (0.8; 0.7-0.92) compared to their female counterparts.

CONCLUSIONS: Sex differences in birth outcomes of infants conceived by ART exist. Further studies are needed to elucidate the biologic mechanisms underlying the relationship between infant sex and these adverse health outcomes among infants conceived by ART.

SUPPORT: NIH R01HD067270.

O-15 Monday, October 14, 2019 11:15 AM

CONCEPTION BY INFERTILITY TREATMENT AND NEWBORN DNA METHYLATION

Edwina Yetung, PhD,a Pauline Lugria, PhD,b Rajeshwari Jamil, PhD,c Xuehuo Zeng, PhD,c WeiHua Guan, PhD,c Michael Y. Tsai, PhD,c Sonia L. Robinson, PhD,c Judy E. Stern, PhD,c Erin M. Bell, PhD,c National Institutes of Child Health and Human Development, Bethesda, MD; cGiotech Inc, Rockville, MD; cUniversity of Minnesota, Minneapolis, MN; cDartmouth-Hitchcock, Lebanon, OR; cUniversity at Albany, Albany, NY.

OBJECTIVE: To determine whether newborns conceived by infertility treatment have different DNA methylation patterns from newborns not conceived by treatment.

DESIGN: The Upstate KIDS Study recruited women and their newborns (2008-2010), oversampling on infertility treatment exposure.

MATERIALS AND METHODS: Mothers reported on use of infertility treatment and the specific type (assisted reproductive technologies [ART] or ovulation induction [OI] / intrauterine insemination [IUI]) at 4 months of age to the Upstate KIDS study, a prospective cohort study of newborns in Rochester, NY. Singletons (n = 385) were enrolled in a longitudinal study of DNA methylation in newborns. DNA methylation was measured using the Infinium Epic microarray. Samples from 855 newborns were used in analysis. Singletons (n = 688) and unrelated twins (n = 167) were included to maintain independent samples. Quantile normalization was applied for probe type normalization and robust linear regression used to model the associations between 837,933 CpGs and any infertility treatment as well as by type (i.e., ART, OI/IUI, none). Bonferroni significance of p < 6.6x10^-10 was used to account for multiple testing. Analyses were adjusted for maternal age, race, education, pregnancy smoking, private insurance, estimated cell type and batch effects.

RESULTS: Newborns conceived with infertility treatment (n = 335, 39%) had higher methylation at one CpG in C14orf166b (cg21616682, p = 4.74x10^-14) compared to newborns not conceived with treatment (n = 514). When the specific techniques were examined, no genome-wide associations were found for conception by OI/IUI (n = 177, 20%). However, ART conceived newborns (n = 158, 19%) had hypomethylation (ranging from 1.5 to 5.3%) at four CpGs in several gene regions (Table 1). Additional adjustment for plurality, infant sex, gestational age and birthweight did not meaningfully alter the findings.

CONCLUSIONS: In one of the largest studies examining differences in newborn DNA methylation by conception with infertility treatment, several genes were identified, lending them to infertility. For instance, SYCE1 encodes for a synaptonemal complex protein, which is necessary for meiosis, and whose mutations were previously found in association with male and female infertility. Ongoing child follow-up will validate whether methylation differences persist.

TABLE 1. Newborn DNA methylation differences between conception by ART versus no treatment

<table>
<thead>
<tr>
<th>CpG</th>
<th>Beta</th>
<th>SE</th>
<th>p-value</th>
<th>Chromosome</th>
<th>Position</th>
<th>Gene</th>
</tr>
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<tr>
<td>cg17676129</td>
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<td>0.002484</td>
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<td>135382545</td>
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<td>135237754</td>
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<td>cg01050010</td>
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<td>0.009847</td>
<td>5.28E-08</td>
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<td>40795974</td>
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O-16 Monday, October 14, 2019 11:30 AM

BABIES BORN FOLLOWING ADMINISTRATION OF NOLASIBAN BEFORE EMBRYO TRANSFER (ET) AFTER IVF: NEONATAL AND INFANT DEVELOPMENT OUTCOMES FROM A DOUBLE-BLIND, PLACEBO-CONTROLLED, CLINICAL TRIAL.

Andrew Humberstone, PhD,a Paul Terrill, PhD,b Lynne Macgregor, MSc,c Ernest Loumaye, MD, PhD,c Ohs Eva SA, Plan-les-Ouates, Switzerland; cCyclc Inc, London, United Kingdom.

OBJECTIVE: Nolasiban, an oral oxytocin antagonist, has been shown to increase live birth rate when administered prior to ET (Visnova 2018). The objective of this study was to assess neonatal and infant development outcomes after administration of nolasiban or placebo at the time of ET.

DESIGN: Multinational, double-blind, randomized, parallel group, placebo-controlled. Phase 3 trial assessing a single oral 900 mg dose of nolasiban or placebo (1:1), administered about 4 hours before ET following IVF. Neonatal outcomes were assessed up to 28 days after birth and infant development assessed using the Ages and Stages Questionnaire-3® (ASQ-3®) completed at 6 months after birth.

MATERIALS AND METHODS: 778 subjects were recruited from 41 fertility clinics in Europe from Mar–Oct 2017. Eligibility criteria included age ≤ 36 years, ≤ 1 failed ART cycle, use of a GnRH antagonist, (19.1%) in the nolasiban group. The most common neonatal morbidities in the placebo group and 5 (3.7%) in the nolasiban group.

CONCLUSIONS: There were 108 deliveries (1 set of twins) resulting in 109 infants in the placebo group and 131 deliveries (5 sets of twins) resulting in 136 infants in the nolasiban group. At birth, mean ± SD 36 years, 1 failed ART cycle, use of a GnRH antagonist, (19.1%) in the nolasiban group. The most common neonatal morbidities in the placebo group and 5 (3.7%) in the nolasiban group.

At 28 days after birth, weight, height and head circumference continued to be similar between groups. 9 (8.8%) infants had been admitted to intensive care in the placebo group and 9 (6.6%) in the nolasiban group. Neonatal morbidities were reported in 29 (26.6%) infants in the placebo group and 26 (19.1%) in the nolasiban group. The most common neonatal morbidities were jaundice (20 (18.3%) placebo, 18 (13.2%) nolasiban) and respiratory distress syndrome (10 (9.2%) placebo, 11 (8.1%) nolasiban).

At 6 months after birth for those subjects with follow-up data, mean ± SD total ASQ-3 scores were 208.7 ± 38.8 in the placebo group and 208.5 ± 44.7 in the nolasiban group. The No. (%) of infants with an ASQ-3 score below the normal range in ≥ 1 domain was 33 (37.5%) in the placebo group and 43 (41.7%) in the nolasiban group.
CONCLUSIONS: The neonatal and infant developmental outcomes were similar between the nolasiban and placebo groups.


SUPPORT: The trial was funded by ObsEva SA.

O-17 Monday, October 14, 2019 11:45 AM

SIMILAR SUCCESS RATES WITH FROZEN OOCYTES BUT INCREASED RATE OF LARGE FOR GESTATIONAL AGE (LGA) INFANTS COMPARED TO FRESH OOCYTES. Channing Burks, MD,* Kristin Van Heertum, MD,* Alexandra C. Purdue-Smith, PhD,* Sunni L. Mumford, PhD,* James Goldfarb, MBA,* and Rachel S. Weinerman, MD,* University Hospitals and Cleveland Medical Center, Cleveland, OH.

OBJECTIVE: Evaluate pregnancy and perinatal outcomes of embryos derived from fresh and frozen oocytes in autologous cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The SART database was used to identify autologous oocyte cycles that resulted in an embryo transfer during 2014 and 2015. Generalized linear regression models were used to compare pregnancy and perinatal outcomes of fresh versus frozen oocytes. Models were adjusted for the following factors: maternal age, BMI, current smoking status, parity, infertility diagnosis, prior IVF attempt, ICSI assisted hatching, number of embryos transferred, multiple gestation and fetal heart reduction. Live birth rate was the primary outcome. Secondary outcomes include miscarriage rate and birth weight.

RESULTS: The mean maternal age in autologous oocyte cycles (N=139,734) was 35 years (SD ±3.6). There was no significant difference in the live birth rates when comparing embryos derived from fresh and frozen oocytes in autologous cycles (25.7% versus 23.9%, aRR 0.94, 95% CI 0.8-1.1). No significant differences were noted in biochemical pregnancy losses (5.8% versus 6.9%, aRR 1.3, 95% CI 0.94-1.79) or clinical miscarriages (10.9% versus 11.2%, aRR 0.94, 95% CI 0.82-1.33) in embryos derived from fresh and frozen autologous oocytes. Increased risk for large for gestational age infants (4.5% versus 12.5%, aRR 2.69, 95% CI 1.66-4.33) was seen in embryos derived from frozen oocytes. No significant difference was noted in low birth weight infants between the two groups.

CONCLUSIONS: Frozen oocytes have similar success rates as fresh oocytes in autologous cycles that resulted in embryo transfer. However, an increased rate of large for gestational age infants was seen in embryos derived from frozen oocyte. This finding warrants further study.

O-18 Monday, October 14, 2019 12:00 PM

PREVALENCE OF CLINICALLY SIGNIFICANT CONGENITAL HEART DEFECTS IN LOW- RISK IVF PREGNANCIES. Sarah H. Bjorkman, MD,* Kurt R. Bjorkman, MD,* Anna K. Skakianakis, MD, MPH, Joshua A. Copel, MD,* Mert Ozan Bahtiyar, MD* Yale School of Medicine, New Haven, CT. Department of Pediatrics, Yale School of Medicine, New Haven, CT; Yale Maternal Fetal Medicine, Fetal Care Center, New Haven, CT.

OBJECTIVE: Current research has shown increased prevalence of congenital heart defects (CHD) among in vitro fertilization (IVF) pregnancies compared to spontaneous pregnancies. We describe the prevalence and characteristics of CHD in IVF pregnancies at a high-volume fetal echocardiography center and outline a low-risk subset of patients for whom echo may not be clinically indicated.

DESIGN: Historical Prospective Observational Study.

MATERIALS AND METHODS: All fetal echocardiograms for singleton and dichorionic twin pregnancies performed January 1, 2004 to December 31, 2018 at a large tertiary care center utilizing gray scale, color Doppler, and spectral Doppler were reviewed and categorized by gestational age (GA), indications for fetal echo, and presence of structural CHD. All initial diagnoses were made by experienced sonographers and a maternal-fetal medicine specialist, recorded on videotape, and confirmed by a pediatric cardiologist. Neonatal echocardiographic examinations were performed to confirm diagnoses in cases with prenatal diagnoses of CHD. Prevalence and 95% confidence intervals (CI) calculated using standard statistical methods. Clinical outcomes were available for cases of CHD after 2011.

RESULTS: 18,879 fetal echocardiograms were completed during the study period. Of those, 3,893 echocardiograms were performed with only indication being IVF gestation. Patients with previous child with CHD, family history of CHD, medication exposure, diabetes, non-cardiac anomaly, anomaly in previous pregnancy, other abnormality noted on ultrasound, or monochorionic twins were excluded. Mean GA at time of echo for IVF only group was 22.2 ± 1.4 weeks. Prevalence of CHD summarized in Table 1. 25 cases were diagnosed with CHD after 2011. 22 were isolated ventricular septal defects (VSD), 10 CHD were not resolved at time of pediatric cardiology follow-up by 16 months, and 3 were clinically significant requiring intervention or cardiology follow-up after 2 years of age. Prevalence of clinically significant CHD in IVF only pregnancies was 0.15% (95% CI [0 - 0.40%]).

CONCLUSIONS: (1) In this low risk IVF cohort, the prevalence of clinically significant CHD is similar to population risk previously reported. (2) A large proportion of CHD in this population are VSD and most spontaneously resolve.

SUPPORT: None.

TABLE 1. Prevalence of CHD in IVF Pregnancies

<table>
<thead>
<tr>
<th>Group</th>
<th># CHD with CHD %</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>All IVF Pregnancies 4242 76</td>
<td>1.79 1.39 - 2.19</td>
<td></td>
</tr>
<tr>
<td>IVF Only Ind. 3893 33</td>
<td>0.85 0.56 - 1.14</td>
<td></td>
</tr>
<tr>
<td>IVF Only (2012-18) 2040 25</td>
<td>1.23 0.75 - 1.70</td>
<td></td>
</tr>
<tr>
<td>IVF Only (2012-18) 2040 10</td>
<td>0.49 0.10 - 1.30</td>
<td></td>
</tr>
<tr>
<td>CHD Not Resolved 2040 3</td>
<td>0.15 0.00 - 0.40</td>
<td></td>
</tr>
</tbody>
</table>

* Cases were Coarct/VSD, Pulmonary Stenosis, and asymptomatic vascular ring.

CONTRACTION AND COMPLEX FAMILY PLANNING

O-19 Monday, October 14, 2019 10:45 AM

TOPICAL LIDOCAINE-PRILOCAINE CREAM VERSUS LIDOCAINE 1% SUBCUTANEOUS INFILTRATION DURING NEXPLANON INSERTION: A RANDOMIZED CONTROLLED STUDY. Ahmed M. Abbas, MD,* Mohamed Khalaf, MD,* Eman El-said, MBBC,* Ahmed Nasr, MD* Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; *Department of Obstetrics and Gynecology, Luxor General Hospital, Luxor, Egypt.

OBJECTIVE: Adequate anesthesia is an important procedural step when inserting contraceptive implants. Subcutaneous injection of lidocaine 1% is a widely used anesthetic method in implant insertion. However, lidocaine injection may be painful due to the penetration of the skin by the needle, and there is a theoretical risk of needle stick injury. This may also cause bleeding or edema which may mislead the intact subdermal insertion of the implant. Lidocaine-prilocaine (LP) cream is an oil/water emulsion in which the oil phase is a eutectic mixture of two anesthetics: lidocaine 2.5% and prilocaine 2.5% in a ratio of 1:1 by weight. Our objective is to compare the anesthetic effect of LP cream versus lidocaine subcutaneous infiltration during insertion of Nexplanon.

DESIGN: Randomized, open-label controlled study (Clinicaltrials.gov: NCT03187392).

MATERIALS AND METHODS: Reproductive-aged parous women requesting Nexplanon insertion for contraception were counseled to participate. Eligible women based on WHO guidelines were recruited and randomized (1:1) to LP cream vs. lidocaine 1% subcutaneous infiltration. In the cream group, 5 mg was applied on the insertion site, and Nexplanon rod was inserted after 5 minutes later. In the injection group, 2 ml of 1% lidocaine was slowly injected through a 24 G needle at the Nexplanon insertion site.
site of skin with the depth of 2-3 mm, until at least 5 mm of wheel was observed, then the needle was further advanced under the skin in the direction of Nexplanon insertion and the remaining lidocaine was injected subcutaneously. Nexplanon rod was inserted within 3 minutes afterward. The main study outcomes were the participant’s self-reported pain utilizing a 10-cm Visual Analogue Scale (VAS) during Nexplanon insertion and 15 minutes post-procedure. A 2-cm difference in VAS score between both arms was considered a clinically significant difference. The secondary outcomes included ease of insertion score, complications of the procedure and patient’s satisfaction using a five-point Likert scale. Student’s t-test and Chi-square test were used for the analysis of the outcomes.

RESULTS: Two hundred sixty women were enrolled and randomized to LP cream arm (n=130) or lidocaine 1% subcutaneous infiltration (n=130). LP cream group reported significantly lower pain scores during Nexplanon insertion (mean±SD: 2.55±0.98 vs. 5.57±1.64, p<0.001) and 15 minutes post-insertion (mean±SD: 2.22±0.89 vs. 4.32±1.27, p<0.001). The ease score of insertion was significantly higher in the LP group (mean±SD: 8.23±0.84 vs. 6.49±0.66, p=0.001). Fifty women (38.5%) in the lidocaine infiltration group suffer from bruising vs. 19 women (14.6%) in the LP group (p=0.001). Additionally, 45 women (34.6%) had bleeding from the insertion site in the lidocaine infiltration group vs. 25 (19.2%) in the LP group (p=0.002). No difference between the patient’s satisfaction levels in both groups (p=0.54).

CONCLUSIONS: Topical application of lidocaine-prilocaine cream before Nexplanon insertion significantly reduces the induced pain with subsequent easier insertions and less rate of procedure-related complications.

SUPPORT: None.

O-20 Monday, October 14, 2019 11:00 AM

A RANDOMIZED CLINICAL TRIAL BETWEEN ULTRASOUND-GUIDED AND UTERINE SOUND-SPARING APPROACH FOR COPPER INTRAUTERINE DEVICE INSERTION. Mohammed Khairy Ali, MD,a Ahmed M. Abbas, MD, MBCh,b M. B. Hassan, MD,c Manal Farouk, MD,a e Entisar Youness, MD, b Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; b Department of Obstetrics and Gynecology, Qous Central Hospital, Qena, Egypt.

OBJECTIVE: The intrauterine device (IUD) is a safe, reliable and long-acting reversible contraceptive method. Pain during insertion may be a barrier to choose IUD use. The trans-abdominal ultrasound guided IUD insertion (TAS-guided IUD insertion) effectively decreases the insertion pain; however, the full bladder during insertion and the need of two investigators may decrease patient satisfaction. In “Uterine Sounding Sparing Approach” (USSA), the sonographer performs a transvaginal ultrasound before IUD insertion to evaluate the uterine position and length without using uterine sounding; this method may increase patient’s satisfaction and acceptance toward IUD use. Our objective was to compare the satisfaction score between both approaches during copper IUD insertion.

DESIGN: Randomized Open-label controlled Trial (Clinical Trials. Gov: NCT03135288).

MATERIALS AND METHODS: All women delivered a live birth greater than 28 weeks’ gestation and requested birth spacing for more than one year were counseled for participation. Eligible women were recruited and randomized (1:1) to Cell-phone assisted (study group) who received a reminder of their postpartum family planning visit five weeks after delivery and a phone call 48 hours before the scheduled visit. They were received two follow-up phone calls to answer any queries and to remind them of the follow-up visits after IUD use. They also provided with a cell phone number working seven days a week from 8 AM to 8 PM to answer any query or questions regarding her family planning program. The control group received the standard postpartum family planning counseling without any phone assistance. A follow-up visit was scheduled at six months to assess the study outcomes. The primary outcome was the rate of initiation of LARC method in the first six months after delivery. The secondary outcomes included the rate of continuation of the LARC method, initiation of another method, and rate of an unplanned pregnancy. Unpaired t and Chi-square tests were used for the analysis of the outcomes.

RESULTS: Eight hundred and sixty-four women were enrolled and randomized (432 women in each group). Both groups were similar regarding age, parity, BMI, educational level, residence and marriage period. The rate of initiation of LARC method was significantly higher in the cell-phone group (30.3% versus 8.4%; p<0.001). Similarly, the rate of continuation was significantly higher in the cell-phone group (95.1% versus 82.9%; p<0.001). Three hundred thirty-one (76.6%) of cell-phone group had started any contraceptive method during the first six months as compared 188 (43.5%) women in the control group (p<0.001). There were no cases of unplanned pregnancy in the cell-phone group compared with ten cases in the control group (p=0.009).

CONCLUSIONS: Adding cell-phone to the postpartum family planning counseling and service can improve the intake of postpartum women to LARC methods and the overall contraceptive performance with a subsequent decrease in the rate of an unplanned pregnancy.

SUPPORT: A fund No. (2016-23) received from The Institutional Grants’ office.

O-22 Monday, October 14, 2019 11:30 AM

INFLUENCE OF GENETIC VARIANTS ON WEIGHT GAIN AMONG ETONOGESTREL CONTRACEPTIVE IMPLANT USERS. Aaron Lazarowitz, MD, MSc,a Eva Dindinger, MPH,a Margaret A. Harrison, BA,a Christina L. Aquilante, PharmD,b Jeannelle Sheeder, PhD,b Stephanie Teal, MD, MPHb *University of Colorado Anschutz Medical Campus, Aurora, CO; bUniversity of Colorado Anschutz Medical Campus, Skaggs School of Pharmacy and Pharmaceutical Sciences, Aurora, CO.

OBJECTIVE: To identify genetic variants that are associated with weight gain related to etonogestrel (ENG) contraceptive implant use.

CONCLUSIONS: USA is associated with higher satisfaction and less pain during insertion than TAS-guided IUD insertion approach. Also, this approach is effective, easy and needs less time for IUD insertion.


SUPPORT: None.
O-24 Monday, October 14, 2019 12:00 PM

BLEEDING PATTERNS AND ENDOMETRIAL SAFETY WITH A 1-YEAR, SEGESTERONE ACETATE/ETINYL ESTRADIOL CONtraceptive VAGINAL SYSTEM. David F. Archer, MD, Kurt T. Barnhart, MD, Michael A. Thomas, MD,* Kelly R. Culwell, MD, MPH,* Clint Dart, MS, Brandi Howard, PhD* University of Cincinnati, Cincinnati, OH; *Evofem, Inc., San Diego, CA; *Health Decisions, Durham, NC.

OBJECTIVE: We analyzed bleeding patterns and endometrial safety of a contraceptive vaginal system (CVS) releasing a daily mean of segesterone acetate (SA) 0.15 mg and ethinyl estradiol (EE) 0.013 mg for up to 13 cycles of use.

DESIGN: Two multicenter, single-arm, open-label, pivotal, phase 3 studies of the SA/EE CVS conducted at 20 US and 7 international sites (3 in Europe, 3 in Latin America, 1 in Australia).

MATERIALS AND METHODS: Participants initiated CVS use on day 2-5 of their menstrual cycle, followed a 21/7-day in/out schedule of CVS use for up to 13 cycles, and recorded vaginal bleeding in paper diaries. We summarized scheduled (occurring on cycle days 22-28) and unscheduled bleeding/spotting (occurring on cycle days 1 to 21) by 28-day cycles. We performed multiple logistic regression analyses to identify factors associated with unscheduled bleeding/spotting from the first 4 cycles of CVS use. Women could also participate in an endometrial safety sub-study at 5 sites. Three blinded pathologists examined histology of endometrial biopsies obtained at screening, at cycle 6 (first 25 women reaching 6 cycles), and at end of study (cycle 12/13) or early study termination in the remaining women. We excluded women with endometrial hyperplasia or cancer at baseline and evaluated histologic changes in women with both screening and follow-up biopsies.

RESULTS: We analyzed bleeding data from the 2070 of 2308 participants in the two phase 3 studies who had daily bleeding diary data for cycle control analysis. Most women (97.9%) documented bleeding/spotting (during ring removal days) with a mean of 4.6-5.2 scheduled bleeding/spotting days per cycle. The proportion of women reporting any unscheduled bleeding/spotting occurred in 13.2%–21.7% of women per cycle, with a mean of 3.4–5.1 days per cycle for those who had unscheduled bleeding. Absence of scheduled bleeding/spotting was 5%-8% of women per cycle; absence of any bleeding/spotting (complete amenorrhea) was 2.6%-4.9% of women per cycle. A low percentage of women (1.7%) discontinued early due to unacceptable bleeding.

O-23 Monday, October 14, 2019 11:45 AM

Efficacy and Safety of a Multipurpose Vaginal pH-Regulator: Results from the Phase 3, AMPower Contraception Clinical Trial. Michael A. Thomas, MD, Kelly R. Culwell, MD, MPH, Clint Dart, MS, Brandi Howard, PhD University of Cincinnati, Cincinnati, OH; *Evofem, Inc., San Diego, CA; *Health Decisions, Durham, NC.

OBJECTIVE: Amphora® (formerly known as Acidform), a multipurpose vaginal pH-regulator (MVP-R), is a novel, non-hormonal, woman-controlled, on-demand, water-based, petroleum-free vaginal gel being investigated for prevention of pregnancy and sexually transmitted infections. Here we present primary results from the confirmatory phase 3 contraception trial, AMPower.

DESIGN: This was a single-arm, open-label study conducted at 112 sites within the US (ClinicalTrials.gov number NCT03243305).

MATERIALS AND METHODS: All sites obtained IRB approval and all women provided informed consent. Eligibility criteria included healthy, monogamous, sexually active women aged 18-35 years who had normal cyclic menses of length 21-35 days, reporting having intercourse ≥3 times per cycle, and were willing to use the study drug as the only method of contraception over the course of the study. Women were instructed to administer a single prefilled applicator of study drug intravaginally immediately before or up to 1 hour before each episode of vaginal intercourse. Women used eDiaries to record timing of product administration, coital information, and side effects. The primary efficacy analysis was the cumulative pregnancy percentage over 7 cycles with typical-use calculated by the Kaplan-Meier method.

RESULTS: A total of 1384 women were included in the Intent-to-Treat (ITT) population; 1182 were included in the primary efficacy analysis (modified ITT [mITT]), and 1330 used at least 1 application of study product and were included in the Safety population. In the ITT population, women’s baseline characteristics were as follows: mean age, 27.7 years (standard deviation [SD], 4.5); mean body mass index, 28.7 kg/m² (SD, 8.1); Caucasian, 69.0% (955/1384); and non-Hispanic or non-Latino origin, 58.2% (805/1384). The mean number of prior pregnancies was 2.5 (SD, 1.8) and the most common contraceptive methods used immediately prior to enrollment were reported to be male condom (56.9% [787/1384], withdrawal method (14.2% [196/1384]), and rhythm method (5.1%, 70/1384). Fewer than 2% of study participants discontinued due to adverse events (AEs) (1.7% [23/1384]). For the primary efficacy analysis in the mITT population, the 7-cycle cumulative pregnancy percentage with typical-use was 13.9% (95% confidence interval [CI]; 10.0%, 17.8%), which met the prespecified primary endpoint of having the upper bound 95% CI ≤21%. The most common AEs (≥2.0%) were vulvovaginal burning sensation (20.0%, 266/1330), vulvovaginal pruritus (11.2%, 149/1330), urinary tract infection (5.7%, 76/1330), vulvovaginal mycotic infection (2.9%, 38/1330), bacterial vaginosis (2.8% [37/1330]), and nasopharyngitis (2.6% [35/1330]). Fourteen women (1.1%) experienced a serious AE with only 1 event (cystitis, 0.1%) considered treatment related.

CONCLUSIONS: In this large phase 3 study, the MVP-R, Amphora, was found to be safe and effective in preventing pregnancy. Amphora provides women with an important new non-hormonal, woman-controlled contraceptive option.

SUPPORT: Evofem Inc.
CRYOPRESERVATION AND FROZEN EMBRYO TRANSFER

O-25 Monday, October 14, 2019 10:45 AM

UNIVERSAL WARMING PROTOCOL* FOR A TRANS-NATIONAL EGG DONATION PROGRAM WITH VITRIFIED OOCYTES: A RETROSPECTIVE MULTICENTRE STUDY. Lodovico Lodovico Parmegiani, PhD, Maria Giulia Minasi, M Sc, Alessandra Arnone, M Sc, Valentina Casciani, PhD, Graciela Estela Cognigni, MD, Rita Viñoles, MD, Maria Teresa Varricchio, MD, Luis Alberto Quintero, MD, Ermanno Greco, MD, Marco Filicori, MD, GynePro Medical Centers- Nexct-Clinics International, Bologna, Italy.

OBJECTIVE: We have previously demonstrated that it is possible to warm vitrified human oocytes using a "universal warming protocol" based on subsequent steps with 1M and 0.5 M of ECCP regardless of the warming kitbrand; this study investigated the clinical efficiency of this protocol on shipped oocytes in a transnational donor program.

DESIGN: Retrospective multi-center observational study on a cohort of 238 patients enrolled in egg donation programs from 02 March 2017 to 19 September 2018. Primary endpoint was the survival rate (n oocytes surviving/n oocytes warmed). Secondary endpoints were fertilization rate (n fertilized oocytes/n injected oocytes), blastulation rate (n blastocysts obtained/n fertilized oocytes), implantation rate (n implanted embryos/n transferred embryos) and live birth rate (n pregnancies giving birth/n of embryo transfer).

MATERIALS AND METHODS: Donated oocytes vitrified in Spain, warmed in 2 centers in Italy where ICSI and embryo transfer (ET) were performed. Number of oocytes 1898, ET 238. Vitrification with Vitrification Kit (Kitazato, Japan); warming with two different kits: Kitazato Warming Kit (Kitazato, Japan); warming in-...

O-27 Monday, October 14, 2019 11:15 AM

CLINICAL FACTORS ASSOCIATED WITH THAW SURVIVAL IN A COHORT OF 6167 VITRIFIED-WARMED, EUPLOID BLASTOCYSTS. Margeaux Oliva, MD,a Christine Briton-Jones, PhD, HCLD,a Dmitry Gounko, MA,a Joseph A. Lee, BA,a Alan B. Copperman, MD,a Lucky Sekhon, MDa “Icahn School of Medicine at Mount Sinai, New York, NY;bReproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Embryo cryopreservation has become integral to IVF treatment. While an embryo failing to survive vitrification-warming is rare, understanding of factors that predict embryo thaw survival could allow for individualized patient counseling. Prior studies on the predictors of thaw survival have been limited by the use of slow-freeze protocols and unscreened embryos. This study analyzed embryo-related factors associated with euploid embryo thaw survival.

DESIGN: Retrospective, case-control.

MATERIALS AND METHODS: This single center study included vitrified-warmed euploid embryos from autologous IVF-PGT-A cycles from 2010-2019. Blastocysts that did not survive warming were compared to those that survived. Independent variables: patient age, basal antral follicle count (BAFC), body mass index (BMI), stimulation protocol, cumulative gonadotropin (GND) dose, estradiol (E2) and progesterone (P4) level at surge, embryo development day, oocytes retrieved, fertilization method, cleavage stage embryo cell number/fragmentation, number of trophectoderm biopsies and vitrification-thawing, embryo sex, Gardner morphology. Student’s t-test, chi-square, and linear regression (generalized estimating equation models) were used.

RESULTS: Of the euploid blastocysts thawed (n=6167), 2.8% (n=175) warmed embryos did not survive. Embryos that did not survive came from women with higher BAFC (OR 0.97, 95% CI 0.95-0.99), E2 levels at surge (p<0.03), and number of oocytes retrieved (p<0.005). Embryos cryopreserved on day 5/6 were more likely to survive than day 7 (OR 4.5, 95% CI 2.5-8.1). Blastocysts that underwent two trophectoderm biopsies had lower odds of survival (OR 0.7, 95% CI 0.5-0.9) than those that had a single biopsy. Repeat vitrification-warming was not associated with thaw survival (OR 0.26, 95% CI 0.14-1.9). While cleavage stage cell count was similar between groups, increased fragmentation was associated with reduced survival (OR 0.97, 95% CI 0.94-0.99). Embryos with expansion grade 4 (OR 4.5, 95% CI 2.5-8.1) and 5 (OR 2.1, 95% CI 1.2-3.7) had higher odds of surviving than fully hatched blastocysts. ICM grade was positive correlated with thaw survival (OR 2.2, 95% CI 1.4-3.4), whereas trophectoderm grade was not. Controlling for relevant confounders, increased BAFC, double trophectoderm biopsy, and fully hatched blastocysts remained associated with reduced thaw survival.

CONCLUSIONS: Blastocysts that undergo a second trophectoderm biopsy, and/or are fully hatched prior to vitrification are less likely to survive warming. Embryos from ‘high responders’ also have reduced odds of thaw survival. These findings may be related to the link between poly cystic ovarian syndrome and poor oocyte quality. Repeat trophectoderm biopsy and increased exposure of fully hatched embryos may reduce vitrification-warming tolerance. Providers can use this data to better counsel patients regarding the risk of their embryo(s) not surviving the thaw. At the molecular level, studies comparing the transcriptome of fresh and vitrified-warmed embryos may provide insights to optimize vitrification protocols.


O-28 Monday, October 14, 2019 11:30 AM

ANTIOXIDANTS INCREASE BLASTOCYST CRYOSURVIVAL AND VIABILITY POST VITRIFICATION. Thi T. Truong, Bachelor of Sciences, David Gardner, Ph.D., School of BioSciences, University of Melbourne, Melbourne, VIC, Australia.

OBJECTIVE: Cryopreservation is important for the preservation of gametes and embryos and consequently is used extensively in human ART. However, cryopreservation can induce oxidative stress resulting in an increase in reactive oxygen species. A combination of antioxidants has been shown to confer significant benefit to mouse IVF and culture, resulting significant improvements in embryo and fetal development. Here, we have examined the effects of the combined antioxidants as a strategy to reduce cellular stress during cryopreservation and hence improve ART outcomes.

MATERIALS AND METHODS: Pronucleate mouse oocytes were collected and cultured in groups under 20% or 5% oxygen to day 4 blastocysts. Expanded blastocysts were vitrified and warmed in medium with and without antioxidants (10 μM Acetyl-L-Carnitine/10 μM N-Acetyl-L-Cysteine/5 μM α-Lipoic Acid), cultured for a further 24 h, and cell numbers and apoptotic cells analysed. Histones H3K9ac and H3K27ac acetylation levels (as a mark of epigenetic impact) were quantified in blastocysts, and outgrowths and synchronous embryo transfers were performed on vitrified blastocysts.

RESULTS: Combined antioxidants supplemented to vitrification and warming media significantly increased ICM (28.34 ± 1.48 vs. 17.92 ± 1.13; P <0.001) and total cell number (91.86 ± 3.71 vs. 77.61 ± 4.44; P <0.01) compared to controls vitrified with no antioxidants. Furthermore, blastocysts vitrified with antioxidants resulted in similar total cell number and higher cleavage rates to non-vitrified controls. Blastocysts vitrified with antioxidants also showed a significant increase in in vitro outgrowth area and perimeter (P <0.05). Subsequent synchronous blastocyst transfer, following culture in 20% oxygen, resulted in increased fetal weight (190.19 ± 4.61 mg vs. 174.29 ± 5.52 mg; P <0.05), crown rump length (11.09 ± 0.10 vs. 10.76 ± 0.11; P <0.05) and limb development (14.89 ± 0.07 vs. 14.56 ± 0.11; P <0.05) when blastocysts were vitrified and warmed with antioxidants. Embryos cultured at 5% oxygen to the blastocyst stage and vitrified with antioxidants also showed increased crown rump length (11.29 ± 0.08 vs. 10.74 ± 0.12; P <0.001) and ear development (14.90 ± 0.05 vs. 14.64 ± 0.11; P <0.05). Importantly, while vitrification reduced acetylation of histones H3K27ac and H3K9ac in vitrified blastocysts, the inclusion of antioxidants significantly ameliorated this (P <0.05).

CONCLUSIONS: Vitrification and warming of blastocysts have detrimental effects on embryo development irrespective of oxygen culture conditions. Combined antioxidants in vitrification media significantly reduced the negative effects, resulting in blastocysts with higher developmental potential in vitro and increased viability. Thus, viability of vitrified human embryos may be improved by the inclusion of antioxidants during cryopreservation.

O-29 Monday, October 14, 2019 11:45 AM

DIFFERENCES IN OOCYTE SURVIVAL BETWEEN DONOR EGG BANKS AND SATELLITE CLINICS WITHIN THE SAME COMPANY. Whitney Hewitt, BS,a Jennifer L. Patrick, PhD,a Lauren Johnson, MD, MSCE,a Matrika Johnson, MD,b Seth Katz, MD,b Joe Whelan, III, MD,a Tyl Taylor, phda "Reproductive Endocrinology Associates of Charlotte, Charlotte, NC; bREACH, Charlotte, NC.

OBJECTIVE: Vitrification of donor oocytes has become a staple in the IVF community. In fact, there are multiple vendors in multiple locations stimulating donors, freezing oocytes, and offering a limited number of oocytes to recipients across the globe. Although oocytes can come from the same company and follow the same protocols, they can come from different satellite locations, thus exposing receiving clinics to different variables that may impact clinical outcomes. This study has two objectives: to compare clinical outcomes of three different egg bank vendors and compare if there are differences between oocytes originating from the same company’s different satellite locations.

DESIGN: Retrospective.

MATERIALS AND METHODS: Frozen donor oocytes that were shipped to our clinic and warmed between 2015-2019 were compared based on the company the oocytes were received from and the clinic from which they were transferred. Clinical outcomes including oocyte survival, fertilization, and usable blastocyst rate (those vitrified or transferred) were compared between different donor egg banks and within the same donor egg bank’s satellite locations. All warming protocols were followed according to each company’s policies.

RESULTS: We performed 139 donor oocyte thaw cycles from three competing egg banks, using a total of 850 frozen donor oocytes from 2015-2019. Bank “A” provided 121 patients with 733 oocytes. Bank “B” provided 8 patients with 63 oocytes, and Bank “C” provided 10 patients with 54 oocytes. Oocyte survival rates post-thaw differed significantly between the different banks, with 630/733 (86.0%), 35/63 (55.6%), and 50/54 (92.6%) surviving from bank “A”, “B”, and “C”, respectively (P<0.001). Fertilization rates and usable blastocyst rate did not differ between the egg banks.

From bank “A”, we compared oocyte survival, fertilization, and usable blastocyst rates between three different satellite clinics within the same egg bank company. A total of 103 donor thaw cycles, with 49 from clinic “A”, 31 from clinic “B”, and 23 from clinic “C”, were performed in our lab from 2015-19. A total of 624 frozen oocytes were thawed, 299, 186, and 139 from clinic “A”, “B”, and “C”, respectively. Oocyte survival post thaw were statistically different between satellite clinic “A” (268/299, 89.6%), clinic “B” (133/186, 71.5%), and clinic “C” (120/139, 86.3%; P<0.001). Fertilization rates and usable blastocyst rate did not differ between clinics.

CONCLUSIONS: Our data suggest that there are differences in oocyte survivability post-thaw amongst the different oocyte banking companies. More importantly, there were differences in oocyte survivability amongst the satellite locations from the same egg bank company. This suggests an impact of the embryologist vitrifying or the stimulation protocol utilized. References: None. SUPPORT: None.

O-31 Monday, October 14, 2019 10:45 AM

EFFECT OF WILDFIRE SMOKE ON PREGNANCY OUTCOMES IN THE NON-HUMAN PRIMATE. Bryn Erin Willson, MD, Kent E. Pinkerton, PhD, Bill Lasley, PhD, Nancy Gee, PhD 1 UC Davis Health, Sacramento, CA; 2 UC Davis Center for Health and the Environment, Davis, CA; 3 Center for Health & Environment, Davis, CA; 4 UC Davis - Center for Health & Environment, Davis, CA.

OBJECTIVE: In November 2018, the “Camp Fire” wildfire was deemed the most destructive and deadliest wildfire in California history. The resulting poor air quality and ambient particulate matter in the Northern California region offered a rare opportunity to study the effect of wildfire smoke on conception and live birth rates in the non-human primates (M. mulatta) that reside outdoors at the California National Primate Research Center (CNPRC) in nearby Davis, CA.

DESIGN: We conducted a pilot prospective cohort study investigating pregnancy outcomes after exposure to ambient smoke from the Camp Fire that burned from 11/8-11/22/18 about 160 kilometers away. This cohort was exposed to elevated fine particulate matter as recorded by California Air Resource Board (CARB). The fine particulate matter (PM2.5 – particles less than 2.5 μm in diameter) measured by CARB indicated a rise above national and state ambient air quality standards (15μg/m3) for 12 days and nights during the 2018-2019 breeding season reaching levels as high as 185μg/m3. The primary outcome of these data is conception and live birth rates.

MATERIALS AND METHODS: Through CNPRC, 66 blood (serum) samples were collected from female macaques in the outdoor colony following exposure to ambient smoke during the 2018-2019 breeding season. The primates have since undergone routine surveillance for conception and birth outcomes. For comparison, data was collected from the 2016 and 2017 breeding seasons.

RESULTS: Preliminary results show that out of 66 primates sampled, a total of 44 primates have confirmed pregnancies by physical exam (palpation) and/or serum marker analysis. Conception and live birth rates in the non-human primates (M. mulatta) that reside outdoors at the California National Primate Research Center (CNPRC) in nearby Davis, CA.

The primates have since undergone routine surveillance for conception and birth outcomes. For comparison, data was collected from the 2016 and 2017 breeding seasons.

RESULTS: No significant differences were observed in 2PN and/or abnormal fertilization rates between the groups. Similarly, on day 3, no significant differences were found in the average cell numbers or in the average number of good (≥ 8 cells; <20% frag.), fair (5-7 cells, any abnormal cleavage stages), and poor (<4 cells) embryos. Similarly, the incidence of abnormal cleavage patterns was similar among the cohort. More embryos were selected for transfer from the 3-hour group than from the 2-hour group (51.1% vs. 48.9%; p = 0.78). There were no significant differences in the utilization rate (the number of embryos transferred fresh plus blastocysts frozen) between the 3- and 2-hour groups (49.6% vs. 49.6%, respectively). The time-lapse morphokinetic data indicated faster-growing embryos in the 3- versus 2-hour group. This difference is apparent in late-stage morphokinetic parameters (r9 to sB). The 3-hour group produced significantly better quality blastocysts in cycles that were either frozen upfront, fresh D3 ET, or PGT (P<0.01).

CONCLUSIONS: The duration of the recovery time post-warming showed no significant differences in overall embryology outcomes prior to blastocyst formation. However, at the BL stage, the 3-hour group demonstrated improvement in morphokinetic parameters and in overall BL quality. Reference: None. SUPPORT: Internal.

ENVIRONMENT AND REPRODUCTION
OBJECTIVE: Women who experienced early life stress (ELS) have aberrant hypothalamic-pituitary-adrenal and autonomic responses as well as an increased inflammatory response to induced stress when compared to ELS naive women. The impact of ELS on infertile women is largely unknown. We sought to determine the prevalence of ELS in the infertile population and the impact of this dysregulated stress reactivity on IVF cycle characteristics and outcomes.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Women aged 18-42 were recruited for enrollment in an autologous IVF cycle. Patients pursuing third party reproduction or fertility preservation were excluded. Consenting participants provided demographic information and completed the CDC-Kaiser Adverse Childhood Experience Questionnaire. Those who indicated ≥24/10 positive responses were considered to be ELS positive. A power analysis indicated that a sample size of 277 subjects would provide at least 80% power to detect a 40% relative difference in live birth rates between groups. Continuous variables were compared using Student’s t-test or Mann–Whitney U test based on normality, while χ² or Fisher’s exact tests were used to compare categorical variables by ELS status. Logistic regression was used to assess for predictors of live birth and early pregnancy failure adjusting for confounders as appropriate.

RESULTS: The prevalence of ELS positivity in this infertile cohort was 29.2% (n=83/284). ELS positive women and controls were similar in age, race/ethnicity, and history of anxiety/depression; however higher BMI s were observed in the ELS positive group (mean BMI 27.4 vs 25.6 kg/m²; p=.02). There were no differences in infertility diagnosis, pregnancy history, number of prior IVF cycles or ovarian reserve parameters. While live birth rates were similar in the two groups (37% vs 35%; aOR 1.13, 95% CI 0.65-2.00), ELS positive women had significantly higher rates of early pregnancy loss (EPL) per transfer (28% vs 17%, p=.04). This association persisted when the analysis was restricted to patients undergoing their first IVF cycle and excluding cycles in which preimplantation genetic testing was performed. After controlling for BMI and parity, ELS positivity remained significantly associated with EPL (aOR 1.95, 95% CI 1.10-3.62, p=.03). However, when EPL rates were considered only among those who achieved a pregnancy (positive pregnancy test), no difference was observed between groups.

CONCLUSIONS: Early life stress has a longstanding impact on adult health. ELS and ELS positivity are associated with increased risk of miscarriage with no differential effects on live birth rates. Early life stress should be considered in the context of infertility and reproductive success.
with a robust error variance. Models adjusted for age, percent body fat, race, and smoking. Models were also adjusted for dietary factors that are potentially related to cadmium exposure and PCOS, such as intakes of rice, total grains, and green leafy vegetables.

RESULTS: Mean (standard deviation) age and percent body fat were 27.3 (8.2) years and 29.7% (6.0), respectively. Median (interquartile range) cadmium levels were 0.30 (0.19-0.43) µg/L. Cadmium was associated with higher total testosterone (2.6% difference; 95% confidence interval [CI] 0.7, 4.5; P = 0.01), SHBG (3.0% difference; 95% CI 0.4, 5.7; P = 0.03), and AMH (7.0% difference; 95% CI 0.2, 14.2; P = 0.04), per 0.1 µg/L increase. Our data also suggests that higher cadmium concentrations were associated with 15% higher probability of having a mild PCOS-phenotype with a borderline significance (relative risk 1.12; 95% CI 0.98, 1.29; per 0.1 µg/L increase; P = 0.09). No associations were found for free androgen index, insulin, and glucose levels. Further adjustment for intakes of rice, total grains, and leafy vegetables did not change these associations.

CONCLUSIONS: Among healthy women, cadmium was associated with endocrine features central to PCOS, including total testosterone and AMH. However, we observed no associations with metabolic markers, such as fasting glucose and insulin. Among women without a PCOS diagnosis, these results suggest a potential role of cadmium in the hormonal milieu associated with PCOS.

O-35 Monday, October 14, 2019 11:45 AM
THE ASSOCIATION OF URINARY CONCENTRATIONS OF BISPHENOL-A, AND DI-ETHYLHEXYL PHthalate Metabolites with Thyroid Function & Autoimmunity in Women from A Fertility Center: RESULTS FROM THE ENVIRONMENT AND REPRODUCTIVE HEALTH STUDY. Irene Souter, MD,
Lidia Mínguez-Alarcón, PhD,a Tim Korevaar, MD, PhD, Jennifer B. Ford, RN,b Jorge E. Chavarro, MD, Sc.D.,c Russ Hauser, MD, MPH, Sc.D.d 1MGH Fertility Center and Harvard Medical School, Boston, MA; 2Harvard T.H. Chan School of Public Health, Boston, MA; 3Harvard School of Public Health, Boston, MA.

OBJECTIVE: To evaluate the association of urinary concentrations of bisphenol-A (BPA) and di-ethylhexyl phthalate (DEHP) metabolites with markers of thyroid function and autoimmunity among women seeking fertility treatments.

DESIGN: Prospective Cohort Study.

MATERIALS AND METHODS: Urine and serum samples were collected from 558 women seeking infertility treatment at an academic institution and participating at the environment and reproductive health (EARTH) study. Urinary BPA and phthalate metabolite concentrations were quantified by isotope dilution tandem mass spectrometry, and the molar sum of four DEHP metabolites was calculated. Biomarkers of thyroid function [thyroid stimulating hormone (TSH), free and total thyroxine (FT4, T3)], and AMH were determined using electrochemiluminescence assays.

Linear regression models adjusted for covariates (age, body mass index, diagnosis, specific gravity, BPA for DEHP metabolites and DEHP metabolites for BPA analyses) were used to estimate the relations between urinary BPA and DEHP concentrations, in tertiles, and serum thyroid function and autoimmune markers.

RESULTS: Higher urinary concentrations of DEHP metabolites were associated with lower serum levels of FT4, TT4, FT3, and TT3 in both adjusted and unadjusted models. The multivariable adjusted means (95% CI) of thyroid function biomarkers for women in the lowest, middle, and highest tertile of urinary DEHP were: 15.6 (15.2, 15.9), 15.3 (14.9, 15.6), and 15.1 (14.7, 15.4) pmol/L for FT4 (p-trend: 0.06); 101 (97.8, 104), 98.6 (95.9, 101), and 94.8 (91.7, 97.8)* mmol/L for TT4 (p-trend: 0.01); 4.9 (4.8, 5.0), 4.8 (4.7, 4.9), and 4.7 (4.6, 4.8)* mmol/L for FT3 (p-trend: 0.01); and 1.9 (1.9, 2.0), 1.8 (1.8, 1.9),* and 1.8 (1.7, 1.8)* mmol/L for TT3 (p-trend: 0.005); * p-value <0.05 when comparing that tertile to the lowest tertile of exposure.

DEHP was not related to either TSH [2.0 (0.8, 2.2), 2.2 (2.0, 2.3), and 1.9 (1.8, 2.1)] µIU/mL, for lowest, middle, and highest tertile respectively; p-trend 0.03]. The thyroid autoantibody biomarkers for women in the lowest, middle, and highest tertile of urinary DEHP were 12.9 (12.5, 13.0), 14.7 (14.3, 15.1), and 14.1 (12.4, 16.1) IU/mL for TPO Ab (p-trend: 0.6); 22.6 (18.8, 27.1), 22.7 (19.5, 26.4), and 19.0 (16.0, 22.6) IU/mL for TgAb (p-trend: 0.02), for lowest, middle, and highest tertile, respectively.

Urinary BPA concentrations were unrelated to thyroid function or thyroid autoimmunity biomarkers.

CONCLUSIONS: Urinary DEHP, but not BPA, was inversely related to markers of thyroid function but not of thyroid autoimmunity. Our data suggest that current levels of exposure to certain phthalates negatively impacts thyroid function of reproductive age women through mechanisms that do not involve autoimmunity.

SUPPORT: National Institute of Environmental Health Sciences (NIEHS): R01ES022955, R01ES009718, and P30ES000002.

O-36 Monday, October 14, 2019 12:00 PM
NON-CHRONIC PRECONCEPTION OPIOD USE AND REPRODUCTIVE OUTCOMES. Kerry S. Flannagan, PhD,a Jeanne G. Radoc, BS,b Sunni L. Mumford, PhD,c Victoria C. Andriessen, BS,c Lindsey A. Sjaarda, PhD,c Matthew D. Johnson, PhD, Jeanna R. Zolton, DO,b Neil J. Perkins, PhD, Kwenaan Kim, PhD,c Robert M. Silver, MD,b Enrique F. Schusterman, PhD,c Epidemiology Branch, DIPHR, NICHD, NIH, Bethesda, MD; bNICHD, Bethesda, MD; cNational Institute of Child Health and Human Development, NIH, Bethesda, MD; dUniversity of Utah, Salt Lake City, UT.

OBJECTIVE: In recent decades, prescription opioid use has increased dramatically among reproductive age women. While much is known about the adverse outcomes of opioid abuse during pregnancy, the risk of limited opioid use during the periconception period is unclear. Thus, we examined associations of preconception and early-pregnancy opioid use with fecundability, live birth, and pregnancy loss in a cohort of women from the EARe trial.

DESIGN: Prospective cohort of 1228 women with 1-2 prior pregnancy losses enrolled in a randomized trial of preconception low-dose aspirin and followed for up to 6 cycles while attempting conception or through pregnancy resolution.

MATERIALS AND METHODS: We measured urinary concentrations of opioids by chemiluminescent immunoassay during preconception and, among women who became pregnant, at weeks 4 and 8 of pregnancy. We defined a positive screen as any opioid detected above manufacturer-defined cut points. Women self-reported use of opioid medications during or in the year prior to their last pregnancy and during preconception follow-up cycles. We estimated fecundability odds ratios (FOR) and confidence intervals (CI) with discrete Cox proportional hazard models. We estimated risk ratios (RR) of live birth and pregnancy loss with log binomial models. We adjusted for age, race, BMI, education, smoking, use of alcohol, marijuana, and antidepressants, time since last pregnancy, and gynecological indications for opioid use (e.g. fibroids, cramping).

RESULTS: 110 (9%) women screened positive for opioids during the preconception period and 33 (4.8% of 8-week pregnancies) screened positive during week 4 or 8 of pregnancy. 166 (13.6%) women self-reported opioid use during or before their previous pregnancy or during preconception follow-up. Most women screened positive or self-reported use only once. Positive preconception opioid use by screening or self-report was associated with longer time to pregnancy (FOR: 0.81; 95% CI: 0.61, 1.03) and marginally associated with probability of live birth (RR: 0.81; 95% CI: 0.64, 1.01). Positive opioid screening during pregnancy was associated with 2.90 times higher risk of pregnancy loss (95% CI: 1.51, 5.55).

CONCLUSIONS: Preconception opioid use was associated with lower fecundability and live birth rate. Use in pregnancy was associated with risk of loss. Opioid use may have adverse reproductive consequences even in non-addicted populations. Further studies are needed to determine the duration of use and specific types of opioids that may be harmful.

SUPPORT: This work was supported by theA Intramural Research Program, Division of Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development.

GENETIC COUNSELING

O-37 Monday, October 14, 2019 10:45 AM
LESSONS LEARNED FROM EVALUATING DECISIONAL REGRET SURROUNDING PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY. Amy Wijekoon, MD,a Mitchell P. Rosen, MD, HCLD,b Molly M. Quinn, MD,a University of California, San Francisco, San Francisco, CA; bUCSF, San Francisco, CA; cUniversity of California, Los Angeles, Los Angeles, CA.
OBJECTIVE: Patients are often expected to make informed decisions about the use of preimplantation genetic testing for aneuploidy (PGT-A) based upon limited knowledge of its risks and benefits. This study aims to assess whether there are differences in degree of decisional regret between patients who decide to undergo/not undergo PGT-A, and to elucidate whether there are personal beliefs or clinical outcomes that correlate with level of decisional regret.

DESIGN: Retrospective cohort survey.

MATERIALS AND METHODS: An online survey was distributed to patients who underwent in vitro fertilization (IVF) with or without PGT-A between January 1st of 2016 to 2018. The survey consisted of 4 sections: 1) Demographic and Clinical Outcomes, 2) Decision-making factors, 3) Beliefs about PGT-A, and 4) Decision regret scale (DRS). Strength of belief in purported risks and benefits of PGT-A were assessed on a 0-100 scale (0: not true; 100: absolutely true). DRS scores ranged from 0-100, with a validated threshold of >25 indicating moderate to severe regret (MSR). Student’s t-test, Wilcoxon Rank-Sum, or Chi square test was applied, as appropriate, to compare baseline characteristics, DRS scores, and MSR rate between those who did or did not complete PGT-A. Multivariate linear regression was used to assess the impact of surveyed factors on DRS scores. Multinomial logistic regression was used to evaluate risk factors for MSR. All patients received evidence-based counseling regarding risks and benefits of PGT-A during a mandatory pre-treatment IVF orientation.

RESULTS: At this time, three hundred and thirty-five women completed the eligibility survey. Of the 261 women deemed eligible, 123 women completed the study survey (47%); 66 underwent PGT-A and 57 did not. There were no differences in demographic characteristics between the two groups. In raw analysis, DRS scores were significantly higher in those who did not complete PGT-A, compared to those who did (Median 20 vs 0, IQR 0-30 vs 0-20, p=0.02); however, that difference diminished after controlling for live birth outcomes. In the group of patients with no live birth after index IVF cycle, there was no statistically significant difference in DRS scores between those who did and did not complete PGT-A (22 vs 34, p=0.15). Participants who completed PGT-A were significantly more likely to believe PGT-A improved the chance of having a healthy baby (88 vs 76, p=0.01); however, that belief correlated with lower DRS scores regardless of live birth outcomes. MSR was noted in 14 women (21%) who had PGT-A compared to 19 women (33%) who did not (p=0.13). Lack of live birth (RR=0.18, p=0.02) and low overall patient satisfaction (RRR=0.98, p=0.03) significantly increased risk of MSR.

CONCLUSIONS: Decisional regret surrounding PGT-A is largely driven by overall patient satisfaction and live birth outcomes. However, our findings suggest that in the setting of a poor clinical outcome, there is no difference in level of decisional regret between those who do or do not elect for PGT-A. Physicians should feel comfortable counseling patients regarding the risks and benefits of PGT-A, and then allow them to choose.


SUPPORT: None.

O-39 Monday, October 14, 2019 11:15 AM

DO BRCA MUTATIONS IMPACT ANEUPLOIDY RATES IN EMBRYOS?

Carrie Chou, MS; Ellen Thomas, MS; Katrina Merrion, MS; Nina Wemmer, MS; Natera, Inc., San Carlos, CA; Affiliation not provided.

OBJECTIVE: Analyze chromosome ploidy results in a patient cohort who pursued preimplantation genetic testing for monogenic/single gene defects (PGT-M) for familial BRCA1 or BRCA2 mutations with concurrent 24-chromosome preimplantation genetic testing for aneuploidy (PGT-A). Prior studies suggest BRCA mutations may be associated with diminished ovarian reserve and infertility, and that the effects of BRCA1 mutations may differ from BRCA2. Furthermore, mouse models have shown

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<th>Embryos (n)</th>
<th>Average number of embryos per case (n)</th>
<th>Euploid Rate ± SD (%)</th>
<th>Aneuploid Rate ± SD (%)</th>
<th>Aneuploid Rate of Maternal Origin ± SD (%)</th>
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<td>54.9 ± 0.9</td>
<td>28.2 ± 1.2</td>
<td>16.9 ± 0.7</td>
</tr>
</tbody>
</table>

TABLE 1. Aneuploidy rates by PA

O-38 Monday, October 14, 2019 11:00 AM

FOCUSING ON PARENTAL ORIGIN OF AНЕУРЗОИДY: DOES PATERNAL AGE IMPACT AНЕУРЗОИДY RATES IN EMBRÝOS?

Katrina Merrion, MS; Diane Ahern, MS; Jessica Adsit, MS; Katherine L. Howard, MS; Dusan Kijacic, MS; Michelle Kiehl, MS; Natera, Inc., San Carlos, CA; Affiliation not provided.

OBJECTIVE: While it is known that aneuploidy rates increase with advancing maternal age (MA) due to deterioration of the oocyte’s meiotic spindle, there has been no proven paternal age (PA) association. Some authors have postulated that advancing PA may be associated with increased risks for aneuploidy, while other studies have shown no association.

In this study, we report the 24-chromosome preimplantation genetic testing for aneuploidy (PGT-A) results for trophectoderm (TE) samples from a series of men who underwent in vitro fertilization (IVF) cycles using oocyte donors, broken down by PA.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: All PGT-A cases with TE biopsy and an oocyte donor between July 2010 and April 2019 were included in the analysis. TE and biological parental samples were run on Illumina Cytol12 SNP-based microarrays with informatics to determine parental origin of each chromosome and establish chromosome copy number. Statistical analysis was performed using a two-tailed t-test.

RESULTS: Results were obtained on 13,018/13,394 (97.2%) of submitted TE samples. The average PA for this patient cohort was 43.5 ± 6.9 years (range 23–73). Aneuploidy rates are broken down by PA using SART age groups (Table 1). Additional analysis performed for men >50 years showed an aneuploidy rate of 704/2031 (34.7%) which was not statistically different from the other PA groups. Moreover, there was no statistical difference in the paternal aneuploidy rates or aneuploidy of mixed origin between PA groups (p>0.05).

CONCLUSIONS: In this study, we did not observe an increase in aneuploidy rates with advanced PA, adding to existing literature showing a lack of PA effect. SNP microarrays with informatics uniquely allows determination of parental origin of aneuploidy rates with advanced PA, adding to existing literature showing a lack of PA effect. SNP microarrays with informatics uniquely allows determination of parental origin of aneuploidy in embryo samples. The difference in overall aneuploidy rates and paternally inherited aneuploidy rates among the PA groups was not statistically significant (p>0.05). This information can be used to aid in patient counseling by providing reassurance that estimates for aneuploidy rates should be based primarily on the age of the oocyte contributor.


SUPPORT: Natera, Inc.
evidence that BRCA1 mutations regulate meiotic spindle assembly and check points, which may infer a link between BRCA1 deficiency and aneuploidy.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: Chart review of all BRCA1 and BRCA2 PGT-M cases referred by in vitro fertilization (IVF) clinics to a lab was completed. PGT-M and PGT-A were performed using SNP microarrays with informatics. A control group of maternal age-matched PGT-A patients was used for comparison. Statistical analysis was done using a two-tailed t-test.

RESULTS: Between Mar 2011 and Sept 2018 a total of 779 embryo biopsies were tested. The overall euploid rate was 56% and mutation positive rate was 50.6%. The euploid rate for controls was 57% (Table 1). A statistically significant difference in the euploid rate of maternal (mat) BRCA1 carriers compared to mat BRCA2 carriers (52% vs 63%; p-value = .02) was observed. There was no difference in the euploid rate between paternal (pat) BRCA1 carriers and pat BRCA2 carriers (56% vs 55%; p-value >.05). Comparison of the control group to all BRCA1/2 carriers, to all mat carrier cases, and to all pat carrier cases showed no difference in euploid rates (p-values >.05).

CONCLUSIONS: Overall, we do not see a decrease in euploid rates among all BRCA1/2 carriers compared to age-matched controls. The statistically significant difference between the euploid rates of mat BRCA1 carriers and mat BRCA2 carriers supports the literature suggesting differing mechanisms and potential risk implications for BRCA1 and BRCA2. BRCA1 mutations in females may increase susceptibility to meiotic errors and aneuploidy; this trend was not observed for male BRCA2. BRCA1 mutations in females may increase susceptibility to differing mechanisms and potential risk implications for BRCA1 and carrier cases supports the literature suggesting overall, we do not see a decrease in euploid rates among all BRCA1/2 carriers compared to age-matched controls.

OBJECTIVE: To investigate a possible association between a TP53 gene polymorphism and ovarian response after IVF/ICSI cycles.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: This study included 136 women submitted to IVF/ICSI cycles. The enrolled individuals met the following inclusion criteria: age ≤ 37 years; normal karyotype; having two ovaries as evinced in ultrasound examination; no history of ovarian surgery, endometriosis, hydrocolpos, infection, or endocrine disorders. DNA extracted from peripheral blood was sequenced on MiSeq (Illumina) to find single nucleotide polymorphisms (SNPs) in the TP53 gene. SNPs were identified using the TruSeq Custom Amplicon (TSCA) Panel (DesignStudio Illumina). The findings from sequencing were associated with age, anti-Müllerian hormone (AMH) levels, antral follicle counts (AFC), total dose of recombinant FSH (r-FSH), follicle size, number of retrieved oocytes, and clinical outcome of IVF/ICSI cycles.

RESULTS: The TP53 (rs1625895) C>T SNP were identified. Women with the TT genotype had significantly poorer ovarian reserve indicators (lower levels of AMH and AFC), poorer ovarian response to rFSH, and poorer clinical outcomes (implantation rate and clinical pregnancy rate/patient). Table 1 presents a summary of the results.

TABLE 1. Results

<table>
<thead>
<tr>
<th>TP53 (rs1625895) Genotypes</th>
<th>CC</th>
<th>TC</th>
<th>TT</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>62 (45.6%)</td>
<td>28 (20.6%)</td>
<td>46 (33.8%)</td>
<td>0.46</td>
</tr>
<tr>
<td>Age (years)</td>
<td>33.3±2.8</td>
<td>33.3±7.4</td>
<td>33.9±3.0</td>
<td>0.01</td>
</tr>
<tr>
<td>AMH (ng/ml)</td>
<td>3.0±3.7^a</td>
<td>2.9±4.1</td>
<td>1.2±1.6^a</td>
<td>0.01</td>
</tr>
<tr>
<td>AFC (n)</td>
<td>17.8±12.1^a</td>
<td>15.8±10.1^b</td>
<td>9.4±6.2^b</td>
<td>^a&lt;0.001;^b0.01</td>
</tr>
<tr>
<td>Total dose of rFSH (IU)</td>
<td>1840±1083^a</td>
<td>2036±1101^b</td>
<td>2642±1027^b</td>
<td>^a&lt;0.001;^b0.007</td>
</tr>
<tr>
<td>Follicles (n):Total</td>
<td>15.5±9.9^a</td>
<td>13.6±10.6</td>
<td>9.1±5.5^a</td>
<td>0.005</td>
</tr>
<tr>
<td>Follicles (n):≥ 18 mm</td>
<td>4.2±2.7^a</td>
<td>4.1±2.8</td>
<td>3.2±1.9^a</td>
<td>0.02</td>
</tr>
<tr>
<td>Retrieved oocytes:Total</td>
<td>11.0±7.5^a</td>
<td>9.3±7.9</td>
<td>6.7±2.4^a</td>
<td>0.01</td>
</tr>
<tr>
<td>Retrieved oocytes:Metaphase II</td>
<td>8.2±6.1^a</td>
<td>6.8±5.9</td>
<td>4.9±2.6^a</td>
<td>0.01</td>
</tr>
<tr>
<td>Fertilization rate</td>
<td>66.5%</td>
<td>67.3%</td>
<td>69.7%</td>
<td>0.66</td>
</tr>
<tr>
<td>Implantation rate</td>
<td>36.8%^a</td>
<td>32.8%</td>
<td>22.0%^a</td>
<td>0.01</td>
</tr>
<tr>
<td>Pregnancy rate/patient</td>
<td>50.7%</td>
<td>45.5%</td>
<td>35.3%</td>
<td>0.23</td>
</tr>
</tbody>
</table>

Values within rows with the same superscript letter were significantly different.
CONCLUSIONS: TP53 (rs1625895) C>T polymorphism was associated with ovarian reserve and apparently affected ovarian response to rFSH and the clinical outcomes of IVF/ICSI cycles. Homozygosity of the C allele was associated with significantly poorer results. The identified SNP might provide an additional tool to test patients for ovarian reserve/reserve and thus help in the individualization of ovarian stimulation protocols. To the best of our knowledge, this was the first study to associate this SNP and ovarian response to gonadotropins.

SUPPORT: Merck Grant for Fertility Innovation (GFI-2014).

### Table: Summary of Results

<table>
<thead>
<tr>
<th>Test Category</th>
<th>PGT-A (n=278)</th>
<th>IVF/no PGT-A (n=155)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean±SD)</td>
<td>37.3±4.6</td>
<td>38.2±5.1</td>
<td>0.06a</td>
</tr>
<tr>
<td>Low risk nuchal translucency (n, %)</td>
<td>187 (of 189), 98.9%</td>
<td>107 (of 107), 100%</td>
<td>0.54c</td>
</tr>
<tr>
<td>First trimester screen normal (n, %)</td>
<td>181 (of 196), 92.4%</td>
<td>105 (of 107), 98.1%</td>
<td>0.006b</td>
</tr>
<tr>
<td>Low risk noninvasive prenatal testing (n, %)</td>
<td>243 (of 244), 99.6%</td>
<td>126 (of 128), 98.4%</td>
<td>0.27c</td>
</tr>
<tr>
<td>Invasive diagnostic testing normal (n, %)</td>
<td>22 (of 22), 100%</td>
<td>11 (of 12), 81.7%</td>
<td>0.35c</td>
</tr>
<tr>
<td>Anatomy ultrasound normal (n, %)</td>
<td>230, 86.8%</td>
<td>128, 85.9%</td>
<td>0.80b</td>
</tr>
<tr>
<td>Placenta normal by ultrasound (n, %)</td>
<td>191, 72.4%</td>
<td>107, 71.8%</td>
<td>0.91b</td>
</tr>
</tbody>
</table>

a: t-test.  
b: chi-square.  
c: fisher’s exact.

### O-42 Monday, October 14, 2019 12:00 PM

**SONOGRAPHIC ABNORMALITIES IN PREGNANCIES CONCEIVED FOLLOWING IVF WITH AND WITHOUT PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY.** Carrie Riestenberg, MD,a Kimberly Moyle, MD,b Neil Silverman, MD,c Lawrence D. Platt, MD,c Christina Shih-chi Han, MD,a Molly M. Quinn, MDa "University of California, Los Angeles, Los Angeles, CA; Cedars-Sinai Medical Center, Los Angeles, CA; Center for Fetal Medicine and Women’s Ultrasound, Los Angeles, CA.

OBJECTIVE: Preimplantation genetic testing for aneuploidy (PGT-A) has been increasingly adopted in IVF clinics across the US. While PGT-A may improve pregnancy rates on a per transfer basis, data demonstrate that patients often hold misconceptions that use of PGT-A will result in a healthy baby. In an effort to improve patient counseling on the benefits and limitations of PGT-A we report the rates and specific types of anomalies detected on anatomy ultrasounds in women who underwent IVF with PGT-A compared to women who conceived following IVF with unscreened embryos.

DESIGN: Retrospective cohort at a maternal-fetal medicine referral practice.

MATERIALS AND METHODS: All patients with singleton pregnancies who had a mid-trimester anatomy ultrasound between January 1-December 31, 2018 at a single clinic were assessed for inclusion. The charts of patients who conceived with IVF with or without PGT-A were systematically examined. The primary outcome was the rate of anomalies detected on anatomy ultrasound. Nuchal translucency (NT), first trimester and/or serum integrated screening, non-invasive prenatal testing (NIPT), and invasive diagnostic testing results were also extracted as available. Statistical analysis was performed using the student t-test, chi-square, or fisher’s exact test where applicable.

RESULTS: Of 4,095 singleton pregnancies during the study period, 433 conceived with IVF, including 278 who had PGT-A and 155 who did not. Rate of low risk nuchal translucency or noninvasive prenatal testing did not differ between patients who did or did not undergo PGT-A. There was a low overall rate of abnormal first trimester and/or serum integrated screen, yet it occurred more commonly in those who had undergone PGT-A (7.6 vs 1.8% p=0.006). Anomalies of fetal anatomy or placenta were found at similar rates between the two groups.

CONCLUSIONS: The rate of abnormal ultrasound findings did not differ in patients who conceived after IVF with PGT-A compared to those who underwent IVF without PGT-A, but there was an increased risk of abnormal anomalies on serum screening. Patients should be counseled that standard prenatal screening and ultrasounds are recommended following IVF with PGT-A.

SUPPORT: None.
O-45 Monday, October 14, 2019 11:00 AM

COMPARISON OF EUPLOID RATES VIA PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) AND SUBSEQUENT PREGNANCY OUTCOMES BETWEEN ASIAN AND WHITE PATIENTS. David Huang, MD, a Eleni A. Greenwood, MD, MS, a Phil Marsh, BS, a Andrew Runge, BS, b Marcellle I. Cedars, MD, b Mitchell P. Rosen, MD, HCLD c University of California San Francisco, San Francisco, CA; cUniversity of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA.

OBJECTIVE: Prior observational studies have suggested Asian ethnicity as a risk factor for poor IVF outcomes. We sought to compare euploid rates by PGT-A between Asian and White patients and their pregnancy outcomes after euploid single embryo transfer (SET).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We analyzed all day 5 and 6 blastocyst trophectoderm biopsy results via PGT-A from 2010-2019 at a single academic center, with the primary outcome being euploid rate. Euploid rate was determined by dividing the number of euploid blastocysts generated from a single egg retrieval cycle by the total number of blastocysts biopsied in the same cycle. Euploid rates were then compared based on self-reported race of the female partner, focusing on White versus Asian ethnicity. Generalized linear models were employed given clustered nature of the data and to control for oocyte age (STATA v14.2). We further compared pregnancy outcomes by race of the female partner after euploid SET in a subsequent frozen embryo transfer cycle, focusing on live birth or ongoing pregnancy as the outcome.

RESULTS: A total of 5,776 blastocyst PGT-A biopsies over 1,291 IVF cycles from 820 White and Asian female patients were identified. Of the blastocyst biopsies analyzed, 3,658 blastocysts were from White female patients and 2,118 blastocysts were from Asian female patients. Overall euploid rates did not vary significantly by female partner race: 57.8% in couples with a White female partner and 43.1% in those with an Asian female partner. After controlling for age of the oocyte, the odds of euploidy in couples with an Asian female partner compared to those with a White female partner were similar (OR 1.02, 95% CI 0.89,1.17, p = 0.75). We also observed no statistically significant differences in ongoing pregnancy or live birth rates between couples with an Asian female partner and those with a White female partner (57.8% vs 54.3%, respectively; p = 0.42) following subsequent euploid SET.

CONCLUSIONS: We observed no significant differences in euploid rates via PGT-A by female partner race (Asian versus White). We also did not note significant differences in pregnancy outcomes between Asian and White female patients in the setting of frozen euploid SET. These findings suggest that the less successful IVF outcomes among Asian patients in prior observational studies may be attributed to mechanisms other than poor oocyte/embryo quality or inferior inherent endometrial receptivity.

O-44 Monday, October 14, 2019 11:00 AM

INTERSECTION OF SEXUALLY TRANSMITTED INFECTIONS AND SUBSTANCE USE AMONG LOW-INCOME MINORITY WOMEN: ROUTINE CARE AS A CRITICAL POINT FOR REDUCING REPRODUCTIVE HEALTH DISPARITIES. Tyler McClung, BS, MS, a Morgan Snow, BA, a Chystal G. Thomas, BS, MMS, a Jamie Perin, PhD, a San Francisco, CA; bUniversity of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA.

OBJECTIVE: The objective of this study to determine the relationship between clinically reported substance use on the prevalence of STIs among AYA women seeking routine well-adolescent and gynecological services in a STI prevalent community.

BACKGROUND: Previous data suggest that adolescent and young adult (AYA) women with sexually transmitted infections (STIs) report only one sexual partner and low condom use. While concurrency may be a key factor, the impact of substance use on effective sexual decision making around condom use may be critically important.

MATERIALS AND METHODS: This analysis utilizes AYA data from the Women’s BioHealth Study (WBS), a large human subjects approved cohort study prospectively enrolling mostly African American low-income female patients 13-29 years during routine well AYA and gynecological visits in which specimens were also collected for Neisseria gonorrhoeae (NG), Chlamydia trachomatis (CT) to assess for sexual risk and infection of Mycoplasma genitalium (MG) and Trichomonas vaginalis (TV). Participants provided demographic, clinical, sexual risk behavior, and biological specimens for Trichomonas vaginalis (TV) and Mycoplasma genitalium (MG) testing. Additionally, for this analysis, serial electronic medical records (EMR) from visits were reviewed to explore STI outcomes associated with reported substance use behaviors during clinical visits for women ≤25 years, a defining point for AYA STI risk.

RESULTS: 443 patients with a mean age of 20.8 years (SD 2.7) were reviewed. Thirty-nine percent had a history of marijuana use, 43% had a history of alcohol use, and 3% had a history of substance use other than alcohol or marijuana. AYA < 21 were 1.5 times more likely AYA ≥ 21 years to use marijuana (OR: 1.53, 95% CI 1.02 to 2.29, P = 0.032). Marijuana was a predictor of increased behavioral risk scores (0.53 average difference, 95% CI 0.26 to 0.80, P = 0.001) and of not always using a condom (OR: 0.54, 95% CI 0.32 to 0.92, P = 0.024). Participants with a history of marijuana use (OR: 1.68 95% CI 1.11 to 2.56, P = 0.015) or other substance use (OR: 3.81, 95% CI 1.33 to 10.95, P = 0.013) were more likely to test positive for an STI.

CONCLUSIONS: A history of marijuana or substance use other than alcohol put AYA patients at a greater risk of not using a condom and contracting an STI, which could negatively affect reproductive health. Strategic approaches to addressing substance use disorders alongside STI prevention efforts among AYA served by practices in low income minority, STI-prevalent communities are warranted.

O-45 Monday, October 14, 2019 11:15 AM

ANTI-MULLERIAN HORMONE (AMH) TRAJECTORIES IN REPRODUCTIVE AGE AFRICAN AMERICAN WOMEN: FINDINGS FROM THE STUDY OF OVARIAN AGING AND RESERVE (SOAR). Emma Giuliani, MD, a Anca M. Tilia, MPH, b Veronica Berrocal, PhD, b Mercedes Carnethon, PhD, b Lia A. Bernardi, MD, b Lisa M. Neff, MD, b Erica E. Marsh, MD b Reproductive Endocrinology and Infertility, University of Michigan, Ann Arbor, MI; bUniversity of Michigan, Ann Arbor, MI; bNorthwestern University, Chicago, IL; bReproductive Endocrinology and Infertility, Northwestern University, Chicago, IL; bEndocrinology, Metabolism, and Molecular Medicine, Northwestern University, Chicago, IL.

OBJECTIVE: AMH, a member of the transforming-growth-factor-b family, is produced by the granulosa cells of preantral and small antral follicles. It has been widely used as the preferred serum hormone to estimate ovarian reserve due to its relative stability over the menstrual cycle. Despite its increasing use, there have been very few studies that have followed AMH levels over time in young, healthy, non-Caucasian women. The objective of this study was to determine AMH trends in reproductive aged African American women (AAW).

DESIGN: Longitudinal study.

MATERIALS AND METHODS: SOAR leveraged an existing cohort of AAW who were recruited from the Detroit, MI community, as part of the Study of the Environment, Lifestyle and Fibroids (SELF). Anthropometric measurements, health information and blood samples were collected from each participant at four time points over a 5-year period. Serum AMH levels were measured using the ultrasensitive picoAMH assay (Ansh Labs, Webster, TX). Summary statistics were derived for the variables of interest, and linear mixed models for logAMH on age and age^2 with random slopes and intercepts were used to estimate trajectories of AMH levels (SAS 9.4 - Cary, NC).

RESULTS: A total of 1,692 women were included in the analysis. The majority of the participants completed all four study visits (66.5%). The mean duration between the first and last visit was 59.0±3.6 months. The median AMH values for the four visits were 5.9±4.2, 4.6±3.9, 4.1±3.7, and 3.9±3.7 ng/mL, respectively. The mean ages at each study visit were 29.2±3.4, 30.9±3.4, 32.5±3.4, and 34.3±3.4 years. At baseline, 59.7% of women were obese, 19.1% were current smokers, and 31% used hormonal contraception within 4 weeks of their visit. In models adjusted for BMI,

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smoking status and current hormonal contraception use at baseline, the overall estimated AMH trajectory showed minimal decrease until age 25 years after which the levels followed a relative linear decline, with accelerated rate after age 30. The correlation between random slopes and random intercepts was -0.93. The rates of AMH decline were similar among women (variance of random slopes: 0.0055) and AMH levels exhibited very little within-individual correlation (intraclass correlation coefficient: 0.17).

CONCLUSIONS: This is the first longitudinal study of AMH trajectories over a substantial period of time in reproductive aged AAW, a group that is largely underrepresented in the ovarian reserve literature. In this population, AMH decline with age seems to follow a common pattern with women with higher AMH levels at baseline exhibiting slightly slower rate of decline than women with lower than average initial levels. As reproductive lifespan and outcomes seem to be influenced by race, a better understanding of AMH trajectories and the role of potential modifiable factors on AMH decline in women of different backgrounds will improve physician counseling and empower women to make well-informed reproductive choices.

O-46 Monday, October 14, 2019 11:30 AM

OBJECTIVE: To determine if the trends in disparities of outcomes between black, non-Hispanic (BNH) and white women undergoing ART over the last 10 years have changed and to identify possible contributing factors that may have influenced such change.

DESIGN: Retrospective, cohort study and comparison of reported outcomes in the SARTCORS database for 2014-2016 with those previously reported in 2004-2006.

MATERIALS AND METHODS: Analysis of 2014-2016 SARTCORS for member clinics that performed at least 50 cycles of ART and reported race in more than 95% of cycles. 125,555 cycles using autologous, fresh, non-donor embryo cycles were analyzed of which 16,551 cycles were from BNH women and 109,004 cycles were from white women. Findings from this analysis were compared with previously analyzed cycles reported for 2004-2006 (Fertil Steril 93:626-35, 2010).

RESULTS: Reporting of race of 60% of cycles was essentially unchanged over the 10 year period. The proportion of cycles from BNH women increased nominally over the same period. When comparing 2014-16 to 2004-06, a greater proportion of BNH cycles were from older ages (2014-16 to 2004-06, a greater proportion of BNH cycles were from older ages (p<0.001), had lower basal E2 (37.8 vs 42.1 pg/ml, P=0.042), higher AMH (3.54 vs 2.84 ng/ml, P=0.018), lower basal Vit D (31.9 vs 36.6 ng/ml, P=0.001), required less gonadotropins (3374.6 vs 3567 IU, P=0.045), had lower peak Vit D (40.8 vs 45.4, P=0.008), and had lower total blastocyst number (2.64 vs 3.1, P=0.036). For those who had a fresh ET (43 SA and 75 C), the live birth rate was lower in SA (52.7% vs 67.4%, P=0.014).

For those undergoing PGT-A, there was a lower incidence of euploid embryos in C (150 cycles in C and 87 in SA) (45.6% in SA vs 35.6% in C, P=0.042).

CONCLUSIONS: Despite being significantly younger and having better ovarian reserve, SA women had significant differences in stimulation parameters. For those who had a fresh ET, SA women had a significantly lower live birth rate compared to Caucasians.


O-47 Monday, October 14, 2019 11:45 AM
SOUTH ASIAN WOMEN HAVE POORER IVF OUTCOMES DESPITE BEING YOUNGER AND HAVING BETTER OVARIAN RESERVE COMPARED TO CAUCASIANS. Fady I. Sharara, M.D., Kaci D. Rogers, MS, Megan Goodwin, MS. Virginia Center for Reproductive Medicine, Reston, VA.

OBJECTIVE: IVF outcomes in ethnic minorities have been reported previously to be worse compared to Caucasians (C), including those of South Asian (SA) descent (India, Pakistan, Bangladesh, Nepal). Little has been published on ovarian stimulation parameters in SA as compared to C.

DESIGN: Retrospective.

MATERIALS AND METHODS: A total of 557 cycles were reviewed (176 in SA and 401 in C). Markers of ovarian reserve (AMH, AFC, FSH, E2) and cycle outcomes were compared between the two groups. The clinical outcome of those who had a fresh embryo transfer were also compared.

RESULTS: SA women were significantly younger (34.3 vs 35.7 yrs, P<0.001), had lower basal E2 (37.8 vs 42.1 pg/ml, P=0.042), higher AMH (3.54 vs 2.84 ng/ml, P=0.018), lower basal Vit D (31.9 vs 36.6 ng/ml, P=0.001), required less gonadotropins (3374.6 vs 3567 IU, P=0.045), had lower peak Vit D (40.8 vs 45.4, P=0.008), and had lower total blastocyst number (2.64 vs 3.1, P=0.036). For those who had a fresh ET (43 SA and 75 C), the live birth rate was lower in SA (52.7% vs 67.4%, P=0.014). For those undergoing PGT-A, there was a lower incidence of euploid embryos in C (150 cycles in C and 87 in SA) (45.6% in SA vs 35.6% in C, P=0.042).

CONCLUSIONS: Despite being significantly younger and having better ovarian reserve, SA women had significant differences in stimulation parameters. For those who had a fresh ET, SA women had a significantly lower live birth rate compared to Caucasians.

Regional disparities in assisted reproductive technology access to care: employing modern technology to close the gap. Sasa Mikhail, MD/MS," Anna Gaidis, MD," Hannah N. Smith, BS," Larisa Gavrilova-Jordan, MD "Medical College of Georgia at Augusta University, augusta, GA;"Medical College of Georgia at Augusta University, Augusta, GA;"Augusta University, Augusta, GA.

OBJECTIVE: Today, significant disparities still exist for access to assisted reproductive technology (ART) treatments in the United States. Only 60% of women who require ART are able to proceed with treatment. One of the major obstacles for access is the scarcity of fertility specialists in some regions of the US. Furthermore, the physical and financial burden associated with
time off from work and travel within or out of state, creates additional barriers. Telehealth is a well-established tool that alleviates these burdens. While other areas of medicine have welcomed this technology, reproductive medicine has yet to utilize it to its full potential. We implemented a regional telehealth program to close the gap in ART access in the rural Southeastern US. Our aim is to evaluate our telehealth program’s ART outcomes and patient satisfaction of those living remotely.

DESIGN: Retrospective cohort and cross-sectional survey study.

MATERIALS AND METHODS: Patients who utilized the telehealth application for ART services at Augusta University (AU) between September 2015 to November 2018 were identified. The study was approved by AU IRB. Demographic variables were collected using the electronic medical record including age, type of ART cycles, travel distance, number of visits, and treatment outcomes. Patients were electronically mailed a validated questionnaire created via the qualtrics™ application. The survey included a patient satisfaction questionnaire as well as travel distance, number of visits, and ART treatment outcome. Data analysis was performed with descriptive statistics methods.

RESULTS: A total of 58 patients were identified of which 53% were < 35 years old (y/o), 16% were 35-37 y/o and 31% >38 y/o. 78% of patients had autologous fresh in vitro fertilization (IVF) cycles, 16% frozen embryo transfer, 3% donor oocytes, 1.4% embryo adoption and 1.4% gestational carrier. The overall clinical pregnancy rate was 60.3% (77% < 35 y/o and 37% > 35 y/o) with an overall live birth rate of 38% (48% < 35 y/o and 22% > 35 y/o). The cohort’s mean number of visits was 2.93 (+/- 0.82). The survey response rate was 7758 (96%), 56% of responders were <35 y/o and 44% >35 y/o. The mean number of visits for responders was 3 (+/- 0.99) and mean travel distance 171.4 miles (+/- 0.67). All responders underwent transvaginal oocyte retrieval and embryo transfer. For surveyors, the clinical pregnancy rate was 19/27 (70.3%) with a live birth rate of 16/27 (59.3%). 93% of patients reported being highly satisfied with the telehealth service to enhance access to ART. All responders stated they would recommend telehealth use for ART to others.

CONCLUSIONS: Our study demonstrates that employing modern telehealth applications improves access to ART care in underserved areas. Fewer office visits maintains high patient satisfaction due to accessibility and cost reduction associated with travel and time off work. Reproductive health providers may consider utilizing telehealth in delivering ART treatment.

SUPPORT: None.

INFERTILITY AND CANCER

O-49 Monday, October 14, 2019 10:45 AM

PREGNANCIES IN CANCER SURVIVORS: OVARIAN RESERVE IS A POOR PROGNOSTICATOR.

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OBJECTIVE: While cancer therapies negatively impact ovarian reserve, few studies have examined factors related to clinical pregnancy rates in survivors. The objective of this study was to prospectively assess pregnancy rate, time to pregnancy, and corresponding measures of ovarian reserve in a cancer survivor cohort compared to similar-aged controls to determine factors associated with pregnancy in cancer survivors.

DESIGN: This is a prospective cohort study of cancer survivors aged 15-39 years who underwent chemotherapy and were ≥1 year post-treatment with no evidence of disease. Comparative controls were post-menarchal females with regular menses (21-35 days). Only survivors and controls at risk for pregnancy, defined by reporting intercourse with a man during the study period, were included in this analysis.

MATERIALS AND METHODS: Participants completed annual study visits with reproductive/contraceptive questionnaires, early follicular phase hormones, and ultrasounds. Demographic characteristics and log-transformed measures of ovarian reserve were compared using Pearson χ² analyses, t-tests, and multivariable regression models. The risk of pregnancy during study follow-up in survivors and controls was compared using Kaplan–Meier curves. Post hoc analyses indicated 80% power to observe a 46% decrease in hazard rates of pregnancy for survivors compared to controls.

RESULTS: 96 survivors and 79 controls were followed for a mean of 4.7 years. There was no difference in age, BMI, or duration of follow-up between groups. At enrollment, 18 survivors and 17 controls reported a pregnancy conceived prior to study; 12 of the 18 pre-study pregnancies in survivors were conceived after cancer treatment. A similar proportion of survivors and controls reported additional pregnancies ‘captured’ during the prospective follow-up time (47/96 [49.0%] survivors; 47/79 [59.5%] controls). There was no difference in the survival distributions for the two groups (p = 0.27).

Four survivors conceived with SOI/UI and seven with IVF. Survivors who conceived were older, more likely to be married or cohabitating, but received similar cyclophosphamide equivalent doses of chemotherapy compared to survivors who did not conceive. Anti-Müllerian hormone measured prior to pregnancy in survivors who conceived was lower than in controls who conceived (1561 vs. 2486 pg/mL, p = 0.02), but similar to survivors who did not conceive (p = 0.26). Importantly, half of the captured pregnancies in both groups were unplanned (52% in survivors vs. 48% in controls, p = 0.9). Among planned pregnancies, survivors reported an average of 16 months (median 9 months) to conceive compared to 11 months (median 1 month) for controls (p = 0.16).

CONCLUSIONS: Pregnancy rate and time to pregnancy was similar in cancer survivors compared to controls despite diminished measures of ovarian reserve. These findings suggest that predictions about the fertility potential of cancer survivors cannot be made on the basis of measures of ovarian reserve alone.

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THE POTENTIAL IMPACT OF NEWER CHEMOTHERAPY REGIMENS ON FUTURE FERTILITY IN MEN AND WOMEN TREATED FOR LYMPHOMA.

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OBJECTIVE: The treatment of lymphoma is rapidly advancing to include more non-ABVD-based chemotherapy regimens. The fertility risks for men and women who receive non-ABVD regimens like BEACOPP are poorly understood.

DESIGN: Systematic review and meta-analysis.

MATERIALS AND METHODS: We searched the MEDLINE, PUBMED, and COCHRANE databases, online trial registries and conference proceedings for published manuscripts and abstracts from 1980 to April 2019. Studies were deemed eligible for meta-analysis if they included reproductive-age women or men with lymphomas (Hodgkin’s and non-Hodgkin’s) and the following were reported: chemotherapy regimen, patient age, duration from chemotherapy to ovarian reserve assessment (Anti-Müllerian Hormone (AMH)) or semen analysis, and rate of either severe oligo- or azoospermia (men). Estimates were pooled using random-effects meta-analysis comparing AMH levels in women, and rates of normospermia in men, with ABVD versus non-ABVD treatment. For the purpose of meta-analysis, normospermia was defined by a lack of either severe oligo- or azoospermia.

RESULTS: Data were extracted from 4 studies involving 440 women and from an additional 7 studies involving 400 men. The range of numbers of women and men included in each of the studies was between 30 to 263 and 19 to 141, respectively. The majority of the cancer diagnoses in all 11 studies were Hodgkin’s lymphomas. Three studies had follow-up AMH levels 36 months after completion of cancer treatment; one study measured AMH levels 18 months after treatment. Post-treatment AMH levels (pmol/L) were higher when comparing women who underwent ABVD versus non-ABVD, however this difference did not reach statistical significance (13.3 [95% CI: 13.3 – 30] versus 3.5 95% CI: [1.8-8.8], p = 0.22). Duration of follow-up for post-treatment semen analyses ranged from one to seven years after completion of treatment. There was a significant difference in the rate of post-treatment normospermia among men who underwent ABVD regimen 89% [95% CI 70 - 96%] versus non-ABVD regimen 28.4% [95% CI 15 - 47.0], p < 0.001).
CANCER TREATMENT IS ASSOCIATED WITH A MEASURABLE DECREASE IN LIVE BIRTHS IN A LARGE, POPULATION-BASED STUDY. Deepika Garg, MD, a Huong Dieu Meeks, PhD, b Erica Johnstone, MD, c Alexander W. Pastuszak, MD, PhD, a Sarah L. Berga, MD, a Ken R. Smith, PhD, a James Hotaling, MD, a Joseph M. Letourneau, MD, a University of Utah, Salt Lake City, UT; UT University of Utah School of Medicine, Salt Lake City, UT.

OBJECTIVE: Research on the impact of cancer treatment on fertility has evolved over time. Initially, studies tracked rates of amenorrhea and, more recently, rates of conception after cancer treatment. The aim of the present study is to define rates of live birth in a large, population-based study of the most common reproductive-age cancers in women.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: We performed a retrospective cohort study using the Utah Population Data Base (UPDB) relating first time cancer diagnosed between 1966 and 2014 to subsequent pregnancy in women in Utah aged 18-45 years. UPDB is a comprehensive source of birth, medical and cancer records of the Utah state population. Women from the study group who had live births after cancer diagnosis (n= 17,960) were compared with age matched controls at the time of cancer diagnosis (n= 89,436) and healthy sisters who had never been diagnosed with cancer (n= 15,099). Age-matched controls were the same age as cancer survivors in the year of cancer diagnosis. Both groups were followed from the year of diagnosis until 2014 and pregnancies achieved during this time recorded. We used conditional Poisson regression models, adjusted for birth year, BMI, and ethnicity, to estimate the association between history of cancer and subsequent live birth.

RESULTS: Based on Poisson regression modeling, the total number of live births was 15% lower among cancer survivors compared to healthy sisters (p < 0.001). When compared to age-matched healthy controls from the general population, cancer survivors had 25% fewer live births (p < 0.01). When compared with their healthy sisters, the reduction in live birth rate was 15% for all cancer types, 16% for breast cancer, 17% for central nervous system cancers, and 36% for soft tissue cancers (p < 0.001). 3% of cancer survivors who had a live birth utilized fertility treatment, compared to 2% (p = 0.13) of healthy controls who achieved live births. In addition, there were more stillbirths among cancer survivors when compared with their healthy sisters (14 per 1000 births versus 11 per 1000 births, p < 0.01).

CONCLUSIONS: In this large, population-based study in the Western United States, cancer and its treatment were associated with lower live birth rates, particularly with regard to preterm birth, pre-eclampsia, and low birth weight, among survivors of cancers diagnosed during the young adult years.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: The Utah Population Data Base (UPDB) was used to identify female cancer survivors (ages 18-45) who were diagnosed from 1966 to February 2014. The UPDB is a comprehensive source of birth, medical and cancer records of the Utah state population. We identified pregnancy outcomes of female cancer survivors (n= 17,960) and compared these with age matched healthy women without a cancer diagnosis who were randomly included based on birth certificates (n= 89,436). Cases were matched to controls who were the same age during the age of the cases during the study period of their cancer diagnosis. Cases and age-matched controls were then followed from the year of diagnosis until 2014 and pregnancies achieved during this time were recorded. Live birth rates, Aggar scores after delivery, pre-term delivery, low birth weight (defined as birth weight between 1500-2500 grams), prevalence of pre-eclampsia, and children with congenital malformations were determined. Descriptive statistics and chi-square tests were used, were appropriate.

RESULTS: Overall, 3128 births to cancer survivors and 19,405 births to healthy controls were included. In comparison to the control group, cancer survivors had significantly lower live birth rates (18% reduction, p < 0.001), an increased rate of preterm delivery (17% vs 13%, P < 0.001), and a higher risk of a child with low birth weight (11% vs 8%, p < 0.001). The higher prevalence of these outcomes was mostly due to cancer related chemotheraphy and radiotherapy. The number of women with pre-eclampsia, children with congenital malformations, and Aggar score (<7) did not differ significantly between groups.

CONCLUSIONS: Currently, a significant focus in onco-fertility is on achieving live birth after cancer treatment. A better understanding of how to achieve a healthy pregnancy after cancer is needed. We find that female cancer survivors have a lower live birth rate and higher risk of pregnancy related complications, including preterm delivery and low birth rate than women without a history of cancer. Whether or not other cancers, endometrial, and/or uterine mechanisms remain to be determined and may shed light on how to ensure healthier reproductive outcomes.

STIMULATION OF THE OVARIAS IN WOMEN WITH BREAST CANCER UNDERGOING FERTILITY PRESERVATION: ALTERNATIVE VERSUS STANDARD STIMULATION PROTOCOLS. E. M. E. Balkenende, MD, a T. Dahlan, M.D., b C. M. M. Beerendonk, M.D. PhD., a K. Fleischer, MD, PhD., a M. A. E. Bos, M.D., PhD., a C. B. Lamberg, MD PhD, a Roelof Schats, MD PhD, b L. Louwe, M.D., b A. E. P. Cantineau, M.D., PhD., b J. M. J. Smeenk, M.D. PhD., a J. P. de Bruin, M.D., PhD., b F. van der Veen, M.D. PhD., Prof., a S. C. Linn, M.D. PhD., Prof., a M. van Wely, Ph.D., Dr., a Mariette Goddijn, MD, PhD. Prof. Dr. a Amsterdam University Medical Center, Amsterdam, Netherlands; Radboud UMC, Nijmegen, Netherlands; Amsterdam AMC, Amsterdam, Netherlands; Leiden University Medical Center, Leiden, Netherlands; UMC Groningen, Netherlands; ETZ, Tilburg, Netherlands; Jeroen Bosch Hospital, Department of Obstetrics and Gynaecology, Den Bosch, Netherlands; Netherlands Cancer Institute, Amsterdam, Netherlands.

OBJECTIVE: To evaluate the effectiveness of ovarian stimulation with tamoxifen or letrozole compared to standard ovarian stimulation on the number of oocytes retrieved in women with breast cancer in the course of fertility preservation.

DESIGN: Multi-center randomized open-label trial in the Netherlands and Belgium.

MATERIALS AND METHODS: Women between 18 and 43 years with breast cancer who opted for banking of oocytes or embryos in the course of fertility preservation were included. We randomly assigned them to one of the three study groups; group 1 ovarian stimulation plus tamoxifen (60 mg per day), group 2 ovarian stimulation plus letrozole (5 mg per day) or group 3 standard ovarian stimulation without additional medication. Primary outcome was the number of oocytes retrieved at follicle aspiration. Secondary outcomes were number of mature oocytes retrieved, number of oocytes or embryos banked and peak E2 levels during ovarian stimulation.

RESULTS: Between January 2014 and December 2018, we randomised 162 women with breast cancer. We analysed the primary outcome for 148 (91%) women of which 142 women (88%) underwent ovum pick up. Mean age of the women was 32 years.51 women underwent ovarian stimulation plus tamoxifen, 51 plus letrozole and 46 standard ovarian stimulation without additional medication. Primary outcome was the number of oocytes retrieved at follicle aspiration. 12.6 (group 1), versus 14.2 (group 2) versus 13.3 (group 3) (mean difference in number of oocytes: group 1 vs. group 3 -0.3, 0.3 vs. 0.3, 0.3 vs. 0.3, 0.3 vs. 0.3) (mean difference in number of oocytes: group 1 vs. group 3 -0.6, 0.6 vs. 0.6, 0.6 vs. 0.6, 0.6 vs. 0.6).

CONCLUSIONS: As lymphoma treatment evolves, fertility preservation physicians need to be aware that lymphomas may increasingly be treated with chemotherapeutic regimens that appear to have a more negative impact on future fertility in men and may likely impact it in women as well, though more data are needed.
group 3.024; 95% CI: -4.2 to 4.7; group 2 vs. group 3.029; 95% CI: -4.2 to 4.8). Mean number of embryos banked was 5.9 (group 1) versus 4.9 (group 2) versus 5.0 (group 3) (mean difference in number of embryos banked: group 1 vs. group 3.085; 95% CI: -3.0 to 4.7; group 2 vs. group 3 -1.33; 95% CI: -4.0 to 3.7).

CONCLUSIONS: These results show that the addition of tamoxifen or letrozole to standard ovarian stimulation did not effect the number of oocytes or embryos banked in the course of fertility preservation for women with breast cancer. Whether the addition of tamoxifen or letrozole to standard ovarian stimulation affects the long-term follow up in terms of safety in women with breast cancer, remains to be seen.

SUPPORT: The STIM trial was funded by the Pink Ribbon foundation.

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DESCRIBING LIVE BIRTHS AFTER CANCER TREATMENTS: WHEN DO PATIENTS CONCEIVE AND HOW MANY CHILDREN DO THEY HAVE? A POPULATION-BASED STUDY IN THE WESTERN UNITED STATES. Deepika Garg, MD,a Huong Dieu Meeks, PhD,b Erica Johnstone, MD,a Alexander W. Pastuszak, MD, PhD,b Sarah L. Berga, MD,a Ken R. Smith, PhD,a James Hotaling, MD,c Joseph M. Letourneau, MD d University of Utah, Salt Lake City, UT; 1University of Utah School of Medicine, Salt Lake City, UT; 2University of Utah School of Medicine Andrology and IVF Laboratories, Salt Lake City, UT.

OBJECTIVE: Oncologists typically advise women to wait for two to five years after cancer treatment before trying to conceive. Age-related fertility concerns can be increased by both this period of waiting and the acceleration of ovarian follicle loss during and after cancer treatment. Little is known about the impact of age on how long it takes women to complete their family building after cancer treatment.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The Utah Population Data Base (UPDB) was used to identify female cancer survivors in Utah state with first time cancer diagnosed between 1966 to 2014. We identified first and last live births of various age groups and reported these relative to the timing of their cancer diagnosis. Descriptive statistics and chi-square testing were used where appropriate.

RESULTS: Our population included 17,960 women with first cancer diagnosis at age 18-45 years. These age groups were split into 18-25, 26-30, 31-35, 36-40, > 40 years old with the fraction of patients included in each group as follows: 18-25 = 14%, 26-30 = 16%, 31-35 = 19%, 36-40 = 23%, >40 = 28%. The most common cancer types among the cohort were breast cancer in 23%, gynecologic cancers in 29%, lymphomas in 4%, and leukemia in 2%. A total of 36% of women had no children at the time of their cancer diagnosis. Nulliparity at the time of diagnosis was more common in the 18-25-year-old age group (62%). Approximately 17% of women had children after their diagnosis of cancer and they tended to have children approximately 2-3 years after cancer diagnosis. Women in the 18-25 age group tended to have their first post treatment child further from diagnosis than women who were >40. Also, women 18-25 years old tend to have their last child 7 years after their cancer diagnosis, whereas women >40 tend to have their last children approximately 2 years after cancer diagnosis. Number of live births after cancer diagnosis was also higher among younger women, as reflected in the table below.

CONCLUSIONS: For both oncologists and infertility specialists, it is important to understand the timeline of when women with a history of cancer tend to build their families, and to incorporate this information into counseling about treatment-related infertility risk. Since the choice of when to build a family is highly personal and may vary across regions, more time-to-pregnancy data from other populations should also be collected.

MALE REPRODUCTION AND UROLOGY: TRAVELING SCHOLARS

O-55 Monday, October 14, 2019 10:45 AM

EVALUATION OF FERTILITY PRESERVATION COUNSELING AND REFERRALS IN US CLINICAL PRACTICES: REVIEW OF ASCO’S QUALITY ONCOLOGY PRACTICE INITIATIVE (QOPI). Taylor P. Kohn, MD, MPH, a Premal Patel, MD, b Benjamin Shiff, MD, c Jaden R. Kohn, MD, MPH, c Ranjith Ramasamy, M.D d Johns Hopkins University School of Medicine, Baltimore, MD; eUniversity of Miami Miller School of Medicine, Miami, FL; fSection of Urology, University of Manitoba, Winnipeg, MB, Canada; gJohns Hopkins University School of Medicine, Department of GYN/ OB, Baltimore, MD.

**P-value Chi-Squared for Trend.** **P-value Chi-Squared.**
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LOWER TOTAL MOTILE COUNT IS ASSOCIATED WITH SMALLER HISTORIC INTERGENERATIONAL FAMILY SIZE: A PEDIGREE ANALYSIS FROM THE UTAH POPULATION DATABASE (UPDB).
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OBJECTIVE: Genetic heritability of male factor infertility may contribute to intergenerational variations in family size. We sought to assess the correlation of total motile count and intergeneration family size within the Utah Population Database (UPDB).

DESIGN: This was a retrospective, population-based, cohort analysis of men with at least a single measure of total motile count (TMC) within the UPDB and with complete pedigree data.

MATERIALS AND METHODS: These men must have at least one generation within their pedigree born in and prior to 1935 for inclusion to reduce the effect of contraception on the results. We identified the average number of generations for each individual overall, as well as the average number of generations and offspring within each generation occurring in and prior to 1935. Linear logistic regression models with clustered sample design were used to assess the relationship between TMC within 5th and 25th percentile and intergeneration family size. Additional generalized estimating equations with independence correlation structure and clustered sample design were created to estimate the change in TMC per increase in number of offspring among proband ancestors.

RESULTS: We identified 2,182 men with a measure of TMC within the UPDB and complete pedigree information. 541 men (24.8%) were within the 25th percentile for TMC while 112 men (5.1%) were within the 5th percentile for TMC (including azoospermic men). The average number of generations within each individual’s pedigree was 4.2 (SD: 1.1). The average number of generations and offspring within each generation occurring prior to 1935 were 3.6 (SD: 1.0) and 6.5 (SD: 1.6), respectively. We found no significant association between intergenerational size and TMC within the 5th percentile (including azoospermic men) (RR = 0.97, 95% CI 0.93-1.01, p = 0.18) or the 25th percentile (RR = 1.00, 95% CI 0.97-1.03, p = 0.98). When TMC was analyzed as a continuous variable, generalized estimating equations suggest that lower TMC is related to smaller intergenerational family size. For every additional child in their historical pedigree back to 9 generations, we saw an increase in TMC of 1.88 million (p = 0.031).

CONCLUSIONS: This is one of the first studies examining the relationship between intergenerational family size and TMC as a marker of male factor infertility. We found a significant association between TMC as markers of male factor infertility and family size, suggesting that lower TMC is related to smaller intergeneration family size. This hypothesis generating data questions an effect of genetic heritability and male factor infertility on intergenerational family size.

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DECISIONAL CONFLICT AND KNOWLEDGE AMONG PATIENTS WITH VARICOCELE SEEKING TREATMENT FOR INFERTILITY.
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OBJECTIVE: To measure disease-specific knowledge and decisional conflict in men with varicoceles being counseled for infertility, and to gain insight into decision-making in male versus female-centric treatments for infertility.

DESIGN: This was a cross-sectional, observational, survey-based study of patients with clinical varicoceles and infertility.

MATERIALS AND METHODS: 84 patients were identified prior to their initial infertility consultation with a fellowship-trained male reproductive surgeon at the University of California, Los Angeles. Following consultation, patients completed a survey instrument measuring disease-specific knowledge, decisional conflict, satisfaction with care, and impression that shared decision-making occurred at the time of consultation. This instrument also queried patients’ preferred infertility treatment modality both before and after consultation. Treatment-associated decisional conflict was measured with the validated SURE metric. Patient characteristics and survey responses were compared between those without decisional conflict (SURE score of 0) and those with some degree of decisional conflict (SURE score of 1-3) using Chi-squared (Fisher’s exact if needed) and Wilcoxon rank-sum tests.

RESULTS: Of 5,887 reproductive age patients, 42.1% discussed the risk of infertility (1540/2831, 54.4%) compared with reproductive-aged patients with newly diagnosed cancer. Our objective had significantly higher rates of fertility risk discussion (48.6% vs 39.6%, p<0.001). Prior to chemotherapy were discussed, male sex (OR 0.73; CI:0.60-0.88) and receiving care in an academic clinic (1.45; 1.05-2.01) predicted higher risk; further research is needed to identify factors that optimize fertility counseling prior to chemotherapy.

CONCLUSIONS: Providers are more likely to counsel younger patients and female patients. State laws improve frequency of discussing fertility risk; further research is needed to identify factors that optimize fertility counseling prior to chemotherapy. Reference: None.

SUPPORT: Department of Urology, University of Miami.
OBJECTIVE: Surgically extracted sperm is generally expected to have inferior IVF outcomes compared to ejaculated sperm. We sought to evaluate sperm quality and IVF outcomes of cryopreserved epididymal sperm samples obtained from patients with obstructive azoospermia (OA) via office-based MIESA. We report sample characteristics and compare fertility outcomes of MIESA patients who underwent IVF with intracytoplasmic sperm injection (ICSI) to a control group of couples who underwent ICSI for unexplained infertility with fresh, normal ejaculated sperm samples.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The MIESA is performed in the office with oral or intravenous sedation using only loupe magnification. Samples are cryopreserved for later IVF/ICSI. Epididymal sperm is extracted in the same manner as an obliterator microsurgical epididymal aspiration (MEA), except without the need for general anesthesia, an operating microscope, or complete epididymal exposure. We analyzed MIESA samples for sperm quality/quantity and compared IVF cycle outcomes to a computer-generated control group of age-matched females who underwent IVF/ICSI for unexplained infertility. All couples with identified female factor infertility were excluded. Chi Square and Student t test analysis were used to determine statistical significance.

RESULTS: 43 MIESA procedures were performed between December 2013 and July 2018. Causes of OA included varicocele (35%), failed vasectomy reversal (55%), congenital bilateral absence of the vas deferens (16%), and other (6%). High quality MIESA samples were obtained with a mean retrieved total motile sperm count of 13.7 million which were cryopreserved in the total number of germ cells per tubule was not uncommon. We envision bodily changes. The consequent reduction in spermatogenesis is quite variable, as clearly demonstrated by the unexpected results of the retrospective analysis is being conducted on these same two patient populations to correlate testicular histology, intraoperative wet prep analysis to identify fully formed spermatozoa, medication type and dosage, and serum levels of Estra-

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GONADAL END ORGAN EFFECTS IN MALE TO FEMALE TRANSGENDER PATIENTS ON HORMONAL THERAPY. Priyanka Bearelly, MD, Jaromir Slama, MD, Robert D. Oates, M.D. Boston University School of Medicine, Boston, MA.

OBJECTIVE: The objective of this study is to investigate changes in spermatogenesis as a consequence of the quantitative reduction in testosterone production and action and/or possible direct effects of estrogen on seminiferous epithelium. This unique patient population provides this unusual opportunity because of the high volume of individuals undergoing gender confirmation surgery.

DESIGN: An IRB-approved retrospective review of 35 neovaginoplasty patients and 21 patients who underwent bilateral orchietomy as a stand-alone procedure was conducted. Testicular histology of 56 patients (112 testicles) was examined by the investigators, and predominant patterns of spermatogenesis were defined. Presently, a prospective, IRB-approved analysis is being conducted on these same two patient populations to correlate testicular histology, intraoperative wet prep analysis to identify fully formed spermatozoa, medication type and dosage, and serum levels of Estradiol, Testosterone (T), Luteinizing hormone (LH), and Follicle Stimulating hormone (FSH) obtained immediately prior to surgery. This is in an effort to refine or define an explanation for the negative effect of these medications on spermatogenesis for later IVF/ICSI. Epididymal sperm is extracted in the same manner as an obliterator microsurgical epididymal aspiration (MEA), except without the need for general anesthesia, an operating microscope, or complete epididymal exposure.

MATERIALS AND METHODS: Between January 2017 to September 2018, 35 transgender women underwent neovaginoplasty, and seminiferous tubule histology was retrospecively examined. In addition, in 2017, 21 patients underwent bilateral orchietomy as a stand-alone procedure. Classification included complete absence of germ cells, spermatocytic maturation arrest (SMA), hypospermatogenesis (mild, moderate, and severe), and normal histology. As part of the early prospective cohort, 6 patients underwent bilateral orchietomy, and 2 patients underwent neovaginoplasty. Intraoperative testicular wet prep findings were recorded as number of spermatozoa per high powered field.

RESULTS: Retrospectively, of the 35 neovaginoplasty patients, the following histology was seen: 2 with complete absence of germ cells, 3 with mild hypospermatogenesis, 8 with SMA only, and the remaining with a combination of SMA with mild (4), moderate (5), and severe (11) hypospermatogenesis. Of the 21 orchietomy patients, the following histology was seen: 4 with SMA only, and the remaining with a combination of SMA and mild (4), moderate (6), and severe (7) hypospermatogenesis. In our early prospective data set, 2 out of 8 patients had spermatozoa seen on intraoperative wet prep (T:70, E2:168: T:18, E2:120).

CONCLUSIONS: Estrogen therapy and testosterone blockers (spironolac-tone) are routinely used in combination in MTF individuals to suppress testosterone and its androgenic effects while promoting welcome estrogenic bodily changes. The consequent reduction in spermatogenesis is quite variable, as clearly demonstrated by the unexpected results of the retrospective review—meiotic progression was uniformly impaired while a decrease in the total number of germ cells per tubule was not uncommon. We envision our nascent prospective study to allow us to formulate some mechanistic models of biological causality.
OBJECTIVE: Marijuana is the most widely used illicit drug in the US, with legalizations further increasing both medical and recreational use. Studies evaluating self-reported use yield mixed results about whether marijuana is harmful in pregnancy. However, there is concern for underreporting due to the illegality of marijuana use as it is not federally legalized. Our aim was to examine associations between preconception marijuana use, via both self-report and urinary tetrahydrocannabinol (THC), and fecundability, live birth, and pregnancy loss. We also evaluated these relationships in the context of ovariocentricity and anti-mullerian hormone (AMH).

DESIGN: A prospective cohort of 1212 women enrolled in the EAGeR trial, aged 18-40 years, with regular menstrual cycles and a history of 1-2 previous pregnancy loss were included.

MATERIALS AND METHODS: Women were screened for urinary THC up to 2 time points prior to conception using a homogenous enzyme immunoassay (Random Laboratories) and reported past year marijuana use at baseline. Women were followed for up to 6 cycles while attempting pregnancy. Anovulation was assessed using fertility monitors and, where available, in the first 2 cycles of follow-up, supplemented with urinary pregnanediol glucuronide measures. Serum AMH was measured at the baseline visit. Cox proportional hazard regression was used to calculate fecundability odds ratios (FOR), and log-binomial regression was used to estimate risk ratios (RR) for live birth, pregnancy loss, anovulation, and low AMH (≤1.0 vs >1.0 ng/ml) adjusting for age, race, BMI, education, smoking, alcohol, and antidepressant use.

RESULTS: Of the 33 (2.7%) women who screened positive for THC, only 14 self-reported marijuana use. A total of 62 women (5.1%) screened positive for THC or self-reported use in the year prior. Women positive for urinary THC or with self-reported marijuana use had reduced fecundability (FOR 0.53, 95% CI 0.33, 0.86). No associations were observed with live birth (RR 0.71; 95% CI 0.41, 1.22) or pregnancy loss (RR 0.78; 95% CI 0.28, 2.18). Further, no associations were observed with anovulation (RR 0.94, 95% CI 0.51, 1.73) or with low AMH (RR 1.25, 95% CI 0.71, 2.20).

CONCLUSIONS: Women who screened positive for THC during preconception, or self-reported use during the past year, had reduced fecundability, though no associations were observed with live birth or pregnancy loss. Associations with reduced fecundability are not likely to be explained by anovulation or AMH levels, suggesting that other mechanisms may be at play. Further investigations are needed to confirm these observations, determine potential mechanisms and what duration and dose of marijuana may negatively impact fecundability.

SUPPORT: Intramural Research Program, Division of Intramural Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development.

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THE ROLE OF MATERNAL PRECONCEPTION VITAMIN D STATUS IN HUMAN OFFSPRING SEX RATIO.

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OBJECTIVE: Experimental data suggests that maternal inflammation is specifically detrimental to the implantation or survival of male embryos, which may contribute to sex ratio reduction on the population scale. However, it is currently unknown whether other factors associated with both pregnancy and inflammation, such as vitamin D status, are associated with altered offspring sex ratio. Our objective was to therefore evaluate the association of preconception serum 25-hydroxyvitamin D levels [25(OH)D] and male live birth among reproductive-age women attempting pregnancy.

DESIGN: This was a prospective secondary analysis of the Effects of Aspirin in Gestation and Reproduction trial, which included 1,228 reproductive-age women attempting to conceive.

MATERIALS AND METHODS: 25(OH)D and high sensitivity C-reactive protein (hsCRP) levels were measured in serum at baseline. Participants were classified as vitamin D sufficient versus insufficient [25(OH)D ≥ 30 vs. < 30 ng/mL]. Fetal sex was ascertained by medical record abstraction among live births and by chromosomal analysis among clinical pregnancy losses. We estimated unadjusted and adjusted relative risks (RRs) and 95% confidence intervals (CIs) for male live birth and pregnancy with a male fetus according to preconception vitamin D status using generalized estimating equations of log-binomial regression with robust standard errors.

RESULTS: Among 1,094 women who completed follow-up, the proportion of male live births was 24% (n=136) and 30% (n=156) in the vitamin D insufficient and sufficient groups, respectively. In multivariable models, women in the vitamin D sufficient group were 25% (RR = 1.25; 95% CI = 1.02, 1.52) more likely to have a live-born male infant compared to the insufficient group. These associations were stronger among women with high versus low levels of preconception hsCRP (>1.95 ng/mL; RR = 1.44;
with increased risk of any loss (HR = 1.21, 95% CI = 1.01, 1.46). Estrogen levels of preconception vitamin D was also positively associated with pregnancy with a male fetus (RR = 1.12, 95% CI = 1.01, 1.24). Further adjustment for nausea and vomiting and other factors that change during early pregnancy showed that caffeine intake at levels lower than those corresponding to current medical recommendation was positively associated with risk of loss (0 vs. ≥ 1 servings/day HR = 1.73; 95% CI = 1.02, 2.94), particularly among hCG-detected losses (HR = 2.83; 95% CI = 1.08, 7.39).

CONCLUSIONS: Our findings suggest that any level of caffeine intake during pregnancy may increase risk of pregnancy loss, particularly in the first 8 weeks of gestation. Women attempting to conceive may benefit from eliminating caffeine intake during preconception and early pregnancy.

SUPPORT: This research was supported by the Intramural Research Program of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (National Institutes of Health, Bethesda, MD, USA; contract numbers HHSN267200603423, HHSN267200603424, and HHSN267200603426).

O-65 Monday, October 14, 2019 11:45 AM
LEPTIN IS A MEDIATOR IN THE ASSOCIATION BETWEEN PERCENT BODY FAT AND DECREASED AMH AMONG HEALTHY WOMEN. Jasmine Aly, MD,a Elizabeth A. DeVilbiss, PhD,b Sunni L. Mumford, PhD,b Micah J. Hill, DO, DO,c Alan H. DeCherney, MD,a Laura Zalles, MD,a Neil J. Perkins, PhD,a Robert M. Silver, MD,d Enrique F. Schisterman, PhD,aProgram in Reproductive Endocrinology and Gynecology, NICHD, NIH, Bethesda, MD; bNational Institute of Child Health and Human Development, Epidemiology Branch, DIPHR, NICHD, NIH, Bethesda, MD; cCooper University Hospital, Department of Obstetrics and Gynecology, Camden, NJ; dUniversity of Utah, Salt Lake City, UT.

OBJECTIVE: While obesity is associated with decreased serum AMH, the mechanism by which this occurs is unknown. Studies have found that increased adipokines produced in the adipose tissue, such as leptin, can directly inhibit ovarian function. A recent study by our group found that increases in leptin were associated with lower serum AMH. Because percent body fat and leptin are closely related there is a need to understand the impact of percent body fat on AMH, and to what extent this relationship is driven by leptin. We hypothesize that increased leptin is associated with decreased AMH and that leptin is a direct mediator of this relationship.

DESIGN: Prospective analysis of 259 women aged 18–44 years from western New York State, followed for up to 2 menstrual cycles.

MATERIALS AND METHODS: Serum AMH and leptin were measured five to eight times per cycle for one (n = 9) or two (n = 250) cycles per participant. Characteristics and mean AMH hormone levels were examined by tertile of average leptin over 2 cycles (First leptin tertile: 4.1-14.2 ng/mL; Second tertile: 14.4-29.8 ng/mL; Third tertile: 29.9-96.8 ng/mL). 248 women participated in a dual energy X-ray absorptiometry (DXA) scan to measure fat and lean mass from which total percent body fat and percent truncal fat were derived. Using the product method, a mediation analysis was performed for percent body fat (exposure), leptin (mediator), and serum AMH (outcome) to determine the extent to which leptin mediates the association between body fat and AMH. Marginal structural models with inverse probability of exposure weights were used to relate body fat to leptin (mediator model) and body fat and leptin to serum AMH at the next visit (outcome model). The mediator model was adjusted for FSH, LH, estrogen, and progesterone, and the outcome model was adjusted for age, smoking status, caloric intake, and physical activity.

RESULTS: Overall, we observed an inverse relationship between percent body fat and serum AMH, such that for each 10% increase in body fat there was a 14% decrease in AMH (95% CI -24.5, -2.1). Mediation analysis results showed that the 14% decrease in AMH was mostly explained by leptin (indirect effect -7.7%, 95% CI -11.6, -3.7), though some of the decrease was also due to other non-leptin mediated pathways (direct effect -5.7%, 95% CI -18, 8.3).

CONCLUSIONS: Among healthy women, higher body fat and serum leptin were both associated with lower AMH concentrations. The inverse relationship between percent body fat and AMH is largely mediated by leptin.

SUPPORT: This research was supported by the Intramural Research Program of the Eunice Kennedy Shriver National Institute of Child Health and Human Development (National Institutes of Health, Bethesda, MD, USA; contract numbers HHSN275200403394C HHSN275201100002I, and Task I HHSN275000001), and the Program in Reproductive and Adult Endocrinology, NICHD, NIH.
OMEGA-3 FATTY ACID SUPPLEMENTATION AND FECUNDABILITY. Jamie Stanhiser, M.D.,* Anne Marie Jukic, Ph.D,* Anne Z. Steiner, MD, MPH “University of North Carolina, Chapel Hill, NC; †National Institute of Environmental Health Sciences, Durham, NC; ‡Duke University Medical Center, Durham, NC.

OBJECTIVE: Omega-3 fatty acids supplementation in animal models have been shown to alter prostaglandin biosynthetic pathways in the ovary and endometrium, and thereby improve folliculogenesis, oocyte maturation, embryo quality, and implantation. However, little is known about the effects of omega-3 supplementation on human fecundity. We sought to determine the association between omega-3 fatty acid supplementation and fecundability, the probability of natural conception in a given menstrual cycle.

DESIGN: Secondary data analysis of Time to Conceive (TTC), a prospective, time to pregnancy cohort study.

MATERIALS AND METHODS: In TTC, women aged 30 – 44 years, trying to conceive < 3 months, with no history of infertility were followed for up to one year of pregnancy attempt using standardized pregnancy testing. While attempting to conceive, women daily recorded intercourse, menstrual cycle events, and vitamin, supplement, and medication intake using the Cerner Multum Drug Database. For this analysis, supplements and vitamins containing omega 3 [for example: docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), prenatal vitamin formulations including omega 3, and fish oil] were identified. The percentage of days in a given menstrual cycle on which a woman took omega-3 supplements was calculated, and, based on the Akaake Information Criterion, a cut-off value of 20% was used to dichotomize omega-3 use in each cycle. A positive urine pregnancy test was used to define conception. A discrete-time Cox proportional hazards model was used to calculate the fecundability ratio, adjusting for age, obesity, history of prior pregnancy, race, and Vitamin D intake in the cycle.

RESULTS: Of 1036 women enrolled in TTC comprising 4,775 cycles, 136 women and 2,265 cycles were missing daily diary data and were excluded. 900 women comprising 2,510 cycles were analyzed: ±3.11 years. Women taking omega-3 supplements were younger, thinner, and more likely to be nulligravid and white compared to women not taking omega-3. After adjusting for age, obesity, previous pregnancy, race, and Vitamin D intake, women taking omega-3 supplements had 1.83 (95% CI 1.42, 2.35) times the probability of conceiving in a given menstrual cycle compared to women not taking omega-3 supplements.

CONCLUSIONS: These data suggest omega-3 supplementation significantly increases the probability of a woman conceiving. Randomized controlled trials are needed to further investigate the benefits from omega-3 supplementation for women trying to conceive naturally.

Reference: N/A.

SUPPORT: N/A.

OVARian STIMULATION
O-67 Monday, October 14, 2019 10:45 AM

A COMPUTERIZED DECISION –SUPPORT SYSTEM FOR DAY TO DAY MANAGEMENT OF OVARian STIMULATION CYCLES DURING IN VITRO FERTILIZATION. Gerard S. Letterie, DO, Andrew MacDonald, MS Seattle Reproductive Medicine, Seattle, WA.

OBJECTIVE: The purpose is to describe a computer algorithm designed for IVF management and to assess accuracy in decision making during ovarian stimulation for IVF when compared to evidence based decisions by the clinical team.

DESIGN: Evaluation study of novel software; comparative; quantitative.

MATERIALS AND METHODS: Data was in the form of IVF cycles. Our data set included estradiol concentrations (pg/ml); ultrasound measurements of follicle diameters in 2 dimensions in mm; cycle day and dose of recombinant FSH during ovarian stimulation for IVF. In a pilot study we evaluated 5 predictive analytics including classification and regression trees, random forests, support vector machines, logistic regression and neural networks. We then developed a hybrid algorithm for automated prediction of 4 decisions critical to management during ovarian stimulation: (1) Stop the cycle (trigger or cancel) or (2) continue and return for follow-up. If decision was to stop, the algorithm added a modifier regarding trigger or cancellation. If the decision was to continue and return, the algorithm identified (3) number of days to follow up and (4) dosage adjustment if needed. Database consisted of 2603 total cycles. (1853 autologous and 750 donor) incorporating 7,376 visits. Seventy percent of the cycles were used for training and validation and 30% for challenge. There were 7,706 data points. We compared DSS performance against evidence based decisions by 12 clinicians. Performance was defined as outcome accuracy or agreement between the clinicians’ decisions and the DSS when challenged using 556 cycles to which the algorithm was naïve (no prior exposure). Algorithms were written in "R" language for stat analysis and data manipulation and converted to C++.

RESULTS: Outcome accuracy of the algorithm, sensitivity and positive predictive value (PPV) for automated prediction are listed in Table 1 for the final trained model on held-out challenge data for the four decisions analyzed.

CONCLUSIONS: We describe a first iteration, predictive analytic algorithm for decision support of 4 key management decisions during ovarian stimulation for IVF. Algorithm performance for the decisions to trigger/cancel, return and days to follow-up was highly accurate and in concordance with clinical decisions. Dose changes (increase or decrease) were relatively infrequent clinical decisions in the database resulting in the lowest outcome accuracy of the algorithm. This algorithm offers the possibility of improved clinical and cost efficiencies for IVF management.

SUPPORT: None.

OMEGA-3 FATTY ACID SUPPLEMENTATION AND FECUNDABILITY. Jamie Stanhiser, M.D.,* Anne Marie Jukic, Ph.D,* Anne Z. Steiner, MD, MPH “University of North Carolina, Chapel Hill, NC; †National Institute of Environmental Health Sciences, Durham, NC; ‡Duke University Medical Center, Durham, NC.

OBJECTIVE: Omega-3 fatty acids supplementation in animal models have been shown to alter prostaglandin biosynthetic pathways in the ovary and endometrium, and thereby improve folliculogenesis, oocyte maturation, embryo quality, and implantation. However, little is known about the effects of omega-3 supplementation on human fecundity. We sought to determine the association between omega-3 fatty acid supplementation and fecundability, the probability of natural conception in a given menstrual cycle.

DESIGN: Secondary data analysis of Time to Conceive (TTC), a prospective, time to pregnancy cohort study.

MATERIALS AND METHODS: In TTC, women aged 30 – 44 years, trying to conceive < 3 months, with no history of infertility were followed for up to one year of pregnancy attempt using standardized pregnancy testing. While attempting to conceive, women daily recorded intercourse, menstrual cycle events, and vitamin, supplement, and medication intake using the Cerner Multum Drug Database. For this analysis, supplements and vitamins containing omega 3 [for example: docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA), prenatal vitamin formulations including omega 3, and fish oil] were identified. The percentage of days in a given menstrual cycle on which a woman took omega-3 supplements was calculated, and, based on the Akaake Information Criterion, a cut-off value of 20% was used to dichotomize omega-3 use in each cycle. A positive urine pregnancy test was used to define conception. A discrete-time Cox proportional hazards model was used to calculate the fecundability ratio, adjusting for age, obesity, history of prior pregnancy, race, and Vitamin D intake in the cycle.

RESULTS: Of 1036 women enrolled in TTC comprising 4,775 cycles, 136 women and 2,265 cycles were missing daily diary data and were excluded. 900 women comprising 2,510 cycles were analyzed: ±3.11 years. Women taking omega-3 supplements were younger, thinner, and more likely to be nulligravid and white compared to women not taking omega-3. After adjusting for age, obesity, previous pregnancy, race, and Vitamin D intake, women taking omega-3 supplements had 1.83 (95% CI 1.42, 2.35) times the probability of conceiving in a given menstrual cycle compared to women not taking omega-3 supplements.

CONCLUSIONS: These data suggest omega-3 supplementation significantly increases the probability of a woman conceiving. Randomized controlled trials are needed to further investigate the benefits from omega-3 supplementation for women trying to conceive naturally.

Reference: N/A.

SUPPORT: N/A.

O-68 Monday, October 14, 2019 11:00 AM

DUAL TRIGGERING OF FINAL OOCYTE MATURATION IN POOR OVARIAN RESPONDERS: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL. Dalia Khalife, M.D., Johnny Awwad, M.D., HCLD, Suleiman Ghuain, M.D., Antoine Abu-Musa, M.D., Christine Beyrouthy, M.P.H., Ghana Said Ghazeeri, M.D. American University of Beirut Medical Center, Beirut, Lebanon.

OBJECTIVE: Women with POR (Bologna criteria) manifest a very low follicular response to controlled ovarian stimulation irrespective of the stimulation protocol utilized. Dual triggering of oocyte maturation was shown to improve follicle collection yield and oocyte maturation in women with predicted normal ovarian response. These benefits have been attributed to the GnRHa-induced FSH surge believed to promote oocyte nuclear maturation and cumulus expansion. The aim of the study is to show whether the co-administration of a GnRH agonist and hCG for final oocyte maturation improve oocyte collection and maturation rates in women with poor ovarian response (POR) compared with hCG alone.

DESIGN: This is an ongoing, prospective randomized controlled trial seeking to randomize 140 women with POR undergoing IVF/FICSI treatment into receiving a dual trigger for final oocyte maturation compared with conventional hCG, between May 2018 and December 2019.

MATERIALS AND METHODS: Women with POR (Bologna criteria) were randomized to receive either a combination of 0.3 mg Triptorelin subcutaneously (Decapeptyl; Ipsen Beaufour; Denmark) and 10,000 IU hCG subcutaneously (Choriomon; IPSA Pharmaceuticals; Switzerland) or 10,000 IU hCG alone. Primary outcomes were oocyte collection and maturation rates. Secondary outcomes were clinical and ongoing pregnancy rates. Chi Square analysis was utilized for categorical data and student t test for continuous variables. A p <0.05 was considered for statistical significance.

RESULTS: Sixty-eight patients have been recruited to this point with a cycle cancelation of 7.35% (5/68). A total of 63 patients were randomly allocated to the dual trigger (n=28) and hCG alone (n=35) groups. Baseline demographic and stimulation characteristics were comparable between the two groups. The total number of oocytes (4 vs. 4.2; p=0.65), number of mature oocytes (3.1 vs. 3.2; p=0.81), and number of 2PN zygotes (2.6 vs.
2.2; p = 0.32) were not significantly different between the dual trigger and hCG alone groups. The oocyte collection (62.5% vs. 64.6%; p = 0.75) and oocyte maturation rates (77.5% vs. 76.2%; p = 0.82) were also comparable. Per embryo transfer, the clinical pregnancy rate (15.2 vs. 12.6; p = 0.96) and ongoing pregnancy rate (13.8 vs. 12.6; p = 0.63) showed no statistical differences.

CONCLUSIONS: There was no significant increase in oocyte collection or maturation rates following dual triggering of final oocyte maturation compared with hCG alone in women with POR. POR (Bologna criteria) represents a subgroup of women with a very poor pregnancy prognosis and also a very challenging fertility management. Although the preliminary findings of this trial do not seem to hold promises in favor of an improved outcome with dual triggering of oocyte maturation in this subgroup of women, conclusive evidence are expected only following completion of the recruitment period.

SUPPOR: None.

O-69 Monday, October 14, 2019 11:15 AM
RISK OF HARM ASSOCIATED WITH THE USE OF LETROZOLE AS A FERTILITY DRUG: A SYSTEMATIC REVIEW AND META-ANALYSIS. Jyotsna Pandir, MD,1 Chiara Achilli, MBBS,2 Priya Bhide, MD,3 Luca Sabatini, MD,3 Richard S. Legro, M.D.,4 Luk Rombaarts, PHD,1 Helena Teede, PHD,1 Javier Zamora, PHD,1 Arri Coomarasamy, PHD,3 Shakila Thangaratinam, PHD5 St Bartholomew’s Hospital and Queen Mary University, London, United Kingdom;6 Hewit Fertility Centre, L, Liverpool, United Kingdom; 7Homerton University Hospital NHS Trust foundation, London, United Kingdom; 8St. Bartholomew’s Hospital, London, United Kingdom; 9Penn State Maternal & Child Health Research, Hershey, PA; 10Monash University, Monash, Australia; 11Queen Mary University of London, London, United Kingdom; 12Tommy’s National Centre for Miseria Research, Birmingham, United Kingdom; 13Women’s Health Research Unit, Queen Mary University of London, London, United Kingdom.

OBJECTIVE: We undertook this systematic review and meta-analysis to find out the harm of congenital malformations (major and minor) and pregnancy loss (first and second trimester loss, still birth, intrauterine death and termination of pregnancy) associated with the use of letrozole as a fertility agent.

DESIGN: Systematic review and Meta-analysis.

MATERIALS AND METHODS: Systematic reviews of literature in accordance with the PRISMA HARM; along with a prospective protocol registration in PROSPERO (CRD42017082260) was performed. Literature was searched (1950 to March 2019), combining the Medical Subject Headings and text words for ‘Letrozole’ and ‘pregnancy’ (ovulation, pregnancy) or ‘fetal’ outcome (fetal, neonatal). The quality of studies were assessed using the Cochrane risk of bias tool for randomised controlled studies (RCTs) and Newcastle Ottawa scale for non-randomised comparative cohort studies (CCS). McMaster tool (McHarm) was used to report on the quality of harms assessment and reporting. Meta-analysis was performed to address zero and ongoing pregnancy on pooling of data from 5 RCTs and 4 CCS (pOR 0.76; 95% CI 0.42, 1.36; I² = 18%; p = 0.28); and in pregnancy loss on combining 14 RCTs and 6 CCS (pOR 0.72; 95% CI 0.48, 1.08; F = 0%; p = 0.92); major congenital malformations on pooling of data from 5 RCTs and 4 CCS (pOR 0.76; 95% CI 0.42, 1.36; F = 18%; p = 0.28); and in pregnancy loss on combining 14 RCTs and 6 CCS (pOR 0.72; 95% CI 0.48, 1.08; F = 0%; p = 0.92). Letrozole when combined with natural conception or other ovulation induction such as gonadotrophins or when used as an adjunct in assisted reproductive cycles showed no significant difference in the outcomes of interest. GRADE of evidence showed moderate to high quality of evidence, downgrading the evidence to moderate instead of high quality, mainly due to sparse data secondary to very few events.

CONCLUSIONS: This large systematic review and meta-analysis, with a moderate to high quality of evidence, shows that when compared with clomiphene or other ovulation induction agents Letrozole is not associated with higher risk of congenital malformations or pregnancy loss.

SUPPOR: None.

O-70 Monday, October 14, 2019 11:30 AM
PREMATUR LUTEINIZATION IN THE ERA OF PGTA: EMBRYONIC REPRODUCTIVE POTENTIAL IS NOT AFFECTED BY ELEVATED PROGESTERONE LEVELS DURING OVARIAN HYPERSTIMULATION. Carlos Hernandez-Nieto, MD,1 Joseph A. Lee, BA,1 Elodie Alkon, MD,1 Melinda Klein, MD,2 Alan B. Copperman, MD,3 Benjamin Sandler, M.D.4 Reproductive Medicine Associates of New York. New York, NY; 5Icahn School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: Premature luteinization or early elevation in progesterone (P4) levels is often observed in patients who undergo a GnRH-antagonist protocol for controlled ovarian hyper stimulation (COH). High levels of P4 have been shown to impair endometrial receptivity which might decrease pregnancy rates. A increased level of P4 has been theorized to be a marker for suboptimal embryo quality. This study aimed to evaluate the impact of premature luteinization during COH on rates of blastulation and embryo aneuploidy.

DESIGN: Retrospective cohort analysis.

MATERIALS AND METHODS: The study included patients who underwent IVF stimulation from 2012-2019. Pre-implantation genetic testing for aneuploidy (PGT-A) were performed on blastocysts reaching criteria for TE biopsy, subsequently embryos were vitrified after biopsy. Cohorts were segregated in two groups: Group 1: blastocysts cryopreserved in the presence of normal P4 levels (P4 < 1.5 ng/mL) the day of ovulation trigger; Group 2: blast cells originated from oocytes retrieved after exposure to premature luteinization (P4 ≥ 1.5 ng/mL) on the day of trigger. Demographic COH parameters, blastulation, and euploidy rates were evaluated. IVF outcomes in a subsequent single euploid FET cycle were assessed. T-test, X², and multivariate regressions with GEE models were used for data analysis. A sample size of 260 patients per group was calculated to create an 80% power to detect a difference of 10% on clinical pregnancy rates (CPR) (α = 0.05).

RESULTS: A total of 3,659 patients with normal P4 (20,038 blasts) were compared to 331 patients with elevated P4 (3,327 blasts). Significant differences were found in BMI, AMH levels, Estradiol, and P4 levels on the day of hCG trigger and oocytes retrieved between cohorts. No difference was found in maturity rates (78.7%, 79.4%, p = 0.1), fertilization rates (81.8%, 82.4%, p = 0.2), cryopreserved blastocysts (76.5%, 75.5%, p = 0.2), and aneuploidy rates (35.3%, 35%, p = 0.7). Blastulation rate was higher in Group 1 (71.8%, 60.2%, p < 0.0001). Furthermore, no differences were found in pregnancy (74.4%, 72.5%, p = 0.4), clinical pregnancy (82.9%, 82.9%, p = 0.5), ongoing pregnancy (70.5%, 68.7%, p = 0.3) and clinical loss rates (9.7%, 14.1%, p = 0.5) after an FET. After adjusting for age, BMI, AMH, and number of embryos biopsied per cycle, no association was found between elevated P4 levels and the odds of increased aneuploidy (OR = 0.90, CI95% 0.7-1.03, p = 0.15), blastulation rate (OR = 0.90, CI95% 0.7-1.05, p = 0.18), or number of good quality embryos (≥4BB) (OR = 1.0, CI95% 0.8-1.22, p = 0.92). Also, no association was found with elevated P4 levels and impaired CPR (OR = 0.82, CI95%0.5-1.2, p = 0.31) after adjusting for age, BMI, embryo quality, and endometrial thickness within our model.

CONCLUSIONS: In an era of PGT-A/FET cycles, premature P4 elevation during IVF stimulation does not represent an obstacle to embryo implantation potential. Our study shows that premature luteinization occurring during COH is not associated with a negative effect on embryonic development, increased aneuploidy rates, or impaired IVF outcomes following subsequent FET.

Reference: None.

SUPPOR: None.

O-71 Monday, October 14, 2019 11:45 AM
DETERMINING CORRELATION BETWEEN BODY MASS INDEX AND MINIMUM REQUIRED HCG DOSE WHEN USING DUAL TRIGGER WITH HCG AND GnRH AGONIST. Lilli D. Zimmerman, MD,1 Kolbe Hancock, MD,2 Nirali J. Shah, MD,3 Chelsea Canon, MD, b
OBJECTIVE: The use of dual trigger for final oocyte maturation using GnRH agonists in conjunction with human chorionic gonadotropin (hCG) has been shown to reduce the risk of developing ovarian hyperstimulation syndrome (OHSS), largely by allowing a lower dose of hCG to be used. It has been well established that absorption of hCG varies by body mass index (BMI), yet there have been no studies published correlating BMI with minimum hCG dose requirements to achieve a targeted post-trigger serum hCG (post b-hCG) level. In previous studies, optimal oocyte maturity with controlled ovarian hyperstimulation (COH) was shown to occur at a minimum post b-hCG value of 50 mIU/mL. This study aims to establish minimum hCG dose requirements per unit BMI to achieve specific post b-hCG levels.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All charts between 1/2009 and 3/2019 were reviewed to identify patients who had undergone COH stimulation at our institution and had received a dual trigger (leuprolide acetate 2mg or 4mg and variable doses of hCG from 1,000 to 10,000 units). The total dose of hCG administered was normalized by BMI, and post b-hCG levels were analyzed. Direct correlation analysis was used to analyze the minimum hCG dose required to achieve a specific post b-hCG level based on BMI.

RESULTS: 4744 IVF cycles met inclusion criteria, derived from 3655 women aged 14-49 years old with a BMI range of 15-54 kg/m². The mean BMI of the cohort was 24.4 kg/m². There was a direct correlation between BMI and the dose of hCG per point of BMI that was administered (y = 0.69x + 75.27, R² = 0.56). To achieve a post b-hCG of 50-54 mIU/mL, 84.1 units of hCG per point BMI (BMI x 84.1) are required.

CONCLUSIONS: Our findings suggest that a dual trigger with a sliding hCG scale in accordance with BMI can be utilized with accuracy to predict a specific post b-hCG value. Our current study analyzed only patients who received a dual trigger, as this cohort encompassed a wide range of BMI and hCG doses, allowing for creation of a dosing scale based on BMI. However, as the absorption and physiologic response to hCG is independent of GnRH agonist administration, these results can be extrapolated for use in hCG-only trigger cycles. This dosing protocol for hCG in dual triggers allows the provider to titrate the desired post b-hCG value in order to achieve optimal oocyte maturation while minimizing side effects and risk of OHSS. This is also applicable for those patients who are not candidates for a pure GnRH agonist trigger and are at risk of OHSS with traditional higher-dose hCG trigger.


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SUPPORT: None.

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**O-72 Monday, October 14, 2019 12:00 PM**

**EFFECT OF DEHYDROEPANDROSTEROONE (DHEA) SUPPLEMENTATION ON INTRACYTOPLASMIC SPERM INJECTION OUTCOME IN INFERTILE WOMEN WITH ANTICIPATED NORMO-OVARIAN RESPONSE.** Mustafa Khodry, MD, HA Hazem Ahmed, MD, AB El-Elaser Ali, MD, SA Sayed Taha, MD, MA Mohammed Fawzy, MD, AM Ahmed M. Abbas, MD. Department of Obstetrics & Gynecology, Faculty of Medicine, South Valley University, Qena, Egypt; Ibn-Sina and Banon IVF Centers, Sohag, Egypt; Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt.

**OBJECTIVE:** To study the effect of dehydroepiandrosterone (DHEA) supplementation in infertile women with expected normal ovarian response before intracytoplasmic sperm injection (ICSI) procedure.

**DESIGN:** Randomized, double-blind, placebo-controlled study.

**MATERIALS AND METHODS:** All women attended the ART unit for first planned fresh embryo transfer ICSI cycles with expected normo-ovarian response were invited to participate in the study. Women were randomized in a 1:1 ratio to either group I (DHEA group) received two capsules of DHEA 25 mg (DHEA组, MRM Co., USA) or group II (placebo group) received two placebo capsules has the same shape, color and consistency starting eight weeks before the date of controlled ovarian hyperstimulation (COH) and continued throughout the whole stimulation period till the hCG triggering day. The primary outcome of the study was the mean antral follicle count (AFC) after eight weeks of treatment. The secondary outcomes included the duration of gonadotrophins stimulation in days, the dose of gonadotropins, the number and quality of retrieved oocytes, the endometrial thickness at hCG triggering day, the fertilization rate, implantation rate, clinical pregnancy rate (CPR) and the adverse effects of the medications.

**RESULTS:** We randomly assigned 108 women into both groups (54 in each arm). No significant difference between both groups regarding the baseline demographic characteristics or serum AMH levels. The mean basal AFC after eight weeks of DHEA supplementation was (10.2±4.4 vs. 13.8±5.3, respectively, p<0.001), while no significant difference in the placebo group (10.4±4.5 vs. 10.7±4.6, respectively, p=0.24). No significant different in the total gonadotropins doses in both groups (p=0.64). DHEA group had statistically significant higher total number of retrieved oocytes (15.3±6.20 vs. 12.9±5.70, p=0.001), and the percentage of good quality oocytes (70.6% vs. 52.3%, p=0.007). No difference between both groups regarding the fertilization rate (62.4% vs. 51.7%, p=0.13), implantation rate (23.1% vs 20.4%, p=0.27), and the clinical pregnancy rate (37.0% vs. 35.2%, p=0.41). Regarding adverse effects, no patients reported major adverse effects during the study period. Only two patients from the DHEA group complained of hot flushes after four weeks of the supplement not interfering with their daily activities.

**CONCLUSIONS:** The use of DHEA in anticipated normal responders eight weeks before ICSI could be valuable in increasing the AFC, the number and quality of the retrieved oocytes relative to placebo, however no improvement in the fertilization, implantation, and clinical pregnancy rates.

**SUPPORT:** None.

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**O-73 Monday, October 14, 2019 10:45 AM**

**PREIMPLANTATION GENETIC TESTING**

**PGT FOR ANEUPLOIDY IMPROVES PERINATAL OUTCOMES COMPARED WITH FET ALONE: AN ANALYSIS OF THE 2014 AND 2015 SART DATA.** Kristin Van Heertum, MD,a Channing Burks, MD,a Kerry S. Flannagan, PhD,b Sunni L. Mumford, PhD,c Alexandra C. Purdue-Smith, PhD,b

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**e30 ASRM Abstracts**

Vol. 112, No. 3, Supplement, September 2019
OBJECTIVE: Clinical studies have shown a difference in the incidence of preterm delivery (PTD) and low birthweight (LBW) following IVF compared with natural conception. In recent years, frozen embryo transfer (FET) and pre-implantation genetic testing (PGT) have become increasingly common. However, few studies have evaluated the effects of embryo biopsy itself on perinatal outcomes. This study aims to assess the differences in perinatal outcomes of autologous FET using embryos that underwent biopsy for PGT versus those that did not.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The Society for Assisted Reproductive Technology (SART) database was used to identify day 5 FET cycles that did and did not undergo PGT from 2014-2015. Log binomial regression models were used to assess associations between embryo biopsy and pregnancy/perinatal outcomes. A sub-analysis analyzed the effects of PGT for aneuploidy (PGT-A) or PGT for monogenic disorders (PGT-M) on perinatal outcomes versus no biopsy. Models were adjusted for covariates including maternal age, race, BMI, smoking, prior IVF cycles, prior preterm/full-term births and cause of infertility. LBW was the primary outcome.

RESULTS: The mean age of the no biopsy patients (N=15,870) and biopsy group (N=10,367) was 33.9 and 35.6 years, respectively (P<0.01). The mean number of embryos transferred was 1.6 and 1.2 (P<0.01) for non-biopsy and biopsy, respectively. Compared to patients whose embryos were not biopsied, patients whose embryos were biopsied were significantly more likely to have a clinical pregnancy (64.9 vs. 57.7%, adjusted risk ratio (aRR) 1.16, 95% confidence interval (CI) 1.13,1.19) and live birth (56.2 vs. 46.8%, aRR 1.25, 95% CI 1.21, 1.3). The incidence of multiple gestation was, unsurprisingly, higher in the non-biopsy group (21.4 vs. 12.6%, aRR 0.68, 95% CI 0.60, 0.77). Of the live births (N=18,457 no biopsy, N=5,815 biopsy), the incidence of LBW was significantly lower following transfer of biopsied embryos versus those that were not biopsied (16.5 vs. 23.8%, aRR 0.74, 95% CI 0.66, 0.83). The odds of PTD was also significantly lower in the biopsy group compared to the non-biopsy group (16.0 vs. 21.5%, aRR 0.79, 95% CI 0.71, 0.88). These differences persisted when comparing PGT-A only versus no biopsy (LBW aRR 0.73, 95% CI 0.65, 0.83; PTD aRR 0.79, 95% CI 0.71, 0.89), but not PGT-M versus no biopsy (LBW aRR 1.08, 95% CI 0.73, 1.58; PTD aRR 0.93, 95% CI 0.63, 1.38).

CONCLUSIONS: The higher incidence of PTD and LBW in the non-biopsy group compared with the biopsy group can likely be, at least in part, explained by the larger proportion of multiple gestation pregnancies seen in that group. PGT-A, by reducing the number of embryos transferred, also incurs improved perinatal outcomes. Further analysis will assess for the contribution of multiple gestations to the differences in perinatal outcomes. However, it is overall reassuring that embryo biopsy is not associated with any negative effects on perinatal outcomes in FETs, and may potentially be associated with improved outcomes.

SUPPORT: None.

O-74 Monday, October 14, 2019 11:00 AM

DOES PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) HARM EMBRYOS? NO—A MULTI-CENTER, PROSPECTIVE, BLINDED, NON-SELECTION STUDY EVALUATING THE PREDICTIVE VALUE OF AN ANEUPLOID DIAGNOSIS AND IMPACT OF BIOPSY.

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OBJECTIVE: Two common concerns regarding PGT-A are: 1) trophectoderm (TE) biopsy may have an adverse effect on embryo reproductive potential, and 2) embryos labeled aneuploid may have the potential to implant and deliver and thus may be wrongly discarded. This study addresses these concerns by 1) comparing implantation rates of the overall study group to a control group, in which biopsy/PGT-A were not utilized, and 2) directly measuring the predictive value (PV) of a diagnosis of embryonic aneuploidy.

RESULTS: The mean age of the no biopsy patients (N=10,367) was 33.9 vs. 35.6 years, respectively (P<0.01). The mean number of embryos transferred was 1.6 and 1.2 (P<0.01) for non-biopsy and biopsy, respectively. Compared to patients whose embryos were not biopsied, patients whose embryos were biopsied were significantly more likely to have a clinical pregnancy (64.9 vs. 57.7%, adjusted risk ratio (aRR) 1.16, 95% confidence interval (CI) 1.13,1.19) and live birth (56.2 vs. 46.8%, aRR 1.25, 95% CI 1.21, 1.3). The incidence of multiple gestation was, unsurprisingly, higher in the non-biopsy group (21.4 vs. 12.6%, aRR 0.68, 95% CI 0.60, 0.77). Of the live births (N=18,457 no biopsy, N=5,815 biopsy), the incidence of LBW was significantly lower following transfer of biopsied embryos versus those that were not biopsied (16.5 vs. 23.8%, aRR 0.74, 95% CI 0.66, 0.83). The odds of PTD was also significantly lower in the biopsy group compared to the non-biopsy group (16.0 vs. 21.5%, aRR 0.79, 95% CI 0.71, 0.88). These differences persisted when comparing PGT-A only versus no biopsy (LBW aRR 0.73, 95% CI 0.65, 0.83; PTD aRR 0.79, 95% CI 0.71, 0.89), but not PGT-M versus no biopsy (LBW aRR 1.08, 95% CI 0.73, 1.58; PTD aRR 0.93, 95% CI 0.63, 1.38).

CONCLUSIONS: The higher incidence of PTD and LBW in the non-biopsy group compared with the biopsy group can likely be, at least in part, explained by the larger proportion of multiple gestation pregnancies seen in that group. PGT-A, by reducing the number of embryos transferred, also incurs improved perinatal outcomes. Further analysis will assess for the contribution of multiple gestations to the differences in perinatal outcomes. However, it is overall reassuring that embryo biopsy is not associated with any negative effects on perinatal outcomes in FETs, and may potentially be associated with improved outcomes.

SUPPORT: None.

O-75 Monday, October 14, 2019 11:15 AM

PREIMPLANTATION GENETIC TESTING (PGT) IS ASSOCIATED WITH HIGHER ODDS OF A HEALTHY LIVEBIRTH AMONG DONOR OOCYTE RECIPIENTS IN THE UNITED STATES: A 2013-2015 NATIONAL STUDY.

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OBJECTIVE: Available evidence suggests that PGT is associated with lower odds of live birth among donor oocyte cycles in the US through 2013. However, outcomes reflective of more current practice are lacking. DESIGN: Retrospective cohort of the Society for Assisted Reproductive Technology Database-Clinic Outcomes Reporting System from 2013 to 2015. MATERIALS AND METHODS: Fresh donor oocyte cycles that resulted in embryo transfer (ET) were queried. Thawed oocytes were excluded. The primary outcome was a "good obstetric outcome (GBO)," defined as singleton live birth at ≥37 weeks with birth weight ≥ 2,500g and <
O-76 Monday, October 14, 2019 11:30 AM

PREGNANCY OUTCOMES FOLLOWING IN VITRO FERTILIZATION FROZEN EMBRYO TRANSFER (IVF-FET) WITH OR WITHOUT PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) IN WOMEN WITH RECURRENT PREGNANCY LOSS (RPL): A SART-CORS STUDY. Swetha Bhatt, MD, Jason Roy, PhD, Sara S. Morelli, MD, PhD, Peter Mcgovern, MD, Rutgers New Jersey Medical School, Newark, NJ; Rutgers - Department of Biostatistics and Epidemiology, Piscataway, NJ; University Reproductive Associates, NJ.

OBJECTIVE: Euploid embryo transfer is thought to optimize outcomes in some couples with infertility, but there is insufficient evidence supporting this approach to management of recurrent pregnancy loss; thus, the aim of this study was to assess the pregnancy outcomes in couples with RPL after use of IVF-FET with PGT-A compared to IVF-FET without PGT-A.

DESIGN: Retrospective cohort study.

RESULTS: Of 25,387 included cycles, 2,372 had PGT performed while 23,015 did not. PGT was associated with increased rates of frozen ET (70% vs 41%; P<0.001), singleton ET (67% vs 44%, P<0.001) and blast transfer (87% vs 65%, P<0.003). Interaction effect between transfer type and PGT was not significant, so the model was fit without an interaction term. Unadjusted rates of live birth and ongoing pregnancy were similar. After adjustment, cycles using PGT significantly increased the probability of a GBO (26.2% vs 23.7%, 1.08 risk ratio (RR), 95% confidence interval (CI) 1.00-1.12, P=0.047). PGT was also associated with an 8% increase in probability of a live birth (95% CI 1.03-1.12), 7% increased probability of a term birth (95% CI 1.01-1.14) and 8% increased probability of a singleton (95% CI 1.03-1.14). When only the first cycle was tested (n=18,417), there was a significant interaction between PGT and transfer type with superior outcomes for PGT in frozen ETs but no effect in fresh ETs (Table).

CONCLUSIONS: PGT, as practiced during the most recently available natural cycles in women using donor oocytes, is associated with improved probability of a healthy live birth.


MATERIALS AND METHODS: This study included data collected by the Society of Assisted Reproductive Technologies Clinical Outcomes Reporting System (SART-CORS) for IVF-FET cycles between years 2010 through 2016. The experimental group included couples with RPL (strictly defined as a history of 3 or more pregnancy losses) undergoing IVF-FET with or without PGT-A. The analysis was restricted to autologous frozen embryo transfer cycles to better compare outcomes with and without PGT-A.

The primary outcome was live birth rate. Secondary outcomes included clinical pregnancy rate and spontaneous abortion rate. Differences were analyzed using generalized estimating equations (GEE) logistic regression models. GEE were used to account for multiple cycles per patient. Covariates included in the model were age, geographic region, race/ethnicity, and indication for assisted reproductive technologies. Analyses were stratified for age less than 35 years versus older than 35 years.

RESULTS: Of 24,007 IVF-FET cycles from the PGT-A group and 43,811 cycles from the control group were included in the analysis (Table 1). The adjusted odds ratio (OR) comparing IVF-FET with PGT-A versus without PGT-A for live birth outcome was 1.30 (95% CI: 1.24, 1.37) for age <35 and 2.01 (95% CI: 1.92, 2.11) for age ≥35. For clinical pregnancy, the OR was 1.26 (1.20, 1.33) for age <35 and 1.82 (1.74, 1.91) for age ≥35. Finally, for spontaneous abortion, the OR was 0.90 (0.82, 0.98) for age <35 and 0.79 (0.73, 0.86) for age ≥35.

CONCLUSIONS: This is the largest study to date assessing the utility of PGT-A in women with RPL. PGT-A was associated with improvement in live birth, clinical pregnancy, and spontaneous abortion rates in women with RPL, with a larger difference noted in women with age greater than 35 years. Couples with RPL warrant counseling on all management options to reduce subsequent miscarriage, which may include IVF with PGT-A for euploid embryo selection.

Reference: N/A.

SUPPORT: None.
OBJECTIVE: NGS provides an unprecedented high-throughput, highly parallel, and base pair resolution data for genetic analysis. In this study, we developed a targeted NGS methodology for simultaneous pre-implantation genetic testing for monogenic/single gene disorders (PGT-M) and aneuploidy (PGT-A) from a single TE biopsy in a single procedure without the need of WGA.

DESIGN: Experimental Study

MATERIALS AND METHODS: Patients whose TE biopsies underwent PGT-M with clinical validated Taqman genotyping were included. Sequencing primers were designed for 11 different variants, including single nucleotide alterations, deletions, and insertions, and then validated on parental genomic DNA. Abnormal embryos donated for research were thawed, re-biopsied, and lysed. Two re-biopsies from each embryo were pre-amplified with a multiplex primer pool for PGT-M and PGT-A, using a two-step PCR strategy to incorporate sequencing library adapters and indexes. Sequencing was performed on Illumina NextSeq 550 using single 150bp reads. The average read depth was approximately 700X. Reads were aligned to a human reference genome (GRCh37/hg19) with the Burrows-Wheeler Aligner (BWA). The variants were called using Samtools for the PGT-M. Karyotypes were analyzed using an in-house clinical validated bioinformatics workflow. Taqman genotyping was performed on the amplified re-biopsies to further confirm the SGD results.

RESULTS: Two TE biopsies of 13 embryos from 7 families, including 9 variants (CFTR c.350G>A, CFTR c.1521_1522delCTT, HEXA c.1421+1G>C, HEXA c.1274_1277dupTATC, PAX6 c.76C>G, TBX5 c.342C>G, PHX c.1180C>T, HMGCL c.122G>A, HMGCL c.497+4A>G), showed 100% concordant PGT-M diagnoses when compared to previous PGT-M based on Taqman qPCR genotyping. The PGT-A from multiple biopsies of the same embryos also demonstrated consistent karyotypes. For one variant, MKS1 c.1411dupG, Taqman genotyping assay design was not possible due to the presence of a string of Gs at the mutation site. The targeted NGS provided accurate genotypes for parental DNA and 5 lymphocyte samples. Another X chromosome-linked nonsense mutation (PCDH19 c.595 G>T) was validated on genomic DNA and 5 fibroblast samples.

CONCLUSIONS: This study provides proof of principle that PGT-M and PGT-A can be reliably and consistently performed simultaneously from the same TE biopsy in only one procedure without additional genotyping assays. For one variant, MKS1 c.1411dupG, Taqman genotyping assay design was not possible due to the presence of a string of Gs at the mutation site. The targeted NGS provided accurate genotypes for parental DNA and 5 lymphocyte samples. Another X chromosome-linked nonsense mutation (PCDH19 c.595 G>T) was validated on genomic DNA and 5 fibroblast samples.

MATERIALS AND METHODS: We collected clinical outcome data (implantation, ongoing pregnancy, birth) for transferred embryos classified as ‘mosaic’ by Preimplantation Genetic Testing (PGT). The following characteristics of mosaicism were considered: general mosaicism versus control (euploidy), type of aneuploidy involved in the mosaicism, level of mosaicism (using 40% or 50% as cutoffs), mosaic monosomies versus trisomies, and age. Chi-squared or Fisher’s test was used to compare groups and evaluate statistical significance.

RESULTS: In the adjoining table we present our results from 372 mosaic embryo transfers, with more data presently being collected. This current analysis (powered to 100%) demonstrates that mosaic embryo transfers can result in pregnancies and births, albeit with decreased success rates compared to euploid embryos. Importantly, complex mosaics involving more than two chromosomes should be deprioritized, and higher levels of mosaicism correlate with poor clinical outcome.

CONCLUSIONS: This is the largest analysis of mosaic embryo transfers to date, and represents a valuable reference to generate guidelines on mosaic embryo selection and prioritization in the clinic.

SUPPORT: Zouves Foundation for Reproductive Medicine.

REPRODUCTIVE BIOLOGY: HUMAN STUDIES

O-79 Monday, October 14, 2019 10:45 AM

THE RELATIONSHIP BETWEEN CHRONOLOGIC AGE, OVARIAN RESPONSE, AND DNA METHYLATION OF WHITE BLOOD CELLS AND CUMULUS CELLS AMONG INFERTILE WOMEN UNDERGOING IVF. Brent M. Hanson, MD,a Xin Tao, Ph.D,b Yiping Zhan, Ph.D,c Timothy G. Jenkins, PhD,d Julia G. Kim, MD, MPH,a Emily K. Osman, MD,a Ashley W. Tieg,a Shelby A. Neal, MD,a Richard Thomas Scott, Jr., MD,a Emre Seli, M.D.a IVI-RMA New Jersey, Basking Ridge, NJ; The Foundation for Embryonic Competence, Basking Ridge, NJ; Overture Life, Madrid, Spain.

OBJECTIVE: Aging is associated with predictable changes in DNA methylation in human somatic cells. An epigenetic clock model has been designed to quantify age. Associations with male and female reproductive function have been identified. The relationship between chronologic age, ovarian response, and DNA methylation of white blood cells and cumulus cells among infertility women undergoing IVF are explored in this study.

MATERIALS AND METHODS: A retrospective chart review of all cycles from 2015 to 2017 was completed. Ovarian response was defined as the number of oocytes retrieved. DNA methylation was measured in white blood cells and cumulus cells from women undergoing IVF. DNA methylation was measured using bisulfite sequencing in white blood cells and methylation sensitive restriction enzyme digestion in cumulus cells.

RESULTS: A total of 769 cycles were included in the analysis. DNA methylation was negatively correlated with age in white blood cells (P=0.044) but not in cumulus cells (P=0.53). DNA methylation was positively correlated with the number of oocytes retrieved in white blood cells (P=0.002) and cumulus cells (P=0.04).

CONCLUSIONS: DNA methylation is negatively correlated with age in white blood cells but not in cumulus cells. DNA methylation is positively correlated with the number of oocytes retrieved in white blood cells and cumulus cells. These findings suggest that DNA methylation may be a potential biomarker for ovarian reserve.

*OP/B = Ongoing Pregnancy/Birth.
*These statistically significant findings stem from an analysis that is >80% powered.

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e33
described by Horvath based on the methylation status of 353 CpG sites on human DNA (1). This model has been shown to accurately predict the chronologic age of individuals. The current study sought to determine whether the age predicted using the Horvath algorithm in white blood cells (WBC) and cumulus cells (CC) is associated with the true age of patients and their response to ovarian stimulation.

**DESIGN:** Prospective cohort study.

**MATERIALS AND METHODS:** Patients undergoing in vitro fertilization (IVF) between July 2017 and December 2018 were recruited under Institutional Review Board approval. On the day of oocyte retrieval, samples of peripheral blood and CC were collected from enrolled patients, and genomic DNA was isolated and stored at -80°C. DNA from WBC was analyzed using the QIAymphony kit (Qiagen, Redwood City, CA, USA). DNA from CC was purified using DNeasy blood and tissue kit (Qiagen, Redwood City, CA, USA). Bisulfit conversion was performed using the Zymo EZ DNA methylation kit (Zymo Research, Irvine, CA, USA). The Illumina 850K DNA methylation EPIC array (San Diego, CA, USA) was then utilized to measure DNA methylation levels. Likelihood ratio tests based on nested linear models were utilized to assess the relationship between predicted age and true age.

**RESULTS:** Methylation data was analyzed for a total of 175 women undergoing IVF (mean age 35.26 ± 4.14 years). The Horvath-predicted age calculation for WBC samples was consistent with the true chronologic age of patients (p=0.0001). However, the predicted age from CC was significantly younger than patients’ chronologic age. The mean predicted age of patients using methylation-based calculations from CC was 8.56 ± 2.07 years. Poor response to ovarian stimulation during IVF, defined as five or fewer oocytes obtained during oocyte retrieval, did not affect the Horvath-predicted age based on calculations from WBC (p=0.131) or CC (p=0.502).

**CONCLUSIONS:** In women undergoing IVF, the epigenetic algorithm described previously by Horvath accurately predicts age when applied to WBC but not to CC. The methylation-based predicted age obtained from analysis of CC is substantially younger than the true age of patients, suggesting that CC exhibit unique methylation patterns that are distinct from those demonstrated by WBC. A poor response to ovarian stimulation is not associated with predictable changes in CpG methylation sites consistent with aging within WBC or CC. CC may have their own distinct methylation pattern which changes with age and must be clearly delineated since this may have implications for reproductive lifespan. Further studies are also required to determine whether alternative CpG sites can accurately predict chronologic age or response to stimulation from CC samples.


**SUPPORT:** None.

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**O-80 Monday, October 14, 2019 11:00 AM**

THE INCLUSION OF BLASTOMERES INTO THE INNER CELL MASS IN EARLY-STAGE HUMAN EMBRYOS DEPENDS ON THE SEQUENCE OF CELL CLEAVAGES DURING THE FOURTH DIVISION.

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**OBJECTIVE:** In mouse embryos, the fate of the inner cell mass (ICM) is known to be determined during divisions that occur from 8-16 cells. The outer cells give rise mainly to trophoderm (TE). In contrast, cells positioned inside the embryo give rise to ICM. However, there is no information on the order of incorporation of blastomeres into the ICM in human embryos. Blastomeres (RBs) are some of the dysmorphic phenotypes that are frequently observed in human oocytes. RBs remain present, and almost unchanged in size, at least until embryos reach the blastocyst stage. Thus, our aim was to examine such early developmental stages using time-lapse recorded data, taking advantage of the large RBs within blastomeres as cellular markers.

**DESIGN:** Time series study.

**MATERIALS AND METHODS:** A total of 201 large refractile bodies in fertilized oocytes progressing through normal 2-cell to 8-cell stages were traced until they developed into a blastocyst. Cluster analysis was conducted to group the blastomeres according to the timing of cell division. Simple and multiple logistic regression analysis were both used to estimate the order in which the cells divided from the second to the fourth division, with the attainment of ICM defined as the endpoint.

**RESULTS:** Following the second division, from 2 cells to 4 cells, the rates of RBs that were distributed to the ICM of blastomeres which cleaved first and second were 20.0% (20/100) and 18.8% (19/101) respectively. During the third division from 4 cells to 8 cells, the rates of RBs that were distributed to the ICM of blastomeres which cleaved first to fourth were 24.1% (13/54), 28.1% (16/57), 10.3% (4/39) and 11.8% (6/51) respectively. During the fourth division from 8 cells to 16 cells, the rates of RBs that were distributed to the ICM of blastomeres which cleaved first to eighth were 35.1% (13/37), 30.8% (9/29), 26.9% (7/26), 30.4% (7/23), 5.3% (1/19), 4.8% (1/21), 0.0% (0/24) respectively. Cluster analysis showed that blastomeres which cleaved earlier tended to reach the ICM and there was a distinct difference between the rates of the second to the fourth divisions. Furthermore, the first 50% of cleaved blastomeres during the fourth division had significantly higher rates of being incorporated in the ICM (p<0.001). Simple logistic regression analysis was used to estimate the order in which the cells cleaved during both the third and fourth division before being included in the ICM, whereas multiple logistic regression analysis was only applied to the fourth cleavage. The third division was thereby removed as a confounding factor and the fourth division was found to be a predictor for ICM (OR:16, CI:4.1-63, p<0.001).

**CONCLUSIONS:** This study found that the cellular composition of the ICM is largely determined at the time of the fourth division. Moreover, it was shown that blastomeres which cleave first to fourth, during the fourth division from 8 cells to 16 cells, gain the ability to be incorporated in the ICM.

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**O-81 Monday, October 14, 2019 11:15 AM**

THE EFFECT OF AGE ON BIOENERGETICS OF HUMAN GRANULOSA CELLS.

Gustavo N. Cecchino, MD a Alberto Pacheco, PhD b Juan A. Garcia-Velasco, PhD b Eduardo Rial, PhD b TIVRMA-Madrid, Madrid, Spain; bIVI Madrid, Madrid, Spain; aAffiliation not provided; bCentro de Investigaciones Biológicas - CSIC, Madrid, Spain.

**OBJECTIVE:** Granulosa cells (GCs) support the synchronization of follicle development along with oocyte growth and maturation, being a potential biomarker of oocyte quality and in-vitro fertilization (IVF) outcomes. However, little is known about GC bioenergetics and its impact on female fertility. We aimed to characterize the bioenergetic profile of human GCs and detect the potential impact of aging on the energy metabolism.

**DESIGN:** Observational prospective cohort study.

**MATERIALS AND METHODS:** From December 2017 to December 2018, the bioenergetic properties of GCs from 53 egg donors aged <35 years and 40 infertile patients ≥38 years were determined. Antagonist protocol was used to carry out controlled ovarian stimulation in all cases and women with diseases that could potentially impair mitochondrial function were excluded. Purified GCs from fresh samples of follicular fluid were seeded in Seahorse XF 24-well microplates. Primary culture was performed for 24 h and followed by a real-time assessment of the oxygen consumption rate (OCR) and the extracellular acidification rate (ECAR) as a proxy for lactate acid. Statistical analysis was performed using SPSS v24 (SPSS Inc., Chicago, IL, USA) and variables were compared using the ANOVA test, as appropriated.

**RESULTS:** GCs from oocyte donors aged <35 years showed a higher basal mitochondrial OCR compared to infertile women ≥38 years (12.8 ± 1.6 pmol O2/min/mg vs. 11.2 ± 1.6; p=0.046). Such difference is unlikely to be a result of reduced mitochondrial mass, once the maximum respiratory capacity remained unchanged (24.5 ± 3.3 pmol O2/min/mg vs. 22.4 ± 4.3; p=0.226). Thus, the difference in the basal mitochondrial respiration was due to a combined decrease in ATP turnover and the rate of proton leakage. Granulosa cells displayed a very high rate of glycolysis as estimated by the ECAR measurements. However, GCs from older patients showed a substantially lower rate of lactate formation (12.9 ± 1.3 mph/min/mg vs. 10.9 ± 0.5; p=0.009). Moreover, GCs from younger patients presented higher ATP/ADP...
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REPEATED IMPLANTATION FAILURE PATIENTS DIS- PLAY A GREATER DELAY OF THEIR RECEPTIVITY WINDOW DIAGNOSED USING A GENOMIC TEST UN- DER HRT TREATMENT COMPARSED TO NATURAL CYCLES.

Delphine Haouzi, PhD,a Frida Entezami, MD,b Charlene Innocenti, Engineer,c Alice Ferrières-Hsa, MD,c Chloë Baron, PhD, student,c Claire Vincens, MD,c Sophie Bringer-Deutsch, MD,c Cecile Brunet, MD,a Antoine Torre, MD, PhD,d Samir Hamamah, MD, PhD*d Inserm U1203, CHU Montpellier, St-Eloi Hospital, Montpellier, France; cAmerican Hospital of Paris, Neuilly-sur-Seine, France; aART-PGD department, Arnaud de Villeneuve Hospital, CHU Montpellier, Montpellier, France; bDivision of Child Health, Obstetrics & Gynaecology department, University of Nottingham, Nottingham, United Kingdom; aArnaud de Villeneuve Hospital, CHU Montpellier, Montpellier, France.

OBJECTIVE: To identify the receptive window in patients with repeated implantation failure prepared for frozen embryo transfer under hormone replacement therapy (HRT) treatment or natural cycle.

DESIGN: Endometrial biopsies were performed during the implantation window 7-9 days after the LH surge in natural cycle or 5-9 days after progesterone administration under HRT respectively. According to genomic testing result, the transfer strategy was: blastocysts transferred at the specific day where endometrium is identified as ‘receptive’; D2/D3 cleavage stage embryos transferred 72/48 hours before the specific cycle day where endometrium is identified as receptive.

MATERIALS AND METHODS: 141 RIF patients with several unsuccessful fresh and/or frozen embryo transfers (FET) were included. The number of previous failed attempts and non-implanted embryos were 4.5±2.1 and 6.6±4 respectively. Genomic testing of endometrial biopsies was performed under natural cycle or HRT. RNAs from biopsies were extracted and mRNA expression levels of specific genes predictive of endometrial receptivity were established using RT-qPCR. Clinical pregnancy was defined by visualization of a gestational sac with a positive fetal heartbeat.

RESULTS: Analyses of endometrial receptivity status in 141 RIF patients (age 37.9±3.8 years) revealed a strong inter-patient variability in the occurrence of the receptive window with mostly a delay between 1 to 3 days. More precisely, biopsies were evaluated under natural cycle (n=29), natural cycle with recombinant human chorionic gonadotropin (hCG, Ovitrelle) (n=7) HRT (n=68) and HRT with GnRH analogue (n=37). In patients evaluated under natural cycle, the majority were receptive at LH+8 (52%). The remaining 48% displayed receptivity equally at LH+6/+7 (24%) and LH+4+9 (24%). Under natural cycle with recombinant hCG, 72 % of RIF patients were receptive at hCG+9 while 14% were at hCG+6/+7 and 14 % at hCG+8. In patients under HRT, 38% and 41% were receptive at Pг+7 and Pг+8, respectively, whereas the remaining 21% were receptive at Pг+4 (21%) or after Pг+9 for 3% of RIF patients. Under HRT with GnRH analogue, the majority of RIF patients were receptive at Pг+8 (67%). Others were receptive at Pг+5/+6 (22%), Pг+7 (5%) and Pг+9 (8%). After personalized embryo transfer using the genomic testing strategy, the clinical pregnancy and live birth rates were 36.2 % and 28.4 % respectively.

CONCLUSIONS: The acquisition of the endometrial receptivity phenotype is more progressive under HRT compared with natural cycle. The majority of RIF patients displayed a delay in occurrence of their receptive window revealing a potential cause for the implantation failure. Personalized embryo transfer according to the specific cycle day where endometrium is said receptive improves both clinical pregnancy and LBR in RIF patients under both HRT and natural cycle.

SUPPORT: This work was partially supported by a grant from the Ferring Pharmaceutical Company.

O-83 Monday, October 14, 2019 11:45 AM

THE ROLE OF VITAMIN D AS A PIECE OF THE UTERINE FACTOR INFERTILITY PUZZLE.

Karine Matevosian, DO,a Lauren Grimm, MA,b Elisabeth Rosen, BS, MA,b Lucas E. Rasnic, BSE, MA,b Jacqueline Sehring, MA,a Jody M. Esquerra, MA,a Anisa Hussain, MA,b Angelene Beltsos, MD,b Roohi Jeeiani, MD,b cAdvocate Lutheran General Hospital, Park Ridge, IL; cViss Fertility Institute, Chicago, IL.

OBJECTIVE: Previous research has proven that there are vitamin D receptors in the endometrial cavity. This study aims to better understand the role of vitamin D on reproductive outcomes and uterine factor infertility. We sought to investigate the impact of vitamin D deficiency on endometrial thickness in patients with an elevated anti-mullerian hormone (AMH) representative of Polycystic Ovary Syndrome (PCOS).

DESIGN: Retrospective chart review at a private multi-location fertility clinic.

MATERIALS AND METHODS: A total of 1065 cycles were identified in patients with an AMH >5 ng/ml between August 2016 to March 2019. All patients underwent timed intercourse or intrauterine insemination. Patients received Letrozole or Clomid therapy and were triggered for ovulation induction following the maturation of 1-3 follicles greater than 18 mm. Patients were divided into two groups: vitamin D < 30 ng/ml in the deficient group, and those with a vitamin D ≥ 30 ng/ml in the sufficient group. The endometrial thickness was compared between the groups. Two sample t-tests and chi-square analysis were used to analyze the data using SPSS 21.0 (SPSS Inc., Chicago, IL, USA).

RESULTS: Baseline characteristic differences between the two groups, including age, race, BMI, and parity were not significant (p>0.05). The majority of RIF patients were in the deficient group (58%) and the deficient group had a thinner endometrial thickness. The mean endometrial thickness in patients with an elevated AMH with vitamin D deficiency and sufficiency was 6.968 mm versus 6.345 mm, respectively (p=0.023). There was a statistically significant negative correlation between vitamin D levels and endometrial thickness. When this data was extrapolated and analyzed in the first phase of the study, pregnancy outcome was compared between the two groups and no difference was noted (p>0.05).

CONCLUSIONS: Vitamin D deficiency is extremely prevalent and affects up to 36% of Americans. It has implications for many aspects of physiology and recent research has explored its effects on reproductive biology. It is hypothesized that decreased vitamin D leads to disruption of estrogen signaling and impaired reproductive outcomes. The endometrium has vitamin D receptors and a deficiency is associated with uterine hypoplasia in animal models. In a human model, vitamin D deficiency may be more prevalent in PCOS patients. Women with PCOS have also been shown to have elevated AMH levels >5 ng/ml. Moreover, previous research in a PCOS model has shown a strong correlation between vitamin D deficiency and uterine factors leading to increased miscarriage risk. Therefore, we sought to explore the connection between AMH, vitamin D and endometrial lining.

Interestingly, our study results were statistically significant and showed that higher levels of vitamin D were correlated with a thinner endometrial lining. Thus, we conclude that though vitamin D plays a role in infertility and the endometrium, it is not a factor in determining endometrial thickness. Future studies are needed to determine how vitamin D interacts with the endometrium in PCOS patients leading to poorer reproductive outcomes and can focus on implantation, receptivity and miscarriage.

SUPPORT: None.

O-84 Monday, October 14, 2019 12:00 PM

DYNAMIC DNA METHYLATION DURING TROPHOBLAST DIFFERENTIATION IN HUMAN PERI-IMPLANTATION STAGE EMBRYOS REVEALED BY SINGLE-CELL WHOLE GENOME BISULFITE SEQUENCING.

Ye Yuan, PhD,a Jiangwen Sun, Ph.D.,b Hao Ming, M.S.c Deirdre M. Logsdon, MS,a William B. Schoolcraft, MD,a Rebecca L. Krisher, PhD,c Zongliang Jiang, Ph.D.c Colorado Center for Reproductive Medicine, Lone Tree, CO; cOld Dominion University, Norfolk, VA; aLouisiana State University, Baton Rouge, LA.

OBJECTIVE: Trophoblast cells play an essential role in the interactions between the fetus and mother. Multipotent trophoblast cells undergo dynamic morphological migration and differentiation around the time of implantation to generate functional placenta, and their coordinated proliferation and differentiation are dependent upon the dynamic expression of a series of genes which are regulated in large part by epigenetic mechanisms. The aim of the
A survey of microsurgery training among urology residency programs.

Thomas A. Masterson, III, MD,a Quinn Carroll Rainer, BS,b Sirpi Nackeeran, BA,c Ranjith Ramasamy, M.D.a

OBJECTIVE: The Accreditation council of graduate medical education (ACGME) establishes surgical minimum numbers of cases for urologic training. Currently there is not a requirement for microsurgery, likely from a belief that residents do not have enough exposure. In an effort to evaluate the availability of microsurgery training among urology residency programs we conducted a survey of the programs. We compared microsurgery to male reconstructive infertility surgery.

DESIGN: Cross sectional survey.

MATERIALS AND METHODS: We obtained a list of the 138 ACGME-accredited urology residencies and contact information from the American Urology Association. We contacted the residency programs by phone or email. For programs that did not reply, we performed a search of the program website. We administered a 3-question survey to assess resident subspecialty training in microsurgery, penile implant and artificial urinary sphincters as a fellowship trained academic faulty member, a private practice fellow, or a non fellowship trained physician. Data are reported as frequencies.

RESULTS: We obtained data from 134 (97%) programs. A total of 104 (78%) of programs had fellowship-trained physicians for training in microsurgery, penile implant and artificial urinary sphincters. The percentage of fellowship-trained microsurgeons per program did not vary significantly when comparing the different sections of the AUA, however the northeast and southeast sections had the lowest percentage (67% and 68%).

CONCLUSIONS: Approximately 80% of urology residency programs have exposure to microsurgery training from a fellowship-trained faculty member. We believe that the lack of a requirement for urologic microsurgery training is unsubstantiated since a majority of programs appear to have fellowship trained faculty. In order to provide an equal exposure to all graduating urology residents, it is imperative that urology residency programs that lack microsurgery as a specialty identify a faculty member who is fellowship-trained.

Reference: None.

SUPPORT: None.
OBJECTIVE: To evaluate the feasibility and effectiveness of embryo biopsy under direct visualization during operative hysteroscopy to avoid maternal contamination of products of conception (POCs) in cases of early miscarriages. Chromosomal analysis of POCs plays a fundamental role in the evaluation and treatment of recurrent pregnancy loss. With traditional Dilatation and Curettage maternal contamination is around 22%.

DESIGN: A series of 20 consecutive operative hysteroscopies was performed in infertile patients with miscarriage between 6-12 weeks from September 2015 through January 2019 in a private infertility clinic.

MATERIALS AND METHODS: Six spontaneous pregnancies plus 14 pregnancies obtained with Assisted Reproductive Technologies (ART): 5 fresh IVF cycles, 3 frozen IVF cycles, 2 fresh egg donation cycles and 4 frozen egg donation cycles. Mean patient age was 39±3.47 years. CRL was 2 to 51 mm. In 80% of cases a heartbeat was seen before miscarriage. Hysteroscopies were performed with a full bladder under transabdominal ultrasound guidance with a Voluson 8 or 6 ultrasound device with a RAB6-D Probe (GE, Austria). A 5 mm compact hystroscope with an operative channel (Wolf, Germany) and hysteroscopic forceps were used for embryo sampling. Resection of the gestational sac was accomplished with hysteroscopic forceps and scissors. Array Comparative Genomic Hybridization or Next Generation Sequencing were used for chromosomal analysis.

RESULTS: Maternal contamination was reported in one case. Of the remaining 19 cases 14 were aneuploidies, 1 was a 45X/46XX mosaic and 4 presented an euploid karyotype (Table). There were no surgical complications. Sixteen of the patients had a sonohysterography performed postoperatively and there was no case of intrauterine adhesions or retained POCs.

CONCLUSIONS: Embryo biopsy under direct visualization during operative hysteroscopy is feasible and could be an effective method to limit maternal contamination and furnish targeted biopsies. By offering the ability to separately sample embryo vs. trophoblast this method could illuminate the implications of mosaicism in trophoblast biopsies. This technique may be less disturbing to the endometrium as shown by absence of intrauterine adhesions in postoperative sonohysterography.

O-88 Monday, October 14, 2019 11:30 AM

UTERUS TRANSPLANTATION - LIVING DONOR OUTCOME. Liza Johannesson, MD, PhD, Giuliano Testa, MD Baylor University Medical Center, Dallas, TX.

OBJECTIVE: Uterus transplantation is a viable treatment option for women with uterine factor infertility. Most surgeries have utilized uterine grafts from living donors.

ED: egg donation; FET: frozen embryo transfer; S: spontaneous pregnancy.

<table>
<thead>
<tr>
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<th>Karyotype</th>
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<tr>
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</table>

FERTILITY & STERILITY® e37

O-89 Monday, October 14, 2019 11:45 AM

PREGNANCY OUTCOMES FOLLOWING HYSTEROSCOPIC CORRECTION OF T-SHAPED UTERI. Shelby A. Neal, MD,* Richard Thomas Scott, Jr., MD,* Linnea R. Goodman, MD#1IVI-RMA New Jersey, Basking Ridge, NJ; bUniversity of North Carolina, Raleigh, NC.

OBJECTIVE: To evaluate pregnancy outcomes following hysteroscopic correction of T-shaped uteri in patients with poor reproductive histories and T-shaped uterine cavities diagnosed by three-dimensional (3D) ultrasound.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: All patients at a single large IVF center undergoing fertility evaluation between 2016 and 2018 with a T-shaped uterine cavity diagnosed by 3D saline infusion sonohysterogram and a poor reproductive history (defined as ≥ 2 of the following events: clinical miscarriage, failed transfer of a euploid blastocyst, ectopic pregnancy, cycle cancellation secondary to endometrial hyperproliferation) were eligible for hysteroscopic correction and inclusion in the study. Surgery was performed in the early proliferative phase under conscious sedation. With saline as a distention medium, a hysteroscopic tissue morcellator was used to shave the lateral walls of the uterine cavity until both tubal ostia could be visualized simultaneously or healthy vascularized tissue was encountered. Post-operative imaging was performed the next month. All patients were followed for up to 6 treatment cycles. The primary outcome was ongoing pregnancy (presence of a fetal heartbeat at 8 weeks gestation). Secondary outcomes included miscarriage (pregnancy loss following documentation of gestational sac), ectopic pregnancy, and mean number of treatment cycles to achieve an

ED: egg donation; FET: frozen embryo transfer; S: spontaneous pregnancy.

<table>
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<tr>
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<tr>
<td>#19</td>
<td>51</td>
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DESIGN: Clinical study.

MATERIALS AND METHODS: Under an IRB approved study protocol 13 living donor uterus transplantations have been performed to date at Baylor University Medical Center Dallas. All donors underwent a thorough evaluation process listed in informed consent was obtained in a private non-coerced environment. A living donor team that included a Nurse Coordinator, a Psychologist, a Living Donor Advocate, Transplant Surgeon, a Gynecologist, and a Fertility Specialist looked after the needs of the donor throughout the evaluation and donation process. The transplant surgeon and gynecologic surgeon decided the best surgical approach and options included abdominal hysterectomy, a robotic hysterectomy, or a laparoscopic hysterectomy. Adverse events related to the surgery were reported in a private non-coerced environment. As per the United Network for Organ Sharing (UNOS) guidelines, every donor was followed at three months, six months, one year and two years.

RESULTS: The median follow-up interval for the living donor is 291 days with a range of 32-892 days. The median surgical time for donor hysterectomy was 6.5 hours. Median estimated blood loss was 0.80 L (0.4-1.7L) with two donors requiring intraproductive blood transfusion. Median hospital stay was 6 days and only one donor required intensive care unit (ICU). Intraoperative complications were uncommon. Five donors had short-term complications (<30 days after surgery) including gluteal claudication with ambulation that resolved 4 weeks post discharge (grade I), UTI (grade I), anemia requiring 1 unit of pRBC (grade II) and clostridium difficile infection (grade II). Three donors experienced long-term (>30 days) postoperative complications. These included vaginal cuff dehiscence (grade IIIb) and UTI (grade II). The vaginal cuff dehiscence was surgically repaired, and the UTI resolved with oral antibiotics.

Two donors were readmitted to the hospital after their surgery due to acute abdominal pain after intercourse on post-op day 97 diagnosed with vaginal cuff dehiscence (surgically repaired [grade IIIb]) and fecal impaction (post-op 27) requiring digital disimpaction under general anesthesia (grade IIb). Both donors required 2 days of hospitalization and recovery was uneventful.

The median sick leave of the donors was 28 days (7-42 days). All donors returned to their normal activities after surgery.

Symptoms after vaginal intercourse were present in 8 out of the 13 donors. Most donors complained of temporary pain, tenderness or discomfort during sexual intercourse. One donor experienced severe pain after her first sexual encounter and was diagnosed with vaginal cuff dehiscence.

CONCLUSIONS: The follow-up data of our initial 13 living uterus donors indicate that the living donor hysterectomy is associated with low risk of complications. Importantly, all living donors returned to their presurgical social and physical outcome.

Reference: None.

SUPPORT: None.
ongoing pregnancy. Patients who achieved an ongoing pregnancy were compared to those who did not using Student’s t-test and Fisher’s exact test.

RESULTS: Sixteen patients (age 37.4 ± 5.4 years, median of 22.5 months attempting conception) with T-shaped uterus were included in this study. Indications for surgery included recurrent pregnancy loss (n=3), recurrent implantation failure (n=2), recurrent ectopic pregnancy (n=1), endometrial hypoproliferation (n=3), or a combination of factors (n=7). There were no surgical complications. Post-operative imaging revealed expansion of the uterine cavity for 14 (87.5%) patients, as assessed by a single independent reviewer.

Following surgery, a total of 34 treatment cycles were attempted by 15 patients, resulting in 6 (17.6%) ongoing pregnancies, 3 (8.8%) miscarriages and 3 (8.8%) ectopic pregnancies. The cumulative ongoing pregnancy rate was 40.0%, with those who achieved an ongoing pregnancy requiring a mean number of 1.5 treatment cycles. There were no differences in age, body mass index, reproductive history or treatment modalities between patients who achieved an ongoing pregnancy and those who did not.

CONCLUSIONS: Patients who underwent hysteroscopic correction of a T-shaped uterus achieved a cumulative ongoing pregnancy rate of 40% over six treatment cycles. Further prospective studies with appropriate control groups are needed in order to ascertain if our findings represent a true improvement in pregnancy outcomes or simply regression to the mean.

O-90 Monday, October 14, 2019 12:00 PM

SINGLE EUPOLOID FROZEN EMBRYO TRANSFER: EVALUATING IMPACT OF INTERVAL SINCE OPERATIVE HYSTEROSCOPY. Allison C. Petrini, MD, Catherine W. Chan, MD, Kelly McCarter, MD, Michi Thompson, BA, Monica Pasternak, MD, Nigel Pereira, MD, Steven Spandorf, MD,* Ronald O. Perlman and Claudia Cohen Center for Reproductive Medicine, New York, NY; NY.

OBJECTIVE: There is limited data on the optimal time between operative hysteroscopy and embryo transfer. Previous studies have demonstrated no difference in pregnancy outcome if the interval between polypectomy or all indications' and embryo transfer (ET) is increased, but did not address operative hysteroscopy solely in the ideal group of patients undergoing single euploid embryo transfers. Our aim was to determine whether a difference in pregnancy outcome exists if the time between operative hysteroscopy and single euploid embryo transfer is increased.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients undergoing single euploid ET at our center over 3 years were examined for history of hysteroscopy prior to ET. Patients were grouped by surgical pathologic diagnosis and were further stratified into groups based on time between hysteroscopy and ET. They were designated as group 1, 2, or 3 to indicate an interval to next menstrual cycle, within 2 menstrual cycles, or within 3 menstrual cycles, respectively. Treatment outcomes were examined and classified as pregnant, not pregnant and then grouped into ongoing pregnancy or pregnancy loss. Student’s and non-parametric t-tests, Mann-Whitney U-test, and chi-square tests were used as indicated with p < 0.05.

RESULTS: A total of 1123 patients met inclusion criteria; 375 underwent hysteroscopy prior to ET during the study period. 77.7% of cases were operative, and 22.3% were diagnostic. Of operative cases, polyps represented 40% (n=98), adhesions 34% (n=84), and myomas 11% (n=28). There were no differences in the baseline demographics between those who were pregnant and not pregnant, or between those with an ongoing pregnancy versus pregnancy loss. The baseline demographics were also comparable between those who underwent hysterectomy and those who did not. There was no difference in the pregnancy rate between the groups who underwent ET 1, 2, or 3 menstrual cycles from operative hysterectomy. In addition, there was no difference in the rate of ongoing pregnancy between groups.

<table>
<thead>
<tr>
<th>Group 1 (ET in next menstrual cycle)</th>
<th>Group 2 (ET in 2 menstrual cycles)</th>
<th>Group 3 (ET in 3 menstrual cycles)</th>
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</thead>
<tbody>
<tr>
<td><strong>Pregnancy rate</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>36.3 (±4.0)</td>
<td>36.7 (±4.1)</td>
<td>0.79</td>
</tr>
<tr>
<td>Mean BMI (kg/m²)</td>
<td>24.0 (±5.7)</td>
<td>24.3 (±5.5)</td>
<td>0.3</td>
</tr>
<tr>
<td>Ongoing pregnancy</td>
<td>52.4%</td>
<td>57.1%</td>
<td>0.8</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>37.1 (±3.7)</td>
<td>37.1 (±3.6)</td>
<td></td>
</tr>
<tr>
<td>Mean BMI (kg/m²)</td>
<td>23.6 (±4.6)</td>
<td>23.5 (±4.6)</td>
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</tbody>
</table>

CONCLUSIONS: The time between operative hysteroscopy and euploid frozen embryo transfer did not have an effect on the ability to become pregnant or the chance of having an ongoing pregnancy. Thus, clinicians can advise patients that they may proceed with a frozen transfer as soon as the next menstrual cycle after operative hysteroscopy.


SCIENTIFIC CONGRESS PRIZE PAPER SESSION 2

O-91 Tuesday, October 15, 2019 10:45 AM

ARTIFICIAL INTELLIGENCE ASSESSMENT OF TIME-LAPSE IMAGES CAN PREDICT WITH 77% ACCURACY WHETHER A HUMAN EMBRYO CAPABLE OF ACHIEVING A PREGNANCY WILL MISCARRY. Rishab Harilaran, BSc, Peter He, Marcos Meseguer, PhD, Marco Toschi, MSc, Jose Celso Rocha, PhD, Nikica Zaninovic, Ph.D., Jonas Malmsit, MSc, Qiansheng Zhan, MSc, Cristina Hickman, PhD "Imperial College London, London, United Kingdom; IVIRMA Global, Valencia, Spain; IVIRMA, Rome, Italy; "State University of Sao Paulo Julio de Mesquita Filho, Assis, Brazil; "Ronald O. Perlman and Claudia Cohen Center for Reproductive Medicine, New York, NY.

OBJECTIVE: To determine whether convolutional neural network (CNN) can be used to predict whether an embryo capable of achieving a pregnancy will ultimately miscarry or lead to live birth based on Artificial Intelligence (AI) analysis of time-lapse (TLM) embryo images.

DESIGN: Diagnostic efficacy assessment of the capability of an Artificial Intelligence system predicting outcome of blind data from two independent clinics, qualitatively assessed using ROC curves with AUC scores and confusion matrices to quantify sensitivity and specificity (True Positive = TP, True Negative = TN, False Positive = FP, False Negative = FN).

MATERIALS AND METHODS: 3412 Time Lapse images of blastocysts with known live birth outcome following a single embryo transfer (“Live Birth”, n= 1756, 51%; “Miscarriage”, n=1656, 49%), were used to train a CNN model for image classification using Tensor Flow. These images were all derived from the same brand of time-lapse incubator (Embryoscope™) and the same time post insemination (111.5 hours) to optimise input data normalisation. Images were allocated into Training (63%, n=2140), Validation (15.5%, n=536) and Test (21.5%, n=736) with an even distribution for confounding factors (patient age cohort, clinic, oocyte donation) and outcome. “Positive” data was labelled as embryos with a Live Birth outcome, “negative” data, as embryos with a Miscarriage outcome.

RESULTS: Following training (AUC=0.85; loss=0.3), the AI had a performance that improved on current embryo selection methods within a blind data set (AUC=0.79); True Positive = 358, True Negative = 207, False Positive = 153, False Negative = 18. 565/376 images were correctly predicted with the blind data set (77% accuracy), with a 58% specificity (207/360) and 95% sensitivity (358/376). Amongst embryos classified as High risk of miscarriage, miscarriage rate was 92% (207/225), compared with 30% (153/511, p<0.001) when embryos were classified as reduced risk of miscarriage.

CONCLUSIONS: This is the first time that such a large data of single embryo transfer embryos from multiple clinics is used to assess AI capabilities.
in predicting miscarriage once pregnancy was confirmed. The high accuracy rate achieved suggests that visible embryo characteristics play a predominant role in maintaining pregnancy to live birth, once the biochemical pregnancy is established, compared to other factors, such as, the endometrium, or other non-visible embryo factors. Additional information (i.e., embryo genetic or proteomic information, or endometrial information) may help improve the specificity of miscarriage prediction.

This technology will now be tested prospectively in other clinics to assess whether these results can be generalised and whether this technology can be used to help advance embryo diagnosis and selection, not only in terms of prediction of live birth, but also miscarriage, an outcome associated with considerable emotional distress to patients.

SUPPORT: This research was funded by São Paulo Research Foundation (FAPESP), grant number 2017 / 19323-5.

O-93 Tuesday, October 15, 2019 11:15 AM

HIGHER INCIDENCE OF POSTPARTUM COMPLICATIONS IN WOMEN WITH POLYCYSTIC OVARY SYNDROME. Snigdha Alur-Gupta, M.D., a Mary Regina Boland, Ph.D., a,b Mary D. Sammel, Sc.D., c Kirt T. Barnhart, MD, MSCE, d Anuja Dokras, M.D., Ph.D., d "University of Pennsylvania Perelman School of Medicine, Philadelphia, PA; eAffiliation not provided; fDepartment of Biostatistics, Epidemiology and Informatics, University of Pennsylvania, Philadelphia, PA; dUniversity of Pennsylvania, Philadelphia, PA; cUniversity of Pennsylvania Health System, Philadelphia, PA.

OBJECTIVE: To assess the risk of perinatal and postpartum depression and postpartum cardiovascular complications in women with PCOS.

DESIGN: Retrospective cohort study using administrative claims from 2000-2016.

MATERIALS AND METHODS: We included women aged 18-50 years enrolled continuously in the claims database Optum for a minimum of 6 months prior to conception, their entire pregnancy and at least 6 weeks following delivery. The PCOS cohort and all comorbidities were identified using specific codes from the International Classification of Diseases (ICD). Primary outcomes were incidence of perinatal and postpartum depression (within 3 months after date of delivery). Secondary outcomes included postpartum preeclampsia, postpartum eclampsia (within 6 weeks after the date of delivery), and peripartum cardiomyopathy (within the last month before or first 5 months after date of delivery). We compared outcomes between the PCOS and non-PCOS cohorts using univariate and multivariable logistic regression models adjusting for covariates including age, geographic location, preterm delivery, ART use, multiple births, pre-pregnancy depression, pre-pregnancy diabetes, pre-pregnancy hypertension, gestational diabetes, gestational hypertension, obesity, history of hyperlipidemia, smoking and race.

RESULTS: We identified 42,391 unique women with PCOS and 795,480 women without PCOS. Women with PCOS were more likely to have depression (4% vs 3%), diabetes (5% vs 1%), hypertension (6% vs 3%) and obesity (15% vs 5%) compared to women without PCOS (p<0.001 for all). They had a higher prevalence of gestational diabetes (24% vs 13%), gestational hypertension (14% vs 8%) and antepartum preeclampsia (5% vs 3%) than women without PCOS (p<0.001). In multivariable models, women with PCOS had a significantly higher odds of both perinatal and postpartum depression and postpartum preeclampsia and eclampsia compared to those without PCOS (Table). Postpartum results remained similar in planned sensitivity analyses in women with at least one year of pre-conception data, when including date of delivery in outcome definition and when varying the definition of perinatal and postpartum depression from the DSM-V criteria of 4 weeks postpartum to a commonly utilized literature length of one year postpartum.

CONCLUSIONS: This study demonstrates for the first time that women with PCOS are at higher risk for depression, preeclampsia and eclampsia in the fourth trimester of pregnancy. Our results highlight the need for comprehensive screening and targeted interventions during the postpartum period in this high-risk population.

SUPPORT: Snigdha Alur-Gupta is supported by the NIH T32 Training Grant: HD007440.

O-94 Tuesday, October 15, 2019 11:30 AM

DEVELOPMENTAL POTENTIAL OF ANEUPLOID HUMAN EMBRYOS BEYOND IMPLANTATION. Marta Nasilia Shahbaz, Ph.D., a Tianshen Wang, M.D., Ph.D., a,b Xin Tao, Ph.D., a,c Li Sun, Ph.D., a,c Yiping Zhan, Ph.D., a,c Antonio Pellicer, MD, Ph.D., a,c Richard Thomas Scott, Jr., M.D., a,d Emre Selc, M.D., a,d Magdalena Zernicka-Goetz, Ph.D., cDepartment of Physiology, Development and Neuroscience, Mammalian Embryo and Stem Cell Group, University of Cambridge, Cambridge, United Kingdom; cThe Foundation for Embryonic Competence, Basking Ridge, NJ; dIVIRMA ROMA, Roma, Italy; aIVI-RMA New Jersey, Basking Ridge, NJ.

CONCLUSIONS: Although subfertility/ART increased LPTB and EPTB (AOR 1.71) and ART (AOR 1.67) groups. The four strongest effectors of LPTB (AOR 1.53) in the ART group and EPTB in UF (AOR 1.79), MAR (P 0.001), chronic diabetes (AOR 1.71 LPTB; AOR 2.01 EPTB), chronic hypertension (AOR 1.85 LPTB; AOR 2.88 EPTB), overweight/obesity, prior hospitalizations, gravidity, gestational diabetes, pregnancy hypertension, placental problems, bleeding, and father's age, race and education) were modeled using multinomial logistic regression. The high accuracy rate achieved suggests that visible embryo characteristics play a predominant role in maintaining pregnancy to live birth, once the biochemical pregnancy is established, compared to other factors, such as, the endometrium, or other non-visible embryo factors. Additional information (i.e., embryo genetic or proteomic information, or endometrial information) may help improve the specificity of miscarriage prediction.

RESULTS: There were 155,997 term, 8,210 LPTB, and 2,756 EPTB deliveries between Massachusetts birth certificates and hospital stays to identify privately insured singleton first births to women ≥ 18 years of age between 2004-2013. Deliveries were classified as ART when they linked to SART CORS, medically assisted reproduction (MAR) when fertility treatment was indicated on the birth certificate, unassisted subfertile (USF) when they had infertility diagnosis in prior hospital records or treatment for fertility in a prior delivery, and fertile if in none of the above groups. Late preterm birth (LPTB: 34-36 weeks) and early preterm birth (EPTB: <34 weeks) deliveries were compared to term deliveries (≥37 weeks). Covariates that significantly influenced the outcome of prematurity were age, race and education) were modeled using multinomial logistic regression.

Syndrome.
OBJECTIVE: Aneuploidy is one of the major limitations of human reproduction. However, the developmental consequences of specific aneuploidies during the early stages of post-implantation development remain poorly characterized. In this study, we investigated the post-implantation development of human embryos with specific aneuploidies compared to euploid embryos.

RESULT: We firstly analyzed the global development of the different aneuploidies, and observed that monosomy 21 embryos had a higher incidence of arrest in culture (p=0.0105), which was specific to the implantation phase of development. The three trisomies analyzed developed similarly up to day 9 in terms of attachment, and preservation of the embryonic and extra-embryonic lineages. However, careful analysis of cell numbers revealed that while trisomy 15 and 18 embryos displayed a marked delay in the extraembryonic lineages on day 9: OCT4+ embryonic epiblast (precursor of the fetus and amnion), GATA6+ extra-embryonic hypoblast (precursor of the yolk sac), and OCT4+ GATA6+ extra-embryonic trophoblast (precursor of the placenta). Chromosome copy number in post-implantation embryos was determined by targeted next generation sequencing (NGS).

RESULTS: We present the first report of the global development of the different aneuploidies, and observed that monosomy 21 embryos had a specific hypoproliferation defect of the trophoblast (p=0.004), while the epiblast and primitive endoderm tissues (derived from the inner cell mass) were not affected (p=NS). In addition, analyses of the specific subset of monosomy 21 embryos that did not arrest during culture, unveiled a similar hypoproliferation phenotype of the trophoblast. To test whether this phenotype was due to mosaicism, embryos were dissected into different pieces for NGS. This revealed 3 non-concordant cases out of a total of 15 embryos analyzed. One case was identified as 45,XX,-21 based on trophoderm biopsy at day 5 and PGT-A by tNGS, but showed 45,XX,-21 and 46,XX on day 9. Remarkably, this embryo developed well up to day 9 in vitro, although it displayed a hypoproliferative trophoblast.

CONCLUSIONS: Our results show that specific aneuploidies lead to specific developmental phenotypes during the first days of post-implantation development. Culturing human embryos beyond day 7 in vitro is a powerful tool to understand how specific aneuploid alterations influence embryo morphogenesis and to detect cases of mosaicism that cannot be identified by sampling trophoderm cells on day 5.


O-95 Tuesday, October 15, 2019 11:45 AM

A LIFESTYLE INTERVENTION TARGETING WOMEN WITH OBESITY AND INFERTILITY IMPROVES THEIR FERTILITY OUTCOMES, ESPECIALLY IN WOMEN WITH PCOS: A RANDOMIZED CONTROLLED TRIAL. Mateia Beltran, MSc,a Belina Carranza-Mamane, MD,a Youssef AinMelk, MD,a Marie-Hélène Pesant, MD,a Karine Duval, PhD,a Farrah Jean-Denis, MSc,a Marie-France Langlois, MD,a Hélène Lavoie, MD,a Guy Waddell, MD,a Jean-Patrice Baillaigean, MD,a Research Center of the Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, QC, Canada; bUniversité de Sherbrooke - Department of Obstetrics and Gynaecology, Sherbrooke, QC, Canada; cFertility Clinic Procrea, Montréal, QC, Canada; dUniversité de Sherbrooke, Sherbrooke, QC, Canada; eUniversité de Sherbrooke, Department of Medicine, Sherbrooke, QC, Canada.

OBJECTIVE: To evaluate the impacts of a lifestyle intervention on fertility outcomes in women with obesity seeking fertility treatments, with or without the polycystic ovary syndrome (PCOS).

RESULT: We randomization controlled trial including 127 women with infertility and obesity, with no major infertility factor (female or male).

MATeRIALS AND METHODS: Women were randomized either in the control group (CG: usual standard of care) or the lifestyle program group (LPG, lifestyle intervention with individual sessions (kinesiologist and nutritionist) and group sessions). A total of 108 women have completed ≥6 months of the study (51 LPG and 57 CG). Since randomization was stratified according to the presence of PCOS (PCOS: CG=35, LPG=33, Non PCOS: CG=22, LPG=18), we present results on fertility outcomes at 18 months of follow-up, and anthropometric and lifestyle changes at 6 months, in all women as well as in women with or without PCOS. Student’s t-test were used to compare means and chi-squared tests for proportions. P-values ≤ 0.05 were considered significant.

RESULTS: As compared to the CG, our lifestyle program increased significantly the pregnancy rates for all women (60.8% vs 38.6%, 1.58 fold, p=0.021) or for women with PCOS (57.6% vs 34.3%, 1.68 fold, p=0.005), but this difference was not significant for women without PCOS (66.7% vs 55.3%, 1.22 fold, p=0.18). This lifestyle program improved significantly the pregnancy rates for spontaneous pregnancy (All: 33.3% vs 12.3%, 2.7 fold, p=0.009; PCOS: 27.3% vs 5.7%, 4.8 fold, p=0.016; Non PCOS: 44.4% vs 22.7%, 2.0 fold, p=0.145) and live birth (all: 51.0% vs 36.8%, 1.39 fold, p=0.139; PCOS: 54.8% vs 31.4%, 1.75 fold, p=0.05; Non PCOS: 66.7% vs 45.5%, 1.47 fold, p=0.18). Pregnancy rates in women using an assisted reproductive technology (ART, n=63) were increased in the LPG for all women (58.6% vs 47.1%, 1.24 fold, p=0.036) and mildly for women with PCOS (51.9% vs 47.6%, 1.09 fold, p=0.744), although this was not statistically significant. Finally, compared to the CG, the LPG has lost significantly more weight at 6 months (all: 3.43± 4.45 vs 0.89± ± 3.67, p=0.003; PCOS: 3.66± 4.47 vs 0.93± ± 4.22, p=0.015), except for non-PCOS women who lost less weight (-2.31± ± 4.34 vs -0.48± ± 2.48,p=0.139). Women in the LPG also improved significantly more the quality of their diet (healthy eating index, all: +18.0± ± 13.7 vs +5.3± ± 12.4 on 100, p<0.001; Non PCOS: +13.6± ± 10.4 vs +6.5± ± 11.3 on 100, p=0.055).

CONCLUSIONS: A lifestyle intervention targeting women with obesity and infertility improves their chances of conceiving, especially spontaneously (with no fertility treatment). Our results suggest that such intervention could benefit women with PCOS even more. It is also possible that lifestyle modifications improve the effectiveness of ART in these women, but to a lower extent. Accordingly, our lifestyle approach could significantly decrease the costs associated with the fertility care of women with obesity and infertility.
CATCHING UP TO THE MANDATE: A MYSTERY CALLER STUDY OF SOCIETY FOR ASSISTED REPRODUCTIVE TECHNOLOGY (SART) MEMBER CLINICS IN STATES MANDATING FERTILITY PRESERVATION (FP) COVERAGE.

Emma C. Trawick, M.D., Kristin Smith, B.S., Maryam Guili, M.D., M.Sc.,1 Eden Cardozo, M.D.,2 Kara N. Goldman, M.D.,6 Northwestern University Feinberg School of Medicine, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Chicago, IL; University of Colorado, Department of Obstetrics and Gynecology, Division of Family Planning, Aurora, CO; Women and Infants Fertility Center, Brown University Warren Alpert Medical School, Providence, RI.

OBJECTIVE: As of April 2019, six U.S. states now mandate private insurers to cover FP for patients facing iatrogenic infertility. In Illinois, this mandate extends to cover Medicaid recipients. We sought to assess how SART clinic representatives address questions relating to insurance coverage for cancer patients seeking FP.

RESULTS: We identified 35 SART member clinics in IL, CT, DE, MD, and RI; 3 were excluded due to nonresponse or conflicts. Of 32 clinics, 29 (91%) offered FP for cancer patients. Less than half (39%, n=11) were confident that insurance would cover FP, and 7% reported they did not accept any insurance. Only 21% (n=6, 4 from IL) referenced legislation mandating FP coverage. Neither practice type nor time since enactment of state mandate influenced clinic responses. Regarding insurance coverage for FP, 85% (n=24) were confident private insurance would cover FP. We found that IL clinics were more likely to report any positive confirmation for coverage if the patient reported she had private compared to Medicaid insurance (81% vs. 14%, p<0.005). 87% of IL clinics did not accept Medicaid, and none provided a direct referral. University-affiliated vs private practice, and time since enactment of state mandate (as of 1/1/2019) and performed individual analyses; responses to “Does insurance [or Medicaid] ever cover FP for cancer patients?” were categorized as positive (yes, usually, sometimes or it depends) versus negative (no, usually not, and I don’t know, and subcategorized as confident (yes, usually, no, and usually not) or not confident (sometimes, it depends, or I don’t know). Data are presented as %, and Fisher’s exact test (p<0.05) was used to compare responses across clinic characteristics and insurer.

RESULTS: We identified 35 SART member clinics in IL, CT, DE, MD, and RI; 3 were excluded due to nonresponse or conflicts. Of 32 clinics, 29 (91%) offered FP for cancer patients. Less than half (39%, n=11) were confident that insurance would cover FP, and 7% reported they did not accept any insurance. Only 21% (n=6, 4 from IL) referenced legislation mandating FP coverage. Neither practice type nor time since enactment of state mandate influenced clinic responses. Regarding insurance coverage for FP, 85% (n=24) were confident private insurance would cover FP. We found that IL clinics were more likely to report any positive confirmation for coverage if the patient reported she had private compared to Medicaid insurance (81% vs. 14%, p<0.005). 87% of IL clinics did not accept Medicaid, and none provided a direct referral. University clinics in IL were more likely than private clinics to accept Medicaid (66.7% vs 0%, p<0.05) and know that Medicaid covered FP (66.7% vs 0%, p<0.05).

CONCLUSIONS: In states where FP coverage is mandated, the SART objective outcome was whether information provided reflected state FP coverage mandates. We called all SART member clinics in FP coverage-mandated states (as of 1/1/2019) and performed a second call for Illinois clinics to assess responses specific to private insurance. Clinics were categorized by state, practice type (university-affiliated vs private practice), and time since enactment of coverage mandate (pre- vs post-1/1/2019). All responses were recorded and coded for analysis; responses to “Does insurance [or Medicaid] ever cover FP for cancer patients?” were categorized as positive (yes, usually, sometimes or it depends) versus negative (no, usually not, and I don’t know, and subcategorized as confident (yes, usually, no, and usually not) or not confident (sometimes, it depends, or I don’t know). Data are presented as %, and Fisher’s exact test (p<0.05) was used to compare responses across clinic characteristics and insurer.

HUMAN SPERM MORPHOLOGY ANALYSIS USING SMARTPHONE MICROSCOPY AND DEEP LEARNING.

Prudhvi Thirumalaraju, BS,1 Manoj Kumar Kanakasabapathy, MS,3 Charles L. Bormann, PhD,4,46 Hemant Kandula, BS,5 Sandeep Kota Sai Pavan, BS,6 Divyank Yarravarapu, BS,7 Hadi Shafee, PhD,8,9 Brigham and Women’s Hospital, Harvard Medical School, Boston, MA; 3Massachusetts General Hospital, Harvard Medical School, Boston, MA.

OBJECTIVE: Sperm concentration, motility and morphology are among the primary measures of a semen analysis. While at-home methods for sperm concentration and motility evaluations have been developed, owing to the complexity of morphology assessments, automated microscopy-based evaluation of sperm morphology at-home has never been possible. Furthermore, all proposed alternative technologies have either been too expensive or inaccurate. An inexpensive, portable and automated sperm morphology assessment tool for at-home testing can improve access to care especially in resource limited settings.

RESULTS: We utilized a smartphone-based microscope that we have developed for sperm concentration and motility analysis 1. Here, we also adapted a deep-convolutional neural network that made use of a layered learning approach described previously, to sperm images acquired using an inexpensive smartphone device 2. For evaluation, clinical samples were prepared by the center’s trained technicians and were evaluated conventionally under a microscope. These slides were then imaged using our smartphone system and the results of the two methods were tested qualitatively (normal/abnormal), to illustrate the system’s applicability and as a training tool.

MATERIALS AND METHODS: A smartphone-based microscope setup was built using 3D printing 1. The total cost of materials for the system was estimated to be $5. Over 170,000 annotated sperm images were used in developing our network and 7000 individual sperm images from 35 semen samples were used in evaluating the network. An android application processes the image on phone, without the requirement of internet access in the smartphone system. The application sends the % of morphologically normal sperm that are present in the sample. The system reports morphological morphology scores were compared to evaluate the performance of the smartphone system.

RESULTS: The smartphone system tested with 35 patient semen samples was able to correctly identify samples based on morphological quality (≥4% good morphological sperm) with 88.5% accuracy with a 95% confidence interval (CI) ranging between 73.3% to 96.8%. Furthermore, a receiver operator characteristic (ROC) revealed an area under the curve (AUC) of 0.928 (CI: 0.788 to 0.988), which confirmed that the artificial intelligence (AI) algorithm can effectively separate the normal and abnormal morphological quality samples. The sensitivity and specificity of the network was 80% and 92% along with a positive and negative predictive value of 80% and 92%, respectively.

CONCLUSIONS: Here, we have reported the first implementation of an automated artificial intelligence-empowered smartphone-based tool for measuring sperm morphological quality. The system is inexpensive, rapid, accurate, and reliable making it suitable at-home screening test. Our future focus is on developing a microfluidic sample handling device that can further sample preparation for at-home use. We have shown that the utilization of AI technologies allows for objective/standardized evaluation of sperm morphology using inexpensive hardware for the first time.


SUPPORT: This work was partially supported by the Brigham Precision Medicine Developmental Award (Brigham Precision Medicine Program, Brigham and Women’s Hospital) and R01AI118502, R01AI138800, and R21HD092828 (National Institute of Health).

HAS THE MASSACHUSETTS INFERTILITY MANDATE LIVED UP TO ITS PROMISE? Katherine Koniaris, MD, Alan S. Penzias, M.D., Eli Adashi, M.D., Tufts Medical Center, Boston, MA; Brigham and Women’s Hospital and R01AI118502, R01AI138800, and R21HD092828 (National Institute of Health).

OBJECTIVE: Massachusetts law mandates coverage for 31 conditions or services including infertility. The public perception is that all residents have
coverage for infertility treatment. In fact, the majority do not. Federal pre-
emptions and other exemptions in state law restrict fertility coverage even
in states with mandates. The goal of this study was to determine the percent-
age of reproductive age women in Massachusetts with coverage for infertility
treatment.

DESIGN: Population based cross-sectional study

MATERIALS AND METHODS: We obtained de-identified population level
data from 3 sources: the State Census Bureau (number of women aged 20-44 living in Massachusetts in 2016); the Center for Health Informa-

CONCLUSIONS: There are notable exemptions to Massachusetts’
mandated health benefits statutes. Self-insured policies provided by em-
ployers are governed by the Federal Employee Retirement Income Security
Act (ERISA) and are not subject to state mandated benefits. Federally-funded
plans covering Military and Civilian federal employees as well as Mas-

As a result, only 36.3% of reproductive aged women in Massachusetts
have health insurance subject to the mandate. Moreover, the Massachusetts
Division of Insurance permits insurers latitude in applying the law. Thus,
women who do not meet certain biological criteria, have exceeded a prede-
termined number of treatment cycles, or have surpassed a total dollar cap are
exempt from coverage. Un-partnered women may not have treatment
coverage until they have paid out-of-pocket for 6-12 months of treatment.

Massachusetts is often cited as the model state for health insurance
coverage of infertility treatment. Yet, only 36.3% of reproductive aged
women are subject to the mandate and even fewer have meaningful access
to services when exceptions are considered. Given that Massachusetts’
mandate has fallen short of affording women real access to care, future study
is warranted with the hope of informing legislative action.

O-101 Tuesday, October 15, 2019 11:45 AM

THE PRICE IS RIGHT? ANALYSIS OF PRICE TRANSPARENCY IN ASSISTED

O-100 Tuesday, October 15, 2019 11:30 AM

RIGHT TO HEALTH: THE SITUATION OF ASSISTED

REPRODUCTION TECHNIQUES WITH GAmETES

DONATION IN ITALY. Giulia Scaravelli, PhD,
Roberto De Luca, Master degree, Robertha Spoletrini, Master de-

OBJECTIVE: The postponement of childbearing age in Italy, determine a
large number of older women wanting a baby. In these cases and in many
others gametes donation could represent an important option for infertility
treatments. Only the recent change of the Law 40/2004 in Italy in April
2014 allowed infertile couples to access to gametes donation. The objective
is to analyze the number and type of gametes donation cycles collected by
The Italian Assisted Reproductive Technology Register (IARTR) since 2014.

DESIGN: In this study IARTR analyzed retrospectively data on 16807
gametes donation cycles performed from May 2014 till December 2017 on
4577 patients. 220 Assisted Reproductive Technology (ART) clinics and
179 Intrauterine Insemination (IUI) clinics sent data to the National Italian
Register and participated in the study with 102 out of 220 (46.4%) and 3
out of 179 (1.7%) performing donation cycles.

MATERIALS AND METHODS: All ART and IUI centres which has
performed at least one cycle with gametes donation, that have sent data
during the study period were included in the study. Parameters regarding
number of patients, number of cycles, treatment indications, age classes,
pregnancies and live births rates were statistically analysed using SPSS
statistic 25.0.

RESULTS: The centers participating in the annual data collection and
which performed at least one donation cycle were 105, of which only
12 were public structures. 14577 patients underwent 16807 initiated cy-
cles (4.4% of all ART and IUI cycles performed in the same period)
that included 14800 cycles performed with complex ART techniques
and 2007 cycles performed with IUI-D. Most cycles (44.6%) were carried
out with oocyte donation, 25.8% with sperm donation and 29.6% with
cyropreserved embryos obtained after a donation. The main indication
for treatment for oocyte donation was the maternal advanced reproductive
age (37.9%), while for sperm donation, 94.0% of indications refer to dis-
eases that affect sperm vitality. Almost all the gametes used for the treat-
ments come from abroad (97.8% of the oocytes and 80.7% of semen).

The pregnancy rate per transfer carried out in the study period was
37.7% for fresh egg donation, 34% for cryopreserved oocytes, 33.5% for
cyropreserved embryos and 36.6% for sperm. The percentage of multi-
tiple deliveries was 32.6%, 17.5%, 13.8% and 18.1% respectively. For the
semen used in intruterine insemination the pregnancy rate per cycle
started was 20% and the multiple delivery rate was 14.4%. In these 4
years 3857 children were born alive, equal to 7.3% of those born from
all ART techniques in the same period.

CONCLUSIONS: The Italian situation regarding gametes donation policy,
raises the question of equity in access to these procedures. The impossibility
of finding donors in our country, dictated by the absence of information cam-
paigns and the lack of possibility of compensation for donors limits the use of
these techniques in public structures. Only a few regions have adopted pol-
icies to improve donation cycles in public centers.

TABLE 1. Population and Coverage

<table>
<thead>
<tr>
<th>Population</th>
<th>#of Women</th>
<th>% of Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Census data: age 20-44 residing in MA in 2016</td>
<td>1,142,542</td>
<td>100%</td>
</tr>
<tr>
<td>Exempt from Coverage</td>
<td># of Women</td>
<td>% of Women</td>
</tr>
<tr>
<td>Self-insured employer sponsored Plans</td>
<td>498,931</td>
<td>43.7%</td>
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<td>Public Assistance Insurance</td>
<td>184,179</td>
<td>16.1%</td>
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<td>5,080</td>
<td>0.4%</td>
</tr>
<tr>
<td>No Insurance</td>
<td>39,746</td>
<td>3.5%</td>
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<td>Subtotal</td>
<td>727,936</td>
<td>63.7%</td>
</tr>
<tr>
<td>Potential Coverage</td>
<td># of Women</td>
<td>% of Women</td>
</tr>
<tr>
<td>Mandate Eligible Insurance</td>
<td>414,606</td>
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Price or Discount Information

<table>
<thead>
<tr>
<th>Clinics Reporting (n = 375)</th>
<th>Mean Cost Reported</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Price Listed</td>
<td>78 (20.8%)</td>
</tr>
<tr>
<td>Consultation</td>
<td>33 (8.8%)</td>
</tr>
<tr>
<td>IU1 Cycle</td>
<td>26 (6.9%)</td>
</tr>
<tr>
<td>IVF Cycle</td>
<td>48 (12.8%)</td>
</tr>
<tr>
<td>FET Cycle</td>
<td>24 (6.4%)</td>
</tr>
<tr>
<td>OC Cycle</td>
<td>33 (8.8%)</td>
</tr>
<tr>
<td>Any Discount/Funding Listed</td>
<td>249 (66.4%)</td>
</tr>
<tr>
<td>Medication Discounts</td>
<td>69 (18.4%)</td>
</tr>
<tr>
<td>Shared Risk Refund</td>
<td>75 (20.0%)</td>
</tr>
<tr>
<td>Lending Programs</td>
<td>151 (40.2%)</td>
</tr>
<tr>
<td>External Financing or Grants</td>
<td>98 (26.1%)</td>
</tr>
<tr>
<td>Internal Financing (e.g.: Multi-Cycle Discounts)</td>
<td>88 (23.4%)</td>
</tr>
<tr>
<td>Military Discounts</td>
<td>74 (19.7%)</td>
</tr>
<tr>
<td>Cancer Discounts</td>
<td>36 (9.6%)</td>
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</tbody>
</table>
OBJECTIVE: A recent influx of assisted reproductive technology (ART) and services promote price transparency, with detailed costs of services listed on websites. Given current market trends, we sought to determine how existing clinics perform in terms of price transparency and to what extent they provide information on available discounts and financial assistance.

DESIGN: Cross-sectional analysis of Society for Assisted Reproductive Technology (SART) registry clinics.

MATERIALS AND METHODS: Clinics were identified through the SART website clinic search function on 4/14/19. Military clinics and those clinics without a website were excluded. Between 4/15/19 and 4/22/19, each clinic’s website was queried. Practice location (city, state) and type (private vs. academic vs. other [e.g.: managed care]) were recorded. Prices for consultation, intrauterine insemination (IUI; including monitoring and sperm preparation), in vitro fertilization (IVF; excluding pre-implantation genetic testing), frozen embryo transfer (FET), and oocyte cryopreservation (OC) were recorded. Mean costs were calculated for each reported price.

RESULTS: 382 clinics were listed on the SART website and 375 met study inclusion criteria. Table 1 illustrates the number and percentage of clinics that provided costs for services, information on discounts, and available financial assistance on their websites. Only 22.8% (67/293) of private practices and 11.7% (9/77) of academic practices reported the price of one or more services.

CONCLUSIONS: Most existing clinics do not report the costs of consultation or of various treatments on their websites. This lack of transparency may actually create barriers to care if costs are lower than anticipated. The majority of clinics provide information on available discounts and/or financing information, the most common being links to lending programs. Full disclosure of cost on clinic websites will not only match new market trends in ART, but also demystify the costs of fertility treatment and potentially democratize fertility care by fostering price competition.

O-102 12:00 PM Tuesday, October 15, 2019

EMERGENCY COS IN ONCOFERTILITY PRESERVATION. Marouen Braham, Associate professor, a Sarah Amari, Medical Degree, b Khadija Feriel Kacem Berjeb, Associate professor, c Mokha Bouricha, resident, d Wissal Jaafar, Medical Degree, e Manel Hamdoun, Medical Degree, f Linda Debabi, Medical Degree, g Olfa Bahri, Sr., Professor, h Anis Fadhlaoui, Associate Professor, i Fethi Zhioua, Pr j Aziza Othmana University Hospital, Tunis, Tunisia; j Gynecology, Obstetric and Reproductive Medicine Department. Aziza Othmana University Hospital, Tunis, Tunisia; k Reproductive Medicine Laboratory. Aziza Othmana University Hospital, Tunis, Tunisia; l Biochemistry Department. Aziza Othmana University Hospital, Tunis, Tunisia.

OBJECTIVE: There is often an urgent need to start cancer treatment. Therefore, protocols with alternative timing to start COS have been proposed in fertility preservation. Is random start COS as effective as conventional start COS in fertility preservation?

DESIGN: We conducted a retrospective study.

MATERIALS AND METHODS: The study included 104 patients recently diagnosed with cancer and in preparation for gonadotoxic therapy, from January 2017 to January 2019.

Patients were evaluated within 2-48h after the referral, clinically, by ultrasound (antral follicular count) and by an AMH dosage. The underlying conditions were mainly: Hodgkin’s Lymphoma (46%), Breast cancer (30%), Rectal cancer (3%), and various other pathologies (Ovarian, Gastric cancer, T Lymphoma, etc.). AMH levels ranged from 0.2ng/ml to a maximum of 10.5ng/ml. All 104 patients underwent IVF cycles using GnRH antagonist protocol. 65 patients underwent an early-follicular start COS (Group 1), whereas 39 had a random (late follicular or luteal) start (Group 2).

The addition of Letrozole was compulsory in case of estrogen-sensitive tumors and E2 levels, closely monitored.

The addition of Letrozole was compulsory in case of estrogen-sen

Oocyte retrieval was done transvaginally in 65% of cases and was trans-urethral in 35%. Oocyte or embryo vitrification were proposed to the patients based on marital status and preference.

OBJECTIVE: To define, using current definitions and prevalence or incidence data, the minimal economic burden of pregnancy in women with PCOS in the U.S.

DESIGN: Systematic literature review and economic burden analysis.

MATERIALS AND METHODS: We performed a systematic review of the published literature to identify studies evaluating the epidemiology of PCOS in pregnancy and its clinical consequences and costs. We selected the three most consistently reported and prevalent pregnancy related health outcomes associated with PCOS to generate our cost analysis: gestational diabetes (GDM), pregnancy-induced hypertension (PIH) and preeclampsia. We linked published cost data for the aforementioned health consequences to their excess incidence attributable to PCOS in order to calculate overall estimated health care-related economic costs.

RESULTS: We estimate that there were 254,463 PCOS-related births in the U.S. in 2017. After accounting for baseline risk, we estimate an excess of 27,177 of these births were complicated by GDM, 16,286 by PIH, and 7,354 by preeclampsia as a result of PCOS. We estimate the mean excess annual cost of pregnancy-related care for women with PCOS in the U.S. due to GDM to be $53,563,896, PIH to be $149,831,200 and preeclampsia to be $84,291,548.

CONCLUSIONS: A conservative estimate of the excess cost of pregnancy-related complications attributable to PCOS in the U.S. exceeds $287 billion in current dollars.


O-104 Tuesday, October 15, 2019 11:00 AM

SEVERE ENDOMETRIOSIS IN RHESUS MACAQUES CONSUMING A WESTERN-STYLE DIET (WSD) AND CHRONICALLY TREATED WITH ANDROGEN. Ov D. Slayden, PhD, a Cecily V. Bishop, PhD, b Emily Mishler, MS, c Lauren Drew Martin, DVM, d Heather M. Sidener, DVM, DAACLAM, e Jon D. Hennebold, PhD, f

FERTILITY & STERILITY® e43
OBJECTIVE: To evaluate the effects of chronic mild hyperandroginemia and/or consumption of a western-style diet (WSD) on the rate of endometriosis in rhesus macaques.

DESIGN: 2 by 2 factorial.

MATERIALS AND METHODS: Female rhesus macaques were treated beginning at menarche (2.5 y) with implants containing cholesterol or testosterone (T). The T implants elevated serum T levels approximately 5-fold and did not prevent menstrual cyclicity (1). Half of the animals in each group were fed a standard monkey chow diet, and the other half received a WSD resulting in 4 treatment groups: controls (C), T, WSD, and T+WSD (n = 9-10/group). After 3 years of treatment, the animals received multiple reproductive manipulations including laparoscopically-guided TruCutTM needle biopsies of the endometrium, ovarian stimulation, laparoscopic follicle aspiration and caesarian section. Beginning in year 5, the animals were evaluated laparoscopically and by transtubal ultrasonography for the presence of endometriosis. Endometriosis was scored for disease stage based on the ASRM Revised Classification criteria. In macaques, stage I animals present with superficial red/brown lesions and mild adhesions. Stage II is defined by extensive lesions (>1 cm² in area in aggregate) and adhesions. Stage III endometriosis includes deep lesions > 2 cm² in size that are identifiable by ultrasound and confirmed by laparoscopy. Stage IV animals present with large lesions and ablation of the uterine cul de sac. Endometriotic stromal cells were isolated from one of the animals with advanced disease. The cells were treated in vitro with steroid hormones (1 ng/ml: E₂, E₂ + P, T, DHT E₂+T and E₂+DHT) in replicate plates (n=5). The cells were analyzed for expression of steroid receptors (ESR1; PGR, AR), aromatase (CYP19A1), and Ki-67 by quantitative real-time PCR (qPCR). Representative lesions were assessed by immunohistochemistry (IHC).

RESULTS: T + WSD animals presented with the highest prevalence (7 out of 10) of severe endometriosis, including 5 animals with Stage IV disease (Table 1). In contrast, 3 of 10 controls possessed only adhesions or Stage I endometriosis. IHC showed strong staining for ER1, PGR and AR staining. Stromal cells, in vitro, expressed minimal ESR1 and PGR regardless of hormonal treatment. However, treatment with T and DHT (with or without E₂) significantly increased AR and aromatase levels (P<0.05). Moreover, treatment with T and DHT significantly increased Ki-67 staining intensity (P<0.05).

CONCLUSIONS: These data support the hypothesis that T in the presence of an obesogenic diet increases the risk for advanced endometriosis. Moreover, androgen alone drives cell proliferation in endometriotic cells obtained from chronically treated T+WSD animals.

Table 1. Frequency and stage of endometriosis (n=10/group).

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>T</th>
<th>WSD</th>
<th>WSD + T</th>
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<tbody>
<tr>
<td>Adhesions</td>
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<td>Stage I</td>
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<td>1</td>
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<tr>
<td>Stage II</td>
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<td>Stage III</td>
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<tr>
<td>Stage IV</td>
<td>0</td>
<td>2</td>
<td>5</td>
<td>7</td>
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<tr>
<td>Total Cases</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>7</td>
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</table>

SUPPORT: NIH P50-HD071835 (RLS/JDH), and NIH 51-OD011092 (ONPRC).
ultrasound) and at least one patent fallopian tube. Women underwent OI with either CC or letrozole for up to 5 cycles. Male partners were required to have a sperm analysis with a normal sperm count of at least 15 million/ml. Chi-Square/Fisher exact. Student’s t, and logistic regression were utilized as appropriate. A p-value of <0.05 was considered statistically significant.

RESULTS: Prevalence of HiBMI was 83.5%, VHBMI 50.8%, and MetS 34.5%. For VHBMI 47% had MetS compared to 21% when BMI < 35 kg/M². The odds for clinical pregnancy (fetal heart rate) were 0.59 (0.38, 0.90) with MetS and 0.60 (0.43, 0.83) with VHBMI in the CC group. Similarly the OR for live birth were reduced, 0.55 (0.34, 0.89) with MetS and 0.61 (0.43, 0.85) with VHBMI. Pregnancy complications occurred in 42.5% with CC and 41.5% with letrozole. In the presence of MetS the OR for GDM was 2.68 (1.22, 5.85) with letrozole, adjusted for VHBMI; and it was 3.31 (1.01, 10.82) with CC. The odds for LGA were higher after adjusting for VHBMI also (both OI agents). VHBMI increased the odds (1.76 [1.25, 2.48]) for Pre-E (CC and letrozole). MetS was not associated with Pre-E in either group.

CONCLUSIONS: MetS and VHBMI lowered the odds of fecundity with CC. MetS was associated with higher odds of gestational diabetes and LGA infants after adjusting for VHBMI with both agents. MetS did not contribute to VHBMI with either agent. VHBMI in contrast was associated with greater odds for Pre-E with either. Incidence of pregnancy complications is high following OI for oligoovulation in PCOS, in part because of MetS and/or VHBMI.

SUPPORT: The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD): U10 HD077680, U10 HD39005, U10 HD38992, U10 HD38249, U10 HD38998, U10 HD355942, HD055944, U10 HD595936, and U10HD55925. This research was made possible by the funding by American Recovery and Reinvestment Act. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NICHD or NIH.

O-107 Tuesday, October 15, 2019 11:45 AM
OXIDATIVE DISEASE IS PRESENT IN LIPOPOLYSACCHARIDE (LPS) TOLERANT MONONUCLEAR CELLS (MNC) OF OBESE WOMEN WITH POLYCYSTIC OVARY SYNDROME (PCOS). Frank González, M.D., Robert V. Condizile, Ph.D., Jianping Xue, Ph.D., Anthony J. Acton, Jr., B.S. 1University of Illinois at Chicago College of Medicine, Chicago, IL; 2Indiana University School of Medicine, Indianapolis, IN.

OBJECTIVE: In PCOS, lipid-induced oxidative stress promotes inflammation.1 In vitro exposure to lipid+LPS suppresses inflammation in LPS tolerant MNC of obese women with PCOS.2,3 We examined the effect of MNC exposure to lipid alone versus lipid+LPS on IL-6 mRNA secretion, and on the mRNA and protein of p47phox, the key component of the ROS producing enzyme NADPH oxidase, in women with PCOS compared with ovarioly controls.

METHODS: Cross-sectional study.

MATERIALS AND METHODS: We studied 20 women with PCOS (10 lean; 10 obese) diagnosed on the basis of oligo-amenorrhea and hyperandrogenemia, and 20 ovarioly controls (10 lean; 10 obese) ages 18-40. MNC isolated from fasting blood samples were cultured with palmitate under pre- (0.4 mM) and post-prandial (0.2 mM) conditions with or without LPS. IL-6 and p47phox mRNA was quantified by RT-PCR. IL-6 secretion was measured by ELISA from blood samples drawn at 0, 24, 48 and 96 hours after HCG administration. Insulin sensitivity was derived by ISOGTT.

RESULTS: In response to lipid alone, the change from baseline (Δ) between pre- and post-prandial conditions increased in lean and obese women with PCOS and obese controls, and was significantly different (p<0.001) compared to the decreases seen in lean controls. ΔIL-6 and Δp47phox mRNA percent change [Δ%: 36±6 vs. 25±5; 2.5±1.2 vs. -1.8±0.6] and p47phox (mRNA: 27±4; 31±4; 22±6 vs. -2±6; protein [pg/ml]: 29±2; 35±4; 22±3 vs. -6±5). The ΔIL-6 response to lipid+LPS increased in lean women with PCOS and obese controls, and was different (p<0.001) compared with the decrease in obese women with PCOS and lean controls (mRNA: 7±1; 6±1 vs. -12±2; -11±1; secretion: 73±123; 59±19 vs. -121±33, -108±22). However, the Δp47phox response to lipid+LPS increased further in lean and obese women with PCOS and controls compared to the decrease in lean controls (mRNA: 38±5; 62±14; 32±6 vs. -9±6; protein: 38±4; 40±2; 31±3 vs. -4±5). Compared with controls, women with PCOS had a greater (p<0.02) HCG-stimulated area under the curve (AUC) for testosterone (T) (lean: 6064±676 vs. 3518±416; obese: 7639±1135 vs. 3683±180) and androstenedione (A) (lean: 510±30 vs. 312±25; obese: 562±48 vs. 321±34). For the combined groups after lipid+LPS, Δp47phox was directly correlated with AUC for T (mRNA: r = 0.66, p<0.0001; protein: r = 0.60, p<0.0001), and was inversely correlated with ISOGTT (mRNA: r = -0.57, p<0.0004; protein: r = -0.58, p<0.0002). In women with PCOS after lipid+LPS, ΔIL-6 secretion was inversely correlated with AUC for T (r = -0.47, p<0.05) and directly correlated with ISOGTT (r = 0.51, p<0.04).

CONCLUSIONS: In PCOS, lipid-induced increases in IL-6 and p47phox are independent of obesity. Oxidative capacity is preserved in the face of LPS tolerance manifested by a two-fold increase in p47phox despite IL-6 suppression when obesity accompanies PCOS. LPS tolerance may be poten-}

O-108 Tuesday, October 15, 2019 12:00 PM
SCREENING FOR ANDROGEN EXCESS IN WOMEN: ACCURACY OF SELF-REPORTED EXCESS BODY HAIR GROWTH AND MENSTRUAL IRREGULARITY.

DYSFUNCTION.

Jessica L. Chan, MD, MSCE, a Marita Pall, MD, PhD, a Uche Ezech, MD, a Ruchi Mathur, MD, a Erica T. Wang, MD, M.A.S, a Ricardo Azziz, MD, M.P.H, a Cedars-Sinai Medical Center, Los Angeles, CA; aUniversity at Albany, SUNY, Albany, NY.

OBJECTIVE: To test the use of a simple telephone questionnaire to iden-}

TIMELINE. 1. HCG-stimulated AUC for testosterone (T) was calculated as the area under the curve (AUC) for testosterone (T) (lean: 6064±676 vs. 3518±416; obese: 7639±1135 vs. 3683±180) and androstenedione (A) (lean: 510±30 vs. 312±25; obese: 562±48 vs. 321±34). For the combined groups after lipid+LPS, Δp47phox was directly correlated with AUC for T (mRNA: r = 0.66, p<0.0001; protein: r = 0.60, p<0.0001), and was inversely correlated with ISOGTT (mRNA: r = -0.57, p<0.0004; protein: r = -0.58, p<0.0002). In women with PCOS after lipid+LPS, ΔIL-6 secretion was inversely correlated with AUC for T (r = -0.47, p<0.05) and directly correlated with ISOGTT (r = 0.51, p<0.04).

CONCLUSIONS: In PCOS, lipid-induced increases in IL-6 and p47phox are independent of obesity. Oxidative capacity is preserved in the face of LPS tolerance manifested by a two-fold increase in p47phox despite IL-6 suppression when obesity accompanies PCOS. LPS tolerance may be poten-}
THE EFFECT OF HIGH HUMIDITY ON EMBRYO CULTURE MEDIA OXIDATION. Carmela Albert, PhD,a Raquel Del Gallego, PhD,b Lucia Alegre, PhD,b Zalou ZL, Larraategui, PhD,c Julian Marcos, Sr, PhD,d Belén Aparicio-Ruiz, PhD,e Marcos Meseguer, PhD,f IVIRMA, Valencia, Spain; fIVIRMA Global, Valencia, Spain; aEMBRYOLOGIST, BILBAO, Spain; aEMBRYOLOGIST, BILBAO, Spain; aIVIRMA Global, Valencia, Spain, Tel Aviv, Israel.

OBJECTIVE: Oil overlay has supported the successful use of a dry incubator to culture human embryos, preventing changes in the pH and temperature. However, dry conditions may affect the osmolality due to the evaporation of the culture media. The use of humid conditions avoids osmolality changes. Our aim in this study was to know how culture conditions might affect embryo culture related to an oxidative stress profile.

DESIGN: Retrospective multicentric study including a total of 7,544 embryos from 1,043 patients undergoing egg donation and autologous IVF treatment.

MATERIALS AND METHODS: Embryos were cultured in a time-lapse incubator system Geri (Genea Biomedix, Australia). Out of its 6 patient-independent chambers, 3 of them worked under a dry atmosphere (DC) and 3 under humid conditions (HC). Retrospectively, blastocyst and good morphology blastocyst rate were evaluated.

For the oxidative stress profiling, a total of 125 spent embryo culture media from the Geri Dishes were analyzed using the TCL (Thermochemiluminescence) Analyzer. 24 (Carmel Diagnostics, Kirtyt-Tivon, Israel). Its mechanism is based on a reduced oxidation leading to the production of light energy counted as photons emitted per second (cps). The use of sequential vs. single-step culture medium was taken into account when HC and DC were compared. Data was analyzed with ANOVA and Chi-squared tests (SPSS software).

RESULTS: No statistical differences were found in terms of embryo development. We obtained a very similar blastocyst rate when the embryos were culture under HC: 71.3% vs DC: 71.0%. Likewise, high quality embryo rate (classified as A or B according to the ASEBIR criteria) was very similar 38.1% in HC vs 37.7% in DC. Regarding the oxidative stress profile, no significant differences were found between groups HC and DC in single-step medium. However, the results showed a trend towards a higher oxidative stress level in media cultured under DC: 127.8±40.6 cps vs. HC: 106.9±44.1 cps. On the other hand, sequential medium did show a significant oxidative status difference (p < 0.05) between media collected on day 3 (75.5±20.4 cps) and media collected on day 5/6 (105.8±39.2 cps). Moreover, no significant differences were found between the oxidative status of media coming from sequential collected on day 5/6 and single-step media. These results were quite interesting as they may depict how the oxidative metabolism in the embryos increase after day 3, when the maternal to zygotic transition takes place.

CONCLUSIONS: In a previous study, our results strongly suggested that culture conditions with a high humidity atmosphere promoted embryo development. However, in an attempt to increase the sample size to confirm these findings, no statistically significant differences have been found. According to the oxidative status of the spent media, DC seem to affects the media oxidation. A larger sample size would be required to confirm this trend.

O-110 Tuesday, October 15, 2019 11:15 AM

HUMAN BLASTOCYSTS DERIVED FROM MONOPRONUCLEAR ZYGOTES: A BIOLOGICAL MODEL FOR THE STUDY OF PLOIDY, EUPLOIDY, TOPOGRAPHY AND HETERO-PARENTAL INHERITANCE. Noelia Grau, PhD,a Nuria Soler, MSc,b Ana Gonzalez-Picazo, MSc,c Xavier Vendrell, PhDb,d Maria José Escribá, PhDe,f Pilar Gámiz, PhDb,f IVIRMA-Valencia, Valencia, Spain; fUniversidad de Valencia, Valencia, Spain; fIVI Foundation, Valencia, Spain; fSistemas Genómicos, Paterna, Spain; fIVIRMA Valencia, Valencia, Spain.

OBJECTIVE: To describe the ploidy and euploidy, chromosomal concordance between different regions of the trophectoderm (TE) and also between TE and inner cell mass (ICM). Besides, we aimed to identify chromosomal inheritance (paternal/maternal) of haploid, diploid and poliploid blastocysts derived from monopronuclear (MPN) zygotes. Additionally, it will be discussed the eventual “rescue” of these blastocysts for reproductive purposes.

DESIGN: Prospective experimental study that includes 910 ICSI cycles from September 2013 to December 2018. 1081 MPN zygotes (1.2%) were obtained. A total of 199 zygotes reached the blastocyst stage (18.5%, blastocyst rate). Seventy-six blastocysts were assigned to three experimental series, according to the genetic analysis performed (ploidy, topography and parental inheritance).

MATERIALS AND METHODS: The study was carried out in 3 series. Series 1: 26 blastocysts were fixed by FISH (chromosomes X, Y, and 18) to assess ploidy. Series 2: 35 blastocysts were biopsied in three samples, two from TE (TE1 and TE2) and ICM. TE1 let us to determinate ploidy by FISH (chromosomes X, Y, 18); TE2 and ICM were used for 24-chromosomes study by NGS. Series 3: 15 blastocysts were biopsied as described in Series 2. TE1: study of 24 chromosomes by NGS. TE2: study of 24 chromosomes and SNPs (single nucleotide polymorphisms) by SNP-array of 750K in a “triploidy, topography and parental inheritance.”
RESULTS: 80.5% of MPN-derived blastocysts were diploid, 8% mosaic and 11.5% haploid (P<0.01). Diploid blastocysts showed a normal sex ratio (1:1); 50% diploid blastocysts were aneuploid. In relation to chromosomal topography, results showed different patterns, according to the chromosomal instability grade. The two green compartments (TE and ICM) was perfectly matched when both compartments were euploid or whole-chromo-some aneuploid (trisomies and monosomies). Incomplete matching between compartments was observed in complex (> 3 chromosomes involved), segmental or mosaic samples, which were more frequently observed in those from TE. 70% MPN-derived blastocysts showed two copies of both parental genomes. In relation to parental inheritance, 40% of blastocysts were diploid heterozygous.

CONCLUSIONS: The MPN experimental model confirms the chromo-somal correlation between ICM and different regions of TE, in cases of euploidy or pure aneuploidy. The chromosomal instability associated to segmental aneuploidy seems to be confined equally to both TE and ICM com-partments. A high percentage of MPN-derived blastocysts showed two copies of both parental and euploid genomes. These data re-open debate on their convenience for clinical reproductive use.

ACIF/2018/076
APOTI/2019/A/010
SUPPORT: IMIDCA/2018/25 (IVACE; PIDCOP-CV)

O-112 Tuesday, October 15, 2019 11:30 AM

USE OF NEXT GENERATION SEQUENCING FOR THE ANALYSIS OF IN VITRO MATURATED OOCYTES AND THEIR POLAR BODIES. Marga Esbert, PhD, Cristina Garcia, MSc, Evelin E. Lara-Molina, MD, Nicolas Garrido, PhD, Dagan Wells, PhD, Emre Seli, M.D., Georgina Cuts, MSc, Agustín Ballesteros, PhD, Javier Herrera, Sr., MSc, Marissa Riqueros, MSc, Elpida Fragouli, PhD, IVI RMA Barcelona, Barcelona, Spain; IVI Foundation IVIRMA Global, Biomedical Research Institute La Fe, Valencia, Spain; IVI Foundation, IIS La Fe, Valencia, IIS, Spain; IVI RMA, Oxford, United Kingdom; IVI-RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: Approximately 15% of retrieved oocytes are immature, 11% at the germinal vesicle (GV) stage, 4% at metaphase I (MI). To date the success rates of in vitro maturation (IVM) have been low. It has been sug-gested that IVM oocytes, if fertilized, may lead to abnormal embryos and an increased risk of spontaneous miscarriages. Consequently, immature oocytes are usually discarded.

The aim of our study was to perform a detailed cytogenetic analysis of in vitro matured oocytes and compare with the chromosome constitution of oocytes which were mature (metaphase II; MII) at the time of retrieval.

DESIGN: Prospective non-randomized study.

MATERIALS AND METHODS: The oocytes examined were generated by sixteen young and healthy oocyte donors participated in the study. The average age was 27 years (range 21-30 years), participants of 34 oocytes were included (22 MII and 21 GV). Oocytes identified to be at the GV stage were cultured individually in 25 μl of Gems® Geri® medium in a time-lapse incubator for up to 50.0 hours to achieve IVM and to determine the time needed for polar body (PB) extrusion. Biopsy of the 1st PB was performed once these oocytes matured to MII. Similarly, mature MII oocytes (n=22) underwent 1st PB biopsy. The cytogenetic constitution of IVM and mature oocyte-PB pairs was assessed using a well validated next generation sequencing (NGS) strategy for the identification of chromosome and chromatid errors arising during female meiosis.

RESULTS: Sixty-two percent of GV oocytes matured in vitro to MII after an average culture of 26.1 hours (95% CI 23.2-29.0). A total of 35 oocyte-PB pairs underwent NGS analysis. Of these, 13 originated from GVs and 22 that were at the MII stage at retrieval. The overall euploidy rate observed was very similar between the two groups, i.e. 76.9% for the oocyte-PB pairs which were retrieved at the GV stage and 78.4% for the mature MII oocyte-PB pairs. The majority of abnormalities (60%) scored were due to unbalanced chromatid predivision, with the remaining 40% arising due to whole chromo-some non-disjunction. No difference in IVM culture length was observed between normal and abnormal GV oocytes that reached the MII stage (26.1 hrs. [95%CI 22.3-30.9] vs. 25.93 hrs. [95%CI 17.4-34.5]).

CONCLUSIONS: To our knowledge, this is the first study to describe the use of NGS for cytogenetic analysis of in vitro matured human oocytes. Our findings suggest that GV oocytes, matured to MII in vitro, segregate their chromosomes in a manner equivalent to those that mature within the follicle. The fact that aneuploidy is not increased following IVM supports the idea that an attempt should be made to “rescue” immature oocytes, rather than discarding them. Further work is required to understand the basis of the poorer outcomes associated with IVM oocytes, but these results indicate that the cause is not cytogenetic in nature.

O-113 Tuesday, October 15, 2019 11:45 AM

TIME LAPSE SELECTED ELECTIVE SINGLE EMBRYO TRANSFER IN HYALURONON ENRICHED TRANSFER MEDIUM IN PCOS IMPROVES LIVE BIRTH RATES COMPARED TO USE OF CONVENTIONAL EMBRYO TRANSFER MEDIA. A POSSIBLE ALTERNATIVE TO FREEZE-ALL CYCLES IN PCOS. Sayali Kandari, MS PhD. CELLUSIRE BIOTECH AND RESEARCH CENTRE, Mumbai, India.

OBJECTIVE: Polycystic ovarian syndrome(PCOS) is shown to impair endometrial receptivity due to disturbed receptor mediation or gene expression affecting implantation rates, miscarriage rates, and live birth rates in fresh embryo transfer(ET). Freeze-all is being used as a strategy to counter ovarian hyperstimulation syndrome(OHSS) and reduced receptivity in PCOS. The added intervention of vitrification and endometrial preparation in subsequent cycles increases cost and time associated with treatment signific-antly. 2014 Cochrane review of use of adherence compounds shows mod-erate evidence that Embryoglue (EG) increases implantation and pregnancy rates, but no study has been designed using EG with sET in PCOS. With time lapse and sET, fresh ETs are advised, avoiding OHSS, but still, implantation rates remain low. We wanted to evaluate whether use of embryo transfer medium enriched with hyaluronan (EmbryoGlue - Vitrolife, Gothenburg, Swe-den) improves outcomes over conventional vitrification and single embryo transfer and miscarriage rates in time lapse(sET) selected fresh sET in PCOS.

DESIGN: Prospective randomized study.

MATERIALS AND METHODS: Fresh embryo transfers between January 2017 and August 2018 in PCOS patients classified by Rotterdam criteria were included. Sample size was calculated with n=152 in each arm for statistical power of the study at 80% with alpha = 0.05, beta =0.2. Time Lapse imaging as discussed by N.Desai et al for embryo selection was adopted for sET. Fertilization and embryo culture conditions were similar in both groups. Fertilization was conducted in CSMC medium (Irvine, CA,USA) and the embryos were transferred into CSMC for uninterrupted time lapse culture in Mini-TL(ESCO,Singapore). Patients were randomly allocated on day of embryo transfer into two groups: In the EmbryoGlue group (153 pa-tients), single cleavage stage or blastocyst was transferred in EmbryoGlue medium that contains 0.5 mg/ml hyaluronan (Vitrolife, Gothenburg, Swe-den). In the control group (168 patients) single cleavage stage embryo or blastocyst was transferred in medium CSMC (Irvine, CA,USA). The Chi square test was used for comparison of proportions and the Mann-Whitney U test was used to compare the differences between the groups.

RESULTS: The EG and control group were similar with respect to age (32.7 +/- 3.6 and 31.7+/- 3.6 respectively), infertility duration (3.8+/-2.1 years and 3.3+/-2.6 years), previous IVF cycles (1.3 +/-1.5 and 1.1+/-1), oocyte number (14.4+/-5.2 and 13.2+/-5), and stage of transferred embryo (17% vs 21% cleavage stage embryos, and 83% vs 79% blastocyst stage embryos). The implantation rate in EG and control group were 39.2% vs 23.8% (p<0.005) and live birth rate were 35.9% vs 17.3%(p<0.001) respec-tively and miscarriage rates were 8.3% in EG vs 28% in control group (p=0.17).

CONCLUSIONS: The use of embryoglue for time lapse selected sET in PCOS shows significant increase in implantation and live birth rates with lower miscarriage rates compared with conventional embryo transfer medium. This strategy should also be explored to improve outcomes as an effect-ive alternative to freeze-all cycles for PCOS patients.

To determine whether the incubator or the dish were responsible for these increases, the Geri dish was used to grow all embryos in Phase II and half of the oocytes placed in the K systems G210 and half in the Geri incubator. While the n is low, more good quality embryos were observed in the Geri incubator. The Geri incubator is an effective incubator yielding good quality blastocysts. More studies are required to determine if a single step media gives the same results.

References: none

SUPPORT: none

EARLY PREGNANCY

O-115 Tuesday, October 15, 2019 10:45 AM

RETAINED PREGNANCY TISSUE AFTER MISCARRIAGE ASSOCIATED WITH HIGH RATE OF CHRONIC ENDOMETRITIS. Dana B. McQueen, M.D., M.A.S., Kruti P. Maniar, M.D., Anne Hutchinson, M.D., Rafael Confino, BS, Jared C. Robins, MD, Lia A. Bernardi, MD, Mary Ellen Pavone, MD, MSCI. Northwestern University, Chicago, IL.

OBJECTIVE: To compare the prevalence of chronic endometritis in women undergoing hysteroscopic resection of retained pregnancy tissue (RPOC) after pregnancy loss to women with unexplained recurrent pregnancy loss (RPL).

DESIGN: Cohort study.

MATERIALS AND METHODS: Institutional Review Board approval was obtained. Women undergoing hysteroscopic resection of RPOC between 6/2008 and 12/2018 were included. In addition, women with unexplained RPL undergoing endometrial sampling between 1/2016 and 12/2018 were included. Unexplained RPL was defined as two or more pregnancy losses with a TSH level under 4 mIU/L, negative antiphospholipid antibodies and normal uterine anatomy. Data on pregnancy history, time since last pregnancy loss and gestational age at time of loss were collected. H&E and immunohistochemical staining for CD138 were performed on all slides. A single pathologist blinded to patient history recorded the number of plasma cells per high power field (HPF). Chronic endometritis was defined as 1 or more plasma cells/10 HPF in addition to stromal changes (spindling, edema, foci of breakdown, presence of other inflammatory cells, and pigment deposition). In order to detect a 25% difference in the rate of chronic endometritis with 80% power and alpha of 0.05, a sample size of 49 women was needed in each group.

RESULTS: Endometrial samples from a total of 100 women were evaluated (50 women undergoing resection of RPOC and 50 women with unexplained RPL). The mean age was similar between groups, 36.4 (SD 4.7) vs 35.2 (SD 4.1) years, P=0.18. The mean number of prior pregnancy losses was 1.9 (SD 1.0) in the RPOC group vs. 3.1 (SD 0.9) in the RPL group, P=0.0001. By H&E staining, chronic endometritis was present in 60% (30/50) of women undergoing resection of RPOC vs. 35% (17/50) of women biopsied for RPL, P<0.0001. By CD138 staining, chronic endometritis was present in 62% (31/50) of women undergoing resection of RPOC vs. 30% (15/50) of women biopsied for RPL, P=0.002. In a subgroup analysis that only included women with RPL, chronic endometritis was present in 71% (20/28) of women with both RPL and RPOC vs. 24% (12/50) of women with RPL alone, P=0.0001 (H&E). Among women with RPL without
suspected RPOC, an implantation site or placental site nodule was reported in three women, and all three of these women had chronic endometritis.

CONCLUSIONS: Following miscarriage, retained pregnancy tissue is associated with a high prevalence of chronic endometritis. A hysteroscopy to evaluate for retained pregnancy tissue may be warranted in women with RPL who are diagnosed with chronic endometritis. Further research is needed to determine if resection of retained tissue is sufficient to treat RPOC associated chronic endometritis, or if additional antibiotic treatment is necessary.

SUPPORT: Friends of Prentice Grant

O-117 Tuesday, October 15, 2019 11:00 AM

IS THERE A PREDISPOSITION TO EMBRYONIC ANEUPLOIDY IN PRE-DIABETIC PATIENTS? Baruch Abititan, M.D.,a Hillary Pearo, M.D.,a,c Randi H. Goldma, M.D.,a Christine Mullin, M.D.,a Weiwei Shan, M.S. Ph.D.,a,b Avner Herslag, M.D.,a Northwell Fertility, Manhasset, NY; aNorth Shore University Hospital, Manhasset, NY; aNorthwell Health Fertility, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY; aNorthwell Fertility; aNorthwell Health Department of Biostatistics, New Hyde Park, NY.

OBJECTIVE: There is a correlation between glycated hemoglobin (HbA1C) values in early pregnancy (> 8%) and frequency of miscarriage and congenital malformations. To date, no study has analyzed the risk of aneuploidy with HbA1C values in the pre-diabetic range. The purpose of this study is to examine the relationship between HbA1C and embryo aneuploidy after IVF with preimplantation genetic testing for aneuploidy (PGT-A).

DESIGN: Retrospective cohort study at an academic medical center.

MATERIALS AND METHODS: We included IVF-PGT-A cycles between 2013-2017. Demographics, oocyte retrieval data, embryo development and ploidy status were reviewed. Patients with a diabetic HbA1C (> 6.5%) were excluded. Pearson correlation compared maternal HbA1C with embryo aneuploidy rate. Wilcoxon rank test compared IVF outcomes and embryo aneuploidy rates between non-diabetic (HbA1C <5.7%) vs. pre-diabetic (HbA1C 5.7-6.4%) patients.

RESULTS: A total of 1,867 blastocysts from 393 patients were analyzed with PGT-A. Three hundred twenty (81.4%) patients had normal HbA1C values and 73 (18.6%) had pre-diabetes. Three hundred thirty-five patients (85.2%) had embryos with autosomal aneuploidy. Fifty-six patients (14.2%) had sex-chromosome aneuploidy of them, 4.8% had embryos with karyotype 45X.

Pre-diabetic HbA1C was significantly correlated with the rate of sex chromosome aneuploidy with HbA1C values in the pre-diabetic range. The purpose of this study is to examine the relationship between HbA1C and embryo aneuploidy after IVF with preimplantation genetic testing for aneuploidy (PGT-A).

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Pre-diabetic HbA1C was significantly correlated with the rate of sex chromosome aneuploidy with HbA1C values in the pre-diabetic range. The purpose of this study is to examine the relationship between HbA1C and embryo aneuploidy after IVF with preimplantation genetic testing for aneuploidy (PGT-A).

CONCLUSIONS: After adjusting for clinical parameters, embryonic expansion, and inner cell mass grade; our data showed euploid embryo TE quality and early levels of a-T-HCG, a biochemical marker of early embryo implantation and placenta. Previously, we demonstrated that embryo TE quality does not correlate with major adverse perinatal outcomes or placental weight at delivery. However, patients who had transfer of embryo(s) with a low TE grade experienced placental histological changes. (Herlihy et al. 2017) This study included patients who underwent a single, euploid frozen embryo transfer (FET) and assessed the correlation between embryo TE grade and early a-T-HCG levels.

DESIGN: Retrospective cohort analysis.

MATERIALS AND METHODS: This study included patients who underwent a single, euploid FET cycle and obtained a positive pregnancy test (serum a-T-HCG ≥5 mIU/mL) from 2015 to 2019. The a-T-HCG measurement was analyzed 9 days after FET using an electrochemiluminescence immunoassays (Immulite 2000; Siemens and/or Cobas e-601; Roche). Only cases that had a first a-T-HCG measurement on day 9 after ET were included in the analysis. Blastocyst morphology was assessed using a center-specific, modified Gardner’s scoring system. ANOVA, χ2 tests, univariate, multivariate linear regression and a mixed effects model with a random intercept model were used to evaluate serum a-T-HCG levels with regard to TE grade.

RESULTS: A total of 2,954 single, euploid FET cycles were included in the analysis. CoHorts were segregated by TE grade: (TE-A: n=1,235; TE-C: n=643), a-T-HCG values were significantly different among cohorts (TE-A: 155.5±97; TE-B: 133.7±80; TE-C: 94.1±73, p<0.0001) and early pregnancy loss (EPL) was significantly higher in embryos with low TE grades: (TE-A:14.6%;TE-B:15.3%;TE-C: 19.2%; p=0.01) There was a significant correlation between TE grade and mean a-T-HCG levels (R2: 0.06, p<0.001). After adjusting for age, BMI, endometrial thickness at ET, ICM grade experienced placental histological changes. (Herlihy et al. 2017) This study included patients who underwent a single, euploid frozen embryo transfer (FET) and assessed the correlation between embryo TE grade and early a-T-HCG levels.

CONCLUSIONS: After adjusting for clinical parameters, embryonic expansion, and inner cell mass grade; our data showed euploid embryo TE grade correlates with a-T-HCG levels at first pregnancy test measurement. The ultrastructural appearance of the TE cells in euploid embryos might represent a surrogate marker of embryo’s capacity to properly adhere and invade the endometrium during the early implantation process. Further studies focusing on syncytiotrophoblast and endometrial cellular and molecular interactions could help reproductive specialists to better understand the mechanisms related to early placental physiology.


SUPPORT: none

O-118 Tuesday, October 15, 2019 11:30 AM

PATERNAL CONTRIBUTIONS IN EARLY EMBRYONIC GENE EXPRESSION: ROLE IN EARLY PREGNANCY LOSS. Vidhu Dhadaw, MD,a Manoj Kumar, Ph.D.,b Neena Malhotra, MD FRCOG, Neeta Singh, MD,b Vatsla Dadhwal, MD,a Rima Dada, MD, Ph.D.a All India Institute of Medical Sciences, New Delhi, India.

OBJECTIVE: A total of 2,954 single, euploid FET cycles were included in the analysis. CoHorts were segregated by TE grade: (TE-A: n=1,235; TE-C: n=643), a-T-HCG values were significantly different among cohorts (TE-A: 155.5±97; TE-B: 133.7±80; TE-C: 94.1±73, p<0.0001) and early pregnancy loss (EPL) was significantly higher in embryos with low TE grades: (TE-A:14.6%;TE-B:15.3%;TE-C: 19.2%; p=0.01) There was a significant correlation between TE grade and mean a-T-HCG levels (R2: 0.06, p<0.001). After adjusting for age, BMI, endometrial thickness at ET, ICM grade experienced placental histological changes. (Herlihy et al. 2017) This study included patients who underwent a single, euploid frozen embryo transfer (FET) and assessed the correlation between embryo TE grade and early a-T-HCG levels.

CONCLUSIONS: After adjusting for clinical parameters, embryonic expansion, and inner cell mass grade; our data showed euploid embryo TE grade correlates with a-T-HCG levels at first pregnancy test measurement. The ultrastructural appearance of the TE cells in euploid embryos might represent a surrogate marker of embryo’s capacity to properly adhere and invade the endometrium during the early implantation process. Further studies focusing on syncytiotrophoblast and endometrial cellular and molecular interactions could help reproductive specialists to better understand the mechanisms related to early placental physiology.


SUPPORT: none
Medical Sciences, Anatomy, New Delhi, India; aAll India Institute of Medical Sciences, Obstetrics & Gynaecology, New Delhi, India.

OBJECTIVE: The dynamic interplay of the vulnerable sperm genomic and extragenomic cargo with the early embryonic development in spontaneous and assisted conceptions has been brought to surface. The suite of sperm transcripts retained in the spermatozoon and the complex epigenetically marked sperm genome synergistically function to influence early embryonic development. Dysregulated gene expression and disrupted genomic integrity resulting in early pregnancy loss needs to be further elucidated.

DESIGN: A case control study.

MATERIALS AND METHODS: Male partners of females who experienced recurrent pregnancy loss (RPL, N=75) and recurrent implantation failures (RIF, n=75) and 75 healthy fertile controls were recruited for the study and semen samples were obtained. Gene expression analysis of the genes critical for embryonic development and DNA damage repair parameters [RPL10A, STAT4, FOXG1, SOX3, RPS6, RBM9, RPL10A, RPS17, RPL29, TOMM7, EIF5A, OGG1 and PARP1] was analyzed by qPCR analysis after normalisation with β-actin and GAPDH. Functional assessment of semen included cardinal biomarkers of oxidative stress by reactive oxygen species (ROS), DNA damage by DNA fragmentation index (DFI) and 8-OhdG levels as well as telomere length in sperm DNA:

RESULTS: The relative gene expression of FOXG1 (P=0.048), SOX3 (P=0.03), RPS6, RBM9 and RPL10A (P=0.001) was seen to differ significantly between RPL patients and controls, while the expression of FOXG1 (P=0.02), RPS6, RBM9 and TOMM7 (P<0.001), RPL10A (P=0.039) and RPS17 (P=0.002) in RIF patients as compared to controls. The levels of ROS, DFI and 8-OHdG were found to be significantly higher as compared to controls and telomere length was found to be significantly different in both RPL and RIF patients with respect to controls. The odds of occurrence of RPL and RIF was 12.41 and 12.68 times greater with ROS>15 [OR 12.41 (6.53-23.55) and 13.68 (6.52-28.71)] respectively. The odds of occurrence was 12.68 and 18.87 time greater with DFI>31 [OR 12.68 (6.28-21.22) AND 18.87 (5.43-27.67)] respectively.

CONCLUSIONS: The orchestration of selective paternal transcripts as well as genomic integrity and telomere length is a critical determinant of early embryonic development and embryo viability. The derangements in sperm functional characteristics and gene expression has the potential to produce adverse transgenerational fetal effects and health of future progeny. The adoption of sperm RNA expression can be established as an integral part of clinical diagnostic measures among other seminal biomarkers.

TABLE 1. Relationships between low day 5 hCG level (<5 IU/L) and transfer outcome.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Risk ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Implantation failure</td>
<td>100</td>
<td>89.3</td>
<td>70.9</td>
<td>100</td>
<td>undefined</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Biochemical pregnancy loss</td>
<td>43.7</td>
<td>92.8</td>
<td>39.2</td>
<td>93.9</td>
<td>6.48 (4.32-9.74)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Eclectic pregnancy</td>
<td>75.0</td>
<td>89.7</td>
<td>3.8</td>
<td>99.9</td>
<td>25.10 (2.64-238.42)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Early SAB</td>
<td>11.8</td>
<td>94.3</td>
<td>31.1</td>
<td>83.0</td>
<td>1.83 (1.15-2.93)</td>
<td>0.017</td>
</tr>
<tr>
<td>Late SAB</td>
<td>20.0</td>
<td>94.3</td>
<td>3.1</td>
<td>99.2</td>
<td>4.04 (0.46-35.09)</td>
<td>0.174</td>
</tr>
<tr>
<td>All pregnancy losses</td>
<td>30.0</td>
<td>93.1</td>
<td>61.2</td>
<td>78.5</td>
<td>2.84 (2.10-3.85)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

O-119 Tuesday, October 15, 2019 11:45 AM

PREGNANCY VIABILITY IDENTIFIED BY EARLY SERUM HCG LEVEL MEASURED IN THE PERI-IMPLANTATION PERIOD FOLLOWING THAWED SINGLE BLASTOCYST TRANSFER. Ankita Raman, MD.a
Angela H. Liu, MD.b, Carrie E. Bedient, MD.b, Leah A. Kaye, MD.b, Forest C. Garner, MS.b, Bruce Shapiro, M.D., Ph.D., H.C.L.D.b
aUniversity of Nevada, Las Vegas, School of Medicine, Las Vegas, NV; bFertility Center of Las Vegas, Las Vegas, NV; cUniversity of Nevada, Las Vegas, NV; dFertility Center of Las Vegas, Las Vegas, NV; eUniversity of Nevada, Las Vegas, NV.

OBJECTIVE: To assess the extent to which outcome of thawed single blastocyst transfer is predicted by serum hCG level measured 5 days post transfer.

DESIGN: Retrospective cohort study of vitrified-warmed single blastocyst transfers performed over a 5-year period at a private fertility center.

MATERIALS AND METHODS: After artificial endometrial preparation, vitrified-warmed blastocysts were transferred on the 6th day of exogenous progesterone exposure. Serum hCG levels were measured 5 and 10 days after transfer. Serum hCG level below 5 IU/L on both days defined implantation failure. Biochemical pregnancy losses were transient hCG elevations that resolved spontaneously without sonographic evidence of intrauterine pregnancy (IUP). Ectopic pregnancies included persisting pregnancies of unknown location that resolved after treatment. Early spontaneous abortions (SAB) were IUPs lost before 10 weeks gestation, while late SABs were those lost after 10 weeks gestation. Implantation failures were analyzed among all transfers. Biochemical pregnancy losses and ectopic pregnancies were analyzed among all pregnancies, early SABs were analyzed among patients with IUP, and late SABs were analyzed among patients with ongoing pregnancies at 10 weeks. Chi-square tests were used in all comparisons. P<0.05 was considered statistically significant.

RESULTS: There were 932 vitrified-warmed single-blastocyst transfers during the study period which resulted in 192 implantation failures, 633 IUPS, 549 ongoing pregnancies and 199 pregnancy losses of all types. Sensitivity, specificity, positive predictive value, negative predictive value, and relative risk are shown in Table 1. Day 5 serum hCG level < 5 IU/ml was found to have high negative predictive value for all adverse pregnancy outcomes except late SAB.

CONCLUSIONS: The eventual fate of an early implanting embryo is largely determined within 5 days of transfer. Even among pregnancies with sonographically confirmed IUP, low day 5 hCG correlated with early SAB. Whether pregnancy losses following low day 5 hCG result from flawed implantation events or inherently non-viable embryos is yet to be resolved.

O-120 Tuesday, October 15, 2019 12:00 PM

SEMINAL EXOSOMES PROTEOME PROFILING REVEAL IMPAIRED CELL SIGNALING AND DEFECTS IN CHROMATIN REMODELING AS PATERNAL CONTRIBUTORS IN RECURRENT PREGNANCY LOSS PATIENTS. Luna Samanta, PhD.a, Soumya Ranjan Jena, M.Phil.b, Jasmine Nayak, M.Phil.b, Gayatri Mohanty, PhD.a, Sujata Kar, MBBS MD.a
aRedox Biology Laboratory, Department of Zoology, Center of Excellence in Environment and Public Health, Ravenshaw University, Cuttack, Odisha, India; bRedox Biology Laboratory, Center of Excellence in
OBJECTIVE: Spontaneous recurrent pregnancy loss (RPL) is most often investigated from the women’s perspective. However, recent evidence suggests the involvement of male factor as a plausible cause particularly in idiopathic RPL. Despite being transcriptionally and translationally quiescent, spermatozoa undergo maturation during transit through epididymal and female reproductive tract. Many proteins and regulatory RNAs associated with the exosomes (epididymosomes and prostasomes) are known selectively transfer their cargo to the sperm thereby modify sperm function. However, the proteome profile of exosomes in general and RPL in particular is largely unknown. Therefore, the main objective of the present study is to identify and understand the possible paternal factors responsible for early pregnancy loss through differential proteomic analysis of seminal exosomal proteins.

DESIGN: Prospective case-control study involving consented participants comprising of fertile donor (n = 21) and partners of spontaneous idiopathic recurrent pregnancy loss patients (n = 21).

MATERIALS AND METHODS: Seminal exosomes were isolated by ultracentrifugation and characterized by western blot, transmission electron microscopy, and nanoparticle tracking analysis followed by label free liquid chromatography mass spectroscopy (LC-MS/MS) and bioinformatics pathway analysis (Ingenuity Pathway Analysis: IPA, Qiagen) and STRING protein-protein interaction (PPI) analysis.

RESULTS: A total of the 998 proteins were detected in the data set (Control: 939 and RPL: 935). Of the 447 differentially expressed proteins 385 underexpressed and 62 overexpressed in RPL while 63 and 59 proteins were exclusive to control and RPL, respectively. Immune response (HSA:168256; false discover rate p = 2.67e-28), signalling proteins (HSA:376176; false discover rate p = 3.04e-22), chromatin packaging and remodeling (GO:0031497; false discover rate p = 2.78e-05), protein folding and apoptosis (HSA:109581; false discover rate p = 5.93e-06) were the major pathways impaired in RPL as revealed by STRING-PPI analysis. Pathway analysis by IPA showed developmental, hereditary and immunological disorders were the top diseases while cell death and survival, cellular assembly and organization, DNA replication, recombination and repair, gene expression were the major functions that were deregulated in RPL spermatooza. Overexpression of HNRNPC and HNRNPU in RPL may be responsible for defective chromatin organization and shortening of telomere-length while underexpression of RUVBL1 may be responsible for altered centrosome function leading to abnormal embryo development.

CONCLUSIONS: The result of this pilot study implies the importance of exosomes in sperm maturation and function, particularly in RPL. Further validation alongside the proteome profiling of spermatooza may lead to identification of candidate biomarkers for determination of male factors in RPL.

SUPPORT: Higher Education Department, Government of Odisha, A University Grant Commission and Department of Science and Technology, Government of India.
OBJECTIVE: Historically, a large percentage of IVF clinics did not adhere to Society for Assisted Reproductive Technology (SART) guidelines for online advertising. New website guidelines, effective January 2018, are clear in expectations requiring a link to clinics’ success rates on the SART site and statistical explanations alongside explicit rules about presenting supplemental data in its entirety specifying that “no partial presentation is allowed”. SART emphasizes that “adherence to this advertising policy is a requirement for membership in SART”. This study examined if SART member IVF centers adhere to this new SART advertising policy.

DESIGN: Cross-Sectional Evaluation.

MATERIALS AND METHODS: 203 IVF center websites were examined. Univariate analysis was used for descriptive data and Fisher’s exact test was used to compare categorical data between subgroups.

RESULTS: Only 50.5% of clinics provided a link to the SART website and, similarly, only 51.9% provided the required disclaimer statement regarding their outcome statistics. Disturbingly, only 9.5% of websites followed SART requirements about the presentation of supplemental data. There were no significant differences between academic and non-academic centers, those in mandated vs non-mandated states, or East versus West Coast clinics in any of the above areas (table 1).

CONCLUSIONS: Only half of surveyed websites adhere to SART’s core guidelines surrounding reporting with lower compliance percentages in other areas. Consideration for additional education could be considered and enforcement of guidelines should be enhanced.

SUPPORT: None

O-123 Tuesday, October 15, 2019 11:15 AM

INFERTILITY IN THE DIGITAL AGE: AN OPPORTUNITY FOR REI PHYSICIANS TO COMBAT THE SPREAD OF MISINFORMATION AND FILL SUPPORT GAPS IN INFERTILITY CARE ONLINE. Emily A. Jacobs, MD, Ginny L. Ryan, MD, MA. University of Iowa Carver College of Medicine, Iowa City, IA.

OBJECTIVE: To examine infertility related content posted on Instagram, including content of posts and identity of content posters.

DESIGN: Retrospective content analysis.

MATERIALS AND METHODS: Data from Instagram were obtained on April 20, 2019. One author queried 42 popular hashtags, including both medical and lay person terminology, related to infertility diagnosis, treatment and procedures. The total number of posts from each hashtag was recorded. Each of the top ten posts (as determined by Instagram’s internal algorithm) for the 42 hashtags was then analyzed to qualitatively identify the content of each post. The post category was determined by the lead author based on the content of the post and the overall message it sent to its readers. The number of likes and comments were also recorded for each post. Lastly, data on the individual who posted were also recorded by analyzing that poster’s Instagram profile.

RESULTS: A total of 5,814,691 posts were tagged with the 42 unique hashtags queried for this study. 315 of the 420 “top posts” met inclusion criteria. Of the hashtags, #PCOS had the highest number of posts associated with it (2,000,000 posts). From the 315 included posts, 271 unique posters were identified. 239 of these posters were non-healthcare related individuals (88%) and 32 (12%) were healthcare related persons. There were 14 self-identified US physicians. All but one had verified credentials. By far, the most common type of post for non-healthcare related individuals was related to their infertility journey (60%). In contrast, the majority of posts created by healthcare-related individuals were educational (41%).

When comparing US verified physician posting versus all other posters, US physicians were more likely to post educational (33% vs 9%, p<0.0006) and promotional posts (33% vs 1%, p<0.0001) and less likely to post about a personal infertility journey (5% vs 58%, p<0.0001). There was no significant difference in ‘likes’ between the two groups (194±200 for US physicians vs 430±787 for all other posters, p=1.71). There was a significant difference in the number of comments between the two groups, with fewer comments in response to US physicians than all other posters (1.2±16 vs 36±51, p=0.015).

No infertility postings by verified US physicians contained medical advice or medical questions. In contrast, 5% and 2% of postings by all other individuals gave medical advice or asked a medical question, respectively. Some of the medical advice given included taking 40mg/day of black cohosh for ovulation induction, using cannabis suppositories to shrink fibroids, and recommending supplements to increase fertility (who were often sold by the poster).

CONCLUSIONS: Instagram and other social media platforms have the potential to be highly influential in the infertility population. Physicians, particularly board-certified reproductive endocrinologists, should consider taking steps towards having a stronger presence online to combat the spread of misinformation that currently dominates these highly used platforms, and to help bridge gaps in access to infertility care.

O-124 Tuesday, October 15, 2019 11:30 AM

ADVANCING LAWS TO PERMIT SURROGACY IN US STATES: CHALLENGES & SOLUTIONS FOR ART PROVIDERS & OTHERS. Robert Klitzman, MD. Columbia University, NY, NY.

OBJECTIVE: To understand how to advance legalization of surrogacy, through data addressing opponents’ concerns

DESIGN: Analysis of state laws & discussions with state policymakers & others

MATERIALS AND METHODS: N/A

RESULTS: Many prospective parents face legal barriers to hiring traditional or gestational surrogates, posing critical questions of whether ART providers & others can address these obstacles & if so, how. A few US states (e.g., California) allow paid gestational surrogacy, upholding legal contracts that prohibit birth mothers from keeping the baby. Yet following the Baby M case, & largely due to fears of exploiting women as surrogates, US states range widely in whether they permit, prohibit, or limit surrogacy & how they enforce such laws. Recently, traditional surrogacy is allowed (since it is not explicitly banned) in 16 states; permitted by statute without much detail in 5; permitted by statute with restrictions in 2; permitted only if unpaid in 4; permitted but with unenforceable contracts in 9; practiced, though contracts are banned, in 2; not practiced because contracts are banned in 4; & unpredictable in 9. Gestational surrogacy is allowed by law in 3 states; allowed (since not explicitly banned) in 22; allowed by statute without much detail in 7; permitted with restrictions in 6; allowed with unenforceable contracts in 1; supported but with no law in 6; practiced, though contracts are prohibited in 5; & not practiced since contracts are prohibited in Washington, DC. States differ in how much surrogates can be paid (e.g., whether more than basic expenses); whether surrogates can change their minds & if so, in when; whether court approval & state residency are needed; & whether an intended parent must provide gametes.

Advocates have unsuccessfully tried altering laws in NY & elsewhere. Opponents tend to draw on conservative Christian arguments (and wariness of much ART) or feminist concerns that most surrogates will be poor & thus taken advantage of. Yet no data exist about these claims. Crucial questions thus arise of why women choose to be surrogates - e.g., who surrogates in fact are & how they see these issues. Anecdotally, many such women are middle class, fully grasp the risks & benefits, having given birth to their own children & feel that the rewards are worth it. Data on gestational surrogates are thus essential - e.g., on their socioeconomic status, motivations & views of their experiences – how they perceive & experience it & whether they view it, retrospectively, favorably or regretfully – to assess whether claims of exploitation are correct. Such data, if they reveal few concerns, can prompt other states to permit surrogacy, assisting many parents. These data can also be vital in educating patients, providers & the public at large about these issues. ART providers could thus help by collecting such data. Widening use of electronic medical records can facilitate collection of some of these data. Providers could also work closely with patient groups on these goals.

CONCLUSIONS: ART providers & others can advance legislation of paid gestational & other surrogacy & thus aid patients through collection of key data.

O-125 Tuesday, October 15, 2019 11:45 AM

EVALUATING THE SART CLINIC SUMMARY REPORTS – IS IT ONLY ABOUT THE LIVE BIRTH RATES? WHAT ABOUT THE SIGNIFICANT MORBIDITY/MORTALITY RISK FACTORS ASSOCIATED WITH MULTIPLE GESTATIONS?. Carrie Riestenberg, MD, A Alin Lina Akopians, MD, PhD, Deborah E. Johnson, MA, Zachary Haimowitz, BS, Hal C. Danzer, MD, Mark W. Surrey, MD, Jason A. Barratt, PhD. University of California, Los Angeles, Los Angeles, CA; Southern California
OBJECTIVE: In 1992, HR 4773, the Fertility Clinic Success Rate and Certification Act, also known as the Wyden bill, was passed mandating public reporting of fertility clinic pregnancy success rates. Currently, >90% of ART clinics in the USA report to SART. The CDC, SART and ASRM work together to publish annual reports of clinic’s pregnancy outcomes. SART warns that “Accurate and complete reporting of ART success rates is complicated. Clinics may have differences in patient selection, treatment approaches, and cycle reporting practices which may inflate or lower pregnancy rates relative to another clinic. This report is best understood in consult with your physician.” Furthermore, “success rates should not be used to compare treatment centers.” In spite of this, patients rely on this information to decide which center they will ultimately choose for their fertility treatment. The objective of this study was to compare the ranking of live birth (LBR) singleton live birth rate (SLBRR) and weighted `risk score' ranking based on risk factors for morbidity/mortality associated with multiple gestation in clinics reporting ≥ 1000 total cycles annually.

DESIGN: Cross-sectional evaluation.

MATERIALS AND METHODS: The 2017 SART Preliminary Data report was reviewed for all reporting ART clinics. Those clinics reporting ≥ 1,000 total cycles annually were included in our analysis, for a total of 62 clinics. LBR, SLBRR, twin and triplet rates were recorded for each of the clinics. A weighted `risk score' was then calculated for each clinic in the following manner: twin rate x 8 + triplet rate x 21. The weighted `risk score' assigned to twin and triplet gestations was derived from published relative risk data of prematurity and low birth weight of twin and triplet gestations compared to singletons, as these have been shown to be the principal risk factors for morbidity/mortality in multiple gestation pregnancies. All clinics were subsequently ranked into quartiles with regards to LBR and `risk score'.

RESULTS: Of 15 15 clinics included in the top quartile with respect to LBR, one clinic also ranked in the lowest quartile of `risk score'. Of the remaining 14 clinics, 5 ranked in the highest `risk score' quartile and 5 in the second highest `risk score' quartile. Therefore, <30% of the clinics ranking in the highest quartile for LBR also ranked in the top two quartiles for safety.

CONCLUSIONS: Our study showed that out of the 62 highest volume ART clinics reporting to SART, two thirds of those in the top quartile for LBR were included in the bottom two quartiles with respect to weighed `risk score', with one third ranking in the highest `risk core' quartile. Only one clinic was in the top quartile in both fields. This is a manifestation of the incentive to achieve a higher LBR, commonly acknowledged to be the most referenced statistic reported by SART, at the cost of a higher risk of multiple gestation. Though not intended to be a tool for clinic comparison and ranking, SART is clearly used in this manner. We argue that more attention should be brought to the balance of success and risk in order to optimize patient outcomes and encourage increased responsibility among ART clinics.

SUPPORT: None

O-126 Tuesday, October 15, 2019 12:00 PM

INSTITUTIONAL POLICIES ON POSTHUMOUS REPRODUCTION USING OOCYTES AND EMBRYOS: PRELIMINARY RESULTS FROM A CROSS-SECTIONAL STUDY. Emma C. Trawick, M.D. a Amani Sampson, B.A. a David L. Keefe, M.D. a Arthur L. Caplan, Ph.D. a Kara N. Goldman, M.D. b Gwendolyn P. Quinn, Ph.D. b Northwestern University, Feinberg School of Medicine, Chicago, IL; aNew York University School of Medicine, Department of Obstetrics and Gynecology, New York, NY; bNew York University School of Medicine, Department of Population Health, Division of Medical Ethics, New York, NY; cNorthwestern University Feinberg School of Medicine, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology and Infertility, Chicago, IL.

OBJECTIVE: Posthumous assisted reproduction (PAR) raises complicated ethical and legal issues. ASRM recommends that assisted reproductive technology (ART) and fertility preservation (FP) programs develop written policies regarding PAR, though little is known about such policies and how they have been implemented. Our objective was to assess the presence and content of policies toward PAR using oocytes and embryos amongSociety for Assisted Reproductive Technology (SART) member clinics in the U.S.

DESIGN: Cross-sectional questionnaire-based study.

MATERIALS AND METHODS: Our study consists of three phases of communication: email-, postal mail-, and phone-based survey. We report on the first phase of anonymous email survey responses. Surveys were emailed to ASRM-member medical directors of all SART member clinics (n = 332) during March and April 2019 using a modified Dillman Method; contact information was acquired from SART and ASRM membership data. The survey included 23 multiple-choice and 3 opened-ended questions assessing practice characteristics (practice type, location, IVF cycle volume), presence of a clinic policy towards PAR, and the content of such policy. Descriptive data are presented as %, with Fisher’s exact test used where appropriate, and thematic content analysis was applied to open-ended responses.

RESULTS: The first phase of the study received 39 clinic responses (12% response rate). Respondents were distributed across the U.S.; average volume of IVF cycles per year ranged from < 250 to > 1500. More than one-third (35.9%, n = 14) of clinics reported participating in any cases of PAR over the past five years, and 51.1% (n = 2) reported participation in more than five cases. Participation in cases of PAR was not significantly associated with practice type or IVF cycle volume (p > 0.05). 57.9% (n = 22) had written policies towards PAR using oocytes or embryos, while 36.8% (n = 14) reported they did not have a policy. Practice type, IVF cycle volume, FP volume, and prior participation in cases of PAR were not significantly associated with the presence of a policy (p > 0.05). Of those with a policy, 52.4% (n = 11) reported they had used that policy, 66.7% (n = 10) without a policy reported they had considered adopting one, and 60.0% (n = 9) reported they had received a request for PAR services. Only 44% (n = 15) of clinics specified that patients not expected to survive to use oocytes due to terminal illness were eligible for oocyte cryopreservation, while 50.0% (n = 17) did not specify. Open-ended comments suggested need for case-by-case appraisal and firm consent policies regarding gamete disposition.

CONCLUSIONS: Our preliminary results suggest that SART programs are receiving an increasing number of requests for PAR services, but many SART programs lack PAR policies, and those with policies do not always follow ASRM recommendations. As PAR cases become more common, clinics should be equipped to manage the complexities of PAR. More data are needed as this study continues, and future research is needed to understand barriers to the creation and implementation of these increasingly needed policies.

IMAGING AND REPRODUCTIVE MEDICINE

O-127 Tuesday, October 15, 2019 10:45 AM

ORAL HYOSCINE BUTYL BROMIDE PLUS CERVICAL LIDOCAINE 5% CREAM IN REDUCING PAIN DURING HYSTEROSALPINGOGRAPHY. Ahmed M. Abbas, MD.a Yehia Ali, MD, b Tarek Farghaly, MD, a Mohamed Khalaf, MD. aDepartment of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; bDepartment of Obstetrics and Gynecology, Faculty of Medicine, Qena, Egypt.

OBJECTIVE: Infertility is defined as the failure of a couple to conceive during 12 months of regular unprotected intercourse. Tubal abnormalities account for 30-40% of the causes of female infertility. Hysterosalpingography (HSG) is a diagnostic procedure in the evaluation of infertile women and considered to be the traditional and the gold standard in the assessment of the patency of the fallopian tubes. The major disadvantage of HSG is pain. Our objective is to evaluate the analgesic effect of combining oral Hyoscine Butyl Bromide (HBB) with cervical lidocaine cream in alleviating pain during HSG.

DESIGN: Randomized double-blinded controlled trial (clinicaltrials.gov: NCT02710305).

MATERIALS AND METHODS: The study included reproductive-aged infertile women scheduled for HSG. Eligible women were recruited and randomized (1:1) to HBB plus lidocaine or Placebo group. All women received oral 20 mg HBB or placebo tablets 30 minutes before HSG, and then 4 ml of lidocaine 5% cream or placebo was applied to the anterior cervical lip, followed by 2 ml placed in the cervical canal using a sterile needleless syringe. The study outcomes were the mean pain score reported during speculum placement, cervical tenaculum placement, injection of the dye, 5 minutes and 30 minutes post-procedure using a 10-cm Visual Analogue Scale (VAS). A 2 cm difference in VAS score between both groups was considered a clinically significant difference. Other outcomes included the number of women who asked for additional analgesics and the adverse effects of the study medications. Mann Whitney test and Fisher’s exact test were used for the analysis of the outcomes. Multivariate regression analysis was
performed to determine the independent predictors of pain with the dependent variable (VAS score during the injection of the dye).

RESULTS: One hundred forty women were enrolled and randomized to HBB plus lidocaine arm (n=70) or placebo arm (n=70). Both groups were similar in age, parity, BMI, duration of infertility and the prior mode of delivery without statistically significant differences. Women in the HBB plus lidocaine group were more likely to report lower VAS scores during injection of the dye, 5 minutes and 30 minutes post procedure (median: 3 vs. 6, p<0.001; 2.5 vs. 5, p<0.001; 1.5 vs. 3, p<0.001, respectively). Moreover, eighteen women asked for additional analgesics in the placebo group versus seven women in the study group (p=0.02). No difference in the rate of adverse effects. The following variables were not predictors of pain: nulliparity (p=0.48), previous cesarean deliveries (0.28), dysmenorrhea (p=0.13), chronic pelvic pain (p=0.42) and prior HSG (p=0.45).

CONCLUSIONS: Utility of oral HBB 30 minutes before HSG plus cervic- al lidocaine 5% cream significantly alleviate the induced pain during and 30 min after the HSG procedure.

SUPPORT: None

O-128 Tuesday, October 15, 2019 11:00 AM

THE DEVELOPMENT OF A SYSTEM TO AUTOMATICA LLY EVALUATE THE NUMBER OF PRONUCLEI USING DEEP LEARNING TECHNOLOGY. Yuta Kida, M.S., a Noritaka Fukunaga, Ph.D., a Sho Sanami, Ph.D., b Hiroyuki Watanabe, M.S., a Yuji Tsuzuki, M.S., a Hiroya Kitasaka, Ph.D., a Seiji Takeda, M.S., a Yoshimasa Asada, M.D., Ph.D., a Asada Ladies Clinic, Nagoya, Aichi, Japan; b Research & Development Center, Dui Nippon Printing Co., Ltd., Kita-ku, Tokyo, Japan.

OBJECTIVE: Embryo evaluation requires long-term experience and learning to acquire high degree of accuracy. In addition, it is difficult to maintain consistency in the quality of evaluation differences among embryologists. Therefore, we have applied an analysis using Deep learning technology (DL). DL can greatly improve learning accuracy by repeat machine learning utilizing a system called Deep Neural Network (DNN). In this study, we aimed to develop a more objective and automatic evaluation system for pronucleus (PN) evaluation using DL of time lapse images (TL) of PN embryos.

DESIGN: We built a stand-alone framework with DNN as the core to automatic evaluation system of the PN number in human embryos, based on TL.

MATERIALS AND METHODS: Part 1: TL of 0, 1 or 2 PN categories (total 900 embryos) were used to develop algorithms for detecting the PN number. We constructed two methods, one to output the number of PN directly to the input TL by applying general DL (M1) and a modified method (M2) which combined with DNN1 for automatically detecting the PN contours from the input TL and DNN2 for outputting the PN number judged from DNN1. The detection accuracy of the two algorithms was compared using 100 embryos for each PN categories (total 300 embryos) not used for DL. The chi-square test or Fisher’s exact test were used for the significant difference test.

Part 2: TL of 0, 1, 2, 3 or multi (4 or more) PN categories (300 of each) assessed by an experienced embryologist (total 900 embryos) were used to develop algorithms for detecting the PN number. We constructed two methods, one to output the number of PN directly to the input TL by applying general DL (M1) and a modified method (M2) which combined with DNN1 for automatically detecting the PN contours from the input TL and DNN2 for outputting the PN number judged from DNN1. The detection accuracy of the two algorithms was compared using 100 embryos for each PN categories (total 300 embryos) not used for DL. The chi-square test or Fisher’s exact test were used for the significant difference test.

RESULTS: Part 1: The M1 and M2 detection rates were respectively 0 PN (69% vs 99%), 1 PN (33% vs 82%) and 2 PN (91% vs 99%). All detection rates were significantly improved in M2 compared to M1 (P<0.05).

Part 2: The M3 and M4 detection rates were respectively 0 PN (95% vs 100%), 1 PN (68% vs 71%), 2 PN (86% vs 90%), 3 PN (33% vs 81%) and multi PN (53% vs 85%). For 0 PN, 3 PN and multi PN, the detection rate was significantly improved in M4 (P<0.05).

CONCLUSIONS: In this study, the detection accuracy of 2 PN by DL showed a very high correlation with the evaluation of an embryologist. In addition, even for the detection of complex PN, improvement in detection accuracy was observed by adding improvements in learning methods. Embryo evaluation by an embryologist requires long-term experience, but the embryo evaluation accuracy by DL was able to approach that of an embryologist. This evaluation has demonstrated the possibility of DL techniques to guarantee objective gamete evaluation through automatic analysis of the image. As a next step, we are in the process of developing a system that combines automatic detection of PN by TL of WL within a continuous culture system throughout embryo development.

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LOW ENDOMETRIAL VOLUME IS NOT ASSOCIATED WITH DIMINISHED LIVE BIRTH FOLLOWING TRANSFER OF A SINGLE THAWED EUPLOID BLASTOCYST. Shelby A. Neal, M.D., a Richard Thomas Scott, Jr., M.D., b Linnea R. Goodman, M.D., c IVI-RMA New Jersey, Basking Ridge, NJ; dUniversity of North Carolina, Raleigh, NC.

OBJECTIVE: Three-dimensional ultrasound (3D US) facilitates reproducible assessment of endometrial volume (EV)1, but whether or not EV is associated with pregnancy outcomes in women undergoing in vitro fertilization (IVF) is unclear2. The objective of this study is to evaluate the association between EV and pregnancy outcomes following transfer of a single thawed euploid blastocyst.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: All patients planning to undergo a single thawed euploid blastocyst transfer between April and December 2017 at a large IVF center were eligible for inclusion. Subjects underwent endometrial preparation according to a standardized protocol. On the day prior to transfer, 3D US was performed for assessment of EV. Patients then underwent transfer of a single thawed euploid blastocyst.

EV was classified into four quartiles according to the 25th, 50th and 75th percentiles. The primary outcome was live birth. Secondary outcomes included clinical pregnancy (presence of a gestational sac on ultrasound), miscarriage (pregnancy loss after documentation of gestational sac), and ectopic pregnancy. Analysis of variance was used to compare continuous variables and chi square or Fisher’s exact test was used for categorical variables. Multivariate logistic regression was performed to account for potential confounders.

RESULTS: A total of 638 subjects consented to participation and completed the study. There were no differences amongst EV quartiles by age at retrieval, age at transfer, or body mass index. EV was directly associated with gravidity, parity and endometrial thickness (all P<0.01). Table 1 shows pregnancy outcomes by EV quartile. When accounting for potential confounders, there were no associations between EV and live birth [aOR 0.97 (0.90-1.05)], clinical pregnancy [aOR 1.00 (0.92-1.92)] or miscarriage [aOR 1.07 (0.95-1.21)]. There was a non-significant trend between low EV and ectopic pregnancy [aOR 1.59 (0.96-2.63), P=0.07].

CONCLUSIONS: EV is not associated with clinical pregnancy, miscarriage or live birth following transfer of a single thawed euploid blastocyst. It is possible that low EV confers an increased risk for ectopic pregnancy; however this association did not reach statistical significance and warrants further investigation.
COMPARISON OF SINGLETON AND TWIN PREGNANCY OUTCOMES IN WOMEN WITH A CONGENITAL UNICORNATE UTERUS AFTER IN VITRO FERTILIZATION-EMBRYO TRANSFER.

OBJECTIVE: To compare the singleton and twin pregnancy outcomes in women with a congenital unicornate uterus after in vitro fertilization-embryo transfer (IVF-ET).

MATERIALS AND METHODS: A single-center retrospective cohort study was conducted with 336 women who were diagnosed with a congenital unicornate uterus from January 2012 to December 2017. In order to avoid selection bias, only the first pregnancy of each patient were considered. All patients were diagnosed as clinical pregnancies by early transvaginal sonography in our hospital. Ectopic pregnancy, multiple pregnancy, selective or spontaneous reduction and induced labor were excluded from this analysis.

RESULTS: There was no significant difference in the mean maternal age, body mass index, infertility type, infertility duration and infertility factors between the singleton-pregnancy group and the twin-pregnancy group (p > 0.05). When compared to the twin-pregnancy group, singleton-pregnancy group had a significantly lower perinatal mortality (1.8% vs. 15.7%, OR = 0.101 (0.033-0.311), P < 0.001) and live birth weight (3068 ± 514 vs. 2260 ± 476, P = 0.001), and lower rates of preterm delivery (13.0% vs. 57.6%, OR = 0.110 (0.059-0.205), P < 0.001), and low birth weight (11.7% vs. 15.8%, OR = 0.096 (0.53-0.174), P < 0.001), while a markedly higher rate of term birth (65.3% vs. 28.8%, OR = 4.658 (2.517-8.619), P < 0.001). Simultaneously, the rate of miscarriage (20.6% vs. 11.9%, P = 0.122) in the twin-pregnancy group was lower than that in the singleton-pregnancy group, and the live birth rate (76.9% vs. 76.3%, P = 0.918) of the single-pregnancy group was basically consistent with the twin pregnancy group, these differences were not statistically significant.

CONCLUSIONS: Singleton-pregnancy could obtain better pregnancy outcomes than twin-pregnancy in women with a unicornuate uterus anomaly after IVF-ET. Therefore, reducing the incidence of twin pregnancy in women with a unicornuate uterus is clinically necessary.

SUPPORT: The Science and technology project of Health and Family Planning Commission of Hunan Province (No. C20180898) and the Citic-Xiangya Research Fund (No. KYXM-201703).

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TABLE. The comparison between singleton-pregnancy and twin-pregnancy

<table>
<thead>
<tr>
<th>Pregnancy outcomes</th>
<th>Singleton-pregnancy group(n=277)</th>
<th>Twin-pregnancy group(n=59)</th>
<th>P-value</th>
<th>OR (95%-CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miscarriage, % (n)</td>
<td>20.6% (57/277)</td>
<td>11.9% (7/59)</td>
<td>0.122</td>
<td>1.925 (0.830-4.463)</td>
</tr>
<tr>
<td>Preterm delivery, % (n)</td>
<td>13.0% (36/277)</td>
<td>57.6% (34/59)</td>
<td>&lt;0.001</td>
<td>0.110 (0.059-0.205)</td>
</tr>
<tr>
<td>Term birth, % (n)</td>
<td>65.3% (181/277)</td>
<td>28.8% (17/59)</td>
<td>&lt;0.001</td>
<td>4.658 (2.517-8.619)</td>
</tr>
<tr>
<td>Perinatal mortality, % (n)</td>
<td>1.8% (4/217)</td>
<td>15.7% (16/102)</td>
<td>&lt;0.001</td>
<td>0.101 (0.033-0.311)</td>
</tr>
<tr>
<td>Live birth, % (n)</td>
<td>76.9% (213/277)</td>
<td>76.3% (45/59)</td>
<td>&lt;0.018</td>
<td>1.035 (0.534-2.007)</td>
</tr>
<tr>
<td>Birth weight, (g)</td>
<td>3068 ± 514</td>
<td>2260 ± 476</td>
<td>&lt;0.001</td>
<td>0.096 (0.53-0.174)</td>
</tr>
<tr>
<td>Low birth weight, % (n)</td>
<td>11.7% (25/213)</td>
<td>58.1% (50/86)</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

PRE-OPERATIVE MAGNETIC RESONANCE IMAGING VERSUS ULTRASONOGRAPHY FOR PREDICTING THE OPERATIVE OUTCOMES OF ABDOMINAL OR LAPAROSCOPIC MYOMECTOMY.

CONCLUSIONS: Singleton-pregnancy could obtain better pregnancy outcomes than twin-pregnancy in women with a unicornuate uterus anomaly after IVF-ET. Therefore, reducing the incidence of twin pregnancy in women with a unicornuate uterus is clinically necessary.

SUPPORT: The Science and technology project of Health and Family Planning Commission of Hunan Province (No. C20180898) and the Citic-Xiangya Research Fund (No. KYXM-201703).

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PRE-OPERATIVE MAGNETIC RESONANCE IMAGING VERSUS ULTRASONOGRAPHY FOR PREDICTING THE OPERATIVE OUTCOMES OF ABDOMINAL OR LAPAROSCOPIC MYOMECTOMY.

Nigel Pereira, MD.a Catherine W. Chan, MD.a Niralj J. Shah, MD.a Isaac Kligman, M.D.a Zev Rosenwaks, M.D.b Ronald O. Perlman and Claudia Cohen Center for Reproductive Medicine, New York, NY; Weill Cornell Medicine, New York, NY; bThe Ronald O. PERELMAN and CLAUDIA COHEN Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To compare the utility of pelvic magnetic resonance imaging (MRI) and pelvic ultrasonography (US) in predicting the operative outcomes of patients undergoing abdominal myomectomy (AM), laparoscopic myomectomy (LM), or robot-assisted laparoscopic myomectomy (RALM).

DESIGN: Retrospective cohort study.
MATERIALS AND METHODS: Women <45 years undergoing AM, LM or RALM for symptomatic leiomyomata were included. Pre-operative pelvic MRI or US was performed based on physician preference. Baseline demographics were recorded for all patients, including the number, location and dimensions of all leiomyomata on MRI or US. Total leiomyomata volumes were calculated based on recorded dimensions. Primary operative outcomes of interest were total operating time, leiomyomata weight and estimated blood loss (EBL). Spearman’s correlation was used to evaluate the correlation between leiomyomata volume and operative outcomes. Receiver-operator characteristic (ROC) curves were constructed for outcomes showing statistical significance.

RESULTS: A total of 117 patients were included; there was no difference in the demographics or leiomyomata characteristics of patients undergoing MRI or US in the AM (n=69), LM (n=13) or RALM (n=35) groups. The mean age and leiomyomata volume of patients undergoing LM was 36.7±7.1 years and 152.1±90.9 mL, respectively. The was a strong positive correlation between MRI leiomyomata volume and operating time (rho=0.90; P<0.001) and leiomyomata weight (rho=0.89; P=0.02). Patients in the RALM group had a mean age and leiomyomata volume of 36.9±4.1 years and 242.4±136.1 mL, respectively. A significant positive correlation between MRI leiomyomata volume and operating time (rho=0.83; P=0.03) and leiomyomata weight (rho=0.79; P=0.01) was noted in the RM group as well. These correlations were non-significant in the LM and RALM groups when using US leiomyomata volume. MRI leiomyomata volume was also predictive of LM and RALM conversion to laparotomy (area-under-the-curve=0.92). These correlations were positive but non-significant in AM group. No correlation was observed between MRI and US leiomyomata volume and EBL in all groups.

CONCLUSIONS: Pre-operative pelvic MRI in patients undergoing LM or RALM strongly correlates with operating time and leiomyomata weight and predicts conversion to laparotomy.

SUPPORT: None

IVF OUTCOME PREDICTORS

O-134 Tuesday, October 15, 2019 11:00 AM

IN VITRO FERTILIZATION WITH PERSONALIZED BLASTOCYST TRANSFER VERSUS FROZEN OR FRESH BLASTOCYST TRANSFER: A MULTICENTER, RANDOMIZED CLINICAL TRIAL. Carles Simon, MD, PhD,1 Carlos Gomez, M.Sc.,1 Sergio Cabanillas, M.D., Ph.D.,2 Iavor K. Vladimirov, M.D., Ph.D.,3 Gemma Castillon, M.D., Ph.D.,3 Juan Giles, M.D., Ph.D.,4 Fazilet Kubra Boyrmukalin, M.D., MSc,5 Necati Findikli, Ph.D.,6 Israel Ortega, M.D., Ph.D.,6 Carmen Vidal, M.D., Ph.D.,6 Alexandra Izquierdo, M.D., Ph.D.,7 Susana Portela, MD,8 Nilofrzt, M.D.,9 Sagiri Taguchi, M.D., Ph.D.,10 Elena Labarta, MD, Ph.D.,10 Francesco Colucci Coelho, M.D., Ph.D.,11 Shari Mackens, M.D.,12 Xavier Santamaria, M.D., Ph.D.,13 Elkin Muñoz, M.D., Ph.D.,14 Suel Gumillero Barrera, Sr., M.D., Ph.D.,15 Manuel Fernández-Sánchez, MD, Ph.D.,16 Marcos Ferando, M.D.,17 Antonio Pellicer, M.D., Ph.D.,18 Ben W. Mol, M.D., Ph.D., Prof.15 Diana Valbuena, M.D., Ph.D.,18 University of Valencia, Igenomix Foundation-Incliva, Valencia, Spain;14 Igenomix SL, Paterna, Spain;15 IVI-RMA Valencia, Valencia, Spain;16 Sbalagram-Sofia, Sofia, Bulgaria;17 IVI-RMA Barcelona, Barcelona, Spain;18 Bahciheci Health Group-Fulya IVF Centre, Istanbul, Turkey;19 IVI-RMA Madrid, MADRID, Spain;20 IVI-RMA Valencia, Valencia, Spain;21 Proces Tecn, Madrid, Spain;22 IVI-Vigo, Vigo, Spain;23 Nilofrant Reproductive Medicine, Porto Alegre, Brazil;24 Oak Clinic, Japan, Osaka, Japan;25 IVI-RMA, Valencia, Spain;26 Centro de Infertilitad e Medicina Fetal do Norte Fluminense, Campos dos Goytacazes, Brazil;27 Universitat Ziekenhuis Brussel, Jette, Belgium;28 IVI-RMA Vigo, Vigo, Spain;29 IVI-RMA Panama, Panama City, Panama;30 IVI-RMA Sevilla, Sevilla, Spain;31 IVI-RMA Bilbao, Bilbao, Spain;32 Monash University, Monash Medical Centre, Department of Obstetrics and Gynaecology, Melbourne, VIC, Australia.

RESULTS: Demographics for the HP-hMG and rFSH arms were similar. The primary non-inferiority end-point of ongoing pregnancy was met, but a higher average number of oocytes/patient was retrieved in the rFSH (22.2) vs. the HP-hMG arms (15.1). Cumulative live birth rates were similar, but OHSS and cumulative early pregnancy loss rates were significantly higher in subjects who received rFSH. Although serum estradiol (E2) concentrations were significantly elevated on day 6 and day 6 and trigger in the HP-hMG group, serum E2 adjusted by follicle number was instead higher in the HP-hMG group on the day of trigger. Progesterone levels remained higher in the rFSH group independent of model. Androstenedione and testosterone levels were significantly higher regardless of adjustment, in the HP-hMG group on the day of trigger (Table).

CONCLUSIONS: Data suggest that gonadotropin specific follicular steroidogenic responses exist. After accounting for ovarian response, HP-hMG drives higher androgen and estradiol with lower progesterone levels. Additional investigation will determine whether changes in ovarian follicle steroid output might be linked to the differences in safety parameters observed.

SUPPORT: Ferring Pharmaceuticals

<table>
<thead>
<tr>
<th>DAY 6</th>
<th>TRIGGER DAY</th>
</tr>
</thead>
<tbody>
<tr>
<td>rFSH</td>
<td>rFSH</td>
</tr>
<tr>
<td>HP-hMG</td>
<td>HP-hMG</td>
</tr>
<tr>
<td>ADJ rFSH</td>
<td>ADJ rFSH</td>
</tr>
<tr>
<td>ADJ HP-hMG</td>
<td>ADJ HP-hMG</td>
</tr>
</tbody>
</table>

| Androstenedione pmoL/L | 5279 | 4984 | 5230 | 5100 |
| Testosterone nmol/L | 1.2 | 1.2 | 1.2 | 1.3 |
| Estradiol nmol/L | 2627 | 2864 | 2533 | 930 |
| Progesterone nmol/L | 2407 | 2867 | 2328 | 2755 |

Androstenedione pmoL/L | 5279 | 4984 | 5230 | 5100 |
Testosterone nmol/L | 1.2 | 1.2 | 1.2 | 1.3 |
Estradiol nmol/L | 2627 | 2864 | 2533 | 930 |
Progesterone nmol/L | 2407 | 2867 | 2328 | 2755 |

ADJ rFSH | ADJ HP-hMG
Value | 95% Confidence Interval

O-134 Tuesday, October 15, 2019 10:45 AM

GONADOTROPIN-SPECIFIC FOLLICULAR STEROIDOGENESIS IN OVARIAN STIMULATION: EVIDENCE FROM THE MENOPUR IN GnRH ANTAGONIST SINGLE EMBRYO TRANSFER - HIGH RESPONDER (MEGASET-HR) TRIAL. Fady I. Sharara, M.D., a Andreas F. Schuh, M.D.,1,2 Ana-Maria Oprea, M.D.,1,2 Jürgen F. Schäfer, M.D.,1,2 P. Chervenak, M.D.,3,4 Carole F. Eppinger, M.D.,5,6 Alexandra Orlovich, M.D.,3,4 Carlos Gomez, M.Sc.,1,3 Sergio Cabanillas, M.D., Ph.D.,1,3 Iavor K. Vladimirov, M.D., Ph.D.,3 Gemma Castillon, M.D., Ph.D.,3 Juan Giles, M.D., Ph.D.,4 Fazilet Kubra Boyrmukalin, M.D., MSc,5 Necati Findikli, Ph.D.,6 Israel Ortega, M.D., Ph.D.,6 Carmen Vidal, M.D., Ph.D.,6 Alexandra Izquierdo, M.D., Ph.D.,7 Susana Portela, MD,8 Nilofrzt, M.D.,9 Sagiri Taguchi, M.D., Ph.D.,10 Elena Labarta, MD, Ph.D.,10 Francesco Colucci Coelho, M.D., Ph.D.,11 Shari Mackens, M.D.,12 Xavier Santamaria, M.D., Ph.D.,13 Elkin Muñoz, M.D., Ph.D.,14 Saul Guillermo Barrera, Sr., M.D., Ph.D.,15 Manuel Fernández-Sánchez, MD, Ph.D.,16 Marcos Ferando, M.D.,17 Antonio Pellicer, M.D., Ph.D.,18 Ben W. Mol, M.D., Ph.D., Prof.15 Diana Valbuena, M.D., Ph.D.,18 University of Valencia, Igenomix Foundation-Incliva, Valencia, Spain;14 Igenomix SL, Paterna, Spain;15 IVI-RMA Valencia, Valencia, Spain;16 Sbalagram-Sofia, Sofia, Bulgaria;17 IVI-RMA Barcelona, Barcelona, Spain;18 Bahciheci Health Group-Fulya IVF Centre, Istanbul, Turkey;19 IVI-RMA Madrid, MADRID, Spain;20 IVI-RMA Valencia, Valencia, Spain;21 Proces Tecn, Madrid, Spain;22 IVI-RMA Panama, Panama City, Panama;23 IVI-RMA Sevilla, Sevilla, Spain;24 IVI-RMA Bilbao, Bilbao, Spain;25 Monash University, Monash Medical Centre, Department of Obstetrics and Gynaecology, Melbourne, VIC, Australia.

OBJECTIVE: To evaluate gonadotropin related differences in follicle endocrine physiology in predicted high responder women undergoing assisted reproductive technology.

MATERIALS AND METHODS: Ovulatory women aged 21-35 y, BMI 18-30 kg/m 2 and serum anti-Müllerian hormone (AMH) ≥5 ng/mL (N=620) were randomized 1:1 to a 150 IU start dose of HP-hMG or rFSH in a GnRH antagonist cycle; 75 IU dose adjustments were allowed on/after day 6 of stimulation. Additional investigation will determine whether changes in ovarian follicle steroid output might be linked to the differences in safety parameters observed.

SUPPORT: Ferring Pharmaceuticals
OBJECTIVE: To determine the effectiveness of personalized embryo transfer (pET) versus frozen embryo transfer (FET) or fresh embryo transfer (ET) in infertile patients undergoing IVF at their first appointment. In pET, embryo transfer is performed within the optimal window of implantation identified by the endometrial receptivity array (ERA).

DESIGN: Multicenter randomized clinical trial. Participants aged ≤ 37 years scheduled for IVF with elective blastocyst transfer at the first appointment were randomized to undergo pET, FET or ET.

MATERIALS AND METHODS: Setting: 16 reproductive medicine centers in Europe, America and Asia with a common reference genetic laboratory. Patient(s): We recruited 569 women, and 458 were randomly assigned to pET (N = 148), FET (N = 154), or ET (N = 156) groups.

Intervention(s): The ERA test was performed using hormone replacement therapy guiding embryo transfer in the pET arm. Blastocyst vitrification was performed in the pET and FET arms. Blastocyst transfer in all groups.

Main outcome measure(s): The primary outcome was live birth. Secondary outcomes were pregnancy and implantation rates as well as clinical miscarriage, biochemical pregnancy, and obstetric and neonatal outcomes. We performed intention-to-treat and per protocol analyses.

RESULTS: In the per protocol analysis, live birth rates at the first embryo transfer were 45 of 80 (56.2%) in the pET group, 39 of 92 (42.4%) in the FET group, and 43 of 94 (45.7%) in the ET group (pET versus FET relative risk [RR] 1.35, 95% confidence interval (CI) 0.97-1.86; p = 0.09; pET versus ET [RR] 1.26, 95% CI 0.91-1.74; p = 0.17). Cumulative live birth rates after 12 months were 57 of 80 (71.2%) in the pET group, 51 of 92 (55.4%) in the FET group, and 46 of 94 (48.9%) in the ET group (pET versus ET [RR] 1.47, 95% CI)1.01-2.13; p = 0.04; FET versus ET [RR]1.71, 95% CI 1.17-2.49; p = 0.003).

Pregnancy rates at the first embryo transfer in the pET, FET and ET were 72.5%, 54.3% and 58% respectively (pET versus FET RR 1.36, 95% CI 1.01 to 1.82, p = 0.03; ET versus FET 1.42, 0.98-2.08, p = 0.05). Implantation rate at the first embryo transfer were 57.3%, 43.2% and 38.6% respectively, (pET versus FET RR 1.37, 95% CI 1.03-1.82, p = 0.03; PET versus ET RR 1.54, 95% CI 1.15-2.05, p = 0.004).

No differences between groups were found for clinical miscarriage, biochemical pregnancy or any other secondary outcomes. Obstetrical outcomes, type of delivery and neonatal outcomes were similar in all groups.

CONCLUSIONS: In this RCT, we found a statistically significant improvement in cumulative live birth rates in pET compared to FET and ET. Pregnancy and implantation rates after pET over FET and ET at first attempt as well as in cumulative rates were significantly higher. These findings indicate the potential of pET with the ERA test at the first appointment that should be confirmed in larger randomized clinical trials. (ClinicalTrials.gov NCT 01954758).

DIMINISHED OVARIAN RESERVE (DOR) IS ASSOCIATED WITH REDUCED EUPLOID RATES VIA PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) INDEPENDENT OF AGE: EVIDENCE FOR CONCOMITANT REDUCTION IN OOCYTE QUALITY WITH QUANTITY. Eleni A. Greenwood, MD, MSc, a Charles E. McCulloch, PhD, b Marcelle I. Cedars, MD, c Mitchell P. Rosen, MD, HCLD b aUniversity of California San Francisco, San Francisco, CA; bUCSF, San Francisco, CA; cUniversity of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA.

OBJECTIVE: Controversy surrounds whether an age-adjusted reduction in ovarian reserve is accompanied by diminished oocyte quality. We sought to determine whether women with DOR (quantitatively) had lower rates of euploid blastocysts via PGT-A testing, as a proxy for oocyte quality. DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Results from all day 5 and 6 blastocyst trophectoderm biopsies for PGT-A between 2010-2019 at a single academic center were reviewed. Blastocysts graded BB (Gardner) or better are biopsied at our center. In fertility diagnoses were grouped as DOR (assigned by clinicians at initial consultation per Bologna criteria) vs non-DOR infertility. Women >42y were excluded given potential conflation with DOR in this range. Couples without infertility (for example, PGT-A for recurrent pregnancy loss, fertility preservation, or PGT-M) were also excluded. The primary outcome was euploid rate, defined as the number of euploid blastocysts divided by number of blastocysts biopsied per cycle. Generalized linear models were used to account for the clustered nature of the data and control for age of the oocyte. Interactions analyses were performed. A secondary analysis assigned DOR on the basis of age-adjusted mature oocyte (M2) yield, comparing the lowest quartile to the remaining 3/4 by age group. Finally, per-patient comparisons outcomes after euploid single embryo transfer (SET) by DOR status.

RESULTS: 8,042 blastocyst PGT-A biopsies from 1,152 women over 1,675 IVF cycles were identified. 225 women (20%) had DOR as infertility diagnosis. Age was higher among DOR women (39.5y vs 37.0y). Euploid rates varied by DOR vs non-DOR (Table). Controlling for age, women with DOR had 24% reduced odds of a biopsied blastocyst being euploid vs non-DOR (Table). Impact of DOR on euploid rates did not differ by age category (interaction p=0.43). When assigning DOR status to women producing the lowest quartile of age-adjusted M2 yield, this relationship remained (Table). No differences were identified in rates of live birth or ongoing pregnancy between patients with and without DOR after SET of a euploid blastocyst (n=944 transfers) (56.8% vs 54.8%, respectively; p=0.88).

CONCLUSIONS: Blastocysts from women with DOR are less likely to be euploid than those from women without DOR, after adjustment for age. Given the concomitant reduction in euploid rates with quantity of oocytes observed in this study, quantitative ovarian reserve assessments (i.e. follicular machinery) may yield insight into relative ovarian aging.
significantly impacted by a delay in blastocyst development, with both im-
plantation (D5 = 73.6%; D6 = 60.9%; D7 = 39.5%) and live birth rates (D5 = 68.5%; D6 = 55.2%; D7 = 37.0%) being significantly decreased (P<0.0001). Even when compared to a cohort of maternal age-matched counterparts (mean maternal age = 37.6 ± 3.6 years), women achieved poorer live birth outcomes with the SET of a D7 euploid blastocyst (37%) compared to a D5 or D6 euploid blastocyst SET (63%; n = 1,314; P<0.0001).

CONCLUSIONS: Aneuploidy rates and reproductive success were significantly associated with the appropriate timing of blastulation and identification of the ICM. Increased maternal age was associated with a delay in blastocyst development. However, even with maternally aged-matched counterparts, significantly compromised developmental potential was observed for D7 euploid blastocysts compared to D5 or D6 euploid blastocysts. Biochemical, metabolic and epigenetic processes that could impact embryo viability, independent of chromosome enumeration, are potential contributors to the observed halving of the live birth rate for D7 euploid blastocysts. Despite poorer outcomes, these data still suggest that with appropriate patient counseling, extended culture to D7 for blastocyst biopsy is a viable clinical option for poorer prognosis patients.

SUPPORT: None.

O-138 Tuesday, October 15, 2019 12:00 PM

PROTOCOL MATTERS: A PROPENSITY GROUP ANALYSIS SHOWS THAT PROGESTERONE ELEVATIONS ON DAY OF TRIGGER DURING FRESH IVF-PARABOLIC EFFECT ON LIVE BIRTH RATES DIFFERENTLY ACCORDING TO STIMULATION PROTOCOL. Chantal Bartels, MD, a James Grady, PhD, b Chaoran Hu, M.S., b Grow R. Daniel, MD. c aCenter for Advanced Reproductive Services, University of Connecticut, Farmington, CT; bUniversity of Connecticut, Farmington, CT.

OBJECTIVE: To assess the influence of trigger day progestrone (P) levels on live birth rate (LBR) after fresh embryo transfer when using different ovarian stimulation protocols, either gonadotropin-releasing hormone (GnRH) agonist suppression or GnRH antagonist.

DESIGN: Retrospective propensity score matching

MATERIALS AND METHODS: eIVF is a multicenter database that has collected over 122,548 patient IVF cycles, 2004-2018. We use logistic regression with protocol types, namely GnRH agonist suppression and GnRH antagonist, to identify co-variates and perform propensity score matching. The two protocol cohorts were matched for age, smoking status, basal follicle stimulating hormone, number of mature oocytes, stimulation type, cryopreservation of embryos, and number of embryos transferred. Each matched protocol cohort contained 6560 patient cycles. Logistic regression was used to regress the outcome live birth against protocols type and proges-
teron level and the (protocol / progestrone) interaction. Chi-square was used to compare categorical variables. P level on day of trigger was divided into three groups: those with P level less than the mean (<1.0 ng/mL), between the mean and one standard devi-
ation (1.0-1.5 ng/mL), and greater than one standard deviation (>1.5ng/mL).

RESULTS: The P mean on day of trigger (ng/mL) was 1.0 ±0.45 and 1.0 ±0.44 for the agonist suppression and the antagonist groups respec-
tively. The two propensity groups with similar with respect to matched prognostic factors. P level on day of trigger did not differ with different stim-
ulation protocols. LBRs were statistically significantly higher in every P group when utilizing the agonist suppression protocol compared to the antag-

CONCLUSIONS: Elevated serum P levels >1 ng/mL on the day of trigger is associated with a statistically reduced LBR following IVF stimulation pro-
tocols using GnRH antagonist. There is no decrease in LBR with P elevations on day of trigger during ovarian stimulation with the GnRH agonist suppres-
sion protocol. This data suggests that protocol should be considered when recommending a freeze-all approach in the setting of elevated P levels on the day of trigger.

SUPPORT: None

LGBTQ

O-139 Tuesday, October 15, 2019 10:45 AM

REPRODUCTIVE FUNCTION IN A TRANSGENDER MOUSE MODEL FOLLOWING CESSATION OF TESTOSTERONE. Molly B. Moravek, MD, MPH, a Hadrian M. Kinneer, BA b, Versana Padmanabhan, MS, PhD b, c Ariella Shikanov, PhD. b cUniversity of Michigan, Ann Arbor, MI; b University of California, Los Angeles, Los Angeles, CA.

OBJECTIVE: While pregnancy is certainly possible in transgender men previously on gender-affirming testosterone (T), very little is known about overall fecundability, and thus fertility preservation is recommended prior to starting T. Studies of T-exposed ovaries at the time of gender-affirming sur-
gery reveal aberrations in ovarian histology and follicle appearance, but func-
tional studies have not been performed. We have established a mouse model to study the effects of gender-affirming T therapy on reproduction. The objective of the current pilot study was to examine fertility following T cessa-
tion in our mouse model, with the hypothesis that reproductive function would be fully restored.

DESIGN: Translational animal study.

MATERIALS AND METHODS: Ten 8 – 9 week old female C57BL/ 6N mice were injected with T enanthate 0.45mg and 5 control (C) mice were injected with vehicle twice weekly for 6 weeks, then all injections were stopped. Daily vaginal cytology and weekly serum hormone analysis was performed. Once cyclicity resumed, mice were divided into two groups: 1) sacrificed after 3-4 estrous cycles and ovaries harvested or 2) 14 weeks breceding 1:1 with male C57BL/6 mice. Ovifating resulting from group 2 were sacrificed on day of life (DOL) 26 and organs harvested. Descriptive statistics were calculated and confidence intervals calculated via modified Wald method or using a t-distribution, as appropriate.

RESULTS: All T-treated mice stopped cycling after 1–2 T injections and 8/ 9 resumed cycling 7–15 weeks following T cessation (one mouse sacrificed early for vaginal prolapse). Control mice cycled regularly throughout. Despite resumption of cyclicity, T-treated mice sacrificed after 3-4 estrous cycles (n=4) exhibited ovarian stromal hyperplasia and lack of corpora lutea on his-

tologic examination. In the breeding arm, 50% of T-treated (2/4) and 50% of control mice (1/2) produced offspring. We observed a similar sex ratio (50% female in T group, 95% confidence interval (CI): 42.76;57% in control, 95% CI: 33.79) and litter size (4.5 in T vs 4.7 in C) between groups. Mean weight on DOL 4 was 2.44g (95% CI: 1.89, 3) in T offspring vs 3.29g (95% CI: 2.93, 3.64) in control

toffspring, and 14.75g (95% CI: 13.68, 15.82) in T offspring and 16.33g (95% CI: 13.46, 19.2) in control mice on DOL 26. The ovaries of both T and control offspring appeared normal, both grossly and histologically.

CONCLUSIONS: Despite histologic aberrations noted in the ovaries of T-
treated mice early after resumption of cyclicity, their fertility approximated that of controls, with no obvious aberrations noted in the offspring. These pi-

dot data suggest that T-induced subfertility may be reversible following cessa-
tion and may not affect long-term reproductive function. Further, these data justify a larger study of fertility following T cessation, as well as further investigation into the molecular mechanisms underlying T-induced changes in ovarian architecture.

SUPPORT: ASRM/SREI Research Grant; University of Michigan Office of Research Grant

O-140 Tuesday, October 15, 2019 11:00 AM

REPRODUCTIVE LIFE PLANNING AND INTEREST IN FERTILITY PRESERVATION AMONG TRANS-

gender and Gender Non-Binary Individuals. Nina Vyas, MD, Alisse Singer, BA, Armen Ter-Barseghyan, MPH, Alena Kantor, BS, Chris Mann, MSW, ASW, Sylvia I. Lambrechts, MPH, MA, Molly M. Quinn, MD. University of California, Los Angeles, Los Angeles, CA.

OBJECTIVE: Professional organizations agree that all transgender per-

sions should be counseled on the effects of their transition on their fertility

FERTILITY & STERILITY®
O-142 Tuesday, October 15, 2019 11:30 AM

THE BURDEN OF FAMILY BUILDING AS A GAY MALE COUPLE: THE MAJORITY OF GAY MALE COUPLES SEEN AT A LARGE REPRODUCTIVE MEDICINE PRACTICE DESIRE A CHILD WITH EACH OF THEIR GENETICS.

Lisa Schuman, MSW, a Spencer S. Richlin, M.D., b

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OBJECTIVE: In 2012, advances in reproductive endocrinology led ASRM to recommend a single embryo transfer for patients “with a good prognosis and to recipients of embryos from donated eggs”. Progress in gay rights has led to more men seeking fertility treatment to build their families over the past decade. Often same sex male couples (SSMC) desire a child from each of their genetics, which requires a donor and a surrogate, in addition to clinic fees. As a result of the high cost for IVF using an ovum donor, surrogate, surrogacy agency, and legal representation per pregnancy, these patients typically request a double embryo transfer. The aim of our study was to verify our observation that both men typically desire a child from each partner and when counseled, the majority of these men are willing to proceed with a single embryo transfer.

MATERIALS AND METHODS: Between 2017 and 2018, 46 SSMC participated in a meeting with the clinic Medical Director which included a review of risks associated with a twin gestation. These couples also received a counseling session with one of two mental health professionals who also discussed risks involved in proceeding with a double embryo transfer. These clinicians also asked, “are you interested in having children with both of your genetics?”

RESULTS: 45 (98%) couples said they desired a child from each of their genetics. One couple said they were “not sure” if they would have more than one child. Two couples had one child when they came to the clinic. Of the forty one couples who were beginning their path to parenthood, 27 (66%) decided to pursue a single embryo transfer after completing counseling.
CONCLUSIONS: Scientific literature addressing the importance of pur- sing a single embryo transfer in regard to childhood outcome is particularly relevant when using an ovum donor (Fert. Stert. 2012; 4:838). Consideration of patient desires, including the interest to transfer two embryos for an improved chance of a successful pregnancy and concomitant costs for a sec- ond journey needs to be understood. Many clinics are only willing to transfer a single embryo created with a donor oocyte into a surrogate without further discussion. Additional consideration should be given to SSMC who face the expenses of ovum donation and surrogacy since both want to be genetic fa- thers. As surrogacy agencies and the public become more aware of the health risks associated with a twin gestation, it is likely fewer male couples will request a double embryo transfer. For now, fertility clinics should consider the financial difficulties inherent in two surrogacy journeys and counsel these men with sensitivity.

References: None

SUPPORT: None

PREGNANCY SUCCESS RATES FOR LESBIAN COU- PLES UNDERGOING INTRAUTERINE INSEMINATION. Jamyn K. Johal, MD, MSc,1 Sara J. Vaughan, MD,1 Eleni A. Greenwood, MD, MSc,1,2,3 Lusine Aghajanova, MD PhD.1,2 1Stanford University School of Medicine, Stanford, CA; 2University of California San Francisco, San Francisco, CA.

OBJECTIVE: To compare pregnancy rates in lesbian women undergoing donor sperm intrauterine insemination (IUI) to heterosexual women under- going IUI using partner or donor sperm; we hypothesized that pregnancy rates would not differ significantly between the two populations.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: This study included all IUI cycles completed at Fertility centers of University of California, San Francisco from 2009-2016 and Stanford University from 2016-2017. The primary outcome of interest was clinical pregnancy rates per cycle. Student t-test and chi square test were used for statistical analysis. Significance was accepted at p<0.05.

RESULTS: A total of 11,845 IUI cycles were included, 341 of which were lesbian women using donor sperm and 11,504 of which were heterosexual women with unexplained or male factor infertility using either partner or donor sperm. Baseline characteristics including maternal age, type of IUI cy- cle, and total motile sperm count were similar between the two groups. Lesbian women had a clinical pregnancy rate of 11% per IUI cycle similar to that of heterosexual women who had a clinical pregnancy rate of 12% (p=0.17). Among both lesbian and heterosexual women, age was inversely correlated with clinical pregnancy rate (p=0.005 and p=0.02, respectively).

CONCLUSIONS: Increasing numbers of lesbian women are attempting to achieve pregnancy using IUI with donor sperm. Lesbian women generally seek these treatments for procreative management and not for infertility. Nonetheless, they have an increased prevalence of smoking, obesity, sexually transmitted diseases and polycystic ovary syndrome compared to heterosex- ual women, which may affect their fertility and IUI success (1). Previous studies are limited with conflicting findings. More information is desperately needed and will help guide counseling, management, and treatment in this population. Despite the majority of lesbian females not having a diagnosis of infertility, in this study pregnancy rates were similar in lesbian women un- dergoing IUI for procreative management and heterosexual women undergo- ing intrauterine insemination for unexplained or male factor infertility. Pregnancy rates for both groups were comparable to nationally reported IUI success rates (2).


OBJECTIVE: There is an increasing trend for SSMC and SM to have children through ART. However, research on their experience accessing care is limited. Our objective was to evaluate decision-making considerations throughout the ART process which are unique to SSMC and SM who have used, or are currently using, ART.

DESIGN: This study was approved by the University of Toronto REB (#32847). A 58-item anonymous online questionnaire accessible through Survey Monkey was administered in order to collect quantitative data. This initial study includes only those undergoing ART in Canada.

MATERIALS AND METHODS: Data collection began in 08/2018 using convenience sampling techniques to recruit participants and is still ongoing. To date, 72 completed surveys have been used for this analysis.

RESULTS: The sample consisted of 63 partnered men and 9 SM, of which 21 had a child using ART, and 51 were actively pursuing ART at the time of filling out the survey. There were similar number of Canadian (n=32, 44.4%) and international intended parents (n=39, 54.2%) who completed the survey. The majority (n=48, 66.7%) were in their 30s at the time of pur- suing ART. The sample cohort was predominantly Caucasian (n=50, 69.4%) and had a high socioeconomic status; 80.6% were university graduates and the median individual income before tax was $79,500 CAD ($59,360 USD).

With respect to the decision to pursue parenthood, the majority of partici- pants (n=63, 87.5%) had a ‘deep desire to have a child’ and felt that having a child was ‘a natural next step in their life’ (n=50, 69.4%). Common resources for learning about ART were internet search (58.3%), social media platforms (41.7%), friends (38.9%), and attending seminars, workshops, and conferences (33.4%) focused on men pursuing parenthood. Twenty-five participants (34.7%) ‘never’ experienced social stigma regarding their family building plan; almost all (n=70, 97.2%) had some form of social support.

When choosing an egg donor, characteristics that were of highest impor- tance to consider included: medical history, physical attributes, personality and temperament, ethnicity, and education. Of coupled participants, 45 (71.4%) intended to use or had used both their and their partner’s sperm to fertilize eggs. Three quarters of participants (n=54) used, or intended to use, preimplantation genetic testing (PGT-A) to screen their embryos. On average, participants spent 3-6 months to find a suitable surrogate. Of partici- pants who had acquired a surrogate, the majority ‘strongly agreed’ with their surrogates on several value and lifestyle issues. Agencies were used in 62 cases (91.1%) for egg donor recruitment, and in 54 cases (90.0%) for surro- gate recruitment.

CONCLUSIONS: The present study provides novel data on the unique considerations that SSMC and SM take into account when using ART in Can- ada to build their families. For future planned studies we will collect data from those who underwent ART in other countries and compare that data with these results.
THE PREVALENCE OF Y-CHROMOSOME MICRODELETIONS IN OLIGOZOOSPERMIC MEN: A SYSTEMATIC REVIEW AND META-ANALYSIS OF NORTH AMERICAN AND EUROPEAN STUDIES. Taylor P. Kohn, MD, MPH,a; Jaden R. Kohn, MD, MPH,b; Robert M. Coward, MD; Johns Hopkins University School of Medicine, Baltimore, MD; Johns Hopkins University School of Medicine, Department of GYN/OB, Baltimore, MD; University of North Carolina, Chapel Hill, NC.

OBJECTIVE: European and North American guidelines recommend Y-chromosome microdeletion (YCM) screening in azoospermic and oligozoospermic men with sperm concentrations <5 million sperm/mL; however, numerous studies have suggested that YCM are rare when sperm concentrations are >1 million sperm/mL. We systematically reviewed and meta-analyzed European and North American studies to determine the prevalence of complete YCM in oligozoospermic men with sperm concentrations of >0–1, >1–5, and >5–20 million sperm/mL and to determine whether 1 or 5 million sperm/mL is the most appropriate sperm concentration threshold for YCM screening.

DESIGN: Systematic Review and Meta-Analysis.

MATERIALS AND METHODS: We performed a systematic review of MEDLINE, EMBASE, Cochrane Library, and ClinicalTrials.gov for studies from database inception through February 2019 evaluating the prevalence of complete YCM in oligozoospermic men in North American and European studies. We specified a priori the sperm concentration threshold of 1 million sperm/mL. Random-effects meta-analysis was used to examine prevalence of complete YCM in oligozoospermic men with sperm concentrations of >0–1 million sperm/mL, 1–5 million sperm/mL, and >5–20 million sperm/mL.

RESULTS: Thirty-seven studies were identified during systematic review (n = 2,492 oligozoospermic men). All complete YCM in oligozoospermic men were AZFy microdeletions. Eighteen studies contained data conducive to meta-analysis (n = 10,866 men). Comparing the pooled estimated prevalence by sperm concentration, complete YCM were significantly more common in men with sperm concentrations of >0–1 million sperm/mL (5.0% [95% CI: 3.6–6.6%] vs <1–5 million sperm/mL [0.8% [95% CI: 0.5–1.3%], p < 0.001]). YCM were similar in men with sperm concentrations >1–5 million sperm/mL and >5–20 million sperm/mL (0.8% [95% CI: 0.5–1.3%] vs 0.5% [95% CI: 0.2–0.9%], p = 0.14).

CONCLUSIONS: In Europe and North America, the majority of YCM occur in men with sperm concentrations ≥1 million sperm/mL, with less than 1% identified in men with >1 million sperm/mL. Male infertility guidelines for North America and Europe should reconsider the sperm concentration screening thresholds to recommend.

SUPPORT: None.

THE EFFECT OF ADVANCING PARENTAL AGE ON PREGNANCY AND NEONATAL OUTCOMES FOLLOWING A SINGLE EUPLOID FROZEN EMBRYO TRANSFER IN A DONOR OOCYTE MODEL. Sydney Chang, MD,a; Dmitry Gounko, MA, a; Joseph A. Lee, BA,a; Natan Bar-Chama, MD,a; Alan B. Copperman, MD,a; Robert M. Coward, MD, Johns Hopkins University School of Medicine, Baltimore, MD; Johns Hopkins University School of Medicine, Department of GYN/OB, Baltimore, MD; University of North Carolina, Chapel Hill, NC.

OBJECTIVE: Advanced maternal age is a significant determinant of oocyte quality and a risk factor for adverse obstetrical outcome. Less is known about the effect of paternal age on in vitro fertilization (IVF) and neonatal outcomes. Population-based studies have suggested that advanced paternal age is associated with preterm birth and low birth weight.2 Previously, our center demonstrated no association between paternal age and birth weight, gestational age at delivery, and neonatal birth weight. Data were evaluated using multivariate linear regressions with generalized estimating equations.

RESULTS: A total of 303 single euploid FET cycles from 187 patients were included in this study. Paternal age ranged from 27.6 to 66.7 years (44.5 ± 6.5). There was no statistically significant association between paternal age, CP rate (OR 1.01 [95% CI 0.96–1.07], p = 0.62), OP/LB rate (p = 0.09 [95% CI 0.94–1.05], p = 0.75), or EPL rate (OR 1.00 [95% CI 0.96–1.07], p = 0.96) after controlling for oocyte age, BMI, endometrial thickness at transfer, embryo morphology grade, and days required for blastulation.

No association between paternal age and birth weight (β = 8.17, p = 0.83).

CONCLUSIONS: In a large, homogeneous cohort of single, euploid FETs derived from donor oocytes, paternal age was not associated with pregnancy or perinatal outcomes. Our results are encouraging, as they did not demonstrate a link between paternal age and preterm delivery or birth weight. While reassuring, this does not address other multifactorial diseases such as schizophrenia and autism that have been associated with advanced paternal age.1 As the diagnostic capabilities of preimplantation genetic testing expand to include the detection of de novo mutations and higher resolution detection of copy number variants, future studies might investigate the impact of paternal age on the embryonic genome, pregnancy outcomes, and newborn health and development.

SUPPORT: None.

O-147 Tuesday, October 15, 2019 11:15 AM
THE EFFECT OF TETRAHYDROCANNABINOL ON TESTOSTERONE AMONG MEN IN THE UNITED STATES: RESULTS FROM THE NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY. Richard Jacob Fantus, MD,a Taylor P. Kohn, MD, MPH,b Ranjith Ramasamy, M.D.a University of Chicago, Chicago, IL; Johns Hopkins University School of Medicine, Baltimore, MD; University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: Smoking tetrahydrocannabinol (THC) causes central suppression of gonadotropins resulting in testosterone deficiency. Emerging literature suggests that this effect may not occur, and that men using THC may actually have increased testosterone (T). Given this discrepancy, we sought to determine the association between different levels of THC usage and T levels using a nationally representative cohort.

DESIGN: This is a retrospective review of a cross-sectional data set, the National Health and Nutrition Examination Survey (NHANES). A survey designed by the center for disease control (CDC) to determine the health of the United States.

MATERIALS AND METHODS: All men ages 18-80 years who answered the substance use questionnaire and underwent laboratory testing for T were included. THC use was self-reported and categorized by number of times used monthly. Multivariate modeling, controlling for confounders identified on univariate analysis, was then used to determine the relationship between THC use and T levels using a nationally representative cohort.

RESULTS: Among the 5,146 men who met inclusion criteria, 1477 (28.7%) endorsed smoking THC at least once in their lifetime, 509 endorse smoking in the last year (15.7%), and 625 (12.1%) reported smoking the last month. Mean T level of the cohort was 430 ± 381 ng/C6. Mean T level of the cohort was 430 ng/C6. Mean T level of the cohort was 430 ng/C6. Mean T level of the cohort was 430 ng/C6. Mean. Multivariate modeling, controlling for confounders identified on univariate analysis, was then used to determine the relationship between THC use and T levels using a nationally representative cohort. THC use was self-reported and categorized by number of times used monthly. Multivariate modeling, controlling for confounders identified on univariate analysis, was then used to determine the relationship between THC use and T levels using a nationally representative cohort. THC use was self-reported and categorized by number of times used monthly. Multivariate modeling, controlling for confounders identified on univariate analysis, was then used to determine the relationship between THC use and T levels using a nationally representative cohort.

Multivariate analysis controlling for age, body mass index, exercise level, alcohol use, and race demonstrated an inverse U association between THC use in the past year and T (Table), (p<0.001).

**CONCLUSIONS:** Analysis of a nationally representative cohort suggests that there is a dose-dependent effect of THC on T levels. While there is an increase in T in all THC users, increased amounts of THC usage appear to have a detrimental effect on serum testosterone levels. Future prospective work using specific doses of THC and studies elucidating the mechanism of the association is required to corroborate these findings.

**TABLE.** The effects of THC use on testosterone when controlling for age, body mass index, exercise level, alcohol use, and race

<table>
<thead>
<tr>
<th>THC use within last year</th>
<th>Difference in T Level (ng/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never</td>
<td>—</td>
</tr>
<tr>
<td>Once a month</td>
<td>49.96</td>
</tr>
<tr>
<td>2-3 times a month</td>
<td>66.77</td>
</tr>
<tr>
<td>4-8 times a month</td>
<td>52.18</td>
</tr>
<tr>
<td>9-24 times a month</td>
<td>41.81</td>
</tr>
<tr>
<td>25-30 times a month</td>
<td>33.44</td>
</tr>
</tbody>
</table>

* Controlling for age, body mass index, exercise, alcohol use, race, comorbidities, study years.
** Linear/Quadratic trend significant.

**O-148 Tuesday, October 15, 2019 11:30 AM**

**UTILIZING THE YO® HOME SPERM TEST NOVICE USERS OBTAINED ACCURATE RESULTS AS COMPARED TO TRAINED TECHNICIANS.**

**MATERIALS AND METHODS:** The YO home sperm test is an FDA approved OTC device to measure Motile Sperm Concentration (MSC). Results are reported as a LOW MSC of <6x10^6/mL or MODERATE/NORMAL MSC of ≥6x10^6/mL. This MSC cut-off is based on the WHO 5th edition reference values for semen analysis. Statistical analysis was based on positive (PPA) and negative percent agreement (NPA) between NOVICE and TRAINED user’s results. Positive results were defined as below the MSC cut-off and negative results above it, indicating absence of the condition being tested. Analysis was performed using MedCalc statistical software.

<table>
<thead>
<tr>
<th>Site Name, Location</th>
<th>N</th>
<th>PPA</th>
<th>NPA</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xytex Corp., Augusta, GA</td>
<td>82</td>
<td>96.3%</td>
<td>100.0%</td>
<td>98.15%</td>
</tr>
<tr>
<td>Xytex Corp., New Brunswick, NJ</td>
<td>136</td>
<td>97.1%</td>
<td>97.0%</td>
<td>97.05%</td>
</tr>
<tr>
<td>Medical Electronic Systems, Caesarea, IL</td>
<td>98</td>
<td>96.4%</td>
<td>100.0%</td>
<td>98.20%</td>
</tr>
<tr>
<td>OVERALL</td>
<td>316</td>
<td>96.7%</td>
<td>98.7%</td>
<td>97.70%</td>
</tr>
<tr>
<td>Inter-site CV</td>
<td></td>
<td>0.5%</td>
<td>1.7%</td>
<td>0.7%</td>
</tr>
</tbody>
</table>

* Controlling for age, body mass index, exercise, alcohol use, race, comorbidities, study years.
** Linear/Quadratic trend significant.

**O-149 Tuesday, October 15, 2019 11:45 AM**

**UNDERUTILIZATION OF PRIMARY MEDICAL CARE AMONG MEN PRESENTING FOR FERTILITY EVALUATION.**

**OBJECTIVE:** A growing body of evidence demonstrates an association between male infertility and significant medical comorbidities including cardiovascular disease, cancer, and even mortality. As such, it is essential that men with subfertility establish and maintain a relationship with a primary care physician (PCP). We sought to determine the proportion of young men presenting for fertility evaluation who reported an established relationship with a PCP.

**MATERIALS AND METHODS:** We retrospectively examined all men presenting for initial male infertility consultation at a tertiary care center with a single reproductive urologist between 2000 and 2018. All men were asked to provide the name of their PCP at the time of initial visit. Descriptive statistics and multivariable regression were utilized to characterize the proportion of men with a PCP at the time of evaluation and associations between PCP status, patient age, and comorbidity.

**RESULTS:** Among 4,127 men presenting for initial fertility consultation, 1,324 had PCP data recorded. Of these, 480 (36.3%) did not have an established PCP at the time of evaluation. Men with a PCP were older than those without - median age 35 years (interquartile range [IQR] 23–40) versus 34 years (IQR 31–38), p<0.001. A smaller proportion of men with a PCP had elevated blood pressure (46.2% versus 56.8%, p=0.03), however a similar proportion of men in both groups were obese (21.7% versus 24.6%, p=0.31). Among 513 men who had a documented visit with an internal medicine physician within our tertiary care network prior to initial fertility consultation, 184 (35.9%) had not seen an internal medicine physician in over a year.

**CONCLUSIONS:** Over one-third of men presenting for fertility evaluation did not have an established PCP, and among those who did, a sizable proportion had not seen their PCP in the previous year. Given the strong link between male infertility and medical comorbidities, reproductive urologists are uniquely positioned to encourage and facilitate the critical relationship between men with subfertility and primary care physicians.

**O-150 Tuesday, October 15, 2019 12:00 PM**

**SAVAGE ULTRASOUND GUIDED TARGETED CRYOABLATION OF THE PERI-SPERMATIC CORD FOR PERSISTENT CHRONIC SCROTAL CONTENT PAIN AFTER MICROSURGICAL DENERVATION OF THE SPERMATIC CORD.**

**OBJECTIVE:** Pain after microsurgical denervation of the spermatic cord is often persistent and refractory. We present a new procedure, vasa tapering, designed to further reduce neural outflow from the testicle to the scrotal skin.
University of Central Florida, Clermont, FL; "PUR Clinic, Clermont, FL; "Keiser University, Cooper City, FL.

OBJECTIVE: To assess the efficacy of Ultrasound Guided Targeted Cryoablation (UTC) of the peri-spermatic cord as a salvage treatment for patients who failed microsurgical denervation of the spermatic cord (MDSC) for the treatment of chronic scrotal content pain (CSP).

DESIGN: Retrospective review of 279 cases (221 patients: 58 bilateral) undergoing UTC between Nov 2012 to July 2016, performed by two fellowship trained microsurgeons.

MATERIALS AND METHODS: UTC was performed using a 16-gauge cryo needle (Endocare, HealthTronics, Austin, TX). Branches of the genito- femoral, ilioinguinal and inferior haugynaeric nerves were cryoablated medial and lateral to the spermatic cord at the level of the external inguinal ring. Level of pain was measured preoperatively and postoperatively using the Visual Analog Scale (VAS) and Pain Index Questionnaire (PIQ-6) (QualityMetric Inc., Lincoln, RI).

RESULTS: Median age was 43 years, operative duration 20 minutes, and post-operative follow-up 36 months (24 to 60). Subjective VAS outcomes: 75% significant reduction in pain (11% complete resolution and 64% ≥ 50% reduction in pain). Objective PIQ-6 outcomes: 53% significant reduction at 1 month (279 cases), 55% at 3 months (279 cases), 60% at 6 months (279 cases), 63% at 1yr (279 cases), 65% at 2ys (275 cases), 64% at 3yrs (232 cases), 59% at 4ys (128 cases) and 64% at 5 yrs (53 cases) post-op. Complications: two wound infections, four penile pain cases (resolved in a few months).

CONCLUSIONS: Ultrasound Guided Targeted Cryoablation of the perispermatic cord is a safe potential treatment option for the salvage management of persistent CSP in patients who have failed MDSC.

SUPPORT: None.

MENTAL HEALTH

O-151 Tuesday, October 15, 2019 10:45 AM
THE IMPACT OF KLINEFELTER SYNDROME ON QUALITY OF LIFE – A MULTICENTRE STUDY. Sebastian Franik, MSc, MD, a Kathrin Fleischer, MD, Ph.D, b Barbara Kortmann, MD, Ph.D, c Kathleen D’Hauwers, MD, Ph.D, d Joanna IntHout, Ph.D, e Claire Bouvattier, MD, f Jolanta Slowikowska-Hilczer, MD, Ph.D, f Solange Grunenwald, MD, f Tim van de Steene, MD, Ph.D, Audrey Cartault, MD, f Annette Richter-Unruh, MD, Ph.D, e Ute Thyen, Ph.D, f Hedi Claassen - van der Grinten, MD, PhD. f a Resident in Obstetrics and Gynaecology, Nijmegen, Netherlands; b Department of Obstetrics and Gynaecology, Radboudumc, Nijmegen, Netherlands; c Department of Pediatric urology, Nijmegen, Netherlands; d Department of Urology, Nijmegen, Netherlands; e Department for Health Evidence, Nijmegen, Netherlands; f Department of Endocrinology, Paris, France; g Department of Gynecology, University of Antwerp, Belgium; h Department of Endocrinology, Medical University of Lodz, Lodz, Poland; i Department of Endocrinology and Metabolic Disease, Toulouse, France; j Vu medisch centrum, Amsterdam, Netherlands; k Department of pediatrics, Toulouse, France; l Department of Pediatric Endocrinology, Bochum, Germany; m Department of Pediatrics, Lübeck, Germany; n Department of pediatric endocrinology, Radboudumc, Nijmegen, Netherlands.

OBJECTIVE: Klinefelter syndrome (KS) is associated with an increased risk of lower socioeconomic status and a higher risk for morbidity and mortality, which may have a significant impact on quality of life (QOL). The objective of this study is to investigate QOL in a large European cohort of men with KS and associate QOL with socioeconomic status, prevalence of somatic disease and mental illness, testosterone supplementation and age of diagnosis.

DESIGN: This study was part of the European dsd-LIFE study, a non-interventional, clinical, cross-sectional study.

MATERIALS AND METHODS: Participants were recruited in 14 clinical study centres in 6 European countries which participated in the European dsd-LIFE study. 218 men with KS were eligible for inclusion. Male normative data from the European Social Surveys (ESS) was used for comparison. Clinical data, related to quality of life, social activity and health status were collected.

RESULTS: The WHO physical domain score of men with KS (66.2 ± 19.4; n=206) was significantly lower compared to the healthy reference population (75.5 ± 16.2; n=1324; p<0.001). The WHO psych domain score of men with KS (n=206) was significantly lower (63.0 ± 17.9) compared to the healthy reference population (67.8 ± 15.6; n=1324; p<0.05). The WHO environment domain score of men with KS (69.7 ± 14.9; n=206) was comparable to the healthy reference population (70.5 ± 20.7; n=1324; p=0.5). The WHO social domain score of men with KS (59.1 ± 22.1; n=206) was significantly lower compared to the healthy reference population (68.2 ± 13.8; n=1324; p<0.001). Men with KS reported less engagement in social activities compared to others of the same age (33% vs 49%, p<0.001), and had less intimate friendships (p<0.001). Experienced discrimination and the presence of somatic or mental health problems led to a significantly worse QOL.

CONCLUSIONS: Quality of life is significantly impaired in men with Klinefelter Syndrome, most likely due to discrimination and the presence of somatic and mental health problems. A multidisciplinary approach of healthcare providers might help to provide adequate counselling and treatment to improve quality of life.

SUPPORT: The research leading to these results has received funding from the European Union’s Seventh Framework Programme (FP7/2007–2013) under grant agreement n° 305373.

O-152 Tuesday, October 15, 2019 11:00 AM
INTIMATE PARTNER VIOLENCE AMONG POST-PARTUM WOMEN REPORTING PRIOR FERTILITY TREATMENT. Jerinne Renee Morris, MD, MPH, Jennifer F. Kawwass, MD, Heather S. Hupp, MD Emory University, Atlanta, GA.

OBJECTIVE: To determine the prevalence of intimate partner violence (IPV) among women reporting use of fertility services compared to those who conceived spontaneously in a national sample of postpartum women.

DESIGN: A cross-sectional population-based study using data from the Pregnancy Risk Assessment Monitoring System (PRAMS), which included women with recent live births between 2009-2016.

MATERIALS AND METHODS: Women self-reported use and type of fertility treatment as well as IPV before or during their most recent pregnancy. Weighted percentages for reported IPV were calculated and compared between women with and without a prior history of fertility treatment preceding their recent pregnancy. We adjusted for maternal age, maternal race/ethnicity, maternal education, marital status, pre-pregnancy BMI, number of stressors (e.g. homelessness) experienced in the preceding 12 months prior to delivery, tobacco use in the three months prior to pregnancy, pre-pregnancy health insurance, annual household income, number of prior live births, outcome of prior pregnancy (including preterm or low birth weight), birth plurality, outcome of most recent pregnancy (including NICU admission or neonatal death), breastfeeding status of most recent neonate. Using multivariate logistic regression, the adjusted odds of IPV as a function of fertility treatment status were calculated.

RESULTS: Of the 37,114 women, 4,664 (12.6%) reported fertility treatment and 766 (2.1%) reported IPV. Of the women who reported use of fertility treatment, 59 (1.3%) reported IPV prior to or during their most recent pregnancy. Women who reported use of fertility treatment prior to their most recent pregnancy were twice as likely to endorse IPV as compared to women who did not report use of fertility treatment prior to their most recent pregnancy (p<0.0001). After adjustment, the odds of IPV were similar among women who received fertility treatment and those who did not (adjusted odds ratio 1.10, 95% confidence interval 0.64-1.89). There was no difference in type of fertility treatment and IPV (including fertility-enhancing drugs, artificial or intrauterine insemination, assisted reproductive technology, or other medical treatment). Predictors of IPV within this population included age less than 20, greater number of reported stressors, tobacco use prior to pregnancy, and household annual income less than $52,000. Non-Hispanic White race/ethnicity and being married were protective against IPV.

CONCLUSIONS: Despite the known adverse psychosocial implications of infertility, its treatment did not confer greater risk of IPV within this postpartum population. The increased use of fertility treatment was less likely to endorse IPV as compared to women who did not report use of fertility treatment prior to their most recent pregnancy. This finding may be associated with infertility, however, may have been mitigated by successful treatment but could be potentiated if unsuccessful. The preconception period, inclusive of encounters with infertility specialists, represents a unique opportunity to screen and counsel women, especially those who may be at higher risk for IPV.

O-153 Tuesday, October 15, 2019 11:15 AM
IMPACT OF IN-CENTER STRESS REDUCTION MODALITIES ON SART-REPORTED LIVE BIRTH RATES. Jessica N. Tozour, MD, PhD, a Randi H. Goldman, M.D, a Christine Mullin, M.D. a a NYU Winthrop Hospital, New York, NY; b PRAMS National Data Coordinating Center, New York, NY; c University of Central Florida, Clermont, FL; d PUR Clinic, Clermont, FL; e Keiser University, Cooper City, FL.
OBJECTIVE: To determine whether infertility centers that offer in-center stress reduction modalities (SRM) have higher live birth rates compared to centers without such services.

DESIGN: Retrospective cohort study comparing LBR among a sample of SART-affiliated fertility clinics with and without in-center SRM. Information on in-center availability of massage therapy and acupuncture were collected through standardized “secret shopper” phone conversations with clinic staff and/or navigation through each center’s website.

MATERIALS AND METHODS: The LBR from SART-affiliated fertility clinics from 6 states (NY, NJ, MA, PA, AZ, WA) were collected. Cycles utilizing gestational carriers were excluded, as were centers without finalized SART data or with unknown SRM treatments. Information regarding in-center acupuncture or massage was gathered via the centers’ websites or anonymous phone conversations with center staff. The primary outcome was LBR in the primary outcome per egg retrieval cycle. LBR was weighted based on the number of cycles performed in each age group for each center. The mean LBR was compared between centers who offer in-center SRM and those who do not stratified by SART maternal age group (<35, 35-37, 38-40, 41-42, >42) using student’s t-test; p<0.05 determined significance.

RESULTS: Ninety-four centers in 6 states (NY, NJ, MA, PA, AZ, WA) were identified using the SART website; 9 centers were excluded due to non-finalized 2016 data and 16 centers were excluded due to unavailable SRM information. Of the 69 fertility clinics included, 16 offered acupuncture and/or massage therapy in-center. LBR was significantly higher in women ages <35 (41.8% vs 37%, p-value 0.02) and 35-37 (32.8% vs 13.7%, p-value 0.04) in clinics offering SRM compared to those who do not (Table).

<table>
<thead>
<tr>
<th>SART Age Category</th>
<th>Live Birth Rate with SRM (n=16)</th>
<th>Live Birth Rate without SRM (n=55)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>41.8</td>
<td>37.0</td>
<td>0.02</td>
</tr>
<tr>
<td>35 - 37</td>
<td>32.8</td>
<td>13.7</td>
<td>0.04</td>
</tr>
<tr>
<td>38 - 40</td>
<td>20.5</td>
<td>10.0</td>
<td>0.17</td>
</tr>
<tr>
<td>41 - 42</td>
<td>11.1</td>
<td>5.5</td>
<td>0.20</td>
</tr>
<tr>
<td>&gt;42</td>
<td>4.2</td>
<td>2.0</td>
<td>0.30</td>
</tr>
</tbody>
</table>

CONCLUSIONS: To our knowledge, this is the first study to examine the impact of stress reduction modalities including massage and acupuncture on SART-reported LBR among affiliated clinics. LBR was found to be significantly higher for women ages <35 and 35-37 among clinics that offer these complementary therapies. This suggests that incorporating alternative medical treatments, such as acupuncture and massage, may improve IVF outcomes for younger patients. It is possible that older patients have less of a benefit due to the profound relationship between age and fertility; however, expanding this analysis to include more centers may similarly suggest a benefit for a broader patient population, and help to ascertain the true utility of SRM.
RESULTS: The study included 6,656 eligible patients. Among the PGT-A group, 19.1% of those without a delivery in the first cycle did not return for a second cycle compared to 13.3% in the non-PGT-A group (P = 0.02) (Table 1). The proportion not returning after subsequent cycles did not differ (all P ≥ 0.14). The cumulative incidence of live birth after up to six IVF cycles was similar in the PGT-A (76.1%, 95% CI: 67.3–82.6%) and non-PGT-A (72.9%, 95% CI: 71.2–74.5%).

CONCLUSIONS: Couples utilizing PGT-A were more likely than those who did not to terminate treatment after the first unsuccessful IVF cycle. In subsequent cycles, those using PGT-A were just as likely as those who did not to terminate treatment prior to achieving a live birth. Although it is accepted that PGT-A improves the likelihood of live birth per transfer, it is likely many couples did not return to care due to a lack of euploid embryos or due to the stresses of fertility treatment independent of PGT-A.

SUPPORT: None.

O-156 Tuesday, October 15, 2019 12:00 PM

HAIR CORTISOL AS A NEW BIOMARKER OF UNDERLYING CHRONIC STRESS, ANXIETY AND DEPRESSION IN INFERTILITY: A PILOT STUDY

Diana C. Santa-Cruz, MSc, a Rafael Caparros-Gonzalez, PhD, b Juan A. Garcia-Velasco, MD, PhD, b 1IVI-RMA Madrid, Madrid, Spain; 2Universidad de Jaen, Jaen, Spain.

OBJECTIVE: To study the viability of hair cortisol levels as new biomarker of chronic stress and explore its relationship with perceived anxiety levels and depressive symptoms.

DESIGN: Prospective, observational, cross-sectional study.

MATERIALS AND METHODS: A total of 50 non-smoking women, with body mass index of 19-30 kg/m2 and no previous fertility treatments, undergoing IVF were eligible for the study. Interested patients were asked to give a sample of their hair in their second consultation with the doctor and twelve weeks later. Study exclusion criteria included subjects with any recognized psychiatric or immune health condition; no drugs, alcohol consumption or high caffeine consumption. To reduce the confounding effect of risk variables, patients diagnosed with Cushing disease, asthma, on steroid medication, diabetes or other conditions known to influence cortisol levels, were excluded. The State-Trait Anxiety Inventory (STAI) and Depression Subscale (DEP) from Symptom Checklist 90-R (SCL-90-R) were used to assess anxiety and depression respectively at the time of the treatment. Over all patients had more Trait Anxiety than T2 (mean: 24.4, p < 0.001) than T2 (mean: 29.8, p < 0.001) than T2 (mean: 24.4, p < 0.001) while there was a mild difference in terms of depression (mean: 0.8 vs 1.5, p < 0.001) from T1 to T2. Cortisol levels increased from T1 to T2 (mean: 239.2 vs 246.9, p < 0.001). On T2, 52% of women had a positive pregnancy test, and their cortisol levels were reduced from T1 to T2 (mean: 357.2 vs 151.1, p < 0.001) while women who had a negative result had higher cortisol levels at T2 (mean: 106.5 vs 378.6, p < 0.001). Regarding correlation only frequent physical exercise showed a significant association to lower cortisol secretion at T1 but not at T2 (0.03 vs 0.09, p < 0.05). Neither age, infertility diagnosis, anxiety levels had any significant association with cortisol.

CONCLUSIONS: We have shown that hair cortisol is a promising new biomarker to evaluate chronic stress in infertility patients. Cortisol secretion interacted with stress to accelerate the development of depressive symptoms, especially in those patients with a negative pregnancy test. Replication of these findings in a larger population will allow further explorations of the possible physiological mechanisms underlying stress and treatment outcomes.

PEDICIAN AND ADOLESCENT GYNECOLOGY

O-157 Tuesday, October 15, 2019 10:45 AM

ADOLESCENTS AND ECTOPIC PREGNANCY: TRENDS IN EMERGENCY DEPARTMENT UTILIZATION BETWEEN 2006-2014

Emma Giuliani, MD, a Monica W. Rosen, MD, b Elisabeth H. Quint, MD, b Erica E. Marsh, MD, a Yolanda R. Smith, MD, a Reproductive Endocrinology and Infertility, University of Michigan, Ann Arbor, MI; University of Michigan, Ann Arbor, MI.

OBJECTIVE: Ectopic pregnancies (EP), if not promptly diagnosed and treated, are associated with significant morbidity and mortality and can negatively impact future fertility in young women. A substantial portion of the work-up and management of EP occurs in the Emergency Department (ED). To better understand this condition in adolescents, we investigated trends in ED utilization for EP in girls aged 13 to 19 years old over a 9-year period.

DESIGN: Retrospective cross-sectional study.

MATERIALS AND METHODS: The Nationwide Emergency Department Sample (NEDS), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality, was queried for all ED visits in adolescents between 13 and 19 years old with a primary or secondary diagnosis (ICD-9-CM) of EP from 2006 to 2014. Parameters assessed included national estimated numbers of ED visits, ED charges adjusted for inflation, hospital geographic locations, patient’s demographic characteristics, and methotrexate (MTX) administration (SAS 9.4 - Cary, NC).

RESULTS: Approximately 75% of adolescents who presented to the ED for EP between 2006 and 2014 were 18 or 19 years old. While the number of ED visits for EP in adolescents remained fairly stable between 2006 and 2010 (3,264 versus 3,180), there was a 17.0% drop in 2011 (2,707) and another 17.9% drop in 2014 (2,221). In the most recent year analyzed, 2014, the majority of ED visits for EP in adolescents were seen in metropolitan areas in the southern regions (38.4%), in patients with Medicaid insurance (57.1%) and those in the lowest quartile for household income based on zip code (35.5%). Average ED charges per visit for EP progressively increased from $5,301 in 2006 to $9,066 in 2014, while total ED charges for this condition remained relatively stable ($17.2M in 2006 versus $20.1M in 2014). Overall, admission rates decreased for household income based on zip code (35.5%). Average ED charges per visit for EP progressively increased from $5,301 in 2006 to $9,066 in 2014, while total ED charges for this condition remained relatively stable ($17.2M in 2006 versus $20.1M in 2014). Overall, admission rates decreased from 43.7% to 18.4% through the years analyzed. Admission rates were higher in 16 and 17 years old adolescents living in metropolitan areas and in the western states. Finally, the percentage of ED visits associated with MTX administration increased from 1.7% in 2006 to 6.9% in 2014.

CONCLUSIONS: The number of ED visits for EP in adolescents decreased substantially between 2006 and 2014, which aligns with lower teenage pregnancy rates recorded by the CDC and easier access to emergent and non-emergent contraception as made available by government initiatives.

TABLE 1. Comparing women who had PGT-A to women who did not have PGT-A in their first cycle

<table>
<thead>
<tr>
<th>Cycle</th>
<th>Cycle cohort</th>
<th>Did not return for treatment</th>
<th>N/Total N (%)</th>
<th>Cycle cohort</th>
<th>Did not return for treatment</th>
<th>N/Total N (%)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6,656</td>
<td>NA</td>
<td>273</td>
<td>NA</td>
<td>6,383</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>4,483</td>
<td>704/5,187 (13.6)</td>
<td>174</td>
<td>41/215 (19.1)</td>
<td>4,309</td>
<td>663/4,972 (13.3)</td>
<td>0.02</td>
</tr>
<tr>
<td>3</td>
<td>2,470</td>
<td>593/3,063 (19.4)</td>
<td>108</td>
<td>21/129 (16.3)</td>
<td>2,362</td>
<td>572/2,934 (19.5)</td>
<td>0.37</td>
</tr>
<tr>
<td>4</td>
<td>1,427</td>
<td>379/1,806 (21.0)</td>
<td>58</td>
<td>22/80 (27.5)</td>
<td>1,369</td>
<td>357/1,726 (20.7)</td>
<td>0.14</td>
</tr>
<tr>
<td>5</td>
<td>816</td>
<td>270/1,086 (24.9)</td>
<td>38</td>
<td>11/49 (22.5)</td>
<td>778</td>
<td>259/1,037 (25.0)</td>
<td>0.69</td>
</tr>
<tr>
<td>6</td>
<td>507</td>
<td>162/669 (24.2)</td>
<td>18</td>
<td>6/24 (25.0)</td>
<td>489</td>
<td>156/645 (24.2)</td>
<td>0.93</td>
</tr>
</tbody>
</table>

*P compares PGT-A with no PGT-A.
over the same time period. The drop in admission rates suggests an opportunity to shift the low-acuity cases of EP from the ED to the less expensive outpatient clinics. Additionally, adolescents who utilized the ED for EP more frequently belonged to the lowest income quartile and had Medicaid coverage, which presents potential disparities in access to care and highlights a need for improved pediatric and adolescent gynecology outpatient services.

O-158 Tuesday, October 15, 2019 11:00 AM

PARENT COMPREHENSION FOLLOWING VIDEO-BASED EDUCATION FOR PEDIATRIC FERTILITY PRESERVATION. Nicole Handa, BS,1 Courtney J. Harris, MD,2 Kristine S. Corkum, MD,2 Aminata Bangoura, BS,2 Shaina M. Goff,3 Monica M. Laronda, PhD,4 Erin E. Rowell, MD,4 Nor- thwestern University Feinberg School of Medicine, Chicago, IL;1 Depart- ment of Pediatric Surgery, Ann & Robert H Lurie Children’s Hospital of Chicago, Chicago, IL;2 Stanley Manne Children’s Research Institute, Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL;4 Division of Pediatric Surgery, Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL.

OBJECTIVE: Decisions about whether to pursue fertility preservation (FP) can be particularly difficult in the pediatric patient population because parents are making decisions for their children. Additionally, the therapies for prepubertal children and surgical FP are experimental. Parents often cite lack of knowledge about infertility risk and experimental nature of options as barriers in deciding whether to pursue FP. This study was designed to gauge comprehension of FP video-based educational tools and to assess parent attitudes towards the tools.

DESIGN: This was a prospective randomized survey-based study completed 2018-2019 at a single tertiary care children’s hospital with Institutional Review Board approval.

MATERIALS AND METHODS: Participants were parents of pediatric patients (0-18 years old) admitted to a general surgery floor. Parents of children with a diagnosis putting them at risk for infertility or who had previously undergone FP were excluded. Participants completed pre-assessment questions, viewed two publicly available videos about FP, and completed post-assessment questions. Video A was colorful, animated, and used simple vocabulary. Video B was mostly black-and-white, more detailed, and used more complex vocabulary. Participants were randomized into two groups, each viewing the videos in a different order. Survey questions included participants’ FP knowledge, comprehension, and video preference. Statistics were gathered using chi-squared analyses and Wilcoxon rank sum tests.

RESULTS: 45 participants completed the survey. The average age was 37.5 years old; the majority were female (76%) and had completed high school/GED or above (98%). At baseline, 64% of participants indicated that they knew nothing about options for children at risk for infertility. After watching both videos, baseline knowledge scores improved in 73% of all participants and 61% felt like they knew some or a lot about FP. There was no difference in the number of participants that improved from baseline between the two groups (p = 0.946). After viewing both videos, 87% of participants correctly answered >50% of the comprehension questions with no difference after video A compared to video B (p = 0.832). However, 70% of participants reported a preference for video A because it was interactive, colorful, and concise.

CONCLUSIONS: After utilizing FP video-based educational tools, parents experienced an increase in FP understanding, including the risk of infertility and options available for children, with preference for videos that are colorful and interactive. Our work indicates that video-based educational tools are an effective way to increase parent knowledge of FP options in the pediatric setting.

O-159 Tuesday, October 15, 2019 11:15 AM

FACTORS ASSOCIATED WITH CHOOSING FERTILITY PRESERVATION IN A PEDIATRIC, ADOLESCENT AND YOUNG ADULT POPULATION. Megan R. Sax, MD,1 Tara Schafer-Kalick, MA,2 Brycen Ferrara, BS,2 Olivia Jaworek Frias, MSN, RN, CNL,3 Lesley Brecher, MD,3 Karen Burns, MD, MS,4 Andrew C. Strine, MD,4 Julie Srogga Rios, MD,4 University of Cincinnati and Cincinnati Children’s Medical Center, Cincinnati, OH;4 Cincinnati Children’s Hospital Medical center, Cincinnati, OH;4 Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; University of Cincinnati and Cincinnati Children’s Hospital Medical Center, Cincinnati, OH.

OBJECTIVE: To determine patient characteristics associated with the decision to pursue fertility preservation prior to gonadotoxic therapy in a female pediatric, adolescent, and young adult patient population.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: This IRB-approved study involved analysis of patient data in the Comprehensive Fertility Care and Preservation Program patient registry at Cincinnati Children’s Hospital Medical Center from 10/1/2013 through 11/6/2018. All female patients who received a fertility consult from this group were included in the analysis. Demographics, clinical diagnosis, and treatment characteristics were compared between participants that selected fertility preservation versus those that declined. Continuous variables were analyzed by student’s t-test and categorical variables were analyzed using Chi-square test. Results with p < 0.05 was considered statistically significant.

RESULTS: Of the 447 total fertility consults, 320 (71.5%) patients were eligible for fertility preservation options prior to gonadotoxic treatments, and one-third chose to pursue a fertility preservation intervention. In patients with a high-risk fertility assessment, 52.5% opted for fertility preservation.

Patients receiving high risk gonadotoxic therapy and those planning bone marrow transplant (BMT) were more likely to choose fertility preservation. A higher proportion of non-English speaking patients/families declined fertility preservation than selected it (Table 1).

CONCLUSIONS: BMT, high fertility risk assessment, and non-English as primary language but not pubertal status or previous cancer treatment were significant factors affecting patient/family choice for fertility preservation in pediatric, adolescent and young adult setting. Based on these results, it is unclear whether a language barrier or cultural beliefs are affecting the decision making in non-English speaking participants. Further research is needed answer this and to better characterize barriers to fertility preservation in this population.

WHO SEEKS FERTILITY SPECIALISTS? CANCER TREATMENTS AND SEEKING FERTILITY SERVICES IN ADOLESCENTS AND YOUNG ADULTS (AYA) WITH CANCER. Christina Lam, MD,1 Alexa CO Medina, MD,1 Kelsey Pinson, MD,2 Brian W. Whitcomb, PhD,3 Irene Su, MD, M.S.C.E.1 University of California San Diego, La Jolla, CA;4 University of California, San Diego, La Jolla, CA;1 UT Southwestern, Dallas, TX;1 University of Massachusetts, Amherst, Amherst, MA.

OBJECTIVE: Clinical guidelines endorse infertility risk counseling in newly diagnosed AYA cancer survivors and referral to fertility specialists in those who express interest. Limited empirical data exist on whether cancer treatment gonadotoxicity is related to patients seeking fertility services, which would suggest appropriate referrals to care. We hypothesized that AYA cancer survivors with planned gonadotoxic treatments are more likely to undergo infertility risk counseling (counseling) and fertility preservation procedures (FP procedures).
Cancer survivors' use of fertility preservation. Journal of pediatric hematology/oncology
K., Mertens, A. C., & Meacham, L. R. (2015). Perceptions of infertility risks among female adolescents and young adults who received alkylating chemotherapy or abdominopelvic radiation treatments before cancer treatment, indicating a continued gap in care. Survivors who received alkylating chemotherapy, 3% received pelvic radiation (RT), 1% received total body irradiation (TBI), and 8% had cancer recurrence. Adjusted for current age, cyclophosphamide equivalent dose of <7 grams/m2 and ≥7 grams/m2 were significantly associated with higher risk of being in MT stage (RR = 8.6, 95% CI 5.5-60.3). Age was not associated. RT (p = 0.001) and TBI (p = 0.04) were both associated with advanced reproductive aging stages, but small numbers precluded inclusion in multivariable models.

CONCLUSIONS: Known to be gonadotoxic, alkylating chemotherapy increased the risk of being in more advanced STRAW stages, providing novel evidence to support classifying reproductive aging in AYA survivors using STRAW+10 criteria. Menstrual pattern alone classifies AYA survivors with regard to their stage of reproductive aging, supporting the use of AMH and FSH in this population.

SUPPORT: NIH HD80952-05.

O-162 Tuesday, October 15, 2019 12:00 PM
COMPENSATORY OVARIAN HYPERTROPHY AFTER UNILATERAL OOPHORECTOMY: EVALUATION OF OVARIAN VOLUMES IN THE PEDIATRIC AND ADOLESCENT POPULATION. Allison C. Mayhew, MD, Mina Farahzad, MD, PhD, Krista Childress, MD Emory University School of Medicine, Atlanta, GA.

OBJECTIVE: Although unilateral oophorectomy is performed in the pediatric and adolescent population for indications including adnexal mass concerning for malignancy, adnexal torsion and infection, it is infrequent and the true prevalence is unknown. Limited data exists on the morphologic and physiologic effects on the remaining ovary after oophorectomy, especially in the pediatric population. Studies have shown compensatory hypertrophy of the remaining single ovary in animal studies and similar findings have been noted in the testis in human boys. Our aim is to evaluate ovarian volumes on ultrasound following unilateral oophorectomy to determine if compensatory ovarian hypertrophy occurs in the remaining contralateral ovary which may lead to important changes in clinical practice.

DESIGN: A prospective cohort study.

MATERIALS AND METHODS: The charts of 328 female patients who met the inclusion criteria were reviewed and 96 were included in the analysis. Patients were excluded if oophorectomy was not performed, they required subsequent contralateral oophorectomy, lacked follow-up ultrasound following...
oophorectomy, or had sonographic abnormalities (e.g. ovarian cyst) on post-oophorectomy ultrasound. Data collected included: age, race, comorbidities, age of menarche, surgeon specialty, ultrasound findings and bilateral ovarian volumes prior to surgery, indication for surgery, surgical pathology, and ultrasound findings and ovarian volume of remaining ovary following surgery. Descriptive analysis of ovarian volume of the remaining ovary following oophorectomy calculated on ultrasound were compared to known age-matched standard volumes at the time of post-operative ultrasound.

RESULTS: The average age of patients at time of oophorectomy was 10.8 years (2 days – 18 years). Twenty-four (25%) were < 10 years of age and 72 (75%) were > 10 years. Average time from surgery to post-operative ultrasound was 12.1 months (0 – 129 months). Average ovarian volume age < 10 years was 2.5 ml and > 10 years was 13.7 ml. Sixty (63%) of patients had post-operative volumes greater than age-matched standards and 29 (30.2%) had smaller volumes. Of those with increased volume, average was 15.3 ml (< 10 years) and 15 ml (> 10 years). Sixty (62.5%) patients had volumes more than 10% larger than the age matched standards, and 50 (52.1%) patients had volumes more than 50% larger. Of the those with increased post-operative ovarian volume (n=60), 83.3% had volumes > 50% larger than age-matched standards.

CONCLUSIONS: Ovarian enlargement occurs in the contralateral ovary following unilateral oophorectomy in the pediatric and adolescent population which supports the concept of compensatory ovarian hypertrophy that has been previously demonstrated in non-human models. This knowledge is important to the future clinical management of young females who have undergone unilateral oophorectomy.

References: Arai H (1920) On the cause of the hypertrophy of the surviving A ovary after semispaying (albino rat) and on the number of ova in it. A Dev Dyn 28:59–79.

SUPPORT: None.

PRACTICE MANAGEMENT

O-163 Tuesday, October 15, 2010:45 AM
CURRENT STATUS OF REPRODUCTIVE LABORATORY PROFESSION: WORKLOAD, WELLNESS, EARNINGS AND JOB SATISFACTION. T. Arthur Chang, PhD, HCLD, ELD, 1 Ching-Chien Chang, PhD, HCLD, 1 Liel Nel-Themaat, PhD, HCLD, 1 Scott E. Smith, PhD, HCLD, 3 Shane Zozula, B.S., T.S. (ABB), 4 Y. Tina Su, PhD, 5 University of Texas Health Science Center, San Antonio, TX; 6 Reproductive Biology Associates, Atlanta, GA; 7 University of Colorado Anschutz Medical Campus, Aurora, CO; 8 Abing- ton IVF & Genetics, Abington, PA; 9 Ovation Fertility, Newport Beach, CA.

OBJECTIVE: To investigate the current workplace status among reproductive laboratory professionals in the U.S., including trends in earnings and comparison to benchmarks, work environment, job satisfaction, and wellness.

DESIGN: Retrospective analysis of multiple years of Society of Reproductive Biologists and Technologists (SRBT) Salary and Job Satisfaction Surveys with comparable publications and benchmarks.

METHODS: Using data from the SRBT surveys 2000-2010, two step procedures were implemented: a logistic regression for every surgeon to estimate a linear term expressing the relationship between experience and embryos transfers performed by the surgeon on duty on that day were included. For operators with previous experience, the number of previous procedures was their entering threshold.

MATERIALS AND METHODS: A logistic regression model with a random intercept for the surgeon was specified, accounting for the heterogeneity among surgeons. To investigate the role of experience on OPR, a two-step procedure was implemented: a logistic regression for every surgeon to estimate a linear term expressing the relationship between experience and outcome. Finally, when the estimated slopes were compared through meta-analysis techniques.

RESULTS: Total of 1,737 responses were analyzed. Overall, survey re- sponses showed satisfaction with their current jobs and optimism on job market projections. However, the majority of survey responses also indicated significant stress (89% answered medium to extremely high level of stress), burnout (60% answered medium to extremely high level of stress), and overtime work (72.8%). Most common benefits received were health and dental insurance, paid time-off, retirement plan, and support for conference attendance and certification. In 2018, the average annual clinical workflow processed by each hands-on personnel included 108 fresh oocyte retrievals, 86 FETs, 79 biopsies for PGT, and 167 andrology tasks. Throughout the past two decades, nominal compensation (non-inflation adjusted) of reproductive lab professionals steadily increased throughout most of the survey period, with numbers higher than the national average for college/advanced degree workers. Such earnings were higher than most clinical lab specialties as well, with exception in a couple biotechnology sectors. Director earnings in- creases trended higher to advanced degree workers nationwide. Non-director categories showed a more significant salary growth than nationwide college/advanced degree workers and lab directors. Data from recent years revealed a wider distribution in salary range, which may reflect the volatility due to short supply of senior embryologists. Recent data also demon- strated an increasing portion of bonus in the compensation structure, which may indicate a broader utilization of bonus/incentives across all clinical settings, and possibly a contributing factor to the wider range of compensation among lab personnel. Gender-related difference in compensation re- mains significant despite an overall smaller gap than nationwide college/advanced degree workers.

CONCLUSIONS: The salary trend of reproductive lab profession show a steady increase throughout the period, a good indication compared to national labor wage and related clinical lab wage benchmarks. However, work-related stress, burnout, overtime duties, and gender pay gap remain issues to be resolved. Potential factors and impacts on these trends warrant further investigation.

O-164 Tuesday, October 15, 2019 11:00 AM
DOES THE OPERATOR PERFORMING THE EMBRYO TRANSFER SIGNIFICANTLY INFLUENCE THE CYCLE OUTCOME? Federico Cirillo, MD, EFMR ESHE/ EBCOG, 1 Pasquale Patrizio, M.D., 2 Emanuela Morenghi, Prof, 1 Michela Baccini, Prof, 1 Elena Zannoni, MD, 1 Luca Cafaro, MD, 1 Camilla Ronchetti, MD, 1 Annamaria Baggiani, MD, 1 Paolo Emanuele Levi Setti, MD, 2 Humanitas Research Hospital, Rozzano (Milan), Italy; 3 Yale Fertility Center, New Haven, CT; 4 Biostatistics Unit, Humanitas Research Hospital, Rozzano (MI), Italy; 5 Department of Statistics, Computer Science Applications, University of Florence, Florence, Italy.

OBJECTIVE: Although embryo transfer (ET) is recognized to be an operator dependent technique, it is still unclear whether there are factors that can influence a correlation between success and operator. This study sought to analyze whether Ongoing Pregnancy Rate (OPR) is associated to the operator and whether there is a learning curve to become proficient.

DESIGN: Retrospective comparative analysis including all the fresh ET performed between 1996 and 2016 at a University-affiliated Center. Only embryo transfers performed by the surgeon on duty on that day were included. For operators with previous experience, the number of previous procedures was their entering threshold.

MATERIALS AND METHODS: A logistic regression model with a random intercept for the surgeon was specified, accounting for the heterogeneity among surgeons. To investigate the role of experience on OPR, a two-step procedure was implemented: a logistic regression for every surgeon to estimate a linear term expressing the relationship between experience and outcome. Finally, when the estimated slopes were compared through meta-analysis techniques.

RESULTS: We included in the analysis 19,829 fresh ET performed by 32 operators. The random effects logistic model included: woman age, FSH, number of oocytes retrieved, fertilization rate, year of the procedure, number and stage of transferred embryos. The likelihood-ratio test for the heterogeneity among operators was highly significant (p-value = 0.0066). From the estimated OPR, best operator the difference between intercepts varied from a co-efficient of -0.205374 to a coefficient of 0.1458145: this result can constitute a very big burden. Performing a random effects meta-analysis on these slopes, we found that the overall estimate was near zero, with a total pooled effect = 0.000 (-0.001 - 0.001). No evidence arose of an increase in OPR according to the operator’s experience. The f2 of the heterogeneity among slopes was 43.7%. From our data, some operators perform worse than the
mean and do not improve with additional transfers. This observation can be explained because ET is generally performed by a single operator who learns on his own, with little opportunity of comparison.

CONCLUSIONS: This study shows that the operator factor can affect OPR but there is no significant increase in the outcome with experience. In future a very useful method could be the digital simulator, which could help operators to ameliorate without practicing on real patients.

SUPPORT: None.

O-165 Tuesday, October 15, 2019 11:15 AM

ONLINE PATIENT REVIEWS ARE INFLUENCED BY TYPE OF PHYSICIAN-BASED INFERTILITY PRACTICE. Ricci Allen, BA, BS, MSc,1 Shruti Agarwal, DO.1 Mark P. Trolle, MD.1 *University of Central Florida College of Medicine, Orlando, FL; 1UCF College of Medicine/HCA Consortium of Greater Orlando, Kissimmee, FL; 2Fertility CARE: The IVF Center, University of Central Florida College of Medicine – Associate Professor, Winter Park, FL.

OBJECTIVE: In the field of reproductive endocrinology and infertility (REI), physician online presence plays a large marketing role with success rates and procedures reported on clinic/hospital websites and patient assessments on physician rating sites. Compared to other specialties, REI clinics place a strong emphasis on optimizing patient-centered care in order to enhance their experience, increase treatment compliance and patient wellbeing while minimizing anxiety and depression during their often extended treatment cycles. The objective of this study is to determine if patient online ratings are influenced by infertility insurance coverage. We hypothesize that patient reviews of physicians will be more positive in areas where health insurance mandates fertility coverage given that financial burden on patients is often cited as a major stressor of their experience.

DESIGN: Retrospective Cohort Study.

MATERIALS AND METHODS: Online physician ratings submitted between 2016-2019 from popular websites (Vitals, RateMD, Healthgrades) were recorded for REI specialists in the U.S. registered through SART and CDC. Overall rankings of physicians were compared based on infertility insurance coverage, clinic location, and type of clinical practice (university/hospital vs. private practice). Infertility insurance coverage was determined as covered if state health insurance mandates fertility coverage and that financial burden on patients is often cited as a major stressor of their experience.

RESULTS: Data was collected from 1,097 REI specialists. An average rating of 4.09 out of 5 was found for physicians in states with mandated insurance coverage and an average rating of 4.08 out of 5 was found for those without insurance coverage (p = 0.762). The average rating for physicians based within a university/hospital practice was 3.96 compared to 4.13 for physicians in a private practice setting (p = 0.011). Among regions in the U.S., the South scored significantly higher mean average rating (p<0.01) than the Northeast and Midwest region. There was no significant difference (p>0.05) between West and South region (see Table).

CONCLUSIONS: A statistically significant higher rating was found for physicians in private practice compared to those affiliated with a university/hospital. No difference was found between the average rating in states with mandated insurance coverage for infertility treatment compared to states without insurance coverage. Furthermore, the South region had significantly higher mean average ratings compared to other regions in U.S except the west.

<table>
<thead>
<tr>
<th>Region</th>
<th>N</th>
<th>Mean Average Rating +/- standard deviation</th>
</tr>
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<tbody>
<tr>
<td>Northeast</td>
<td>327</td>
<td>3.99 +/- 0.930*</td>
</tr>
<tr>
<td>West</td>
<td>241</td>
<td>4.14 +/- 0.95</td>
</tr>
<tr>
<td>South</td>
<td>354</td>
<td>4.22 +/- 0.85*</td>
</tr>
<tr>
<td>Midwest</td>
<td>175</td>
<td>3.91 +/- 1.01*</td>
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</tbody>
</table>

*p = 0.01 – 0.049; ‘p = 0.765


O-166 Tuesday, October 15, 2019 11:30 AM

FREQUENCY AND CLAIMS BASIS FOR LAWSUITS OVER LOST, DISCARDED AND DAMAGED FROZEN EMBRYOS OVER A 10 YEAR PERIOD. Gerard Letterie, MD.1 2.3. Dov Fox, JD, DPht, LLM.1 2.3. Seattle Reproductive Medicine, San Diego, CA; 1Professor of Law and Director of the Center for Health Law Policy and Bioethics at the University of San Diego, San Diego, CA.

OBJECTIVE: Cryopreservation technology has opened options to preserve fertility and maximize family building options. These opportunities create liability risks for providers not directly related to clinical practice and quality controls but also for maintenance of laboratory equipment and environment. Insights into how best to deliver care and assure optimal outcomes may be gained from a first-ever review of an increasing body of recent case law brought over embryos that have been lost, damaged discarded, mis-implanted or contaminated. Our objectives are to review claims, basis of claims and frequency of lawsuits over lost frozen or damaged frozen embryos.

DESIGN: Retrospective review of case law in state and federal courts over a 10 year period.

MATERIALS AND METHODS: Case law was researched from January 1, 2009 to April 22, 2019. Bloomberg, Westlaw and Lexis Nexis databases were searched to provide coverage of state court dockets regarding allegations and basis of cases made. Bloomberg Law included all federal court dockets. Cross-referenced terms included embryo, fertilized oocyte, frozen or cryopreserved embryo, discarded, lost and damaged embryo/s and implanted embryos. Data extracted included claims arising in federal and state courts.

RESULTS: A total of 131 cases were identified: 121 and 10 lawsuits in the state and federal court dockets respectively. 87 cases involved the recent cases in California and Ohio in 2018-19. Allegations for these relate to freezing the embryo in the wrong tank, loss of the embryo, loss of the tank, or tank failure. In the remaining 44 cases, the majority (37) were brought across a broad range of allegations including: personal injury; breach of contract or warranty; product liability; professional negligence; unfair business practices and miscellaneous tort. A minority of cases (7) were brought for medical malpractice. The locations of these 44 cases included New York, Delaware, Illinois, Arizona and North Dakota.

CONCLUSIONS: The frequency of suits for damaged, lost or destroyed embryos is low with the exception of the recent events in California and Ohio. The basis of the claims is seldom for medical malpractice. These findings suggest that insurance coverage directed to claims outside of medical malpractice may be warranted given the expanding inventories of frozen oocytes, embryos and sperm and varying basis for claims.

SUPPORT: None.

O-167 Tuesday, October 15, 2019 11:45 AM

IMPROVED MONITORING OF HUMAN EMBRYO CULTURE CONDITIONS USING A DEEP LEARNING-DERIVED KEY PERFORMANCE INDICATOR (KPI). Manoj Kumar Kanakasabapathy, MS.1 Prudhvi Thirumalaraju, BS.1 Raghav Gupta, BTech.2 Rohan Pooniwalla, BTech.3 Hemanth Kandula, BS.1 Irene Souter, MD.3 Irene Dimitriadi, MD.2 Charles L. Bormann, PhD.2 Hadi Shafee, PhD.1 2Brigham and Women’s Hospital, Harvard Medical School, Boston, MA; 2Massachusetts General Hospital, Harvard Medical School, Boston, MA.

OBJECTIVE: The clinical outcome of an in-vitro fertilization (IVF) cycle is perhaps the best indicator of system efficiency with ongoing pregnancy rates providing the most robust marker of embryo quality. Several early developmental stage markers are widely used to monitor culture conditions, however, their association with clinical outcomes is unclear. The objective of this study was to determine whether the use of an artificial intelligence (AI) algorithm, trained to predict in-vitro human embryo developmental fate, can be effectively used as a key performance indicator (KPI) for monitoring the performance of the embryo culture system.

DESIGN: Retrospective cohort study using a pre-developed deep neural network. The deep neural network (AI) analyzed embryos images acquired at 70 hours post insemination and provided a score (KPI score) taking into account all embryos within a given group.
FERTILIZATION AND EMBRYO GRADING

ICSI USING DEEP LEARNING-ENABLED INDIVIDUAL EMBRYOLOGISTS PERFORMING AUTOMATED QUALITY ASSESSMENT OF EMBRYO TRANSFER MANEUVERS AND MANIPULATIONS – THE EFFECT ON IN VITRO FERTILIZATION (IVF) OUTCOMES.

MATERIALS AND METHODS: A total of 876 embryos were cultured in 6 different lots of media (Medium A-F; CSC-Complete, Irvine Scientific) and under identical conditions at 37 °C, 5% O2 and 5% CO2 with oil overlay (Ovoil, Vitrolife). The percentage of 2 pronucleus (2PN) zygotes at the 4-cell stage on Day 2, 8-cell, 6 to 10-cell, ≥ 7-cells and those predicted to develop into high quality blastocyst stages using an AI-based generated KPI on Day 3 of embryo development was compared with ongoing pregnancy rates using a regression analysis. The low threshold value for ongoing pregnancy rates in the Massachusetts General Hospital (MGH) fertility clinic is set at 50%.

RESULTS: The AI-based generated KPI for predicting high quality blastocyst formation had the highest association with ongoing pregnancy rates. This was the only cleavage stage KPI examined that was able to detect changes in our embryo culture environment that resulted in the pregnancy rates dropping below the threshold of 50%.

CONCLUSIONS: The most important aspect of quality assurance analysis is the identification of KPIs that will provide meaningful insight into laboratory functioning. This study demonstrated the power of using AI predictions in monitoring the performance of the embryo culture environment.


O-168 Tuesday, October 15, 2019 12:00 PM

AUTOMATED QUALITY ASSESSMENT OF INDIVIDUAL EMBRYOLOGISTS PERFORMING ICSI USING DEEP LEARNING-ENABLED FERTILIZATION AND EMBRYO GRADING TECHNOLOGY. Prudvi Thirumalaraju, MS, a Manoj Kumar Kanakasabapathy, MS, a Raghav Gupta, BTech, a Rohan Pooniwala, BTech, a Hemanth Kandula, BS, a Irene Souter, MD, a Irene Dimitriadis, MD, b Charles L. Bormann, PhD, b Hadi Shafiee, PhD, b Brigham and Women’s Hospital, Harvard Medical School, Boston, MA. a Massachusetts General Hospital, Harvard Medical School, Boston, MA.

OBJECTIVE: Data analysis is a crucial part of an effective in-vitro fertilization (IVF) quality program to ensure proper laboratory functioning and, perhaps more importantly, to identify potential problems to permit timely corrections. Fertilization assessment is the primary outcome used to measure embryology staff proficiency with Intracytoplasmic sperm injection (ICSI). However, tracking the developmental fate of ICSI derived embryos may provide a more complete picture of how well this procedure is being performed. Current quality assessments require manual examination into laboratory functioning. This study demonstrated the power of using AI predictions in monitoring the performance of the embryo culture environment.

MATERIALS AND METHODS: In our study, performances of 7 individual embryologists were calculated through manually analyzing the developmental outcome rates with the outcome rates measured automatically by an AI system through morphological analyses. The AI system developed to evaluate fertilization and blastocyst development was utilized for this work. We compared the rates of fertilization, blastocyst development, and high-quality blastocyst (HQB) development in a total of 947 embryos that were divided between the 7 embryologists. To evaluate the difference between the two analysis methods, we performed a Wilcoxon matched-pairs signed rank test and a coefficient of variation (%CV) analysis.

RESULTS: The Wilcoxon tests revealed that the two approaches performed with negligible differences (P>0.05) for all three rate estimations (Fertilization, Blastocysts, and HQB). The medians of differences for estimations of fertilization, blastocyst, and HQB were -1.3% (P>0.31), 1.8% (P>0.09), and -3.6% (P>0.18), respectively. The %CV estimations also showed that the difference between manual and AI-generated estimations for each embryologist in all three rates was low. The median of %CV between the two approaches in measuring the rates of fertilization, blastocysts, and HQB were 1.9%, 3.4%, and 10.9%, respectively.

CONCLUSIONS: This study is the first to describe the use of artificial intelligence to monitor individual embryologists performing ICSI in a clinical setting. The extremely low coefficient of variation between the manual and AI-based QA assessment methods demonstrate the high accuracy of the automated AI system. This study demonstrates an alternative method for monitoring KPIs in the IVF laboratory without the need for manual assistance.


O-169 Tuesday, October 15, 2019 10:45 AM

EMBRYO TRANSFER MANEUVERS AND MANIPULATIONS – THE EFFECT ON IN VITRO FERTILIZATION (IVF) OUTCOMES. Briana O’Leary, MD, a Andrea Lanes, PhD, a Ann M. Thomas, PhD, a Elizabeth S. Ginsburg, MD, a Malinda S. Lee, MD, MBA, a Brigham and Women’s Hospital, Boston, MA. a Brigham & Women’s Hospital, Boston, MA.

OBJECTIVE: To determine the effect of maneuvers performed on the embryo transfer (ET) catheter during ET on in vitro fertilization (IVF) outcomes.

MATERIALS AND METHODS: This study included all women undergoing IVF/ICSI with a subsequent Day 3 or Day 5 ET at a single academic hospital. IVF practice from 1/2013 to 1/2018. The first ET during the study period was included from each patient. A ‘trial followed by transfer’ method was routinely employed and all ETs were performed under abdominal ultrasound guidance. Each ET was systematically scored on ease by the transferring physician (easy, some difficulty, extreme difficulty) and any additional maneuver or instrumentation that was needed to perform the ET, such as bending the outer sheath of the catheter, extending the outer sheath over the inner catheter, and retaining the external sheath (conversion into an ‘afterload’ method).

The primary outcome was live birth rate. Secondary outcomes included clinical pregnancy rate (CPR), implantation rate (IR), ectopic, biochemical and miscarriage rate.

Direction of the uterus, catheter used, infertility diagnosis, BMI, age, donor egg, fresh versus frozen embryo, use of a gestational carrier, preimplantation genetic testing, endometrial thickness, presence of blood and mucus on the transfer catheter, distance from the fundus, and physician performing the ET
MINIMALLY INVASIVE UTERINE ASPIRATION 24 HOURS AHEAD OF EMBRYO TRANSFER CHARACTERIZES THE COMPROMISED RIF UTERINE MICROENVIRONMENT AND IS PREDICTIVE OF REPRODUCTIVE OUTCOME.

Jason C. Parks, BS, Blair R. McCallie, BS, Mary E. Haywood, PhD, Taylor Pini, PhD, William B. Schoolcraft, MD, Mandy G. Katz-Jaffe, Ph.D., Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Repeat implantation failure (RIF) is particularly challenging to treat in ART, resulting in limited success even when adequate preparation of the endometrium is established and a transfer is performed with a high grade euploid blastocyst. The objective of this study was to utilize a multidisciplinary approach to decipher the complexity of RIF through investigations of the maternal molecular components ahead of an embryo transfer.

DESIGN: Research study.

MATERIALS AND METHODS: Patients were recruited with IRB consent 24 hours prior to a programmed frozen embryo transfer (FET) with a euploid blastocyst. Uterine secretions were collected by gentle aspiration (~2-5ul) under ultrasound guidance and grouped according to reproductive outcomes: Failed euploid FET (RIF patients, ≥ 3 prior IVF failures) and Positive live birth FET (maternally age-matched patients; mean 36.6 ±3.8 years of age) were analyzed for RNA sequencing on the NovaSEQ 6000 (Illumina). Reads were aligned to hg38 using GSNAP and analyzed with edgeR (FDR cutoff of 5%; P<0.01). Metabolite analysis (n = 20) was performed by UHPLS-MS (Thermo) using MassMatrix and Maven (Princeton Univ). Proteomic analysis (n = 6) involved FASP digestion and LC-MS/MS, with protein identifications generated by Mascot (v 2.6) and Scaffold (v 4.8.9) (a = 0.05; fold change >1.5 or <0.5).

RESULTS: A unique uterine microenvironment was observed for RIF patients and negative implantation outcomes 24 hours prior to an embryo transfer (P<0.05). An interplay of several biological processes were evident in RIF failed aspirates with a focused interest on 13 significantly reduced transcripts, 7 significantly increased maternal miRNAs, 12 significantly decreased amino acids and 16 proteins of significantly altered abundance (P<0.05). Specific examples included decreased expression of PLA2G4D (P<0.001), which was positively correlated with NO (n = 20); reduction of tandem reads on the NovaSEQ 6000 (Illumina). Increases in miR-17, a known negative regulator of VEGFA, required for successful implantation (P<0.01). Decreased quantities of arginine, essential for blastocyst activation and trophoblast cell motility (P<0.05). Lastly, increased abundance of SERPING1, a protein associated with inflammation, which suggested a complement activation (P<0.05).

CONCLUSIONS: Analysis of uterine secretions 24 hours prior to FET, allowed for an in-depth molecular characterization of the compromised RIF uterine microenvironment and was predictive of reproductive outcome. The negative influence on key miRNAs and gene transcription levels, in addition to altered amino acid and protein concentrations, were all identified as critical contributors to poor RIF outcomes. Ongoing investigations into the relationships of these molecular networks will lead to the possibility of more effective clinical interventions for this difficult patient population.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Women (age range 20-48) diagnosed with POI based on ESHRE criteria (amenorrhea or oligomenorrhea for at least four months and increased follicle-stimulating hormone (FSH) > 25 IU/l measured twice with a four-week interval) were recruited for the study. Antral follicle counts (AFC), anti-mullerian hormone (AMH), and FSH levels were determined at baseline. PRP was prepared from peripheral blood using routine techniques. PRP injection was performed transvaginally, under ultrasound guidance, into at least one ovary using a 35 cm 1G single lumen needle. Cyclic estrogen (4 mg estradiol daily on days 1-25) and progesterone (200 mg progesterone daily on days 16-25) were used to induce vaginal bleeding after PRP treatment. On the 2-4th days of induced menses after the procedure, AFC, AMH, and FSH levels were re-assessed. Patients with at least one atretic follicle were started on ovarian stimulation for IVF-ICSI and embryo banking at cleavage stage. Markers of ovarian reserve (AFC, FSH, AMH), and IVF laboratory outcome parameters (number of MII oocytes, 2PN embryos, cleavage stage embryos) were followed.

RESULTS: At the time of this submission, a total of 70 patients (mean age ± SD: 40.8 ± 4.8) with the diagnosis of POI were included in the study. PRP treatment resulted in improved AFC (2.6 ± 1.3 vs 0.9 ± 0.8; P<0.01), increased estradiol levels (4.0 ± 3.0 vs 3.4 ± 2.6 IU/l; P=0.08), and lower serum FSH (32.6 ± 9.6 vs 37.4 ± 11.2; P=0.06) levels. Total number of MII oocytes, 2PN and cleavage embryos obtained were 2.38 ± 1.57, 2.00 ± 1.47, and 1.94 ± 1.08, respectively. In 24 patients (34.2%), no changes were observed in terms of AFC or other laboratory parameters after the PRP procedure, therefore IVF-ICSI was not attempted. Another 24 patients (34.2%) failed to respond to stimulation or had fertilization failure. In 21 patients (30%), at least one cleavage stage embryo was obtained and embryo banking was performed. Importantly, spontaneous pregnancy occurred in six patients (7.1%, mean age ± SD: 39.5 ± 5.8) one or two cycles after the PRP procedure. At the time of this report, one of these pregnancies had resulted in missed abortion while the others were ongoing.

CONCLUSIONS: In women with POI, intraovarian injection of autologous PRP might be considered as an alternative experimental treatment option. Future studies with larger sample size and randomized prospective study design will be necessary to determine whether this intervention truly resulted in improved clinical outcomes.
**SAFETY OF OIL-BASED CONTRAST MEDIUM FOR HYSTEROSALPINGOGRAPHY: A SYSTEMATIC REVIEW.** Inez Roest, BSc; Nienke van Welie, M.D., b

**OBJECTIVE:** Previous studies suggest an endometrial receptivity analysis (ERA) may improve implantation and live birth rates for patients with previous frozen embryo transfer (FET) failure. The purpose of this study is to evaluate whether performing an ERA prior to first time FET with a euploid blastocyst improves the live birth rate.

**DESIGN:** This is a single institution retrospective cohort study.

**MATERIALS AND METHODS:** A retrospective review was performed including all patients in 2017 who underwent first time FET with a euploid blastocyst(s) (n=220). All patients in this study underwent PGT-A by NexGen sequencing. The embryos were then vitrified. Patients were stratified by ERA status (n=46) vs. no ERA (n=174) prior to undergoing FET. The primary outcome was to measure the live birth rate. Secondly, we measured the implantation rate and the clinical pregnancy rate. A two-sample t-test was used to compare continuous outcomes between groups, and Chi-square testing was used to compare proportions between the two groups.

**RESULTS:** The implantation rate for patients that underwent ERA vs. no ERA prior to FET was 64.6% vs. 60.5% (p=0.71). The clinical pregnancy rate for ERA vs. no ERA prior to FET was 56.5% vs. 52.8% (0.56). The live birth rate for ERA vs. no ERA prior to FET was 52.2% vs. 51.1% (p=0.9). The single embryo transfer rate was 96% for the ERA group vs. 98% for the non-ERA group.

**CONCLUSIONS:** Performing an ERA prior to first time FET with a euploid blastocyst did not increase the live birth rate compared to patients who did not have an ERA before their first FET. The differences in implantation and clinical pregnancy rates between the two groups were also not statistically significant. Our findings warrant an adequately powered randomized controlled trial to determine the efficacy of ERA prior to the transfer of a euploid blastocyst.

**O-173 Tuesday, October 15, 2019 11:45 AM**

**REPRODUCTIVE BIOLOGY: ANIMAL AND EXPERIMENTAL STUDIES**

**HIGH-FAT DIET CAUSES DYSREGULATION OF OVARIAN ENDOTHELIN-2 EXPRESSION ACROSS THE ESTROUS CYCLE.** Natalie M. Hohos, PhD, Emily M. Elliott, BS, Malgorzata E. Skaznik-Wikiel, MD University of Texas Health Science Center at Houston, TX.

**OBJECTIVE:** To evaluate national trends in embryo transfer training for Reproductive Endocrinology and Infertility Fellows.

**MATERIALS AND METHODS:** Institutional Review Board approval was obtained. Reproductive Endocrinology and Infertility (REI) Fellowship program directors and fellows were surveyed to assess their experience with live embryo transfers performed by fellows and potential barriers to fellowship training in live embryo transfer.

**RESULTS:** Anonymous surveys were sent to 51 REI fellowship program directors and 142 fellows. Responders included 25 program directors and 47 fellows (10 first-year, 14 second-year and 23 third-year fellows). 35% practiced in the Midwest, 35% in the North East/Mid Atlantic, 18% in the South West/South East and 18% in the West/Northwest. Among all 72 responders, 19% (14/72) reported that no live embryo transfers were performed by fellows in their program. 16% (4/25) of program directors and 21% (10/47) of fellows, 70% (7/10) of first year fellows, 43% (6/14) of second year fellows and 44% (10/23) of third year fellows had performed < 10 live embryo transfers at the time of survey. The median number of live embryo transfers performed during fellowship was 20 (range 0-370, mean 65.1, SD 95). On a scale of 1-10, the program directors’ reported level of comfort with fellows performing live embryo transfer was 8.1 in the Midwest, 8.5 in the North East/Mid Atlantic, 6.9 in the South West/South East and 5.9 in the West/Northwest. Barriers to live embryo transfers performed by fellows included: attending physician acceptance (50%, 36/72), perceived patient acceptance (44%, 32/72), physician-patient relationship (42%, 30/72), history of difficulty transfer (25% 18/72), perceived fellow skill (21%, 15/72), concerns regarding competition with private practice (18%, 13/72), and lack of simulator training (8%, 6/72). There was no agreement regarding the number of live embryo transfers that should be performed prior to graduation from fellowship, with program directors reporting a range of 0 to 100 (median 25, mode 25) and fellows reporting a range of 0 to 250 (median 30, mode 50).

**CONCLUSIONS:** There are significant differences between fellowship programs regarding the availability of live embryo transfer training, with nearly half of third year fellows reporting < 10 live embryo transfers. Data suggests that embryo transfers performed by fellows have similar live birth rates to embryo transfers performed by attending physicians. However, perceptions among fellowship program directors regarding physician and patient acceptance likely influence experience during fellowship training. Efforts should be made to address these barriers and set minimum standards for number of transfers performed during fellowship.
expression throughout the estrous cycle in HFD exposed mice and compare it with chow fed controls.

**MATERIALS AND METHODS:** 5-week-old C57Bl/6j mice were fed a standard chow or 60% HFD for 10 weeks. Estrous cyclicity was evaluated daily for the last two weeks of feeding and ovaries were collected in each of the four estrous cycle stages (N = 9/group/stage). T-test and chi-square tests were used for statistical analysis, as appropriate.

**RESULTS:** After 10 weeks of diet, HFD mice weighed more than chow controls (28.8 ± 0.7g, 21.1 ± 0.2g p < 0.0001), HFD mice also had a higher prevalence of abnormal estrous cycles compared to chow controls (58.3% and 21.6% p = 0.0018). In chow controls, Edn2 was expressed as expected with basal levels during diestrus and proestrus, increased 11.6-fold during estrus, and decreased back to basal levels during metestrus. In the HFD mice, Edn2 was dysregulated across the entire estrous cycle (table 1), and when Edn2 expression was examined across all cycle stages in HFD mice, there was no characteristic peak of Edn2 expression in estrus with the lowest levels of Edn2 observed. Endothelin converting enzyme (Ece, cleaves Edn2 pre-peptide to active form) transcript expression levels were found to be uniformly upregulated in the HFD exposed mice across all stages of the estrous cycle (table 1).

**CONCLUSIONS:** Our data suggest that Edn2 and its post-translational regulation is dysregulated across the estrous cycle in HFD-fed mice. Work is currently underway to examine ovarian protein Edn2 levels across the estrous cycle to confirm our gene expression data. Future research should investigate mechanisms behind dysregulated Edn2 expression with HFD feeding. Collectively, this work will allow us to better understand how HFD leads to ovulatory dysfunction and to develop strategies targeting HFD-induced ovulation defects.


SUPPORT: Colorado NORC Pilot Grant (P30DK048520) to M.ES-W.

O-177 Tuesday, October 15, 2019 11:15 AM

**OOCYTE SPECIFIC TRANSCRIPTION REGULATORS, NOBOX AND FIGLA, ARE IDENTIFIED AS KEY CONTRIBUTORS TO THE DECLINE IN FECUNDITY ASSOCIATED WITH OVARIAN AGING.** Jennifer E. Russ, BS, Jason C. Parks, BS, Blair R. Wallace, BS, Mary E. Haywood, PhD, William B. Schoolcraft, MD, Mandy G. Katz-Jaffe, Ph.D.; Colorado Center for Reproductive Medicine, Lone Tree, CO.

**OBJECTIVE:** Advanced maternal age (AMA; ≥35 years) is associated with a decline in fecundity that is largely attributed to loss of oocyte number and quality. The aim of this study is to explore at a molecular level the relationship between aging, ovarian environment and oocyte quality.

**DESIGN:** Longitudinal research study.

**MATERIALS AND METHODS:** Young outbred CD1 female mice (3-4 months old; Young) and naturally aged outbred CD1 female mice (10-12 months old; Aged) were super-ovulated and oocytes collected (n = 10 group) for quantitative immunofluorescence of endoplasmic reticulum (ER) stress indicators, pIRE1 and ATF6. Total RNA was isolated from unstimulated ovaries (n = 6 per group), sequence libraries were prepared using the TruSeq Total RNA library kit (Illumina) and sequenced on the Illumina NovaSEQ 6000. Differentially expressed genes (DEGs) were generated using edgeR, with an FDR cutoff of 5% (q value <0.01) and Student’s t-test significance at p<0.001, followed by Ingenuity Pathway Analysis (Qiagen).

**RESULTS:** Oocyte numbers significantly declined with natural aging (Young: Aged: 4.6, Young = 12.9; p<0.0001). Total RNA sequencing revealed 281 significant DEGs in Aged versus Young ovaries (120 increased and 161 decreased; p<0.0001). Unsupervised hierarchical clustering of the 281 DEGs cleanly separated the ovaries according to female age. Enriched pathway analysis revealed signaling pathways including Citruline-Nitric Oxide Cycle, VEGF Family Ligand Receptor Interactions, and HIF1 signaling. Nitric oxide is a common signaling molecule in these pathways, and has been shown to maintain diopole arrest in pre-ovulatory oocytes. Aged ovaries displayed a significant decrease in nitric oxide gene expression.
SAFE AND EFFICIENT DETECTION OF EGG MATURITY WITHOUT CUMULUS CELL REMOVAL BY NON-INVASIVE TOMOGRAPHY. Rebecca L. Krisher, PhD; Deirdre M. Logsdon, MS; Benjamin B. Goheen, BS; Sandeep K. Rajput, PhD; Travis A. Morgan, MBA; William B. Schoolcraft, MD; Ran An, PhD; Brian A. Levine, MD; Colorado Center for Reproductive Medicine, Lone Tree, CO; Animated Dynamics, Inc., Indianapolis, IN; CCRM NY, New York, NY.

OBJECTIVE: Currently, eggs must be denuded to assess maturity. However, maintenance of the cumulus cell investment is critical to support oocyte quality during maturation. A novel tomography device using near-infra-red light has been developed to detect the first polar body without removing cumulus cells. Our objective was to determine the effect of tomographic imaging for polar body detection on mouse oocyte developmental competence and subsequent embryo quality.

DESIGN: Prospective research study. The experimental design consisted of three treatment groups: control eggs (C, standard IVF/IVC protocol; n=135), imaged eggs (I; n=45), and eggs that were treated identically to I but not exposed to tomography (NI; n=63). Two replicates were performed.

MATERIALS AND METHODS: In vivo matured mouse (outbred CF1, n=8 females) eggs were collected following ovarian stimulation. A subset of oocytes was randomly selected and immediately placed into fertilization medium containing sperm (C). The remaining eggs were placed into two imaging dishes, consisting of 50 µL drops of MOPS buffered medium under oil. Both dishes were moved to a heated stage on the imaging system. Eggs in one dish were imaged (I; 8-10 eggs/microdrops); oocytes in the second dish (NI) served as an environmental control. Presence or absence of the polar body was recorded for each egg. After imaging, both I and NI groups were placed into fertilization medium containing sperm. After IVF, 2PN zygotes were placed into sequential culture medium.

RESULTS: It required 93 seconds on average to image each oocyte and determine if it contained a polar body (range, 40-150 sec/oocyte). Tomography evaluation revealed that 78% of the eggs were mature. After IVF, C had fewer (p<0.01) 2PN zygotes than either I or NI (60%, 87%, 76%, respectively). The percentage of mature eggs (78%) was slightly underestimated compared to the percentage of successfully fertilized zygotes (87%). There were no differences in blastocyst development or hatching between treatments (C, 64% and 57%; I, 67% and 69%; NI, 75% and 67%, respectively). There were no differences in ICM or total cell number between treatments, although NI tended (p=0.08) to have fewer TE cells than C (NI, 83±6.5%; C, 100.8±6.1%). The percentage of ICM cells was increased (p<0.05) in I (12.3±1.1%) compared to C (8.9±0.7%). The expression of 8/9 genes related to blastocyst viability (BMP15, DNM3TA, FOXO3A, GLUT1, GRP78, NANOG, PAG, PLAC8) did not differ between treatments, although expression of ATPI4 was decreased (p<0.05) in I and NI compared to C.

CONCLUSIONS: Assessment of cumulus enclosed mouse eggs to determine maturity using near infra-red tomography does not have any negative effects on fertilization, blastocyst development or embryo quality. This data suggests that tomography could be used to safely make clinical decisions about the most appropriate fate of each retrieved egg prior to cumulus removal, thereby improving quality of the oocyte cohort.

THE PLASMINOGEN ACTIVATOR SYSTEM IN THE PRIMATE ENDOMETRIUM DURING THE OVAINE CYCLE AND MENSTRUATION. Reem Sabouni, MD; Sara Demirel, MD; David F. Archer, MD; EVMS/ Jones Institute for Reproductive Medicine, Norfolk, VA; North Shore University Hospital & Long Island Jewish Medical Center, Manhasset, NY; Eastern Virginia Medical School, Norfolk, VA.

OBJECTIVE: The endometrium undergoes dynamic morphologic changes reflecting hormonal fluctuations. The plasminogen activator system (PAS) is an enzymatic cascade involved in hemostasis and matrix turnover that is activated by tissue plasminogen activator (tPA) and inhibited by plasminogen activator inhibitors-1 (PAI 1). Evidence supports PAS’s role in remodeling the endometrium in human endometrial cancers, yet little is known on the dynamic alterations of these enzymes within a controlled ovarian cycle. This study seeks to characterize the expression of PAI 1 and tPA in the primate endometrium during an artificial cycle.

DESIGN: Animal in vivo experiment.

MATERIALS AND METHODS: Endometrial biopsy samples were obtained from 4 adult cycling female rhesus macaques monkeys during an artificial cycle controlled with estrogen and progestin implants at 3 separate time points: menstrual, proliferative and secretory. The tissue sections were stained via immunohistochemistry (IHC) with specific PAI 1 and tPA antibodies. Controls using immunofluorescence and IHC were captured with standardized settings with 4 representative images of stroma, gland and vasculature from each tissue. Four separate areas of stroma, gland or vasculature were analyzed from different parts of each slide. Values were expressed as integrated optical density and analyzed using ImageJ software. Statistics were performed on means ± standard deviation of n=4/group and subjected to ANOVA with Tukey’s multiple comparison test at p<0.05.

RESULTS: Stromal PAI 1 was highest in the secretory phase (184.7 ± 9.1), then proliferative (151 ± 5.6) and menstrual phase (88.4 ± 18.6) with a statistically significant difference between secretory phase compared to the proliferative and menstrual phases (p<0.0001). Glandular PAI 1 was highest in the secretory phase (99.6 ± 36.9), followed by proliferative (48 ± 9.8) and menstrual phase (44.1 ± 3.1). Vascular PAI 1 was highest in the secretory phase (127.7 ± 23), followed by proliferative (89 ± 16.3) and menstrual phase (61.9 ± 4.7). Statistically significant differences were seen between secretory compared to proliferative and menstrual phases for the gland (p<0.1) and vasculature (p<0.001).

Stromal tPA was highest in the secretory phase (181 ± 17.6), then proliferative (169.6 ± 10.7) and menstrual phase (145 ± 33). Glandular tPA was highest in the secretory phase (123 ± 20.7), then menstrual (113 ± 29) and proliferative phases (109 ± 20). Vascular tPA was highest in the secretory phase (119.9 ± 26.6), followed by menstrual (109 ± 29) and proliferative phase (94.5 ± 6.6). The differences between the menstrual phases for tPA were not statistically significant.

CONCLUSIONS: PAI 1 was noted to be significantly expressed in the secretory phase in the stroma, gland and vasculature supporting its possible role in the endometrial decidualization. High PAI 1 levels in the secretory stroma may reflect pro tease activity with the onset of menses. Comparing expression of PAI 1 and tPA demonstrates that PAI 1 appears to have a more dynamic expression within the monkey endometrium suggesting a larger role in endometrial remodeling.

THE ROLE OF GLYPHOSATE IN INFERTILITY: THE MECHANISTIC LINK. Charalampos Chatzicharalampous, MD, PhD; Zeina A. Yahouf, BS; David Bai, BS; Awoyini Olumide Awonuga, MD, Husam Abu-Soud, PhD Wayne State University, Detroit, MI.

OBJECTIVE: In light of the recent Roundup lawsuit, glyphosate has been widely accepted as a significant environmental toxin that may affect humans in various ways including cancer and infertility. Exposure to even low doses of glyphosate-based herbicides during pregnancy has been found to impair fertility, cause intrauterine growth restriction and induce fetal malformations. In this study...
we sought to determine the underlying mechanism by which glyphosate negatively impacts oocyte quality, fertilization rates as well as embryo development.

DESIGN: Experimental case-control study of mouse oocytes and pronucleate embryos, exposed in vitro to increasing glyphosate concentrations and followed through day 5 of development. We utilized multiple assays including reactive oxygen species (ROS) generation and zinc depletion to examine the possible underlying detrimental mechanisms.

MATERIALS AND METHODS: Metaphase II mouse oocytes (n=200) were retrieved from 8-10 week female mice and a subset (n=100) were fertilized using IVF. The oocytes as well as the fertilized mouse embryos were then exposed to increasing concentrations of glyphosate (0-200 µM) for 2h - 4h as per protocol. The oocytes were divided into four groups that were treated as follows: Group A: ROS detection assay, Group B: Zinquin ethyl ester assay, Group C: fixed, stained and scored based on the spindle structure (microtubule morphology -MT and chromosomal alignment - CH) as indicators of the oocyte’s capacity to sustain exposure. All groups were compared to Group 4: untreated controls.

Exposed embryos were incubated for up to 120 hours post fertilization and evaluated for full and hatching blast rate conversion. They were photographed and graded daily based on their appearance and development using published embryo grading protocols. A subset of the treated embryos (n = 10 for each concentration) were treated, in a similar fashion as the oocytes, in order to evaluate for ROS overproduction and zinc depletion. Confocal microscopy was used to assess the embryos. Statistical analysis was performed using t-test, ANOVA and chi-square. A p-value < 0.05 was considered statistically significant.

RESULTS: Oocytes treated with increasing glyphosate concentrations > 50 µM were found to have poor scores for MT and CH and that difference was statistically significant as compared to controls (p < 0.05). Embryos followed to 96 hours post fertilization (early blastocyst) and 120 hours (full and hatching blastocyst) after glyphosate exposure (0-200 µM) were assessed and those exposed to glyphosate concentrations > 100 µM showed significantly increased arrest rates and poor morphology scores compared to controls. ROS overproduction as well as zinc depletion was evident in embryos treated with high glyphosate concentrations. These observations were statistically significant compared to untreated controls (p < 0.05).

CONCLUSIONS: This work suggests the possible underlying mechanisms by which glyphosate negatively affects reproductive health in the mouse model. Possible fertility implications in humans will require further research. SUPPORT: None.

ART LAB: TECHNOLOGY

O-182 Wednesday, October 16, 2019 11:00 AM
NON-INVASIVE OOCYTE SELECTION INCREASES CLINICAL PREGNANCY RATE: A PROSPECTIVE STUDY OF 108 PATIENTS. Inge Van Vaerenbergh, PhD, Tom Adriaenssens, MSc, Nazli Akin, MSc, Wim Coucke, PhD, Ilona Mateziel, PhD, Greta Verheyen, PhD, Eileen Van Hecke, Msc, Andre Rosenthal, Prof, Johan Smits, MD, PhD, Prof, Follicle Biology Laboratory, Vrije Universiteit Brussel, Brussels, Belgium; Quality of Laboratories, Sciensano, Brussels, Belgium; Centre for Reproductive Medicine, UZ Brussels, Brussels, Belgium; Fertiga, Lede, Belgium.

OBJECTIVE: To compare clinical pregnancy outcome by non-invasive cumulus testing using gene expression in combination with embryo morphology versus morphology alone in eSET patients.

MATERIALS AND METHODS: Planned free transfers of day-3 ICSI eSET. Patients were stimulated with GnRH antagonist and HP-HMG. Oocytes underwent single denudation after pick-up. The cumulus cells were analysed with QRT-PCR for three predictive genes CAMK1D, EFNB2 and SASH1 (Corona Test) and two control genes. The analysis resulted in a single score for each oocyte. The score was used to select and transfer a single day 3 embryo with excellent or good morphology. The control group was matched (blinded for outcome) under the same conditions as the intervention group (same age, same number of embryos, same stimulation protocol).

The primary outcome was clinical pregnancy (fetal heartbeat confirmed by endovaginal ultrasound at 7 weeks), with stratification for age and number of excellent/good quality embryos (GQE). Secondary outcome included cumulative pregnancies from frozen embryo transfers. Outcomes were compared among treatment arms using one-tailed chi-square test.

RESULTS: A total of 108 patients underwent the Corona Test and were matched with 108 control patients nearest in time to the treated cases. There was an 80% increase compared to day 5 blastocyst transfer. These data indicate that morphology selection supported by non-invasive cumulus testing can drastically increase pregnancy rates.
OBJECTIVE: To apply Artificial Intelligence (AI) technology on time-lapse (TLM) embryo images and morphokinetic parameters to predict live birth.

DESIGN: The morphokinetic parameters (n = 131, ICIS only), with known live birth data from single blastocyst transfers, and 131 TLM images of embryos at 111.5 hours post ICSI were used to train (70%), validate (15%), and blindly test (15%) for prediction of live birth by an AI feature-extraction system. Inclusion criteria involved recipients from our oocyte donation program with single blastocyst transfer and non-PGT.

MATERIALS AND METHODS: Absolute and interim cleavage time points (t2 to t8) were used, along with 33 independent numerical variables extracted from standardized TLM images as an input data. The artificial neural network (ANN) architecture associated with the genetic algorithm was used to produce a predictable output of livebirth. The efficacy of prediction of live birth was quantified and assessed using ROC curves, AUC and confusion matrices (True Positive - TP, True Negative - TN, False Positive - FP, and False Negative - FN).

RESULTS: Overall accuracy of prediction of live birth by AI using morphokinetic data was 96.2% (126/131; TP = 37, TN = 69, FP = 1, FN = 4, AUC = 0.946). In the training dataset, the accuracy was 95.5% (86/91, AUC = 0.96), and in the blind test dataset, accuracy was 100% (20/20, AUC = 0.961). The overall accuracy of live birth by AI using image analysis was 90.1% (100/111, TP = 39, TN = 61, FP = 7, FN = 4, AUC = 0.91). In the training dataset, the accuracy was 89% (81/91, AUC = 0.887), and in the blind test dataset, accuracy was 95% (19/20, AUC = 0.67-0.94). The combination of morphology and morphokinetics, the AUC for positive were similar (0.96) but for negative live birth were less predictive (0.65).

CONCLUSIONS: This is the first time that AI is used to evaluate human embryo quality using morphokinetic and morphological assessment in a data set of single embryo transfers from an oocyte donation program with known live birth. Our data suggests that AI can be used to enhance the efficacy of embryo selection performed by the standard morphology or the existing algorithms of morphokinetics. Applying AI in conjunction with morphokinetic or image analysis has the potential for being the platform of embryo selection, with similar predictive abilities when treated independently although its combination may not improve the performance of AI.

O-185 Wednesday, October 16, 2019 11:45 AM

A DEEP LEARNING FRAMEWORK OUTPERFORMS EMBRYOLOGISTS IN SELECTING DAY 5 EUPLOID BLASTOCYSTS WITH THE HIGHEST IMPLANTATION POTENTIAL.

Eduardo Hariton, MD, MBA, Irene Dimitriadis, MD, Manoj Kumar Kanakasabapathy, MS, Prudhi Thirumalaraju, BS, Raghav Gupta, BTech, Rohan Poonwala, BTech, Irene Souter, MD, Sarah T. Rice, MS, Pragati Bhownick, MD, Leslie B. Ramirez, PhD, Carol Lynn Cuchhoe, PhD, TS (ABB), Jason E. Swain, PhD, Lynn M. Boehnlein, BS, Charles L. Bornmann, PhD, Hadi Shafiee, PhD.

Massachusetts General Hospital, Harvard Medical School, Boston, MA; Brigham and Women’s Hospital, Harvard Medical School, Boston, MA; Extend Fertility, New York, NY; San Diego Fertility Center, San Diego, CA; CCRM Fertility Network, Lone Tree, CO; Division of Reproductive Endocrinology and Infertility, Department of Obstetrics and Gynecology, University of Wisconsin, Madison, WI.

OBJECTIVE: To evaluate the performance of an artificial intelligence-based approach, using a deep convolutional neural network (CNN) combined with a genetic algorithm (GA), in selecting top quality day 5 euploid blastocysts compared to those selected by highly trained embryologists.

DESIGN: Historical Prospective Double-Blinded Multi-Center Cohort Study.

Overall clinical pregnancy (n=108) (%) 61
Overall cum. clinical pregnancy (n=108) (%) 79
Clint. preg. Age <35 (n=68) (%) 62
Clint. preg. Age [35-38] (n=43) (%) 60

Corona Test group Control group Chi-square (p-value)

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SUPPORT: This study was funded by IWT/VLAIO and Vrije Universiteit Brussel IOFPOC26.
MATERIALS AND METHODS: Using a dataset of 3,469 embryos, the deep CNN model was trained and tested to primarily classify images of embryos captured at 113 hours post insemination (hpi). A non-overlapping set of 97 euploid embryo images with known implantation outcomes was then used to compare embryo predicting accuracy of trained embryologists from multiple centers in the US to that of the CNN. Only euploid embryos that had undergone preimplantation genetic testing for aneuploidies (PGT-A) were included to remove the bias introduced by chromosomal abnormalities.

RESULTS: The CNN performed with an accuracy of 75.3% while the embryologists performed with an average accuracy of 67.4% (min-max: 64.5%-70.2%) in differentiating euploid embryos based on their implantation outcome. The CNN performed with a sensitivity and specificity of 84.2% (CI: 72.1% to 92.5%) and 62.5% (CI: 45.8% to 77.3%), respectively. The positive predictive value (PPV) and negative predictive value (NPV) of the network were 76.2% (63.8% to 86.0%) and 73.5% (55.6% to 87.1%), respectively. A one sample t-test revealed that the CNN significantly outperformed embryologists in predicting embryo implantation of euploid embryos using a static image obtained at a single time-point (113 hpi) (P<0.0001).

CONCLUSIONS: The trained artificial intelligence framework outperformed trained embryologists in identifying PGT-A euploid embryos destined to implant. A large randomized controlled trial is warranted to confirm that the developed CNN can improve in-vitro fertilization outcomes by prospectively selecting embryos with higher implantation potential than those selected with the current methods.

SUPPORT: This work was partially supported by the Brigham Precision Medicine Developmental Award (Brigham Precision Medicine Program, Brigham and Women’s Hospital) and R01AI118500, and R21HD092828 (National Institute of Health).

O-186 Wednesday, October 16, 2019 12:00 PM
THE ASSOCIATION BETWEEN RAPIDLY DIVIDING EMBRYOS AND EMBRYONIC EUKARYOTIC歐PE LAY DIETED VIA NEXT GENERATION SEQUENCING (NGS). Jenna Friedenthal, MD, Dmitry Goukos, MA, BA, Joseph A. Lee, BA, Lawrence Grunfeld, MD, Alan B. Copperman, MD, Icahn School of Medicine at Mount Sinai, New York, NY; Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Previous research has suggested that rapid embryo development may be a strong predictor of outcomes. [1] Rapid cell division of the early embryo was thought to be "chaotic," and cleavage stage embryos with >8 cells thought to have poor developmental potential. However, others have found that early cleavage embryos have higher implantation rates [2]. Studies evaluating the relationship between cleavage development and embryonic aneuploidy [3] are limited by use of older technologies. Thus, our goal was to assess whether rapid cell division of an early embryo is correlated with copy number abnormalities and embryonic competence.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The study included patients at a single academic center who underwent in vitro fertilization and had at least one embryo that reached cleavage stage from 2016 to 2019. Day 3 embryos were divided into 3 groups: slow (<6 cells), intermediate (6-8 cells), and fast (≥8 cells). Our primary outcome was euploidy as diagnosed by trophoderm (TE) biopsy for preimplantation genetic testing for aneuploidy (PGT-A). All tested embryos were evaluated using NGS. Secondary outcomes included number of blastocysts, biopsied blastocysts, ongoing pregnancy/live births (OP/LB), and clinical losses (CL). Data were analyzed using students ANOVA, chi square tests, and a multivariate logistic regression, with p<0.05 considered significant.

RESULTS: A total of 40,916 Day 3 embryos from 3,565 patients were assessed in this study. In a multivariate analysis, there were significant differences between slow (n=6,651), intermediate (n=23,907), and fast (n=11,358) Day 3 embryos that developed to blastocysts (30.3%; 77.5%; 80.8%; p<0.0001) and that were biopsied (9.68%; 46.89%; 52.22%; p<0.0001). Euploidy was similar among groups (47.71%; 49.07%; 50.76; p=0.07). A sub-analysis of intermediate vs fast embryos showed a higher rate of euploidy in the fast group (p=0.04). After adjusting for confounders, and using the intermediate group as a control, fast Day 3 embryos were significantly associated with increased odds of reaching blastocyst stage (OR 1.13, CI 1.06-1.20, p=0.0001) and having blastocysts that were eligible for TE biopsy (OR 1.18, CI 1.12-1.24, p<0.0001). After controlling for confounders, we found no association between fast growing Day 3 embryos and odds of euploidy (OR 1.04, CI 0.97-1.11, p=0.23). There was no association between fast growing Day 3 embryos and odds of OP/LB (OR 0.97, CI 0.82-1.14, p=0.69) or CL (OR 1.02, CI 0.77-1.35, p=0.09).

CONCLUSIONS: Rapidly dividing cleavage embryos perform as well as, if not better than, intermediate or slow growing cleavage embryos. Prior cleavage of rapidly dividing embryos may have advantages for improving patient dysynchrony and not necessarily implantation failure related to embryonic competence. Our study demonstrated that rapidly dividing embryos have high rates of euploidy and clinical potential. Morphokinetic measurements combined with genomic and non-genomic markers provide the ideal support to optimize embryo selection and improve patient outcomes.


ENDOMETRIOSIS

O-187 Wednesday, October 16, 2019 10:45 AM
CORRELATION BETWEEN FOLLICULAR LEVELS OF INTERLEUKIN 6 (IL-6) AND ANTI-MULLERIAN HORMONE (AMH) AND ICSI OUTCOME IN WOMEN WITH PROVEN ENDOMETRIOSIS. Khadija Fierel Kacem Berjeb, Associate Professor, Marouen Braham, Associate professor, Cirine BEN. Massaoud, Research Master’s Degree in Biomedical Sciences, Manel Hamdoun, Medical Degree, Asma Chaabene, Bachelor’s degree in medical biology, Anis Fadhlaoui, Associate Professor, 0. Bahri, Sr. Professor, Fethi Zhioua, Pri2 Aziza Othmana Hospital, Tunis, Tunisia; Aziza Othmana University hospital, Tunis, Tunisia; Aziza Othmana hospital, Tunis, Bardo, Tunisia; Biochemistry Department, Aziza Othmana University hospital., Tunis, Tunisia; Affiliation not provided.

OBJECTIVE: Investigating a potential correlation between follicular AMH and IL-6 in women with endometriosis and thus a potential influence of the inflammatory process in endometriosis on ICSI outcome.

DESIGN: A matched case-control study was conducted in the Reproductive Medicine center at Aziza Othmana Hospital in Tunis. The study population included a total of seventy-five patients; twenty-five patients with proven endometriosis and fifty patients diagnosed with other causes of infertility, each undergoing an ICSI cycle between March and August 2018.

MATERIALS AND METHODS: All patients followed a controlled ovarian stimulation protocol for an ICSI cycle. The follicular fluid was collected from 75 patients at 72h and 75h after the administration of gonadotropin, then stored at -80°C until assay. AMH and IL6 concentrations in follicular fluid were determined by electrochemiluminescence immunoassay. Comparisons of data between the two groups were preformed with t student test and with chi 2 test. Correlations were assessed with the Pearson correlation test.

RESULTS: Two groups were formed; an endometriosis group and a control group. Both groups were comparable regarding clinical parameters and those of the ovarian stimulation. As for the biological parameters measured in the follicular fluid, IL-6 levels showed a statistically significant increase in the "endometriosis" group compared to the "control" one (162.32 vs 19.93; p=0.02). The follicular AMH levels were comparable between the two groups (2.22 vs 2.71; p=0.41). No correlation was shown between the follicular levels of IL6 and AMH (r = 0.01, p = 0.3). The comparison of ICSI outcomes between the "endometriosis" group and the "control" group showed that the fertilization rate (69.99% vs 62.98%; p<0.05) the Top embryos rate (41.71% vs 37.64%; p<0.05) and the pregnancy / transfer rate (38.09% vs 34%; p<0.05) were comparable between the two groups. The miscarriage rate was higher in women with endometriosis (37.5% vs18.75%; p<0.05).

CONCLUSIONS: The higher miscarriage rate in women with endometriosis suggests that the endometrial receptivity is the target of the deleterious effects of the inflammatory process. As for the follicular AMH, it seems to have a greater predictive value than the ovarian function or the oocyte quality. Further investigations are needed to confirm such a theory.

SUPPORT: This study was funded by the research department of Aziza Othmana Hospital in Tunis.
OBJECTIVE: One conundrum in endometriosis arising from a recent study is that, while endometriotic epithelial and stromal cells supposedly co-exist, the two cellular components seem to take independent developmental trajectory. This is due to the finding that, while cancer-associated somatic mutations were found to be enriched in the epithelial component, the stroma does not carry much. Given that endometriotic lesions are fundamentally wounds undergoing repeated tissue injury and repair that ultimately progress to fibrosis, we hypothesized that the stromal component of endometriotic lesions may recruit other cells and turn them into mesenchymal cells. One possible candidate cell is endothelial cell. Essentially, endothelial cells in lesions transdifferentiate into mesenchymal cells, likely induced by transforming growth factor β1 (TGF-β1) released by activated platelets, contributing further to lesional fibrosis. This study was undertaken to test this hypothesis.

DESIGN: Laboratory study using human tissues, in vitro experimentation using an human umbilical vein endothelial cell line HUVEC.

MATERIALS AND METHODS: Immunofluorescent analysis of 30 each ovarian endometrioma (OE) and deep endometriosis (DE) tissue samples, using antibodies against CD31 and fibroblast-specific protein 1 (FSP-1), was performed. Immunohistochemistry analysis of CD31, FSP-1 and α-smooth muscle acting (α-SMA) was also performed. Masson trichrome staining was used to evaluate the extent of lesional fibrosis. In in vitro experiments, we evaluated morphological changes, gene and protein expression levels, migratory and invasive propensity, cellular contractility, and collagen production for HUVEC co-cultured with vehicle, activated platelets or thrombin only. We used A83-01, a TGF-β1 inhibitor, to neutralize TGF-β1.

RESULTS: Endometriotic lesions clearly exhibited signs consistent with EndoMT, especially in OE lesions. Activated platelets, through the induction of TGF-β1 signaling pathway, induced EndoMT in HUVECs, resulting in increased migratory and invasive propensity, cellular contractility, and collagen production. Prolonged exposure of HUVECs to activated platelets induced increased expression of α-SMA, desmin and F-actin suggesting further transdifferentiation into smooth muscle-like cells. Neutralization of TGF-β1 abolished these changes. DE lesions had significantly higher staining levels of CD31, but lower α-SMA and FSP-1 staining, concomitant with lower lesional fibromuscular content than that of DE lesions. The staining levels of CD31 correlated negatively with the staining levels of α-SMA, as well as the extent of lesional fibrosis.

CONCLUSIONS: EndoMT contributes to fibrogenesis in endometriosis. Because of EndoMT, the endometriotic stroma is constantly replenished by endothelial cells and other cells. These cells generally have much lower mutation rates than that of the endometriotic epithelium. Thus, we provide an explanation for the above mentioned conundrum of apparent independent developmental trajectories taken by endometriotic epithelium and stroma.

OBJECTIVE: To determine whether cancer driver mutations contribute to the development and progression of endometriosis and endometriosis-associated cancers.

DESIGN: Endometriosis lesions might arise as an autotransplant, as a hemizygous driver mutation. The majority of the cancers developing in these 18 women were cancers known to be associated with endometriosis. Of note, the mean age of endometriosis diagnosis for the 18 women with a somatic driver mutation who developed cancer was 53.2, and the age at diagnosis was 36.3 for those with no cancer to date (Wilcox p<0.0001).

CONCLUSIONS: Somatic cancer driver mutations are common in endometriosis lesions. When a cancer driver mutation is present in an endometriosis lesion, the risk of a secondary cancer appears to be elevated.

SUPPORT: Jounce Biosciences, LLC.
OBJECTIVE: Endometriosis affects an estimated 1 in 10 women during their reproductive years, and up to 30% to 50% of women with endometriosis may experience infertility. Classically, endometriosis is a surgical diagnosis, and excision or ablation of endometriosis is known to be technically challenging with little added benefit for patients undergoing in vitro fertilization (IVF). However, the presence of an endometriosis diagnosis may impact clinical recommendations during fertility treatment. A previous study developed classifiers for prediction of endometriosis in a cycle-phase specific manner by using margin tree classification within one dataset. Our aim was to build on this research by utilizing machine learning to predict and independently validate the presence or absence of endometriosis, regardless of cycle phase and other uterine pathology, through endometrial biopsy (EMB) samples.

DESIGN: Retrospective cohort analysis of publicly available genomic data.

MATERIALS AND METHODS: We trained Random Forest classifiers on ten gene-expression based modules, derived from spectral decomposition of the discovery dataset (n = 148) to predict the presence of endometriosis. These classifiers were validated in an independent gene expression dataset (n = 37) of eutopic EMB samples obtained from patients with and without endometriosis.

RESULTS: We identified a 280-gene predictor of endometriosis using Random Forests that was found to predict the presence of endometriosis, regardless of the endometrial phase and other pathology, with an accuracy of 84% (area under ROC = 0.84; p-value: 6.14e-05), with a negative predictive value of 86% and a positive predictive value of 81%. We reduced model over-fitting by performing 10-fold cross-validation of our discovery data.

CONCLUSIONS: Using machine learning, we developed a new genomic signature with the ability to accurately predict the presence of endometriosis from an EMB sample regardless of cycle phase or other pathology. Ongoing work is interrogating the findings in the IVF population, and the role played by DNA methylation in regulating expression of key genes and pathways in our predictive model. In a move towards personalized, noninvasive medicine, the EMB diagnosis of endometriosis could provide meaningful clinical information without subjecting patients to the risks and expense of surgery.


TABLE 1.

<table>
<thead>
<tr>
<th>Gene Set</th>
<th>Description</th>
<th>Gene Set Size</th>
<th>Expected Count</th>
<th>Observed Count</th>
<th>Fold Enrichment</th>
<th>P Value</th>
<th>FDR</th>
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<tr>
<td>GO:0005887</td>
<td>Integral plasma membrane</td>
<td>1596</td>
<td>65.6</td>
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<td>1.92</td>
<td>3.58E-13</td>
<td>2.75E-10</td>
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<td>GO:0044430</td>
<td>Cytoskeletal part</td>
<td>1620</td>
<td>66.6</td>
<td>127</td>
<td>1.91</td>
<td>4.68E-13</td>
<td>2.75E-10</td>
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<td>GO:0009986</td>
<td>Cell surface</td>
<td>782</td>
<td>32.1</td>
<td>67</td>
<td>2.08</td>
<td>9.24E-09</td>
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<td>GO:0098590</td>
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<td>GO:0030054</td>
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<td>83</td>
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Non-eg-08 INVASIVE DIAGNOSTIC OF ENDOMETRIOSIS: USING MACHINE LEARNING INSTEAD OF THE OPERATING ROOM. Kathryn L. Shai, MD, MHA,^a^ Chaitanya R. Acharya, PSM, PhD,^b^ Stephanie Snellitzer, MD,^c^ Herbert K. Lyerly, MD,^d^ Kelly S. Acharya, MD,^e^ Division of Reproductive Endocrinology and Infertility, Duke University Medical Center, Durham, NC; ^f^Duke Center for Applied Therapeutics, Department of Surgery, Durham, NC.

OBJECTIVE: Endometriosis affects an estimated 1 in 10 women during their reproductive years, and up to 30% to 50% of women with endometriosis may experience infertility. Classically, endometriosis is a surgical diagnosis, and excision or ablation of endometriosis is known to be technically challenging with little added benefit for patients undergoing in vitro fertilization (IVF). However, the presence of an endometriosis diagnosis may impact clinical recommendations during fertility treatment. A previous study developed classifiers for prediction of endometriosis in a cycle-phase specific manner by using margin tree classification within one dataset. Our aim was to build on this research by utilizing machine learning to predict and independently validate the presence or absence of endometriosis, regardless of cycle phase and other uterine pathology, through endometrial biopsy (EMB) samples.

DESIGN: Retrospective cohort analysis of publicly available genomic data.

MATERIALS AND METHODS: We trained Random Forest classifiers on ten gene-expression based modules, derived from spectral decomposition of the discovery dataset (n = 148) to predict the presence of endometriosis. These classifiers were validated in an independent gene expression dataset (n = 37) of eutopic EMB samples obtained from patients with and without endometriosis.

RESULTS: We identified a 280-gene predictor of endometriosis using Random Forests that was found to predict the presence of endometriosis, regardless of the endometrial phase and other pathology, with an accuracy of 84% (area under ROC = 0.84; p-value: 6.14e-05), with a negative predictive value of 86% and a positive predictive value of 81%. We reduced model over-fitting by performing 10-fold cross-validation of our discovery data.

CONCLUSIONS: Using machine learning, we developed a new genomic signature with the ability to accurately predict the presence of endometriosis from an EMB sample regardless of cycle phase or other pathology. Ongoing work is interrogating the findings in the IVF population, and the role played by DNA methylation in regulating expression of key genes and pathways in our predictive model. In a move towards personalized, noninvasive medicine, the EMB diagnosis of endometriosis could provide meaningful clinical information without subjecting patients to the risks and expense of surgery.

O-193 Wednesday, October 16, 2019 10:45 AM

METABOLIC SYNDROME (MetS): FECUNDABILITY AND ADVERSE PREGNANCY OUTCOMES IN UNEXPLAINED INFERTILITY. Sushila Arya, MD, a Karl R. Hansen, MD PhD, b Michael P. Diamond, MD, c Robert A. Wild, M.D., M.P.H. PhD, d NICHD’s Reproductive Medicine Network. eUniversity of Oklahoma Health Sciences Center, Oklahoma City, Oklahoma city, OK; aAugusta University, Augusta, GA.

OBJECTIVE: To determine the association of MetS with fecundability and pregnancy complications after ovarian stimulation–intrauterine insemination (OS-IUI) for unexplained infertility.

DESIGN: Secondary analysis of a randomized clinical trial (RCT) investigating clinical pregnancy, live birth, and multiple pregnancy rates with OS-IUI for couples with unexplained infertility.

MATERIALS AND METHODS: This secondary analysis included all 900 couples undergoing OS-IUI as part of The Assessment of Multiple Intratruerine Gestations from Ovarian Stimulation (AMIGOS) clinical trial. Briefly, this trial enrolled women at 12 sites, age 18-40 with at least one patent fallopian tube and regular menses who underwent OS-IUI with letrozole, clomiphene citrate (CC) or gonadotropins for up to four treatment cycles. Male partners were required to have a semen analysis with at least 5 million total motile sperm in the ejaculate. Chi-Square/Fisher exact, Student’s t, and logistic regression were utilized as appropriate. A p-value of < 0.05 was considered statistically significant. MetS was defined by the International Diabetes Federation (IDF) criteria. Overweight/obese = BMI ≥25 kg/M².

RESULTS: Prevalence of Hi BMI was 51.09%, VHBMI 10.4%, and MetS 17.6%. BMI or MetS was not associated with clinical pregnancy or live birth rates. Pregnancy complications occurred in 40.18% overall (CC 30.0%, letrozole 41.4% and gonadotropins 46.9%). For CC and letrozole, the odds for any pregnancy complication with MetS were 2.72 (1.27, 5.82). With MetS, 22.7% had Pr-E and 27.3% had gDM vs. 5.2% and 8.3% without MetS. When given gonadotropins, MetS was not associated with complications, however multiple pregnancies were more common (33% of triplet pregnancies had Pr-E). For those with VHBMI, the odds of a complication were 4.30 (1.17, 15.79), and 65% had MetS. The overall odds for a complication with MetS present were 3.10 (1.44, 6.67) adjusting for VHBMI and multiple pregnancies.

CONCLUSIONS: MetS did not influence fecundability. However, it is significantly associated with pregnancy complications beyond the risk conferred by obesity alone. MetS portends pregnancy complications, as does VHBMI, with OS-IUI for patients with unexplained infertility.

REFERENCES:
A The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD): U10 HD077680, U10 HD39005, U10 HD38992, U10 HD27049, U10 HD38998, U10 HD055942, U10DS05944, U10 HD055936, and U10HD055925. This research made possible by the funding by American Recovery and Reinvestment Act. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NICHD or NIH.

FEMALE REPRODUCTION

O-194 Wednesday, October 16, 2019 11:00 AM

THE AROMATASE INHIBITOR, LETROZOLE: A NOVEL TREATMENT FOR ECTOPIC PREGNANCY. Mohamed F. Mitwally, MD, FACOG, a Wala G. Hozayan, PhD, b Kamel M. A. Hassanin, PhD, b Kamal A. Abdalla, MD, c Noha K. Abdalla, B.Sc. c Odessa Reproductive Medicine Center, Helotes, TX; aBiochemistry Division, Chemistry Department, Faculty of Science, Beni-Suef University, Beni-Suef, Egypt; bBiochemistry Department, Faculty of Veterinary Medicine, Minia University, Minya, Egypt; cDepartment of Obstetrics & Gynecology, Faculty of Medicine, Minya University, Minya, Egypt.

OBJECTIVE: Study the use of the aromatase inhibitor, letrozole, for the treatment of ectopic pregnancy compared to methotrexate.

DESIGN: Non-randomized prospective cohort study.

MATERIALS AND METHODS: A series of 42 consecutive patients with undisturbed ectopic pregnancy were counseled regarding the treatment options including surgical treatment (control group), medical treatment with the methotrexate (study group 1) or letrozole (study group 2). Each group included 14 patients. Primary outcome was complete resolution of ectopic pregnancy determined by serum hCG levels below laboratory immunodassay detection. Secondary outcomes included changes in the biochemical parameter of ovarian reserve, Anti-Mullerian Hormone (AMH), as well as hematological and hormonal changes associated with the two medical treatments compared to surgical treatment.

RESULTS: Complete resolution of ectopic pregnancy occurred in equal number of patients, 12 out of 14 (86%) in each of the two study groups. The two patients who failed methotrexate treatment had to undergo surgery after becoming hemostatically unstable, while in the letrozole group, one patient had to go to surgery when she became hemostatically unstable, while in the second patient, a decision to do surgery was due to failure of hCG level to decline four days after letrozole treatment. Treatment with methotrexate was associated with higher levels of liver enzymes, and lower levels of platelets (the differences in both parameters were statistically significant). The decline in hCG levels was faster in the letrozole group, when compared to the methotrexate group. Three months after treatment, AMH levels were lower in the methotrexate group when compared to the letrozole and the surgery group. However, the decline in the hCG and AMH levels were not statistically significant.

CONCLUSIONS: Up to our knowledge, this is the first report in the literature on the success of letrozole in medical treatment of ectopic pregnancy. In the absence of estrogen priming, progesterone may not exert its physiological function due to a negative effect on progesterone receptors. It is hypothesized that by inhibiting the estrogen synthetase (the aromatase enzyme), the progesterone would not exert its physiological function in maintaining pregnancy, including ectopic pregnancy. The small sample size and non-randomized design of our study would limit our conclusion about letrozole success in treating ectopic pregnancy. However, the promising high resolution rate and better safety profile that letrozole has over a chemotherapeutic agent like methotrexate, should encourage studying the letrozole as a promising medical treatment for ectopic pregnancy through more definitive randomized clinical trials, that are adequately powered. Furthermore, letrozole may also be a safer alternative instead of surgical approach in managing early pregnancy loss, and pregnancy termination when medically indicated and ethically appropriate. In our study, a long follow up is intended to compare ovarian reserve in the two study groups and the surgery control group.


O-195 Wednesday, October 16, 2019 11:15 AM

REPRODUCTIVE OUTCOMES FOLLOWING A RUPTURED ECTOPIC PREGNANCY. Barry E. Perlman, DO,a Kavitha Krishnamoorthy, MD, a Ruchi Karsalia, BS,b Debra Heller, MD.b Rutgers New Jersey Medical School, Newark, NJ; bRutgers-New Jersey Medical School, Newark, NJ.

OBJECTIVE: Ectopic pregnancies account for 2% of all pregnancies in the United States. Subsequent pregnancy outcomes following ruptured versus non-ruptured ectopic pregnancy have been poorly reported in the literature. Non-peer reviewed websites have reported that ruptured ectopic pregnancies are damaging for future fertility; however, only one single study has reported no difference. As rupture of an ectopic pregnancy could lead to hemoperitoneum, inflammation, and scar formation, we hypothesized that ruptured ectopic pregnancies will decrease future fertility. Therefore, the primary objective of this study is to determine if fewer subsequent intrauterine pregnancies occur following surgical excision of a ruptured tubal ectopic compared to surgical excision of a non-ruptured ectopic pregnancy.

DESIGN: Retrospective cohort study at a University-affiliated hospital.

MATERIALS AND METHODS: All patients undergoing salpingectomy for a tubal ectopic pregnancy from 1/1991-12/2016 were considered. Patients were excluded if: it was not possible to determine ruptured versus non-ruptured status; if the patient had documented contraceptive use or no sexual activity; pregnancy included 14 patients. Primary outcome was complete resolution of ectopic pregnancy occurred in equal number of patients, 12 out of 14 (86%) in each of the two study groups. The two patients who failed methotrexate treatment had to undergo surgery after becoming hemostatically unstable, while in the letrozole group, one patient had to go to surgery when she became hemostatically unstable, while in the second patient, a decision to do surgery was due to failure of hCG level to decline four days after letrozole treatment. Treatment with methotrexate was associated with higher levels of liver enzymes, and lower levels of platelets (the differences in both parameters were statistically significant). The decline in hCG levels was faster in the letrozole group, when compared to the methotrexate group. Three months after treatment, AMH levels were lower in the methotrexate group when compared to the letrozole and the surgery group. However, the decline in the hCG and AMH levels were not statistically significant.

CONCLUSIONS: Up to our knowledge, this is the first report in the literature on the success of letrozole in medical treatment of ectopic pregnancy. In the absence of estrogen priming, progesterone may not exert its physiological function due to a negative effect on progesterone receptors. It is hypothesized that by inhibiting the estrogen synthetase (the aromatase enzyme), the progesterone would not exert its physiological function in maintaining pregnancy, including ectopic pregnancy. The small sample size and non-randomized design of our study would limit our conclusion about letrozole success in treating ectopic pregnancy. However, the promising high resolution rate and better safety profile that letrozole has over a chemotherapeutic agent like methotrexate, should encourage studying the letrozole as a promising medical treatment for ectopic pregnancy through more definitive randomized clinical trials, that are adequately powered. Furthermore, letrozole may also be a safer alternative instead of surgical approach in managing early pregnancy loss, and pregnancy termination when medically indicated and ethically appropriate. In our study, a long follow up is intended to compare ovarian reserve in the two study groups and the surgery control group.


SUPPORT: None.
RESULTS: A total of 1,171 tubal ectopic pregnancies were identified, 77 of which met inclusion criteria. Ruptured ectopic pregnancies did not result in a significant decrease in subsequent intrauterine pregnancy rate nor a significant increase in future ectopic pregnancy rate during the 12-month follow-up period. 10 out of 27 (37%) patients with ruptured ectopic pregnancy had an intrauterine gestation within 12 months, while 17 out of 50 (34%) patients with a non-ruptured ectopic achieved an intrauterine pregnancy within 12 months (p<0.007). 4 out of 27 (15%) cases with a ruptured ectopic and 7 out of 50 (14%) cases with a non-ruptured ectopic had a subsequent ectopic pregnancy within 12 months (p=0.99).

CONCLUSIONS: Ruptured ectopic pregnancy did not adversely affect the intrauterine pregnancy rate nor recurrent ectopic pregnancy rate 12 months following the rupture, compared to non-ruptured ectopic pregnancies.


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PROGESTIN THERAPY FOR WOMEN WITH COMPLEX ATYPICAL HYPERPLASIA: LEVONORGESTREL INTRAUTERINE DEVICE VERSUS SYSTEMIC THERAPY.

Rachel S. Manzella, MD, Marissa O. McLean, MD, Marcia A. Ciccone, MD, David J. Nusbaum, BS, Heena Purswani, MD, Elise B. Marcuso, MD, Christina E. Dancz, MD, Begum Ozel, MD, Lynda D. Roman, MD, Mahli Khoshchereh, MD, MS, Meghan B. Smith, MD, Richard J. Paulson, MD, MS, Koji Matsuo, MD, PhD, University of Southern California, Los Angeles, CA.

OBJECTIVE: For women with complex hyperplasia with atypia (CAH) who do not undergo hysterectomy, either for fertility preservation or due to poor surgical candidacy, the effectiveness of the levonorgestrel-releasing intrauterine device (LNG-IUD) compared to systemic therapy has not been well studied. We sought to examine differences in treatment response between the LNG-IUD and systemic therapy in women with CAH.

METHODS: A retrospective observational study at a tertiary care center between 2003-2018.

MATERIALS AND METHODS: Time dependent analyses of complete response (CR) and progression to cancer were performed for LNG-IUD vs. systemic therapy. A propensity score inverse probability of treatment weight (IPTW) model was used to create a weighted cohort that differed based on treatment type but was similar with respect to other characteristics. An interaction-term analysis was performed to examine the impact of body habitus on treatment response, and an interrupted time-series analysis was employed to assess changes in treatment patterns over time.

RESULTS: Among 245 women with CAH, 69 (28.2%) had the LNG-IUD and 176 (71.8%) received systemic therapy. Mean age and body mass index were 36.9 years and 40.0 kg/m², respectively. In the patient level analysis (Table 1), women who received the LNG-IUD were three times more likely to have CR and had a 75% lower likelihood of progression to cancer compared to those who received systemic therapy (both, P<0.001). In particular, women with class III obesity derived significant benefit from the LNG-IUD vs. systemic therapy (CR rates, 70.3% vs. 40.6%, HR 4.34, 95%CI 2.75-6.86, P<0.001) compared to those with class II-II obesity (95.3% vs. 53.5%, HR 1.85, 95%CI 1.16-2.97, P=0.010). In the cohort level analysis, LNG-IUD used significantly increased after 2007 (6.3% to 82.7%, 13.2-fold increase, P<0.001), and this increase was associated with an increasing number of women who achieved CR (32.9% to 81.4%, 2.5-fold increase, P=0.005).

CONCLUSIONS: Our study suggests that the LNG-IUD may be more effective than systemic therapy with oral progestins for women with CAH who opt for non-surgical treatment, particularly in morbidly obese women.

O-197 Wednesday, October 16, 2019 11:45 AM

PRECONCEPTION A1C AND TIME TO PREGNANCY, PREGNANCY LOSS, AND LIVE BIRTH.

Jessica R. Zolton, DO, Kerry S. Flannagan, PhD, Sunni L. Mumford, PhD, Jeannie G. Radoc, BS, Samratwi F. Yisakha, PhD, Neil J. Perkins, PhD, Keween Kim, PhD, Robert M. Silver, MD, Micah J. Hill, DO, Alan H. DeCherrey, MD, Enrique F. Schisterman, PhD, National Institute of Child Health and Human Development, NIH, Bethesda, MD; University of Utah, Salt Lake City, UT.

OBJECTIVE: Reproductive aged women are increasingly at risk of co-morbid conditions resulting from obesity and sedentary lifestyles. Past research indicates that increasing A1c in healthy populations is positively associated with markers of inflammation and the development of diabetes in the future. It is unknown if increasing A1c in healthy women during the preconception period impacts reproductive success. Our goal was to examine the relationship of preconception A1c and time-to-pregnancy (TTP), pregnancy loss, and live birth.

METHODS: Prospective cohort from the Effects of Aspirin in Gestation and Reproduction trial included 1,228 healthy women ages 18-40 years with a history of one or two pregnancy losses attempting spontaneous conception, and no known diagnosis of infertility, diabetes, or PCOS.

MATERIALS AND METHODS: A1c was measured using high performance liquid chromatography (Tosoh Bioscience) at the baseline visit prior to conception. Pregnancy was detected with hCG and ultrasound. Fecundability odds ratio (FOR) and 95% confidence intervals (CI) were estimated using discrete Cox proportional hazards regression models, accounting for left truncation and right censoring. Weighted log-binomial regression models were used to estimate relative risk (RR) and 95% CIs for live birth and pregnancy loss, Models were adjusted for age, BMI, race, income, and treatment arm.

RESULTS: Preconception A1c results were available for 1,194 participants. The lower 10th percentile consisted of A1c values of 3.8-4.6% (n=121), the middle group A1c of 4.7-5.5% (n=975), and upper 90th percentile A1c was 5.5-7.5% (n=98). Increasing preconception A1c was associated with longer TTP (FOR 0.74; 95% CI 0.57, 0.96) in unadjusted models, however, there was no association in adjusted models after accounting for BMI and other markers of obesity and insulin resistance (FOR 0.92; 95% CI 0.69, 1.22). Preconception A1c was not associated with differences in live birth (RR 1.03; 95% CI 0.84, 1.25) or pregnancy loss (RR 0.74; 95% CI 0.49, 1.12).

CONCLUSIONS: Among healthy women, we observed no association of A1c with live birth rate or pregnancy loss. The association of A1c and TTP appeared to be influenced by BMI, a strong risk factor for both diabetes and...
FERTILITY & STERILITY

O-198 Wednesday, October 16, 2019 12:00 PM

A LONGITUDINAL ASSESSMENT OF OVARIAN RESERVE AFTER MYOMECTOMY. Devora Aharon, MD.a Lucky Sekhon, MD.b Joseph A. Lee, BA,b Mackenzie Naert, BA,a Ahmad Kerr, MD, b Charles Ascher-Walsh, MD.a Alan B. Copperman, MD.a 1Cahn School of Medicine at Mount Sinai, New York, NY; 2Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Myomectomy is the preferred treatment option for symptomatic fibroids in women desiring fertility-sparing treatment. However, the effect of myomectomy on ovarian reserve is largely unknown. There is evidence to show that other treatments for fibroids including uterine artery embolization and hysterectomy may diminish ovarian reserve. Additionally, the use of a tourniquet transiently decreases blood supply to the ovaries, which may impact ovarian reserve. This study sought to determine whether open and minimally invasive myomectomy are associated with immediate and/or long-term changes in serum anti-Mullerian hormone (AMH).

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Patients undergoing minimally invasive (robot-assisted or laparoscopic) or open abdominal myomectomy by one primary surgeon from May 2018 through March 2019 were included. A Penrose drain tourniquet was used for all open myomectomies. Vasopressin was injected into the myoma subserosa for all minimally invasive myomectomies (MIS). Baseline data collected included age, BMI, and race. Surgical data collected included surgical approach, additional procedures, estimated blood loss (EBL), length of procedure, and weight of fibroids removed. Serum AMH was collected prior to the procedure. Follow-up serum AMH levels were measured at 2 weeks, 3 months, and 6 months after the procedure. To achieve 80% power to detect a 15% difference in mean AMH level, with p <0.05, a minimum of 43 subjects needed to be recruited. Paired t-tests were used to detect the mean difference between baseline AMH and 2 week, 3 month, and 6 month AMH respectively. Univariate linear regression was used to detect the effect of surgical approach and covariates on the percent difference in AMH from baseline to each follow-up time point. All follow-up visits will be completed by September 2019, therefore a preliminary analysis was conducted for the purpose of this abstract.

RESULTS: A total of 56 patients were included in the study. 32 had open myomectomies and 24 had minimally invasive myomectomies. A significant decrease in serum AMH was found between baseline and 2 weeks post-operatively (n=42) (b=0.26 ± 0.75 (95% CI 0.03-0.49) p=0.029). This transient effect was no longer significant after 3 months (n=20) and 6 months (n=14). Linear regression showed a significantly greater decrease at 2 weeks post-operatively in the open compared to MIS group (b=-0.56, p=0.039). No significant differences in AMH were seen between open and MIS groups at 3 and 6 months. Surgical factors such as EBL, length of surgery, and fibroid weight were not significantly associated with post-operative changes in serum AMH level.

CONCLUSIONS: AMH levels appear to undergo a transient decline in the immediate post-operative period after myomectomy, with a more pronounced effect with an open compared to MIS approach. The use of a tourniquet might cause a more significant decrease in AMH in the immediate post-operative period, but does not appear to have a sustained effect. Patients can be reassured that undergoing a myomectomy does not have a long-term impact on ovarian reserve, regardless, of the approach.

Reference: None.

SUPPORT: None.

FERTILITY PRESERVATION

O-199 Wednesday, October 16, 2019 10:45 AM

HOW OPEN IS THE WINDOW OF OVARIAN FUNCTION AFTER CANCER TREATMENT? Brian Kwan, PhD,a Shaylyn S. Stark, MPH,a Mary D. Sammel, ScD,b Brian W. Whitcomb, PhD, b Andrew C. Dietz, MD, MSCR,a Elena Martinez, PhD,a Loki Natarajan, PhD,a R. Irene Su, M.D., M.S.C.E.a University of California San Diego, La Jolla, CA; 2UNIVERSITY OF PENNSYLVANIA HEALTH SYSTEM, PHILADELPHIA, PA; 3University of California San Diego Moores Cancer Center, San Diego, CA; 4University of California, San Diego, Family and Preventive Medicine and Public Health, La Jolla, CA.

OBJECTIVE: The remaining window of ovarian function after cancer treatment is clinically important, yet largely unknown. This study estimated the trajectory of AMH over two decades following cancer treatment in female survivors of adolescent and young adult cancers (AYA survivors). We hypothesized that AMH levels would initially rise, then plateau and finally fall over time after cancer treatment, and trajectories would vary by treatment gonadotoxicity.

DESIGN: Cross-sequential.

MATERIALS AND METHODS: Female AYA survivors who were ages 18-39, were diagnosed with cancer at ages 15-35, completed primary cancer treatment and had at least one ovary were recruited from cancer registries, clinics and advocacy groups between 2015 and 2018. Followed for 18 months, participants collected dried blood spots (DBS) and answered questionnaires every 6 months. DBS were assayed for AMH levels (LOD 0.03 ng/mL, inter- and intra-assay CV <10%) using the picoAMH assay (Ansh-Labs, Webster, TX). Cancer treatment data were abstracted from primary records. Functional Principal Component Analysis (FPCA) modeled AMH trajectory over time since treatment. Principal components were compared by gonadotoxicity (low, moderate, high) and age at diagnosis (<25, 25-35, ≥35) groups.

RESULTS: 763 survivors, mean age 33.3 (SD 4.7), contributed 1968 AMH levels at a median of 6.5 years post-treatment (IQR 2.0-9.1). The most common cancers were breast (27%), lymphoma (25%) and thyroid (18%). By treatment gonadotoxicity, 30% were low, 62% were moderate, and 8% were high. For the overall trajectory, post-treatment AMH levels began high and rose to plateau by 2.5 years, and maintained at similar levels up to 10 years. FPCA showed that trajectories differed significantly by gonadotoxicity (p<0.001) and age at cancer diagnosis (p<0.05). The low group displayed rising levels until 2.7 years post-treatment, then maintained at similar levels until 10 years post-treatment before levels began to fall. The moderate group trajectory was similar, but the magnitude of peak AMH recovery was approximately two-thirds of the low group. In contrast, the high group displayed a quick recovery (plateau by 1.5 years) and no appreciable time interval during which AMH was maintained before a steep fall of levels. Younger age at diagnosis was associated with higher levels of AMH at plateau, but similar maintenance intervals prior to fall of levels, compared with older age at diagnosis. The predicted trajectories showed overlapping among groups.

CONCLUSIONS: Using the hybrid longitudinal and cross-sectional design, with the FPCA approach, we show novel data on the trajectory of AMH beyond the first 5 years after cancer treatment. The AMH trajectories suggest that for low and moderate toxicity groups, the duration during which AMH stays plateaued appears long, in contrast to a narrow window in the high toxicity group. These trajectories aid in counseling AYA survivors on their family building plans.

SUPPORT: NIH HD080952-05.

O-200 Wednesday, October 16, 2019 11:00 AM

IN SEARCH OF THE CRYSTAL BALL - HOW MANY EGGS TO A LIVE BIRTH? A 2-STEP PREDICTION MODEL FOR EGG FREEZING COUNSELING BASED ON INDIVIDUAL PATIENT AND CENTER DATA. Serena H. Chen, M.D.a Yajing Angela Xie, Ph.D.a Natalie A. Cekleniak, MD.a Debbra A. Keegan, MD.a Mylene WM. Yao, MD.a Division of Reproductive Medicine, IRMS at St Barnabas, Livingston, NJ; 2Univty Inc., Los Altos, CA.

OBJECTIVE: We aim to develop a two-step egg freezing counseling tool that provides personalized expected live birth (LB) rates before oocyte retrieval (Pre-OR) and adjusts the expectations after oocyte retrieval (Post-OR), when the oocyte yield is known.

METHODS: We applied machine learning (ML) to a retrospective IVF-LB outcomes data set. Due to limited LB outcomes from egg freezing itself, this large, diverse IVF patient population served as proxy for women considering egg-freezing to preserve fertility potential.

MATERIALS AND METHODS: We applied the boosted tree method and cross-validation to train and test Pre- and Post-OR models in predicting LB outcomes. The dataset comprises linked IVF-ET data from 1,166 IVF cycles started at our center in 2015 for women under 42. Both Pre- and Post-OR
models use clinical predictors such as age, BMI, AMH, day 3 FSH, any clinical infertility diagnosis, reproductive history, and semen analysis, but only the Post-OR model uses the oocyte yield. Models with optimal discrimination (AUC) and prediction accuracy relative to an age-control model were selected. It is possible that not only the oocyte live birth rates or per-embryo aneuploidy rates, but also 1) the expression of PECAM in the Akt pathway and hence results indicate that cyclophosphamide suppresses rather than activating Akt.

RESULTS: Model Evaluation: The AUC for the Pre-OR, Post-OR and age-control models were 67%, 73%, and 57%, respectively. Compared to age-control, AUC improved by 17% (Pre-OR) and 28% (Post-OR). Prediction accuracy, measured by the posterior log of odds ratio compared to age-control (i.e. “how many times more accurate compared to age-control”) is improved by 25-folds (Pre-OR) and 67-folds (Post-OR) using natural log scale. Based on the Pre-OR model, 84% of our IVF patients have a personalized LB rate over 32% from transfer(s) of embryo(s) generated from one IVF-COH cycle. Relevance for Egg Freezing Counseling - Example 1: Based on the Pre-OR model, a 30 year old woman (BMI 26, AMH 3.5 ng/mL, no infertility) has 69-70% (95% CI) LBR per egg-freezing cycle (per cycle here on) which would be adjusted if oocyte yield is less than expected. For example, if her oocyte yield were 5-9 oocytes (less than the expected 10-15), her expected LBR per cycle would decrease to 48-53% (95% CI). Example 2: Based on the Pre-OR model, a 36 year old woman (BMI 28, AMH 2.5 ng/mL, no infertility) has 52-53% (95% CI) LBR per cycle. However, if her oocyte yield were > 15 oocytes (higher than expected), her expected LBR per cycle would increase to 60% (95% CI).

CONCLUSIONS: We have developed a two-step egg freezing counseling tool that sets expectations about LB outcomes before and after knowing the actual oocyte yield while personalizing LB expectations to each woman’s reproductive health profile and maximizing transparency with ML-based models validated against our center’s IVF outcomes. User experience testing is required to optimize how to best convey LB expectations provided by the models.

SUPPORT: Each organization funded its own research efforts.

O-201 Wednesday, October 16, 2019 11:15 AM

CHEMOTHERAPYCAUSES PRIMORDIAL FOLLICLE DEATH IN THE HUMAN OVARY VIA MULTIPLE APOPTOTIC PATHWAYS AND NOT BY “BURN OUT”.

Shiny Titus, Ph.D., Kutluk H. Oktay, M.D., Ph.D., Yale University School of Medicine, New Haven, CT.

OBJECTIVE: It has been proposed that gonadotoxic chemotherapy results in the “burn out” of primordial follicle reserve by activating PI3K/PTEN/Akt signaling pathway. Others have challenged this concept and put forward DNA damage and apoptosis as the main mechanism of follicle loss. We conducted this study to answer this controversy and conclusively determine the mechanism of chemotherapy-induced damage to ovarian reserve in women.

DESIGN: Ovarian cortical pieces from organ donors aged ≤ 32 years were xenografted subcutaneously to SCID mice (n=12 mice/tissue from 4 donors each). After 10 days, the mice were given an injection of cyclophosphamide (75mg/kg) or the vehicle. The tissues were recovered 12 hours later.

MATERIALS AND METHODS: The female C57BL/6 mice aged 6-8 weeks were randomized into five groups (n=8 per group), including the control group without any medical treatment, the CP-alone group (75mg/kg, i.p. weekly), the treatment groups which CP was co-administered with either oral metformin (50mg/kg/day) or two specific mTOR inhibitors (sirolimus 0.67mg/kg/day or everolimus 0.167mg/kg/day). After four weeks of treatment, five mice per group were sacrificed to collect the ovarian tissue and serum, and three mice per group were mated with male breeders 8 weeks after the end of treatment. The data were analyzed by one-way analysis of variance, the chi-square test or Fishers exact test where appropriate. A P value of < 0.05 was considered statistically significant.

RESULTS: The number of the primordial follicle, tertiary follicle, and corpus luteum significantly decreased in the CP-alone group compared with the control group. The deleterious effects of CP were significantly rescued when oral metformin was given that the follicular counts were significantly higher in the CP + metformin group than CP-alone group (number of primordial follicle: 16.7 ± 6.3 vs. 9.6 ± 4.7, p<0.004; tertiary follicle: 5.4 ± 1.1 vs. 2.6 ± 1.8, p=0.002; corpus luteum: 8.2 ± 1.5 vs. 5.6 ± 1.3, p=0.029). The other two specific mTOR inhibitors, sirolimus and everolimus, also exhibited similar protective effects on the ovarian follicular counts against CP damage. The serum level of anti-mullerian hormone, a reliable objective marker of ovarian reserve, was significantly decreased in the CP-alone group and increased in CP + metformin group (control vs. CP-alone vs. CP + metformin: 5.8±0.3 vs. 2.1±1.0 vs. 4.6±1.2 ng/ml, p<0.0001). The number of the oocytes was also significantly decreased in the CP-alone group and increased in the CP + metformin group (control vs. CP-alone vs. CP + metformin: 6.7±1.2 vs. 1.0±1.0 vs. 4.0±2.0, p=0.004). The IHC stain showed that the expression of phospho-mTOR and TUNEL protein within mice ovaries were increased when treated with CP and were significantly decreased when co-treated with metformin. The reduction in the number of the follicular population in the CP-alone group was accompanied by enhanced colocalization of the pro-apoptotic BAD-Bcl2 complex ( p=0.006) in the primordial follicles, confirming that cyclophosphamide induces follicle death via apoptosis.

CONCLUSIONS: This single cell transcriptomic and immunohistochemical analysis of human primordial and primary follicles prove that gonadotoxic chemotherapy agents do not cause follicle activation; they rather create a pro-apoptotic state resulting in massive loss of ovarian reserve. Future research on pharmacological fertility preservation should target preventing DNA damage and apoptosis rather than follicle activation.

SUPPORT: This work was supported by ROI HD061259 from NICHD.

O-202 Wednesday, October 16, 2019 11:30 AM

METFORMIN: A NOVEL OPTION OF FERTILITY PRESERVATION DURING CYCLOPHOSPHAMIDE-CONTAINING CHEMOTHERAPY.

Chu-Chun Huang, MD,³ Mei-Jou Chen, MD, PhD,³ Shee-Uan Chen, MD, PhD,³ Hong-Neng Ho, MD, PhD,³ Yu-Shih Yang, MD, PhD,³ aDepartment of Obstetrics and Gynecology, National Taiwan University Hospital, Taipei, Taiwan; bNational Taiwan University Livia Shangyu Wan Scholar, Taipei, Taiwan; cTaipei Medical University, Taipei, Taiwan; dDepartment of Obstetrics and Gynecology, Fu Jen Catholic University Hospital, New Taipei, Taiwan.

OBJECTIVE: Cyclophosphamide (CP) could cause premature primordial follicle activation and depletion, and finally premature ovarian failure, through the imbalanced activation of mTOR signaling pathway. Whether metformin, a widely prescribed anti-diabetes agent with mTOR inhibitory effect, could preserve fertility during CP treatment is still unknown.

DESIGN: A murine study.

MATERIALS AND METHODS: The female C57BL/6 mice aged 6-8 weeks were randomized into five groups (n=8 per group), including the control group without any medical treatment, the CP-alone group (75mg/kg, i.p. weekly), the treatment groups which CP was co-administered with either oral metformin (50mg/kg/day) or two specific mTOR inhibitors (sirolimus 0.67mg/kg/day or everolimus 0.167mg/kg/day). After four weeks of treatment, five mice per group were sacrificed to collect the ovarian tissue and serum, and three mice per group were mated with male breeders 8 weeks after the end of treatment. The data were analyzed by one-way analysis of variance, the chi-square test or Fishers exact test where appropriate. A P value of < 0.05 was considered statistically significant.

RESULTS: The number of the primordial follicle, tertiary follicle, and corpus luteum significantly decreased in the CP-alone group compared with the control group. The deleterious effects of CP were significantly rescued when oral metformin was given that the follicular counts were significantly higher in the CP + metformin group than CP-alone group (number of primordial follicle: 16.7±6.3 vs. 9.6±4.7, p<0.004; tertiary follicle: 5.4±1.1 vs. 2.6±1.8, p=0.002; corpus luteum: 8.2±1.5 vs. 5.6±1.3, p=0.029). The other two specific mTOR inhibitors, sirolimus and everolimus, also exhibited similar protective effects on the ovarian follicular counts against CP damage. The serum level of anti-mullerian hormone, a reliable objective marker of ovarian reserve, was significantly decreased in the CP-alone group and increased in CP + metformin group (control vs. CP-alone vs. CP + metformin: 5.8±0.3 vs. 2.1±1.0 vs. 4.6±1.2 ng/ml, p<0.0001). The number of the oocytes was also significantly decreased in the CP-alone group and increased in the CP + metformin group (control vs. CP-alone vs. CP + metformin: 6.7±1.2 vs. 1.0±1.0 vs. 4.0±2.0, p=0.004). The IHC stain showed that the expression of phospho-mTOR protein and TUNEL protein within mice ovaries were increased when treated with CP and were significantly decreased when co-treated with metformin. The reduction in the number of the follicular population in the CP-alone group was accompanied by enhanced colocalization of the pro-apoptotic BAD-Bcl2 complex (p=0.006) in the primordial follicles, confirming that cyclophosphamide induces follicle death via apoptosis.

CONCLUSIONS: This single cell transcriptomic and immunohistochemical analysis of human primordial and primary follicles prove that gonadotoxic chemotherapy agents do not cause follicle activation; they rather create a pro-apoptotic state resulting in massive loss of ovarian reserve. Future research on pharmacological fertility preservation should target preventing DNA damage and apoptosis rather than follicle activation.

SUPPORT: This work was supported by grant MOST 105-2314-B-002-109-MY3 (H.N. Ho), MOST 102-2321-B-002-093-MY3 and 105-2628-B002-043-MY4 (M.J. Chen), and MOST 105-2628-B-002-031-MY3 (C.C. Huang) from the Ministry of Science and Technology of Taiwan and the National Taiwan University Hospital (107-00405S, 108-004536).

e84 ASRM Abstracts Vol. 112, No. 3, Supplement, September 2019
MATERIALS AND METHODS: 115 patients, age 2 to 35 years, had frozen ovary cortex stored at our center since 1997. 15 of them up till now have had the tissue thawed and re-implanted. Three were leukemia, one was multiple sclerosis, two were premature ovarian failure, and the rest were solid tissue cancers. All were menopausal for at least 3 years. The technique for re-implantation was the same in all cases. After thaw of cortical tissue, three to five slices were quilted into one piece with 9-0 nylon interrupted sutures. The dead cortex was removed in entirety, and the quilted slices were sutured to the underlying medulla with 9-0 nylon interrupted sutures. The dead cortex was removed in entirety, and the quilted slices were sutured to the underlying medulla with 9-0 nylon interrupted sutures after hemostasis was achieved with micro-bipolar forceps and irrigation with pulsatile heparinized media to avoid adhesions. All transplants were orthotopic so that the patients could be allowed to conceive spontaneously. Patients were followed monthly for hormones, return of menses, and pregnancy, and delivery. In addition, the literature was reviewed to try to tabulate the number of live births to date in the world.

RESULTS: Of the fifteen patients who had their frozen tissue re-implanted, none underwent IVF, all pregnancies were spontaneous from intercourse. 15 healthy babies were delivered to 10 of the 15 women (66%). Two women delivered the thawed, transplanted tissue. Two of the three with leukemia had a total of 4 healthy babies. In the literature, we counted a total of 170 babies in addition to our 15, making a total of 185. Live baby pregnancy rate in the literature ranged from a low of 31% to our 66%, in the only four reported series, including ourselves, thus far. There have been no cases of transmission of cancer.

CONCLUSIONS: Ovarian cryopreservation for cancer patients should no longer be labeled "experimental".

FIBROIDS

O-204 Wednesday, October 16, 2019 12:00 PM
ARE GENDER DYSPHORIA PATIENTS COUNSELED ON FERTILITY PRESERVATION PRIOR TO INITIATING HORMONAL THERAPY? - Ross G. Everett, MD MPH, Bryce A. Thompson, BA, Kaylee M. Luck, BS, Johnathan Doolittle, MD, Jay I. Sandlow, MD, Medical College of Wisconsin, Milwaukee, WI.

OBJECTIVE: National guidelines recommend counseling patients with gender dysphoria on the impacts of hormone or surgical therapy on their fertility prior to beginning either intervention. In this study, we aim to identify the compliance to these guidelines at our institution.

DESIGN: Retrospective, single institution chart review.

MATERIALS AND METHODS: Utilizing ICD codes, we identified patients with a diagnosis of gender dysphoria [GD] treated at our institution between 2008-2018. Various parameters regarding medication regimen, surgical intervention, fertility counseling, and fertility preservation were obtained through retrospective review. Patient demographics and interventions were compared. All data was analyzed in a standard statistical fashion utilizing Stata software.

RESULTS: Upon review, 269 patients met inclusion criteria. Of these, 114 (42.4%) had a chromosomal sex of female and 155 (57.6%) were chromosomal males. Race was divided as 75.5% White, 16.7% Black and 7.8% Other. The average age was 30.9 (S.D.:±13.7). Regarding management of GD, 63.6% had been managed by Gynecology, 25 (9.3%) had seen Urology, 74 patients (27.5%) ultimately pursued some surgical intervention. 97 patients (36.1%) were on hormonal therapy for GD prior to evaluation at our institution and were excluded from subsequent analysis. Another 26 patients did not have record of pursu-
SUBLINGUAL MISOPROSTOL 400 VS. 200 MCG FOR REDUCING BLOOD LOSS DURING ABDOMINAL MYOMECTOMY: A RANDOMIZED DOUBLE-BLIND CLINICAL TRIAL. Ahmed M. Abbas, MD, a Hossam Ramadan, MSc,b Shyama Ali, MSc, c Yehia Ali, MD, d Mohammed Khairy Ali, MD,a Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; bDepartment of Obstetrics and Gynecology, Faculty of Medicine, Arsan University, Arsan, Egypt; cDepartment of Obstetrics and Gynecology, Faculty of Medicine, Suez University, Suez, Egypt; dDepartment of Obstetrics and Gynecology, Faculty of Medicine, Qena, Egypt.

OBJECTIVE: Uterine leiomyomas are the most frequent benign gynecologic pelvic tumors in women, which originate from the myometrial cells of the uterus. Minimizing blood loss during the surgical procedures and the need for blood transfusion and iron therapy are major challenges with abdominal myomectomy. Our objective is to compare the effectiveness of preoperative sublingual misoprostol 200 vs. 400 mcg for reducing blood loss during and after abdominal myomectomy.

MATERIALS AND METHODS: Patients with documented uterine fibroids on pelvic imaging and scheduled for abdominal myomectomy were invited to participate in our study. We included women aged (18-50 years) with five or less symptomatic subserous or intramural fibroids, Preoperative hemoglobin level is >8 g/dl, and uterine size is less than 24 weeks gestation. The eligible women were randomized (1:1) to either (group A) received two tablets of sublingual misoprostol 400 mcg at 3 hours and 1 hour before the surgery, or (group B) received one tablet of sublingual misoprostol 200 mcg and one placebo tablet at the previously mentioned schedule. The primary outcome was the difference in the mean amount of intraoperative blood loss during myomectomy. The secondary outcomes included the change of hemoglobin (HB) before and 24 hours after surgery, duration of surgery, postoperative blood transfusion and the side effects of the drug. Mann Whitney test and Fisher’s exact test were used for the analysis of the outcomes.

RESULTS: Eighty women were enrolled and randomized (n=40 in each arm). No difference between both groups regarding age, parity, BMI, type, number, size of fibroids and the total uterine size. Estimated blood loss was significantly lower in the misoprostol 400 mcg group (373.3 ± 55.6 vs. 560.0 ± 105.2 ml, p<0.001). Moreover, the reduction in HB level was significantly lower in the misoprostol 400 mcg group (0.8 ± 0.18 vs. 1.7 ± 0.38 g/dl, p<0.001). The operative duration was significantly shorter in the misoprostol 400 mcg group (91.3 ± 57.2 vs. 111.2 ± 63 minutes, p<0.001). Seven cases required a blood transfusion in the misoprostol 200 mcg group versus two cases in the other group (p=0.03). No difference between both groups reading the side effects of misoprostol.

CONCLUSIONS: Sublingual misoprostol 400 mcg is an effective and safe method for reduction of blood loss and need for blood transfusion during abdominal myomectomy.

SUPPORT: None.

MATERIALS AND METHODS: Patients with documented uterine fibroids on pelvic imaging and scheduled for abdominal myomectomy were invited to participate in our study. We included women aged (18-50 years) with five or less symptomatic subserous or intramural fibroids, Preoperative hemoglobin level is >8 g/dl, and uterine size is less than 24 weeks gestation. The eligible women were randomized (1:1) to either (group A) received two tablets of sublingual misoprostol 400 mcg at 3 hours and 1 hour before the surgery, or (group B) received one tablet of sublingual misoprostol 200 mcg and one placebo tablet at the previously mentioned schedule. The primary outcome was the difference in the mean amount of intraoperative blood loss during myomectomy. The secondary outcomes included the change of hemoglobin (HB) before and 24 hours after surgery, duration of surgery, postoperative blood transfusion and the side effects of the drug. Mann Whitney test and Fisher’s exact test were used for the analysis of the outcomes.

RESULTS: Eighty women were enrolled and randomized (n=40 in each arm). No difference between both groups regarding age, parity, BMI, type, number, size of fibroids and the total uterine size. Estimated blood loss was significantly lower in the misoprostol 400 mcg group (373.3 ± 55.6 vs. 560.0 ± 105.2 ml, p<0.001). Moreover, the reduction in HB level was significantly lower in the misoprostol 400 mcg group (0.8 ± 0.18 vs. 1.7 ± 0.38 g/dl, p<0.001). The operative duration was significantly shorter in the misoprostol 400 mcg group (91.3 ± 57.2 vs. 111.2 ± 63 minutes, p<0.001). Seven cases required a blood transfusion in the misoprostol 200 mcg group versus two cases in the other group (p=0.03). No difference between both groups reading the side effects of misoprostol.

CONCLUSIONS: Sublingual misoprostol 400 mcg is an effective and safe method for reduction of blood loss and need for blood transfusion during abdominal myomectomy.

SUPPORT: None.
monitoring showed a statistically significant reduction of 18F-FDG uptake in both VitD-treated groups (p<0.05), indicating a reduction in LM size. Likewise, macroscopic LM size diminished significantly in VitD 1 mg/kg/day dose group (p<0.025). Besides, the high dose of VitD significantly decreased cell proliferation in LM (p<0.025). Further, CAPSASE 3 expression was induced by VitD in a dose-dependent manner and apoptotic cells increased in VitD 1 mg/kg/day group (p<0.009). Regarding ECM, VitD treatment decreased COLLAGEN I expression at both doses (p<0.02) and at the highest dose we observed decrease of PAI-1, TGFβ1, and MMP2 and MMP9 expression (p<0.05).

CONCLUSIONS: VitD short-term treatment is only capable to maintain human uterine LM size, while at long term VitD significantly reduces LM size by cell proliferation inhibition and ECM degradation and apoptosis increase, without side effects. Our data strongly suggest that long-term treatment with VitD could be considered as an effective adjuvant treatment for uterine LM in women.

AC & HF contributed equally.

SUPPORT: P11500312; P1701039; P18/00323; CD15/00057; ACIF/ 2016/444.

O-209 Wednesday, October 16, 2019 11:45 AM

MULTICENTRIC ANALYSIS OF UTERINE LEIOMYOMAS IN AFRICAN AMERICANS AND CAUCASIANS: INSIGHTS INTO HEALTH DISPARITY. George L. Maxwell, MD, a Christopher Tarney, MD, b Nicholas Buteman, PhD, c Anthony R. Soltis, PhD, c Brian L. Hood, PhD, c Clifton L. Dalgard, PhD, d Matthew Wilkerson, PhD, d Kathleen M. Darcy, PhD, d Yovanni Casablanca, MD, d Ayman Al-Hendy, MD PhD, c Thomas Conrads, PhD, d Department of Obstetrics and Gynecology, Inova Fairfax Hospital, Falls Church, VA; a Gynecologic Cancer Center of Excellence, Muhra Cancer Center Research Program, Uniformed Services University of the Health Science, George Washington University, Bethesda, MD; c Gynecologic Cancer Center of Excellence, Muhra Cancer Center Research Program, Uniformed Services University of the Health Science, Bethesda, MD; b The American Genome Center, Uniformed Services University, Bethesda, MD; d The American Genome Center, Bethesda, MD; d University of Illinois College of Medicine, Chicago, IL.

OBJECTIVE: Uterine leiomyomas (ULMs) are the most common tumor of the female genital tract. Prevalence of ULMs are higher in African-American (AA), who also experience greater severity of symptoms and different responses to treatment than Caucasian (CA) women.

DESIGN: We performed whole genome sequencing (WGS) and in-depth global proteomic analyses of ULMs from Black and White women to evaluate for a biologic basis underlying the health disparities seen in this disease.

MATERIALS AND METHODS: Fresh-frozen ULMs from AA (n=23) and CA (n=25) patients and matched myometrium (n=20 total cases) were obtained from a single institution. Tissues were processed for genomic DNA to support WGS analysis (Illumina HiSeq X) or by pressure cycle-amplification prior to support global proteomic analysis using liquid chromatography-tandem mass spectrometry (Thermo Fusion Lumos) using a multiplexed, quantitative proteomics/tandem mass tag-10 labeling strategy. Differential expression and functional inference analyses was performed using commercial and in-house bioinformatic pipelines.

RESULTS: Standard estimates of ancestral admixture from WGS data revealed that 95% of self-described CA women were of European descent, with remaining clustering as admixed American ancestry. Preliminary somatic mutation analyses of a patient subset (n=14) revealed n=5 AA and n=4 CA cases (>64%) exhibited recurrent mutations or deletions in a hotspot window with the MED12 gene. Proteomic analyses resulted in the quantification of 3,257 total proteins and revealed 401 significantly altered (LIMMA FDR<0.05) between AA vs. CA ULMs. Protein alterations suggested marked remodeling of extracellular matrix in AA versus CA ULMs and included diverse collagen (COL3A1, COL5A2 and COL4A1) as well as matrix metalloproteinases (MMP2/10) isoforms. Functional analyses revealed activation of the glycoprotein VI signaling as well as pathways supporting muscle formation and intercellular signaling, but inhibition of JAK-STAT signaling and pathways supporting fibrinogenesis and proliferation of connective tissue cells in AA versus CA ULMs. Comparative analyses of protein alterations with historic differential gene expression analyses comparing 52 ULMs from AA (n=8) and CA (n=3) women (Davis BJ et al, 2013) revealed >41% (168) of proteins altered between AA vs. CA ULMs were also significantly altered at the transcript level and exhibited high correlation abundance trends (Spearman Rho = 0.559, P<0.001).

CONCLUSIONS: Quantitative analyses revealed distinct proteomic changes among White and Black ULMs, providing insight into the pathogenesis of disparities seen in this common disease. These findings may also clarify novel therapeutic strategies that support individualized treatment.

O-210 Wednesday, October 16, 2019 12:00 PM

PREOPERATIVE TREATMENT WITH LEUPROLIDE ACETATE AND ULIPRISTAL ACETATE BEFORE OUTPATIENT HYSTEROSCOPIC MYOMECTOMY: PROSPECTIVE COMPARATIVE STUDY. Simone Ferrero, MD, PhD, a Fabio Barra, MD, b Umberto Leone Roberti Maggiore, MD, PhD, c Valerio Gaetano Vellone, MD, PhD, d Carolina Scala, MD, e DINOGMI, University of Genova, Genova, Italy; d Department of Gynecologic Oncology, IRCCS National Cancer Institute, Milan, Italy; c DISC, University of Genova, Genova, Italy; Istituto G. Gaslini, Genova, Italy.

OBJECTIVE: Outpatient hysteroscopic myomectomy can be usually performed in case of single submucosal myoma with largest diameter up to 2 cm. The volume of the myoma has a critical role in outpatient myomectomy because larger myomas require a longer resection time and, thus, these procedures may be less tolerated by patients. One of the major advantages of preoperative therapy is to decrease the volume of uterine myomas. This prospective study compared outpatient hysteroscopic myomectomy performed by using the Versapoint system in patients who received 3-month preoperative treatment with leuprolide acetate (LA), ulipristal acetate (UPA) or who did not receive any preoperative hormonal therapy.

DESIGN: Single center prospective non-randomized study.

MATERIALS AND METHODS: This study included patients of reproductive age requiring outpatient resection of single FIGO type 0–1 myoma with largest diameter < 2 cm. Exclusion criteria were: previous surgical treatment of uterine myomas, previous administration of hormonal therapies for uterine myomas, additional endometrial conditions requiring hysteroscopic treatment (such as uterine polyps), additional surgical procedures performed by other approach, such as laparoscopy, suspicion of malignancy. Study patients underwent either preoperative treatment with UPA (5 mg/day; group UPA) or LA (11.25 mg/ml; group LA) for 3 months or immediate surgery (without preoperative hormonal therapy, group S). The choice of receiving preoperative treatment was based on patients’ preference. Hysteroscopic myomectomy was performed by using the Versapoint system. The primary objective of the study was to compare the rate of complete resections in the three study groups. The secondary objective of the study was to compare the operative results between the study groups. The tertiary objective of the study was to assess the characteristics of the myomas and the endometrium in patients treated with UPA and LA. Data were analyzed according to intention to treat.

RESULTS: 138 patients were included in the study. The percentage decrease in the volume of uterine myomas was higher in patients receiving LA than in those treated with UPA (p = 0.015). Before surgery, myoma volume was lower in the LA group (22.2 ± 14.4 cm3, p<0.05) than in group UP (43.3 ± 22.5 cm3, p<0.05). The percentage of complete resection was significantly higher in group LA (83.0%; 39/47) than in group UPA (60.5%; 23/38; p = 0.043, respectively). The percentage of complete resection was significantly higher in group LA (83.0%; 39/47) than in group UPA (60.5%; 23/38; p = 0.020) and in group S (62.2%; 33/53; p = 0.021). The volume of fluid infused was significantly lower in group LA than in group S (p<0.005). There was no significant difference in the volume of fluid absorbed between the three study groups (p = 0.341). Concerning the characteristics of the endometrium, completely atrophic endometrium was significantly more frequent in the LA group compared with the other study groups. The texture of the myoma was rubbery or soft more frequently in the UPA group than in the other groups.

CONCLUSIONS: Compared with UPA or no treatment, LA improves the rates of complete resection in patients undergoing outpatient hysteroscopic myomectomy.

IVF OUTCOME PREDICTORS 2

O-211 Wednesday, October 16, 2019 10:45 AM

IMPACT OF BODY WEIGHT ON OVARIAN RESPONSE AFTER INDIVIDUALIZED OR FIXED FOLLICLE-STIMULATING HORMONE DOSING IN WOMEN UNDERGOING IVF: A PROSPECTIVE COMPARATIVE STUDY. Scott M. Nelson, MD, PhD, a Antonio La Marca, MD, PhD, b Juan A. Garcia-Velasco, MD, PhD, c Marie G. Gaslini, MD, PhD, a Fabio Barra, MD, b Umberto Leone Roberti Maggiore, MD, PhD, c Valerio Gaetano Vellone, MD, PhD, d Carolina Scala, MD, e DINOGMI, University of Genova, Genova, Italy; d Department of Gynecologic Oncology, IRCCS National Cancer Institute, Milan, Italy; c DISC, University of Genova, Genova, Italy; Istituto G. Gaslini, Genova, Italy.

OBJECTIVE: To assess the impact of body weight on ovarian response in women undergoing in vitro fertilization.
OBJECTIVE: To explore the influence of body weight on ovarian response and related clinical outcomes after individualized follicle-stimulating hormone (FSH) dosing versus fixed starting dosing of 150 IU FSH in women undergoing in vitro fertilization (IVF).

DESIGN: Randomized, assessor-blind, controlled trial; 1326 women undergoing their first ovarian stimulation cycle were randomized 1:1 to follicitropin delta or follicitropin alfa. In the follicitropin delta group, women with anti-Müllerian hormone (AMH) <15 pmol/L received fixed daily doses of 12 μg and women with AMH ≥ 15 pmol/L received individualized doses, based on AMH level and body weight. Women randomized to follicitropin alfa received a fixed starting dose of 150 IU, regardless of their AMH and body weight.

MATERIALS AND METHODS: Oocytes retrieved 36±2 hours after triggering final follicular maturation were inseminated by IVF or intracytoplasmic sperm injection. Good-quality blastocysts (≥3 BB) was based on Gardner-Schoolcraft classification (1999), blastocyst transfer was performed on day 5, and ongoing pregnancy was confirmed by ultrasound at 10-11 weeks after transfer. Data were evaluated descriptively by calculating the mean number of oocytes, good-quality blastocysts, and the ongoing pregnancy rate for nested subgroups of women based on increasing body weight.

RESULTS: Exposure to serum FSH showed an inverse relationship with body weight for both follitropin delta and follitropin alfa. In women with AMH <15 pmol/L, the ovarian response in terms of number of oocytes did not show any body weight dependence. In women with AMH ≥15 pmol/L treated with follitropin alfa, the number of oocytes decreased from an overall mean of 13 oocytes to a mean of 10 oocytes with increasing body weight. In the individualized follicitropin delta group, the number of oocytes was not affected by body weight. Accordingly, the number of good-quality blastocysts decreased with increasing body weight in women with AMH ≥15 pmol/L in the follitropin alfa group, from an overall mean of 2.3 to a mean of 2.0, whereas body weight did not affect the number of good-quality blastocysts in the individualized follitropin delta group. The ongoing pregnancy rate after fresh transfer tended to decrease with increasing body weight in the follitropin alfa group but not in the individualized follitropin delta group. Finally, MA, GATUS, and YSD were identified by multinominal logistic regression model as significant predictors of EPL. The multinominal logistic model could be used to calculate the probability of EPL and thus, proper early treatment could be applied to the high-risk patients.

TABLE. The predictive factors for the EPL

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<th>Parameters</th>
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<tr>
<td>GATUS</td>
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<td>.034</td>
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<td>GSD</td>
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<td>YSD</td>
<td>0.632</td>
<td>0.532</td>
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SUPPORT: The Science and Technology Project of the Health and Family Planning Commission of Hunan Province (No. C201802829) and the Citic-Xiangya Research Fund (No. KYXM-201703).

O-213 Wednesday, October 16, 2019 11:15 AM

THE IMPACT OF AGE BEYOND PLOIDY: OUTCOME DATA FROM 9,101 EUPLOID SINGLE EMBRYO TRANSFERS. Andres Reig, M.D., Richard Thomas Scott, Jr., Emre Seli, M.D., Yale University - Bridgeport Hospital, Bridgeport, CT; IVI-RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: Rate of embryonic aneuploidy increases significantly with increasing female age and is the primary cause of lower pregnancy and live birth rates observed in older reproductive age women. This study evaluates single euploid embryo transfers to eliminate the impact of aneuploidy on reproductive efficiency. It then seeks to determine if an age-related decline in reproductive efficiency persists indicating that other factors may contribute to impaired outcomes in aging women.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A total of 9,101 single embryo transfers that had undergone pre-implantation testing for aneuploidy (PGT-A) and cryopreservation were included. These were divided into five groups according to the age of the woman at the time of oocyte retrieval: <35 years old (n=4,585 embryos transferred), 35-37 years old (n=2,272), 38-40 years old (n=1,665), 41-42 years old (n=330), and ≥42 years old (n=249). Biochemical (positive serum ß-hCG 10 days after transfer), clinical (visualized gestational sac), and live birth rates were calculated for each group as percentage of embryos.
transferred, and then compared using a Chi-square for trend. Similarly, the clinical pregnancy rate was also analyzed for trend as a percentage of biochemical pregnancies, and the live birth rate as a percentage of clinical pregnancies, in order to detect at what stage increasing age has the greatest impact.

The implantation rates as a percentage of embryo transfers negatively correlated with oocyte age, with the percentage of embryos transferred ranging from 73.1% in the oldest group to 81.5% in the youngest (p < 0.0001). This difference was consistent throughout clinical pregnancy rates (57.4% - 67.5%; p < 0.0001), and live birth rates (50.5% - 58.5%; p = 0.01). Interestingly, the proportion of clinical pregnancies which were lost did not change with age, strongly suggesting that factors contributing to decline in reproductive potential with age have their impact prior to the establishment of a clinical pregnancy.

CONCLUSIONS: Age-related diminution in reproductive efficiency is largely overcome by selection of euploid embryos for transfer. However, an age-related decrease in implantation, clinical pregnancy, and live birth rates persists indicating that aneuploidy is not the only factor contributing to reproductive senescence. The additional factors, which remain to be defined, seem to impact the reproductive process prior to implantation as the inability of progressing to delivery after implanting was not impacted by age.

O-214 Wednesday, October 16, 2019 11:30 AM
THREE-DIMENSIONAL ULTRASOUND DIAGNOSIS OF ADENOMYOSIS IS NOT ASSOCIATED WITH DIMINISHED LIVE BIRTH FOLLOWING SINGLE THAWED EUPLOID BLASTOCYST TRANSFER: A PROSPECTIVE COHORT STUDY. Shelby A. Neal, MD, Scott J. Morin, MD, Marie D. Werner, MD, Ndeye-Aicha Gueye, MD, Paul Pirтеa, MD, George Patounakis, MD, PhD, Richard Thomas Scott, Jr, MD, Linnea R. Goodman, MD. IVI-RMA New Jersey, Basking Ridge, NJ; IVI-RMA Northern California, San Francisco, CA; IVI-RMA Pennsylvania, Allentown, PA; IVI-RMA Florida, Lake Mary, FL; University of North Carolina, Raleigh, NC.

OBJECTIVE: To evaluate the impact of adenomyosis, diagnosed using three-dimensional ultrasound (3D US), on pregnancy outcomes following single thawed euploid blastocyst transfer.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Patients planning to undergo a single thawed blastocyst transfer between April and December 2017 at a large IVF center were eligible for inclusion. Exclusion criteria were body mass index ≥ 40 kg/m², uterine anomalies, history of myomectomy, use of a gestational carrier, and communicating hydroalpinx. Consenting patients underwent endometrial preparation according to a standardized protocol. On the day prior to embryo transfer, 3D US was performed and images were reviewed for the diagnosis of adenomyosis. Subjects were then classified into two categories: single thawed euploid blastocyst and pregnancy outcomes were accrued. All 3D US images were de-identified and independently reviewed by five reproductive endocrinologists for the presence of seven sonographic features of adenomyosis: globular uterine configuration, asymmetry of the myometrial walls, heterogeneous echotexture, irregular junctional zone, myometrial cysts, linear striations, and presence of an adenomyoma. Adenomyosis was considered to be present if at least three of out five reviewers noted a minimum of one sonographic feature. Inter- and intra-rater agreement was evaluated using Fleiss’ kappa. Clinical and cycle characteristics of subjects with and without adenomyosis were compared using Student’s t-test and chi-square test. The primary outcome of interest was live birth rate. Secondary outcomes included clinical pregnancy rate and miscarriage rate. Logistic regression was performed to account for potential confounders.

RESULTS: The prevalence of adenomyosis in the study population was 15.3% (99/648). The inter- and intra-rater agreement amongst five independent reproductive endocrinology and infertility specialists who conducted 3D US assessment of adenomyosis were fair (k = 0.23) and moderate (k = 0.58), respectively. Subjects with adenomyosis were older (37.1 versus 35.9 years, P=0.02) and more likely to have undergone a GnRH agonist downregulation protocol when compared to subjects without adenomyosis (16.2% vs. 5.1%; P=0.02).

Clinical pregnancy (80.0% vs. 75.0%) and live birth rates (69.5% vs. 66.5%) were similar between groups. When adjusting for potential confounders, there was no difference in clinical pregnancy [aOR 1.47 (0.85-2.56)], miscarriage [aOR 1.3 (0.62-2.72)] or live birth [aOR 1.28 (0.78-2.08)] in subjects with adenomyosis and those without adenomyosis. No individual sonographic marker of adenomyosis was found to be predictive of pregnancy outcomes.

CONCLUSIONS: Adenomyosis diagnosed on 3D US is not associated with pregnancy outcomes following transfer of a single thawed euploid blastocyst. These findings suggest that routine screening for adenomyosis in an unsel ected infertile patient population following frozen embryo transfer is not warranted.

O-215 Wednesday, October 16, 2019 11:45 AM
ART OUTCOMES AMONG PRE-PREGNANCY CANCER SURVIVORS: LINKAGE OF MASSACHUSETTS ART CORS AND CANCER REGISTRY. Leslie V. Farland, Sc.D. a Judy E. Stern, PhD b Chia-Ling Liu, ScD c Howard Cabral, PhD, MPH d Richard Knowlton, MS, Susan T. Gershman, PhD, MS, MPH e Hafsaot Diop, MD, MPH. Stacey A. Missmer, Sc.D. a University of Arizona, Tuscon, AZ; dartmouth-Hitchcock, Lebanon, OR; MAPD, Bureau of Family Health and Nutrition, Boston, MA; Boston University, Boston, MA; MAPDH, Massachusetts Cancer Registry, Boston, MA; Michigan State and harvard T.H. Chan SPH, grand Rapids, MI.

OBJECTIVE: To investigate fertility treatment outcomes among childhood, adolescent, and young-adult cancer survivors.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: ART cycles in Massachusetts to women ≥ 18 years old from 2004-2013 from the Society for Assisted Reproductive Technology Clinic Outcome Reporting System (SART CORS) (n=90,928 cycles) were linked to the Massachusetts Cancer Registry. Main outcomes of interest were treatment patterns, number of oocytes retrieved, number of oocytes fertilized with or without ICSI, number of embryos transferred, implantation rates, and clinical intrauterine gestation (CIG). We used generalized linear mixed models to accommodate multiple pregnancies per woman with a log link and a Poisson distribution to estimate relative risks (RR) and 95% confidence intervals (CI) a priori adjusted for maternal age and cycle year. To investigate mechanism of association, we stratified by autologous/donor gametes and compared autologous embryo quality between women with and without cancer history.

RESULTS: Among women who utilized ART, 587 (1,273 ART cycles) were childhood and young-life cancer survivors. In crude models, women cancer survivors undergoing ART were more likely to use donor gametes (RR:1.27 (1.01-1.61)) compared to women with no history of cancer, although this attenuated after adjustment for age and cycle year (RR:1.04 (0.82-1.30)). We saw no difference in number of oocytes retrieved (RR:1.02 (0.96-1.09)) or proportion of oocytes fertilized (RR:0.97 (0.94-1.01)) between autologous cycles with and without a history of cancer, however cancer survivors had higher total FSH administered (375.9 IU/mL; RR:1.14 (1.09-1.19)) compared to cycles with no history of cancer (3362.2 IU/mL). Among cycles starts, cycles to women with a history of cancer were less likely to result in CIG (RR: 0.71 (0.64-0.78)) compared to cycles without a history of cancer; this relationship was strongest among autologous cycles (RR:0.64 (0.57-0.72)) but absent from donor cycles (RR:1.06 (0.91-1.23)). When restricted to cycles with embryos transferred, there was no difference in CIG between cycles with and without a history of cancer (RR:0.98 (0.90-1.08)). Among autologous single embryo transfers, no significant difference was seen in the proportion of good quality embryos transferred at the cleavage (RR: 1.13 (0.91-1.42)) or blastocyst (RR:1.20 (0.98-1.47)) stage in cancer survivors compared to women with no history of cancer.

CONCLUSIONS: Women cancer survivors may require more FSH and potentially different ART protocols compared to women with no history of cancer. Our analyses further suggest that cancer may influence ovarian stimulation response, given that autologous cycles to cancer survivors were less likely to result in CIG among cycle starts but not among embryo transfers. Future studies should investigate stimulation protocols to maximize successful implantation and CIG among women starting ART cycles who have a history of cancer.

SUPPORT: NIH R01HD067270.

O-216 Wednesday, October 16, 2019 12:00 PM
ENDOMETRIAL COMPACTION (DECREASED THICKNESS) IN RESPONSE TO PROGESTERONE RESULTS IN HIGHER ONGOING PREGNANCY RATE. Eran Zilberman, M.D. a Dan Nayot, M.D. b Ramsey Genco Smith, B.Sc.c James Meriano, M.Sc.c Eran Barzilay, M.D. Ph.D.d Jigal Haas, M.D.e Robert F. Casper, M.D.f aTrio Fertility, Toronto, ON, Canada; bTRIO Fertility, Staff Physician, Toronto, ON, Canada; cTRIO Fertility, Toronto, ON, Canada; dDepartment of Obstetrics and Gynecology, Samson Assuta Ashdod University Hospital, Ashdod, Israel; eRobert F Casper, M.D. fUniv of Family Health and Nutrition, Boston, MA; gBoston University, Boston, MA; hIVI-RMA Pennsylvanian, Allentown, PA; iUniversity of Ari-
OBJECTIVE: For a pregnancy to occur, implantation of an embryo into a receptive endometrium is crucial. There are few methods to reliably assess the receptivity of the endometrium during an in-vitro fertilization (IVF) cycle. Some methods are invasive such as endometrial biopsy for histologic dating or for the Endometrial Receptivity Array (ERA) and cannot be done in the cycle of interest. Other non invasive methods that can be performed in the treatment cycle include ultrasound (US) for endometrial pattern & thickness or for sub-endometrial waves. We have previously shown a significant increase in ongoing pregnancy if the endometrium became thinner (compacted) during the progesterone phase in hormonally replaced (HRT) frozen embryo transfer (FET) cycles with untested embryos. The objective of the present study was to evaluate whether endometrial compaction was also associated with improved ongoing pregnancy rates in fresh IVF cycles and in FET cycles involving euploid embryos after preimplantation genetic testing for aneuploidies (PGT-A).

DESIGN: A retrospective observational cohort study.

MATERIALS AND METHODS: We retrospectively evaluated cycles from 3 cohorts: 271 HRT cycles with untested single blastocyst FET, 250 HRT single FET cycles of euploid embryos, after PGT-A, and 370 cycles of single fresh embryo transfers after controlled ovarian hyperstimulation. We evaluated recorded digital US images of the endometrium using imaging software and measured endometrial thickness. We calculated the change in endometrial thickness from the end of the estrogen stage/trigger day to the day of embryo transfer. We divided the patients into two groups: 1) cycles with a compaction rate of 10% or greater; 2) cycles with no change or an increase in thickness. The primary outcome was ongoing pregnancy defined as visualization of fetal cardiac activity at 12 weeks gestation or later.

RESULTS: Similar to our previous findings in HRT cycles with untested single blastocyst transfers, we found a significantly higher ongoing pregnancy rate in the euploid embryo cohort and in the fresh embryo transfer cohort with a 10% or greater compaction of the endometrial lining thickness.

Ongoing pregnancy:

<table>
<thead>
<tr>
<th></th>
<th># of cycles</th>
<th>Compacted</th>
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<th>p Value</th>
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<tbody>
<tr>
<td>Frozen Embryo Transfer</td>
<td>271</td>
<td>43/83</td>
<td>45/188</td>
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</tr>
<tr>
<td>Euploid embryo FET</td>
<td>250</td>
<td>47/99</td>
<td>49/151</td>
<td>0.017</td>
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<td>Fresh Transfers</td>
<td>370</td>
<td>52/130</td>
<td>61/240</td>
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</tr>
</tbody>
</table>

CONCLUSIONS: Compaction of the endometrial lining results in a better ongoing pregnancy rates in FET cycles with euploid embryos and in fresh embryo transfers. Our results suggest that an US measurement in the estrogen phase and again in the progesterone phase demonstrating endometrial compaction may be a new non-invasive determinant of endometrial receptivity in IVF cycles.

MALE FACTOR

O-217 Wednesday, October 16, 2019 10:45 AM

A MICROFLUIDIC SPERM-SORTING DEVICE REDUCES THE PROPORTION OF SPERM WITH DOUBLE STRAND DNA FRAGMENTATION.

FRAGMENTATION. Aida Pujol Masana, PhD, Agustín García-Peiró, Sr., PhD, Rafael Lafuente, PhD, Karinna Lattes, MD, MSc, Rita Vassena, DVM, PhD, Daniel Martaró, MD, PhD, CIRH (Centro de Infertilidad y reproducción Humana), Barcelona, Spain; "Barcelona Male Infertility Center (CIMAB), Vallcorba street, 1, Sant Quirze del Vallès, Spain; "Affiliation not provided; "CIRH (Centro de Infertilidad y Reproducción Humana), Barcelona, Spain; "Clinica EUGIN, Barcelona, Spain.

OBJECTIVE: To determine whether the use of the microfluidic sperm sorting device Fertile Chip diminishes the proportion of sperm with double strand DNA fragmentation (dsSDF) compared to swim up.

OBJECTIVE: This is a matched cohort study of samples from nine patients. All were diagnosed with 60% or more dsSDF in their spermatozoa, as assessed by a neutral COMET. The study was approved by the local IRB. The number of patients included was calculated to detect a difference of 20% in dsSDF between study groups, with an alpha risk of 0.05 and a beta risk of 0.05.

MATERIALS AND METHODS: One semen sample of each participant was collected for the study. After a basic sperm analysis, a part was frozen and a part was split into two further aliquots; one aliquot was processed using Fertile Chip and then frozen, and the other was processed using swim up and then also frozen. The three frozen aliquots were analysed by neutral COMET assay for the detection of dsSDF.

RESULTS: The nine patients included in the study had a mean age of 38.9 years (range 34 – 53) and their mean BMI was 26.78 kg/m² (range 20.9 – 32.84). Five of them had a history of miscarriage (range: 1-7). Their basic semen characteristics were: the mean volume was 2.88 ml (range: 1-4); the mean concentration was 94.13 M/ml (range 5.98 - 321.4) and the mean percentage of motile sperm (+b forms) was 39.77% (range 20.9 - 59.8). Processing semen samples using swim up did not change the percentage of spermatozoa with dsSDF (64.8% in the raw samples and 65.1% post swim up). On the other hand, microfluidic sorting of the fresh semen sample using Fertile Chip lowered the percentage of dsSDF to 34.9%; a reduction of 45.2% (p<0.001).

CONCLUSIONS: The selection of spermatozoa using Fertile Chip diminishes significantly the percentage of spermatozoa with dsSDF, either compared to the fresh ejaculate or after swim up. Fertile Chip can be used in patients with a high proportion of spermatozoa carrying dsSD (non-viable), although this study did not evaluate reproductive results, it is reasonable to expect an improvement of clinical variables in this kind of patients.

SUPPORT: None.

A STEP TOWARDS THE AUTOMATION OF INTRACYTOPLASMIC SPERM INJECTION (ICSI): REAL-TIME CONFIRMATION OF OOCYTE PENETRATION BY ELECTRICAL RESISTANCE.

MEASUREMENT. Amir Mor, MD PhD, Man Zhang, MD, PhD, Ecem Esencan, M.D., Burcin Simsek, Ph.D., Stephanie M. Nichols-Burns, PhD, Yifei Liu, PhD, Jonathan Lo, MSc, Dawn A. Kelk, Ph.D., HCLD, Xiao-Bing Gao, PhD, Emre Selî, M.D., Yale School of Medicine, New Haven, CT; University of Pittsburgh, Pittsburgh, PA; Yale University, New Haven, CT.

OBJECTIVE: Automated (robotic) intracytoplasmic sperm injection (ICSI) requires confirmation of plasmatic membrane penetration. Visual assessment using image processing algorithms have been developed but remain unreliable. We hypothesized that an increase in electrical resistance upon oocyte plasmatic membrane piercing during ICSI can serve as an objective tool to confirm oocyte penetration.

DESIGN: Experimental study.

MATERIALS AND METHODS: Oocyte membrane piercing with the ICSI pipette was performed by advancing the pipette towards mature (metaphase II) oocytes collected from 6 to 12-week-old mice and immature (germinal vesicle stage and metaphase I) oocytes donated by women who underwent oocyte retrieval. Electrical resistance at the ICSI pipette tip was measured using a conventional electrophysiological setup that includes an electrical resistance meter and two electrical wires located in the lumens of the holding and ICSI pipettes. Our mouse experiments included four groups: a study group, two negative and one positive penetration control groups. In the study group, egg penetration was determined visually by 3 investigators through 2D light microscopy. The first negative penetration control group consisted of oocytes with fragmented membrane non-viable. In the second negative control group, the ICSI pipette tip was advanced to the perivitelline space and the absence of oocyte penetration was confirmed by applying fluid pressure to demonstrate oocyte compression and zona pellucida expansion. In the positive penetration control group, the plasmatic membrane was ruptured after the application of pressure through the pipette tip (confirming that the tip was inside the egg and not in the perivitelline space). A high proportion of spermatozoa carrying dsSDF (non-viable) were included in the treatment group. For four patients, we found an increase of resistance with ICSI use compared to swim up (p<0.001). These patients had a significantly lower ongoing pregnancy rate (R in M2) compared to the swim up group.

RESULTS: In mouse oocytes, significant electrical resistance (R in M2) increases were detected in all positive penetration control group cases (n=11). \( \Delta R = 8.2 \times (3.0 - 10^{-6}) \), P < 0.001. In these cases, rupturing the
membrane, by positive pressure, led to an immediate resistance drop to around the extracellular resistance values. In the two negative penetration control groups (n=19), no significant resistance changes were detected. In the study group (n=45), resistance increase was detected after visual observation: ΔR = 6.5 (0.1 - 191.7), P < 0.001. In human oocytes, a marked increase in resistance was observed in all visually normal (viable) oocytes (n=28): ΔR = 2.2 (0.9 - 6.7), P < 0.001. In the fragmented/non-viable oocytes (n=6), no significant change in resistance was detected.

CONCLUSIONS: An electrical resistance increase can serve as a reliable tool to confirm oocyte penetration, independent of optical visualization. Following further validation and safety assessment, this technology can potentially be integrated into manual or robotic IVF systems.


O-219 Wednesday, October 16, 2019 11:15 AM

SIMPLE VITRIFICATION OF A SMALL NUMBER OF TESTICULAR SPERMATOZOA USING RAPID-I CARRIERS IN NON-OBSTRUCTIVE AZOOSPERMIA. Yozo Nagao, MS, Keiko Tanaka, MS, Hitomi Osubo, BS, Shigetoshi Mizumoto, PhD., Takeshi Kuranoto, M.D., Ph.D., Masao Murakami, PhD. Kuramoto Women’s Clinic, Fukuoka, Japan.

OBJECTIVE: Testicular sperm extraction (TESE) combined with ICSI has made biological fatherhood possible for many men with non-obstructive azoospermia (NOA), the most severe form of male infertility. For the men with a limited number of testicular spermatozoa, efficient sperm storage is crucial to avoid complications related to repeated TESEs in cases of failed ICSI cycles. However, reports on ideal carriers and techniques for cryopreserving a small number of spermatozoa that can be used universally are still limited. Our aim is to evaluate the efficacy of a previously described method for cryopreserving a small number of spermatozoa using Rapid-i carriers (ESHRE 2011) was evaluated for men with NOA and a small number of testicular spermatozoa.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Vitrification of a small number of spermatozoa was performed for 14 men with NOA following conventional (3 men) or micro-dissection (11 men) TESE from February 2012 to January 2019. Vitrification: 1-10 sperm were aspirated into an ICSI pipette and added to 1.5 μL of cryoprotective solution (K-SISC, Cook Medical) on a Rapid-i carrier strip (Vitrolife), which was placed in LN$_2$ vapor (2 min), inserted into a pre-cooled LND$_2$ storage vessel. Following further validation and safety assessment, this technology can potentially be integrated into manual or robotic IVF systems.

CONCLUSIONS: An electrical resistance increase can serve as a reliable tool to confirm oocyte penetration, independent of optical visualization. Following further validation and safety assessment, this technology can potentially be integrated into manual or robotic IVF systems.


O-220 Wednesday, October 16, 2019 11:30 AM

COMPARISON OF CRYOPROTECTANT FREE VITRIFICATION OF HUMAN SPERMATOZOA IN A NEW SEMEN SIMULANT WITH RAPID FREEZE OF SPERMATOZOA IN GLYCEROL. Sounndarya Janani Senthil Kumar, MBBS, M.Sc.; N. Sanjeeva Reddy, MD (Obstetrics and Gynaecology), DGO; Manjula Daniel G, PhD.; Sindhuja Namboori Srinivasan, MBBS, M.Sc. Clinical Embryology, PhD Research Scholar. Clinical Embryology Sri Ramachandra Institute of Higher Education and Research, Chennai, India; Assistant Professor, Department of Reproductive Medicine and Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, India; Assistant Professor, Department of Reproductive Medicine and Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, India; Lecturer, Department of Reproductive Medicine and Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, India.

OBJECTIVE: Seminal fluid contains materials with cryoprotectant properties. However, ROS and free radicals generated by the spermatozoa and seminal leukocytes within the semen may have a detrimental role in the protection of spermatozoa during cryopreservation. The purpose of this study was to formulate a new medium similar to the seminal fluid and to compare the effects of vitrification of spermatozoa in the newly prepared semen simulant medium with rapid freezing of sperms in glycerol and to survey the effect of these two methods on the sperm quality parameters and DNA fragmentation after thawing/warming.

DESIGN: This prospective study was done in 100 normozoospermic semen samples from male partners who attended our infertility clinic from February 2018 to February 2019.

MATERIALS AND METHODS: A semen simulant embodying the salient physical and chemical properties of human semen was prepared in-house. It had all energy sources including fructose, glucose, pyruvate and lactate along with antioxidants such as ascorbic acid and urate that are naturally present in the seminal fluid. Consenting men attending the infertility clinic provided their semen samples. The sperm quality parameters were analysed according to WHO and the DNA fragmentation Index (DFI) was analysed by sperm chromatin dispersion test. Each sample was divided into two aliquots; one half was vitrified in the semen simulant and the other half was frozen by rapid freeze in Glycerol. Post-thaw samples were subjected to all the tests performed in the fresh semen sample and the results were compared. Statistical analysis was done with IBM/SPSS software. Repeated measures of ANOVA was used for multiple comparison. The probability value 0.05 was considered as significant level.

RESULTS: There was a significant increase in the total motility and vitality in the samples vitrified with the semen simulant after warming when compared with the rapid freeze group (mean ± SD Total motility; 31.85±8.52 vs 29.53±8.15 p=0.001; Vitality; 45.84% vs 43.65% p=0.034 respectively). The percentage of normal morphology in the samples frozen by rapid freeze with glycerol was significantly lower in comparison with those vitrified in the semen simulant (1.33±0.33 % vs. 4.57±2.05% p=0.0005). There was a significant increase in DFI in the samples frozen by rapid freeze when compared to those frozen-warmed by vitrification with the semen simulant (32.7±6.68% vs. 26.11±5.45 % p=0.0005).

CONCLUSIONS: The total motility, viability and the sperm chromatin integrity was comparatively better in the sperms vitrified in the semen simulant. The current work assumes that the main cause of damage in the rapid freezing group was osmotic shock, because it requires cryoprotective agent (CPA). On the other hand, CPA was not used in vitrification and the speed of cooling is high, avoiding extracellular ice formation. In conclusion, vitrification in the semen simulant medium has great potential for human sperm cryopreservation and does not require CPA. Due to the cost effectiveness and inhouse preparation, vitrification in the semen simulant could be an effective alternative for commercial media.

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SURGICAL SPERM EXTRACTION VS. SEMEN CENTRIFUGATION: METHOD OF SPERMATOZOA RECOVERY DOES NOT CORRELATE WITH EUPLOIDY RATES IN PATIENTS WITH CRYPTOZOOSPERMIA. Carlos Hernandez-Nieto, MD; Joseph A. Lee, BA; Martha Luna-Rojas, MD; Tamar Alkon, MD; Christine Britton-Jones, PhD; Natan Bar-Chama, MD; Alan B. Copperman, MD; Benjamin Sandler, MD.
OBJECTIVE: Cryptozoospermia is defined as spermatozoa not identified in the ejaculate, but observed in pellet following centrifugation (World Health Organization). Fertility specialists differ in opinion whether there might be benefits to surgically retrieving sperm in these patients. Previous studies have described a correlation between testicular extracted sperm and spermatic aneuploidy in patients with non-obstructive azoospermia (1). However, there are currently no peer reviewed publications associating rates of embryonic ploidy with Cryptozoospermia. The aim of this study is to evaluate the rate of embryonic euploidy in blastocysts derived from testicular versus ejaculated sperm in cryptozoospermic patients.

DESIGN: Retrospective cohort analysis.

MATERIALS AND METHODS: The study included couples who suffer from Cryptozoospermia and underwent an autologous IVF cycle(s) with pre-implantation genetic testing (PGT-A) from 2014 to 2019. Only cases where oocyte insemination was conducted with intra-cytoplasmic sperm injection (ICSI) were evaluated. Cohorts were separated based on the source of sperm (Ejaculated vs. Testicular (TESE)). Demographic and clinical embryology parameters were compared. Student’s t-test, Wilcoxon rank test, chi-square test, and multivariable logistic regression models were used for data analysis.

RESULTS: Of the 87 IVP/PGT-A cases on cryptozoospermia patients (matrix 187 blastocysts), 74 cases (n = 47, blastocysts) utilized ejaculated sperm (male 13 cases = 99 blastocysts) utilized testicular sperm. No significant differences were found in demographic and stimulation parameters among cohorts. No differences between the ejaculated and testicular cohorts were found in fertilization (63.2%; 61.1%, p = 0.32); blastulation (64.5%; 66.6%, p = 0.69); and rate of embryo euploidy (49.7%; 52.1%, p = 0.76) respectively. No differences were found in rate of cycle cancellation due to unavailable embryos for TE biopsy (18.9% vs 7.6%, p = 0.32). After adjusting for female and male’s age, BMI, AMH, and number of biopsied embryos, there were no association with utilizing surgical extracted sperm and lower odds of embryo euploidy (OR 0.69, 95% CI 0.11-4.3, p = 0.69).

CONCLUSIONS: Normal chromosomal composition is a primary driver of embryonic competence and reproductive success in patients undergoing ART. In our review of the literature, this is the first study analyzing the euploidy rate on a large cohort of embryos in patients with Cryptozoospermia. Our data demonstrate that the odds of the resulting embryo being euploid is not associated with the source of sperm recovery. Regardless of the method of collection, a number of researchers have raised concerns about genetic and epigenetic risks of utilizing sperm cells prone to increased DNA integrity damage or exposed to different environmental factors (i.e. free oxygen radicals). Our study findings show that there is no genomic advantage to surgical sperm retrieval in cryptozoospermic patients. These data can be used to counsel patients who suffer from cryptozoospermia about the potential chromosomal composition of their embryos.


SUPPORT: None.

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OBJECTIVE: To map the level of sperm chromatin fragmentation (SCF) at different areas of the male genital tract.

DESIGN: Male partners from consenting couples had their ejaculated specimens screened for SCF with a commercially available kit. ICSI clinical outcomes compared with sperm retrieved from the same male when sperm from both semen and testes were screened for SCF.

CONCLUSIONS: Our data could be useful in discerning the optimal methods for sperm retrieval for reproduction in males with abnormal semen parameters.

MALE REPRODUCTION AND UROLOGY: RESEARCH

O-233 Wednesday, October 16, 2019 10:45 AM

A NOVEL MOUSE MODEL TO INVESTIGATE PLACEMENT, PROCESSING AND REMOVAL OF SPERM PROTAMINES. Samantha B. Schon, MD, MTR; Lindsay Moritz, BS; Sue Hammoud, Ph.D. University of Michigan, Ann Arbor, MI; University of Michigan, Cellular and Molecular Biology Graduate Program, Ann Arbor, MI.

OBJECTIVE: Protamines, consisting of protamine 1 (P1) and protamine 2 (P2) are essential for packaging paternal DNA into the sperm nucleus. Proper histone-to-protamine exchange is critical for normal fertility with aberrations in this process associated with infertility, altered semen parameters, decreased fertilization rates in couples undergoing IVF and even decreased pregnancy rates. Despite their critical importance, our understanding of the mechanism by which protamines are processed, placed into the nucleus, and finally removed is far from complete.

MATERIALS AND METHODS: Epitope-tagged P2 mice were generated via CRISPR/Cas9. Incorporation of two tags was validated with western blot and immunofluorescence (IF). Phenotypic and fertility assessments were performed using tests and epididymal weights, sperm counts, motility assessment and breeding trials. Immunoprecipitation followed by mass spectrometry (IP-MS) from whole testes using both transgenic (P2Egfp) and wild-type control mice was performed for identification of interacting proteins. Novelty identified proteins were validated via reciprocal IP-MS, western blot and IF.

RESULTS: We demonstrate successful incorporation of both of the two tags in sperm. P2Egfp and P2Egfp mice are fertile with normal litter size and fertility parameters. IP-MS revealed over 500 interacting proteins, a
number of which have been validated and are known to have enzymatic or chaperone/chromatin remodeling roles in other cell types.

CONCLUSIONS: We have successfully generated an epitope-tagged protamine 2 transgenic mouse. Through IP-MS we have further identified a number of candidate interacting proteins. Future studies will focus on continued validation of these proteins and investigation of their specific functions. This work is critical to elucidating the currently unknown mechanism by which protamines are placed, processed and removed in both sperm the early embryo.

SUPPORT: 5K12HD065257-07 (SBS) and 1DP2HD09149-01 (SSH).

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POLYMORPHISMS IN THE HUMAN PRDM9 GENE MAY LEAD TO MEIOTIC ARREST AND AZOOSPERMIA. M. Blake Evans, DO, Sherry Ralls, BA, Mohamed Mahgoub, Mohamed, MD, PhD, Alan H. DeCherney, MD, Todd Macfarlan, PhD NIH-NICHD, Bethesda, MD. 

OBJECTIVE: PRDM9 is responsible for directing the location of programed double strand breaks and subsequent crossover events between homologous chromosomes during meiosis in human gametes. Prdm9 is also essential for meiosis and fertility in mice, with PRDM9 knockout males displaying complete azoospermia. PRDM9 contains a rapidly evolving DNA binding zinc finger array that is coded by a ~84 nucleotide repeating unit mini-satellite sequence. The human A-type allele, which accounts for ~90% of the alleles in the human population, contains 13 repeating units. We sought to develop a strategy to effectively genotype this mini-satellite with PacBio sequencing and to determine whether PRDM9 variation, including mini-satellite length polymorphisms, is associated with infertility in the human male.

DESIGN: Observational study.

MATERIALS AND METHODS: Using a normospermic human control, a two-step polymerase chain reaction (PCR) protocol was established to successfully amplify the PRDM9 zinc finger array mini-satellite and sequence it using both Sanger and PacBio next generation sequencing, which has the advantage of circular consensus sequencing and long reads. We next amplified PRDM9 from the genomic DNA of 48 azoospermic men and 5 controls. The samples were visually analyzed with gel electrophoresis, and potential mutant alleles that had an atypical band appearance were compared to the wild type.

RESULTS: PacBio sequencing results from the normospermic control were found to be an identical match to the known human A allele, confirming our ability to effectively genotype the mini-satellite array in a single PacBio run. Gel electrophoresis of PCR amplified PRDM9 alleles from azoospermic men identified 6 potential mutant variants of distinct mini-satellite lengths differing from the A-allele.

CONCLUSIONS: We have developed a protocol to effectively genotype the human PRDM9 zinc finger array mini-satellite to evaluate a potential etiology of azoospermia in the infertile human male. We found 6 potential PRDM9 alleles differing from the known A-allele in a small (n = 48) azoospermic men population. Current/ongoing research includes applying our PacBio sequencing protocol to genotype all 48 azoospermic men in comparison to a control group and evaluate if there is an association between PRDM9 mini-satellite repeat length, polymorphisms, or de novo mutations and azoospermia.

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A RANDOMIZED CONTROLLED ANIMAL TRIAL: EFFICACY OF A 4K3D VIDEO MICROSCOPE VERSUS AN OPTICAL OPERATING MICROSCOPE FOR UROLOGIC MICROSURGERY. Russell P. Hayden, MD, Haixing Chen, MD, Hülya Ar-ris Y. Collier, MD, Emily A. Seidler, MD, Laura E. Dodge, ScD, MPH, Anna Merport Modest, PhD, MPH, Ai-ris Y. Collier, MD, Emily A. Seidler, MD, Laura E. Dodge, ScD, MPH, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA; Boston IVF; Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA.

OBJECTIVE: Advanced maternal age has been extensively studied and is known a risk factor for adverse pregnancy outcomes including ischemic placental disease (IPD), defined as the obstetrical diagnosis of preeclampsia, small for gestational age (SGA), or placental abruption. Advancing maternal age has been associated with decreased fecundity, early pregnancy loss, and adverse outcomes for the offspring; however, little is known about the impact of advanced paternal age on IPD. Our objective was to evaluate the association between male partner age and the risk of IPD among pregnancies 20 weeks of gestation or greater.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We identified all deliveries from January 1, 2004 to December 31, 2013 at a tertiary hospital that resulted from autologous in vitro fertilization (IVF) cycles. Cycles using donor sperm were excluded. Male partner age at the time of oocyte retrieval was categorized as <30, 30-<35, 35-<40, and 40 years or older. Couples whose male partner was 30-<35 was used as the reference group. IPD was defined as preeclampsia, placental abruption, SGA, or intrauterine fetal demise due to placental insufficiency. We identified pregnancies complicated by preeclampsia or placental abruption using ICD-9 codes and medical record review. We defined SGA as <10th percentile using gestational age and sex-adjusted U.S. growth curves. All IUFDS were reviewed in the medical record to determine the cause, if known. We used log-binomial regression and generalized estimating equations with an independent correlation matrix to estimate risk ratios (RR) and 95% confidence intervals (CI), accounting for multiple

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pregnancies per woman. All models were adjusted for maternal age, paternal age, year of delivery, cycle number, and nulliparity.

RESULTS: We identified 1,133 deliveries from 1,023 couples. The overall incidence of IPD was 26.4%. The risk of IPD was similar across categories of male age (range: 23.0-29.4%). When compared to couples with a male partner under 35 years of age, the risk of IPD was 0.72 (95% CI 0.43-1.2) in the male age <30 group, 0.89 (95% CI 0.65-1.2) in the male age 35-<40 group, and 1.1 (95% CI 0.60-1.9) in the male age 40+ group. When evaluating subgroups of IPD, compared to couples whose male partner was 30-<35, deliveries from couples whose male partner was <30 had a lower risk of SGA (RR 0.28, 95% CI 0.10-0.76). The risk of the other individual components of IPD was similar in all of the male partner age categories.

CONCLUSIONS: There is no association between male partner age and the risk of IPD; however, the risk of SGA is lower in the youngest male age category. Larger studies are needed to confirm these findings.

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EVALUATION OF SPERM PROTEOME IN CANCER PATIENTS PRIOR TO TREATMENT. Manesh Kumar Panner Selvam, PhD, Ashok Agarwal, PhD, Peter Natesan Pushparaj, PhD. American Center for Reproductive Medicine, Cleveland Clinic, Cleveland, OH; Center of Excellence in Genomic Medicine, Faculty of Applied Medical Sciences, King Abdullah University, Jeddah, Saudi Arabia.

OBJECTIVE: Cancer has an adverse effect on sperm health. Conventional semen analysis does not explain the fertility status of cancer patients. Currently, proteomics is being used as a powerful tool to identify the fertility associated molecular pathways affected in spermatozoa. The objective of this study was to evaluate the sperm proteome of cancer patients compared with healthy fertile men and infertile men.

DESIGN: Cryopreserved semen samples of cancer patients before starting cancer therapy were used in the current study. Type of cancer patients included were: Testicular cancer (n=28), Hodgkin’s disease (n=20), Lymphoma (n=8) and Leukemia (n=5). Pooled samples from the cancer patients were used for proteomic analysis. The proteome of cancer group, was compared with fertile men (n=7) and infertile men (n=9).

MATERIALS AND METHODS: Proteomic profiling of sperm (cancer patients, fertile men, and infertile men) was performed using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Proteins and peptides were identified using search programs Mascot and SEQUEST. Sperm proteins of cancer patient group were compared separately with fertile and infertile men groups. Differentially expressed proteins (DEPs) obtained from two different analysis were subjected to comparison analysis using ingenuity pathway analysis (IPA) software.

RESULTS: The functional bioinformatic analysis revealed that proteins associated with mitochondrial dysfunction, oxidative phosphorylation, and mitogen signaling pathways are dysregulated in cancer patients in comparison to fertile and infertile men. Furthermore, comparison analysis of two sets of DEPs predicted deactivation of oxidative phosphorylation and TCA cycle (Table 1).

CONCLUSIONS: Current proteomic findings indicate that the cellular pathways associated with oxidative phosphorylation and TCA cycle are affected in spermatozoa of cancer patients. Further in-depth investigation and validation of specific proteins associated with both the pathways in cancer patients are warranted.

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NOVEL EX VIVO CULTURE OF NEONATAL MOUSE TESTICULAR ORGANOID MAINTAINED IN A HANGING DROPLET WITH RETINOIC ACID. Philip Xie, B.S., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D., The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To propose a method to sustain germ cell characteristics of neonatal germlinal epithelial cells in the form of self-organized organoids and initiate meiotic differentiation under the exposure of retinoic acid (RA).

DESIGN: We tested the feasibility of utilizing an ex vivo three-dimensional culture system maintained in a hanging droplet (HD) to sustain and induce maturation of murine neonatal testicular cells.

MATERIALS AND METHODS: After trypsinization of 5-day-old newborn mouse testicular tissue, isolated cells were cultured in medium designed for spermatogonial stem cells (SSCs) composed of DMEM/F12 with GDNF, FGF2, 2-mercaptoethanol, L-glutamine, and B27 supplement in a gelatin-treated well for 3 days. Cell culture was then trypsinized and washed in SSC medium. The resulting cell pellet was resuspended in SSC medium void (control) or with 1 μM RA (HDRA). Cell suspensions were then adjusted to 40,000 cells/ml, and approximately 1,000 testicular cells were placed in each 25-μl HD. Cell characterization was performed every 3 days by germ cell stage-specific markers on an H&E-stained background.

RESULTS: After culturing neonatal testicular cells in HDs, initial aggregate was observed 48 hours after HD culture. The earliest complete self-formation of spherical organoids was observed at day 3 for both control and HDRA. In the control group, continuing and consistent expression of OCT4 (>70%) and nuclear DAZL (>75%) throughout the experiment until day 21 determined that the SSCs retain stemness. In HDRA, a downregulated expression of OCT4 was recorded as early as day 3 in approximately 50% of the cells. A shift from nuclear to perinuclear positivity of DAZL in 16% of the cells in the HDRA group at day 21 confirmed differentiation in spermatocytes. Cytoplasmic VASA expression in the HDRA group confirmed meiotic/post-meiotic differentiation of the germ cells. Positive vimentin staining in 25% of the cells indicated the presence of nurturing pre-Sertoli cells in both groups.

CONCLUSIONS: The attempt to maintain germ cell characteristics of neonatal testicular cells in the form of self-organized organoids appears to be an effective strategy for studying ex vivo spermatogenesis in the long-term. With the essential supplement of RA, germinal epithelial maturation was achieved. Once the ability to induce late-stage gametogenesis is confirmed, this technique may benefit cancer survivors who underwent gonadotoxic therapy in prepubertal age with irreversible damage of the germinal epithelium.
ELECTIVE EGG FREEZING AND MALE SUPPORT: A QUALITATIVE STUDY OF MEN’S HIDDEN ROLES IN WOMEN’S FERTILITY PRESERVATION. Marcia C. Inhorn, PhD, MPH,1 Daphna Birenbaum-Carmeli, PhD,2 Pasquale Patrizio, M.D.3 *Yale University, New Haven, CT; 1University of Haifa, Haifa, Israel; 2Yale Fertility Center, New Haven, CT.

OBJECTIVE: Do men participate in women’s fertility preservation decisions and procedures? Emerging evidence suggests that lack of a male partner is the primary reason why women are pursuing elective egg freezing (EEF). However, this qualitative study asked women whether men played any supportive roles in their fertility preservation decisions and procedures.

DESIGN: In this binational, qualitative study, 150 women (114 in the United States, 36 in Israel) who had completed at least one cycle of EEF were interviewed by two senior medical anthropologists, one in each country, during the period from June 2014 to August 2016.

MATERIALS AND METHODS: Study participants were recruited through 4 American IVF clinics (2 academic, 2 private) and 3 in Israel (1 academic, 2 private). In-depth, semi-structured, open-ended interviews were audio-recorded, transcribed, and entered into a qualitative data analysis program (Dedoose) for thematic analysis, along with detailed interview summaries.

RESULTS: Although 85% of women identified the lack of a male partner as their main reason for pursuing EEF, nearly two-thirds (63%) relied on some form of male support during their EEF decision making processes and procedures. Five categories of men, in order of support, included: 1) father(s), if any; 2) male friends (past or present); 3) male partners; 4) sons, if any; 5) friends and family. More than a dozen different forms of assistance were offered by men in four major categories (instrumental, financial, physical, and psychological).

CONCLUSIONS: Five different categories of men played supportive roles in women’s EEF, offering 12 forms of instrumental, financial, physical, and psychological assistance. Although one-third of women went through EEF alone or with only female support, this study reveals the “hidden” roles men play in supporting female family members, friends, and partners.

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ELECTIVE EGG FREEZING AND MALE SUPPORT: A QUALITATIVE STUDY OF MEN’S HIDDEN ROLES IN WOMEN’S FERTILITY PRESERVATION. Marcia C. Inhorn, PhD, MPH,1 Daphna Birenbaum-Carmeli, PhD,2 Pasquale Patrizio, M.D.3 *Yale University, New Haven, CT; 1University of Haifa, Haifa, Israel; 2Yale Fertility Center, New Haven, CT.

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SUPPORT: US National Science Foundation, Cultural Anthropology Program, BCS-1356136.

O-231 Wednesday, October 16, 2019 11:15 AM
THE EFFECTIVENESS OF EDUCATION USING VIDEOS WITH SMART PHONES AND A BOOKLET ON FERTILITY WOMEN - FOCUSED ON THE PRO-CESS OF IN VITRO FERTILIZATION. Eun Hee Seo, MS,* Hwayeon Cho, Master,* Eunjung Jeon, master,* Kyongyol Kim, MS,* Jiuk Lee, BS,* Hyunjoo Choi, BS,* Mi Ok Moon, MS,* Hayoung Lee, MS,* Tae Ki Yoon, M.D, Ph.D.* *Yeoik Kim, MD, PhD* CHA University, CHA fertility center, Seoul station, Seoul, Korea, Republic of (South); *CHA Fertility Center Seoul Station, Obstetrics and Gynecology, Seoul, Korea, Republic of (South).

OBJECTIVE: The purpose of this study was to develop a Q&A related to in vitro fertilization for the first-time trial women and to produce a booklet with the contents of the existing video education ‘In Vitro fertilization’ and compare the effectiveness of education through knowledge and educational satisfaction surveys and to find a more effective educational plan for women with in vitro fertilization.

DESIGN: Retrospective study.

MATERIALS AND METHODS: From September 30th, 2016 to October 25th, 2016, a total of 131 women who participated in the first trial of in vitro fertilization in the CHA Fertility Center Seoul Station, and 9 participants were eliminated those who did not see the educational data to the end or did not respond to the questionnaire sincerely. The selection of educational materials was selected by the participants. The selection result was selected by a total of 122 participants: 45 pamphlets, 35 videos, and 42 videos and pamphlets. The survey tool, Knowledge Measurement Problem Questionnaire, consisted of 17 items by the validity of the total score has 3. The characteristics of the expert group and the difficulty of the content of the general population. It modified and supplemented education satisfaction items in web-based virtual classrooms developed by Jeong In-seong and Lim Jung-hoon (1999). The reliability of the tool was a = 0.895 for Kronbach. The participants were asked about the level of knowledge and satisfaction of education on the 7th - 8th day of menstruation, which is the next hospital visit. Data analysis was performed using SPSS WIN 21.0. The general characteristics of the participants were asked by descriptive statistics and frequency analysis. ANOVA and crossover analysis were used for homogeneity. ANOVA, Scheffe, regression analysis and correlation analysis were used respectively. Percentage of correct answer which can be an important parameter of the paper was calculated as a percentage using the right answer and the number of samples *100.

RESULTS: As a result of this study, the total score of the knowledge level items was the highest with correct answer rate of 86.83%, and followed by the booklet group with 85.49% and the video group was 82.02%. The results of the ANOVA showed that there was no significant difference in the level of knowledge among the three groups: 13.91 2.369 in the video group, 14.64 1.540 in the booklet group, and 14.74 2.165 in the booklet + video group. It was confirmed that the score of booklet + video group was high in the order of booklet group 4.14 0.534, video group 4.31 0.581, booklet + video group 4.41 0.570.

CONCLUSIONS: Based on the results of this study, it is shown that if the education needs of the participants who are in vitro are analyzed, and if systematic and standardized educational materials are produced accordingly and brochures and videos are appropriately provided, it is possible to increase education satisfaction. The purpose of this study has its meaning in conducting the study about the content and method of education for infertility women and the content and method of education provided to the participants of in vitro baby are specifically specified.

EVALUATION OF ANXIETY IN FREEZE-ALL PATIENTS. Nagihan Dinçer, Bsc.ª Ayseal Salgın, Bsc.ª Necati Findikli, Ph.D.ª Fazilet Kubra Boyunakul, M.D.ª Msc.ª Mustafa Bahçecî, M.D., Ph.D.ª *BAHCÊÇI FULLYA IVF CENTER, ISTANBUL, Turkey; ²Bahçecî Health Group-Fulya IVF Centre, Istanbul, Turkey; ³Bahçecî Health Group-Fulya IVF Centre, ISTANBUL, Turkey.

OBJECTIVE: To investigate the anxiety scores and depression scales of infertile women that applied to Bahçecî Fulya IVF Center for elective frozen blast embryo transfer between February 26, 2019, and April 18, 2019.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: This study is a prospective cohort study which included 178 patients. Face to face interview in the patient’s room 1 hour ago the embryo transfer was performed and Beck Depression Inventory (BDI) with 21 items and Anxiety and Depression Scale (HADS) with 14 items were fulfilled. The age of the patients, number of previous failed trials, total follicle stimulating hormone (FSH) and human menopausal gonadotropin (HMG) doses during ovulation induction period, number of oocytes obtained after oocyte pick up, number of m2, number of frozen embryos, number of embryos remaining were recorded from the patients. The BDI and HADS scores obtained after BDI and HADS were evaluated with SPSS 15.0 program. All these parameters were analyzed in multiple regression analysis.

RESULTS: BDI and HADS score was found to be correlated (rho:0.57 p<0.001). In the multivariate analysis no factor such as women age, number of previous failed trials, FSH and HMG doses during ovulation, number of oocytes retrieved, number of m2, number of frozen embryos, number of embryos remaining were found to have an effect the BDI and HADS. Also, the pregnancy rates were not affected according to the BDI and HADS scores stratified.

CONCLUSIONS: Anxiety scales does not affected by the patient’s ovulation induction and embryological parameters.

CLINICAL EXPERIENCE OF NURSING TEAM IN PRE-CONCEPTION GENETIC COUNSELING AT A LARGE, DIVERSE INFERTILITY PRACTICE. Marlene De La Mota, BS,ª Elizabeth Lipov, BS,ª Karina Yaipen, RN,ª Joseph A. Lee, BA,ª Teresa A. Cacchione, MS, CGC,ª Melissa Bell, RN,ª Maitland Dabney, RN,ª Alan B. Copperman, MD,ª Tanmoy Mukherjee, MD,ª Tcahn School of Medicine at Mount Sinai, New York, New York, NY.

OBJECTIVE: While ethnicity based-carrier screening was once a customary component of preconception genetic testing, expanded carrier screening (ECS) is being increasingly utilized to identify recessive or X-linked mutations. The role of the nursing team has evolved to include provision of genetic counseling for patients facing new information to process and potential use in treatment. This study assesses nursing involvement and patient decision making in infertile couples accessing ECS.

DESIGN: Retrospective.

MATERIALS AND METHODS: The study included patients who underwent ECS (panels with ≥200 diseases) from May 2017 – March 2018. Patients were identified as either non-carriers, carriers whose partner tested negative for the mutation, carrier couples, or female carriers (X-linked pathogenic variant). We evaluated the mutation prevalence and the decision-making process regarding use of preimplantation genetic testing for monogenic/single gene defects (PGT-M).

RESULTS: A total of 2439 patients (980 couples) underwent ECS. 2075 patients (64.6%) patients were found to carry ≥1 mutation. The most prevalent being 8.1% Alpha Thalassemia (n=198), 5.8% Biotinidase Deficiency (n=142), 5.7% GJB2-related Non-Syndromic Hearing Loss (n=139), 4.1% Cystic Fibrosis (n=100), 3.8% Familial Mediterranean Fever (n=93), 864 patients (35.4%) tested negative for all mutations.

Of 980 participating couples, 31 (3.1%) were identified as being carrier couples. Of the 1527 females tested (2.5%) were carriers for X-linked conditions. The 39 X-linked females and 31 carrier couples underwent formal genetic counseling to assist with ART treatment decision-making. 30 proceeded with PGT-M while 30 declined PGT-M.

Of the carrier couples who decided to access PGT-M technology, the most prevalent conditions included Cystic Fibrosis (n=5), Beta-Globin Related Hemoglobinopathies (n=4), GJB2-related Non-Syndromic Hearing Loss (n=3), Familial Mediterranean Fever (n=3), and Gaucher Disease (n=2). Of the females who pursued PGT-M for X-linked conditions, 5 were Fragile X Pre-mutation carriers and 1 a Fragile X Intermediate carrier.

Of the 30 individuals/couples who declined PGT-M, 19 were Fragile X Intermediate carriers, 7 were Fragile X Pre-mutation carriers, 2 were GJB2-related Non-Syndromic Hearing Loss carrier couples, 1 Familial Mediterranean Fever carrier couple, and 1 Beta-Globin Related Hemoglobinopathies (City of Hope variant) carrier couple. Patients positive for intermediate Fragile X were most likely to waive PGT-M.

CONCLUSIONS: Expanded genetic carrier counseling and screening have become integral parts of preconception counseling. Given decreasing costs of sequencing and increasing awareness or the discordance between self-reported ethnicity and ancestral inheritance markers, pan-ethnic is now widely utilized. The modern infertility nursing team is increasingly being called upon to provide pre- and post-test counseling to infertility patients. By educating patients about contemporary reproductive options, patients will obtain a greater sense of autonomy across their family building journey.

Reference: None.

SUPPORT: None.

WHAT IS THE IDEAL NUMBER OF VIALS OF DONOR SPERM TO PURCHASE FOR PATIENTS UNDERGOING DONOR SPERM INTRAVITREAN INSEMINATION (DIUI)? Sydney Chang, MD,ª Dmitry Gounko, MA,ª Joseph A. Lee, BA,ª Melissa Bell, RN,ª Margaret Daneyko, RN,ª Alan B. Copperman, MD,ª Tammy Makherjee, MD,ª Tcahn School of Medicine at Mount Sinai, New York, New York, NY.

OBJECTIVE: Gamete donation has provided patients who would not otherwise have the ability to conceive the opportunity to have a healthy child via screened selected eggs and sperm. Donor sperm is a limited resource, and scare literature exists to inform patients regarding the optimal number of vials to purchase to maximize the chances of conceiving while minimizing cost. The objective of this study is assess the number of donor sperm vials needed to achieve ongoing pregnancy (OP) for patients who are undergoing donor sperm intravitreal insemination (DIUI).

DESIGN: Retrospective, cohort study.

MATERIALS AND METHODS: The study included patients at a single academic center who underwent a natural cycle or medicated ovulation induction cycle (with clomiphene citrate or letrozole) with DIUI from 2010-2019. Exclusion criteria included gonadotropin use or imaging showing tubal pathology, uterine myomas, or polyps >0.5 cm. r-hCG was administered when ≥ 1 18mm follicle was visualized. DIUI was performed 36 hours later. The primary outcome was OP. A Kaplan-Meier curve was created for each SART age group to determine the cumulative probability of OP from each DIUI cycle. A second curve stratified by anti-Mullerian hormone (AMH) levels: [low (<0.7 ng/mL, normal 0.7-8.4 ng/mL, and high >8.4 ng/mL].1 Patients were censored when they dropped out or progressed to IVF.

RESULTS: A total of 913 patients were included in the study (Groups A: 257: B: 199, C: 168, D: 142, E: 147). The cumulative percent of patients that achieved OP in each cycle is shown in Table 1.

CONCLUSIONS: Until now, there has not been a personalized algorithm to predict how many vials of donor sperm should be purchased prior to attempting DIUI. Using Kaplan-Meier curves stratified by age and AMH, we developed a starting point from which clinicians can further tailor their recommendations to incorporate patient characteristics and preferences for family size. The cumulative OP rate per cycle can also be used to counsel patients about when to transition their treatment strategy to one that includes assisted
TABLE 1. Cumulative OP rate per cycle (%)

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SUPPORT: None.

PROFESSIONAL DEVELOPMENT

O-235 Wednesday, October 16, 2019 10:45 AM

IMPROVING THE REI FELLOWSHIP INTERVIEW EXPERIENCE: A SURVEY.

Erka P. New, MD, MPH, Papri Sarkar, MD, Anthony N. Imudia, MD, University of South Florida, Brandon, FL; USF, Tampa, FL; Stanford University, Palo Alto, CA; University of South Florida, Tampa, FL.

OBJECTIVE: The interview process for residents applying to Fellowship in Reproductive Endocrinology and Infertility (REI) is a highly competitive process with many challenges for applicants such as conflicting interview dates, the expense of traveling, and missing days from work. The goal of this study is to collect data on the current REI fellowship interview process so that it may be improved in the future.

DESIGN: An anonymous survey was sent to individuals who have gone through the REI fellowship interview process. In addition, fellowship program directors and coordinators were contacted by e-mail to gain information on typical interview dates for each program.

MATERIALS AND METHODS: The survey designed for applicants was distributed over social media and the REI fellow e-mail list-serv. Some survey questions included:

- How many days of work or vacation did you take off for Fellowship interviews?
- Did you ever miss an opportunity to interview at a program you were interested in? If so, what was the reason?
- How often did you have to travel to the same city more than once for an interview?
- How much money did you spend on average per interview?
- What recommendations do you have for how the interview process could be improved?

The fellowship program information was obtained by contacting each program using the publicly available contact information on the Accreditation Council for Graduate Medical Education (ACGME) website.

RESULTS: There were 44 survey respondents. Of those, 38.6% participated in the 2018 REI interview season, 29.5% in 2017 and 31.8% participated more than 2 years ago. The mean number of interviews attended was 12.6 (range of 1-22). On average 13.4 (0-30) days off work or vacation were used to interview. 67.4% of respondents missed an opportunity to interview at a program they were interested in, with most common reasons: the interview date was the same day as another interview, could not attend due to geographic location, and cost was too great. 72% traveled to the same city more than once for an interview. The average cost per interview was $478 (range $200-$1,000) and average cost per interview season was $5,660 (range $900-$15,000). Fellowship program data was available from 43 of 48 programs contacted. The 2018 interview season spanned from June 4 to August 30. The most popular interview date was Monday, August 27 (5 interviews). The number of dates that had conflicting interviews scheduled were 26. Most programs offered 2 interview dates (46.5%), 30% offered 3 interview dates, 16% offered 1 date, and 6.9% offered 4 dates.

CONCLUSIONS: This data supports the need to coordinate the REI fellowship recruitment process between programs to reduce conflicting interview dates and mitigate cost. Recommendations from respondents include having programs notify applicants of interview offers at the same time, geographically aligning interviews by region, including a virtual component to interviews such as video interviews or interviewing at a central location, and helping applicants with costs such as hotels or flights. Encouraging collaboration between fellowship programs would increase applicant satisfaction.


SUPPORT: None.

O-236 Wednesday, October 16, 2019 11:00 AM

THE STATE OF WOMEN IN ACADEMIC REPRODUCTIVE ENDOCRINOLOGY PROGRAMS. Jessica Selter, MD, Emily Spurlin, MD, Paula C. Brady, MD Columbia University Medical Center, New York, NY.

OBJECTIVE: To identify gender differences in leadership and academic rank within academic reproductive endocrinology programs with fellowships in the United States.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: Official institutional websites of the 2017-2018 American Board of Obstetrics and Gynecology (ABOG)-accredited reproductive endocrinology fellowship programs were reviewed, and gender representation at each leadership position and academic rank (Division and Fellowship Director; Full, Associate, and Assistant Professor) was recorded. Three programs did not consistently report academic rank, so only leadership positions were recorded. Associate Fellowship Directors were rarely reported and therefore excluded. Only medical doctors (MD, DO, MBBS) who completed postgraduate training in OB/GYN were included. Private practice physicians affiliated with universities were included only if present on academic department websites with academic titles. Univariate comparisons were performed using Chi-squared tests, with significance at P<0.05.

RESULTS: Among 49 ABOG-accredited reproductive endocrinology programs, 263 faculty were identified, 129 (49%) male and 134 (51%)
A total of 17 residents completed the office hysteroscopy simulation program. The average age was 28.8 with 87% females, and an even distribution of years of training. The distribution of intended subspecialty training included 11.7% into reproductive endocrinology, 29.4% into gynecologic oncology, 11.7% into minimally invasive gynecologic surgery, and 23.5% into generalist/unknown. All residents reported little to no experience with office hysteroscopy prior to the training experience and 88% felt extremely uncomfortable with performing the office hysteroscopy procedure. Following training, there was a significant increase in subjective comfort (76% vs. 11.4%, P<.01) with a majority of residents reporting slight/moderate comfort with performing the procedure. Following training, all residents agreed that Endosee simulation was a good preparation for office hysteroscopy. Furthermore, there was a significant increase in residents who agreed that office hysteroscopy simulation should be integrated into Ob/Gyn curriculum (68% vs. 94%, P=.04). After training, residents had an improved overall score (218 vs. 242, P<.01), decreased procedure time (116sec vs. 73sec, P<.01), shorter cumulative path length (24.4 vs. 17.8cm, P=.01) and a trend towards improved navigation percentage (61% vs. 70%, P=.06).

CONCLUSIONS: This study demonstrates that office hysteroscopy training using a simulator improves both subjective resident comfort and objective performance. Despite the small sample size, the overall enthusiasm regarding office hysteroscopy simulation suggests the need for a larger study group and a possible role for integrating office hysteroscopy into resident Ob/Gyn curriculum.

SUPPORT: CooperSurgical provided surgical simulators for the study.
rates of assisted reproductive technologies being particularly limited. Knowledge of fertility does not change throughout residency training, demonstrating consistent gaps in fertility knowledge. Knowledge during PGY1 year is consistent with mean scores found in prior research in Internal Medicine residents (65%), as well as a cohort of female medical students and gynecology residents and fellows (64.9%) [1,2].


SUPPORT: None.

O-239 Wednesday, October 16, 2019 11:45 AM

COLLABORATIVE AND MULTIDISCIPLINARY APPROACH TO THE REI FELLOWSHIP

APPLICATION. Randi H. Goldman, M.D., Christine Mullin, M.D., Esther Lopez, M.P.A., Jeanette Tomasino, Ph.D., Martina Borovica, M.B.A., Avner Hershlag, M.D., Northwell Health Fertility, Zucker School of Medicine at Hofstra/ Northwell, Manhasset, NY.

OBJECTIVE: To describe the development and implementation of a Reproductive Endocrinology and Infertility (REI) fellowship program and the process of obtaining initial accreditation, with a focus on the multidisciplinary collaborative effort of the OB/GYN department, GME committee, and affiliated programs.

MATERIALS AND METHODS: This is a descriptive study completed at an academic institution that evaluates the critical aspects of establishing an REI fellowship program. We specifically explored how to utilize the broad network of interdisciplinary opportunities already established at our institution to provide a collaborative, inclusive learning environment for fellowship trainees.

RESULTS: REI sub-specialists are expected to master the medical knowledge and surgical procedures involved with all aspects of reproductive health, including care for infertile women and couples, disorders that threaten fertility such as cancer and systemic disease, pediatric and adolescent gynecologic care, and fertility preservation. When designing our fellowship program, we built upon the multidisciplinary strengths of our institution by consulting with other departments and divisions. Minimally Invasive Gynecologic Surgery, Male Infertility, Endocrinology, Pediatric Endocrinology, and Genetics – disciplines that encompass the broad aspects of our field – have partnered to educate our fellows and actively participated in developing the curriculum. The Feinstein Institute for Medical Research provides methodological, step-wise classes on study design and research, and a thorough biostatistics course for fellow learners. This research-oriented environment is committed to giving fellows the tools to conduct well-designed and meaningful basic, translational, and clinical studies. The process of building our program highlighted the collaborative nature of existing programs, and establishing an REI fellowship became a natural extension for our department. The multidisciplinary nature of the fellowship reflects the ever-expanding horizons of our specialty, equipping our fellows with strong exposure to all aspects of reproductive health both in and out of the division. Our new program was granted two fellowships each year.

CONCLUSIONS: This descriptive study emphasizes the need for a collaborative effort in the accreditation of a new fellowship program. Utilizing existing institutional resources and designing a fellowship program with input from all teams that will comprise the fellows’ education fosters an environment for individual and group learning, opportunities for sharing clinical information between divisions, as well as collaborative research that will support the training of future leaders and advancement of the field. We hope that other programs that are considering establishing a training program will use this model, taking advantage of existing opportunities at their institutions.

O-240 Wednesday, October 16, 2019 12:00 PM

REI EXPOSURE IN RESIDENCY: HOW MUCH IS ENOUGH? Jason A. Schneider, M.D., Tomer Singer, MD, Avner Hershlag, M.D., Randi H. Goldman, M.D.

“Zucker School of Medicine at Hofstra/Northwell at Lenox Hill Hospital, New York, NY; Northwell Health Fertility, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: Exposure to Reproductive Endocrinology and Infertility (REI) is critical for Obstetrics and Gynecology (OB/GYN) resident learners to ensure adequate fund-of-knowledge and for career planning. The purpose of this study is to assess residents’ exposure to clinical and research opportunities in REI and identify how experience and comfort with REI vary by demographic characteristics.

DESIGN: Cross-sectional electronic survey study.

MATERIALS AND METHODS: A web-based questionnaire was completed anonymously by 100 U.S.-based OB/GYN residents, with questions regarding the structure of their residency programs and REI rotations, access to REI faculty, patients, and research, career plans, and demographics. Outcome measures were whether residents felt their REI experience was “too little,” “just right,” or “too heavy,” and whether they anticipated feeling comfortable completing a basic infertility workup at the completion of training. Fisher’s exact tests determined differences in outcomes; p<0.05 determined significance.

RESULTS: Most residents (89%) reported having a dedicated REI rotation and 1/3 of trainees had rotations over multiple years; 24% occurred during the PGY-1 year, 43% during PGY-2, 40% during PGY-3, and 25% during PGY-4. Approximately 1/4 of respondents have an REI fellowship at their institution and 3/4 have the opportunity to participate in REI-related research. Among those who described their REI experience as “too light” (N=53), 66% anticipated feeling uncomfortable completing an infertility workup at the end of residency, while 93% of residents who felt their REI exposure was “just right” (N=46) anticipated feeling comfortable, a statistically significant difference (p=0.001). Residents training in the Northeast felt least prepared to perform a workup vs. the rest of the U.S. (69% vs. 86%, p=0.048). Significantly fewer fellowship-aspiring residents felt their REI exposure was “just right” (32% vs. residents who were undecided or planning to be general OB/GYNs (55%) (p=0.038). Residents planning to pursue REI fellowship were least likely to feel their REI exposure was “just right” (18%, vs. 82% “too light”). Only 1 resident felt that their REI exposure was “too heavy.” Residents whose REI curricula included ASRM teaching modules were significantly more likely to feel their REI exposure was “just right” (62% vs. 38%; p=0.035). No differences were seen based on rotation length, university- vs. community-based programs, having a sub-speciality trained program director, or presence of an institutional REI fellowship.

CONCLUSIONS: Although 53% of residents feel REI exposure during residency is “too light,” most (79%) trainees expect to feel comfortable completing a basic infertility workup upon graduation. ASRM teaching modules may be a simple intervention to standardize REI curricula and help residents feel more content with their REI exposure during training. Importantly, adequate exposure to REI may help inform career choices of trainees.
REGENERATIVE MEDICINE AND STEM CELLS

O-241 Wednesday, October 16, 2019 10:45 AM

OBJECTIVE: To propose a method to sustain mouse embryonic stem cells (mESCs) utilizing a decellularized seminiferous tubule matrix (DSTMs) as a biotechnological scaffold and induce differentiation into male germ line cells in conditioned medium. DESIGN: We tested the potential of a bioreactor concept–based culture system supported by a biological scaffold to allow de novo generation of meiotic male germ line cells from mESCs.

MATERIALS AND METHODS: Male mESCs were cultured in epiblast cell–line cell (EpiLC) medium containing activin A, bFGF, and KSR for 3 days to allow differentiation into EpiLCs. Subsequent exposure to primordial germ cell–like cell (PGCLC) medium subsidized with BMP4, BMP8b, SCF, LIF, and EGF in hanging droplet (HD) allowed the formation of embryoid bodies (EBs) rich in PGCLCs. Isolated cells from 80 EBs were utilized in the bioreactor, in directed contact with DSTMs, and loaded with DMEM in a gelatin–treated culture well equipped with a 0.4–μm pore size mesh inlet. 14–week-old mice were sacrificed for DSTMs and conditioned medium. DSTMs were prepared by immersion in 1% sodium dodecyl sulfate for 24 hours. Eighty-mm sections of DSTMs, longitudinally sliced and flattened, were placed below the mesh; interstitial cells were isolated from the respective contralateral testes by differential plating and loaded above the mesh. Cell characteristics were analyzed by germ cell stage–specific markers on an H&E-stained background.

RESULTS: Culturing mESCs in EpiLC medium, the continuing expression of OCT4 (>90%) and the decreased positivity of Nanog (45%) indicated progression to EpiLCs. EBs rich in PGCLCs expressed positive surface SSEA-1 after 6 days of culture in HD with PGCLC medium. Isolated cells of PGCLCs were derived from the digestion of EBs and layered on the DSTMs. The earliest attachment of PGCLCs onto DSTMs occurred on day 3, and complete recellularization was observed at approximately day 10. Following complete recellularization, about half of all isolated cells obtained from the enzymatic digestion of recellularized tubule displayed decreased expression of OCT4, while 5% displayed nuclear DAZL positivity at day 10. In 1% of the cells, perinuclear DAZL confirmed spermatocyte differentiation at day 21. At around day 16, cytoplasmic VASA positivity in 5% of the cells suggested meiotic/post-meiotic germ line differentiation.

CONCLUSIONS: The timeline of our bioreactor system was comparable to in vivo spermatogenesis in the mouse, occurring in the course of 21 days. Once the ability of a 3D biocompatible scaffold to induce late-stage gametogenesis is confirmed, it will be possible to study spermatogenesis in vitro. Neogametogenesis from genotyped stem cells performed in a scaled-down microfluidic device may help to treat men afflicted by Sertoli cell–only syndrome.

O-242 Wednesday, October 16, 2019 11:00 AM
Efficiency Generation of Granulosa Cell Like Cells from Human Endometrium Derived IPS Cells as a Source for AutoLOGOUS Estradiol Production. Joo Hyun Park, MD, PhD, Heeyon Kim, M.D., Hyun Kyung Kim, MS, SiHyun Cho, M.D., Ph.D. Yeoung University College of Medicine, Gangnam Severance Hospital, Seoul, Korea, Republic of (South).

OBJECTIVE: To derive granulosa cell like cells from induced pluripotent stem cells (iPSCs) which are derived from discarded endometrial stromal cells as a novel source of autologous estradiol production.

DESIGN: iPSCs were driven using human endometrial cells obtained from five benign hysterectomy and stepwise granulosa cells were differentiated to successfully induce estradiol production.

MATERIALS AND METHODS: After pathologic confirmation, human endometrial cells free from pathologic findings were obtained from five hysterectomy specimens of benign indications. Using episomal vectors for Sox2, Oct4, cMyc and Klf4, 3 cell lines were driven per donor. Embryoid bodie(s)(EBs) were first formed from these patient endometrium derived iPSCs and to induce primitive streak-mesendoderm and intermediate plate mesoderm lineage. Consequently estradiol(E2) producing granulosa like cells were obtained from Human embryonicderived from H9 (EBs) line H9 was used as control. To induce mesodermal lineage differentiation, produced EBs were supplemented with BMP4 (10 ng/ml), WNT3a (6 ng/ml), Activin A (6 ng/ml) and bFGF (5 ng/ml) for 6 days. After confirming mesodermal commitment, differentiation was further directed using BMP4 (10 ng/ml), Follistatin (25 ng/ml) and bFGF (5 ng/ml) for an additional 6 days. During the differentiation process markers indicative of granulosa cell differentiation(ALH, FOXL2, FSHR, AMHR2, LHR, CYP19A1) was performed via real-time PCR and FACS analysis. After a differentiation period of 12 days, these cells were seeded at a density of 4x105 per one 6-well plate and after adding androstenedone for an additional period of time, E2 assay was performed using ELISA.

RESULTS: After a differentiation process of 6 days, FACS analysis of brachyury expression for H9 was 30% and 21.7% (SD +/- 3.5%) for human iPSCs. This primitive streak-mesendoderm marker, brachyury showed marked expression at day 6 of differentiation and decreases upto day 12 of differentiation. Donor and cell line variabilities with regards to efficiency and time requirements were observed.

The aforementioned AMH, FOXL2, FSHR, AMHR2, LHR and CYP19A1 expression were increased after estradiol producing granulosa cell differentiation in both iPSCs and H9. Real-time PCR analysis showed relative AMH expression of 10.8 (SE +/- 0.11) in the iPSCs and 2.4 (SE +/- 0.1) in the H9, 10.8 of granulosa cells compared with the undifferentiated state. According to FACS analysis, AMHR2 expression at differentiation day 12 was as follows; 53.2% for iPSCs and 93.6% for H9. FSHR at day 12 for iPSCs was 32.4% versus 30.2% for H9, CYP19A1 expression for H9 differentiation at day 6 was 38.5% and 83.9% at day 12. However, CYP19A1 expression for iPSCs was not observed at day 6 but a 100% expression at differentiation day 12.

Control estradiol concentration in the basal media was 9.38 pg/ml(SE +/- 2.5), 2191.7 pg/ml(SE +/- 211.9) for iPSCs 1364.3 pg/ml(SE +/- 107.9) for H9.

CONCLUSIONS: Granulosa cell like cells expressing the appropriate markers and functional for estradiol production could be successfully derived from human endometrium derived iPSCs. SUPPORT: None.

O-243 Wednesday, October 16, 2019 11:15 AM
Targeting Activated Pro-inflammatory Pathway in Primed Myometrial Stem Cells with Vitamin D3 and paracitiCOL. Hoda Elhossiny Elkafas, MS.c Osama A. Badary, PhD,1 Engy Elmorsy, PhD,1 Rehab Kamel, PhD,1 Ayman Al-Hendy, MD PhD,1 Qiwei Yang, PhD,2 University of Illinois at Chicago, College of Medicine, Chicago, IL, National Center for Drug Control and Research (NODCAR), Giza, Egypt; 2pharmacology and toxicology department faculty of pharmacy Helwan University, cairo, Egypt; 3University of Illinois at Chicago, Chicago, IL, USA.

OBJECTIVE: Uterine fibroids (UFs) are a benign monoclonal neoplasm of the myometrium and recognized as the most prevalent gynecologic tumor among reproductive age women. Previous studies showed that early life exposure to xenosterogens such as diethylstilbestrol (DES) increased the frequency of UF development. However, the underlying mechanism is largely unknown. This study is to determine the pro-inflammatory mediators which contributes to the activated inflammatory pathways in myometrial stem cells (MMSCs) in response to developmental exposures to DES, and characterize the role of vitamin D3 and its analog in reversing the DES exposure-induced activated inflammatory pathway.

DESIGN: Laboratory research studies using the Eker rat fibroid model (Tsc2-mutant Eker (Tsc2+c/-)); MMSCs.

MATERIALS AND METHODS: Female newborn Eker rats were treated S.C. with vehicle (VEH) or 10 μg/kg of DES. After 1 month of environmental effects, on postnatal days (PND) 10-12, a key period of uterine development. MMSCs were isolated from adult (5 months) myometrium tissue (N=5 for each group) using dual Stro-1 and CD44 surface markers. Whole genome RNA-sequencing was performed to identify pro-inflammatory markers in DES- and VEH-MMSCs. The protein expression levels of a panel pro-inflammatory genes were measured using a cytokines antibody array. RNA expression was determined by qRT-PCR.

RESULTS: Ingenuity Pathway Analysis of RNA-seq data demonstrated that inflammatory pathway was activated in response to DES exposure in MMSCs.
RNA-seq demonstrated that several key inflammatory mediators including TNF-$\alpha$, IL1a, IL1b, IL17, IL-12, CINC-1, ICAM-1, IL1ra, CXCL5, and TIMP-1 were upregulated in DES-MMSCs as compared to VEH-MMSCs. The RNA expression of IL-10 which is an anti-proinflammatory mediator was downregulated in DES-MMSCs. q-PCR analysis confirmed the alteration of RNA expression of these inflammatory mediator genes (P<0.05). Cytokines antibody array analysis exhibited an increased expression of CINC-1,ICAM-1, IL1ra, CXCL5,TIMP-1, and VEGF in DES-MMSCs vs VEH-MMSCs. q-PCR analysis demonstrated that treatment with Vitamin D3 and its analogue Paricalcitol reversed the effect of DES exposure by downregulating those pro-inflammatory cytokines (P<0.01). Cytokines antibody array further demonstrated that vitamin D3 and Paricalcitol reversed the DES-induced upregulation of pro-inflammatory mediators including CINC-1, ICAM-1, IL1ra, CXCL5, TIMP-1, and VEGF in DES-MMSCs.

CONCLUSIONS: Our data strongly demonstrate that developmental exposure to DES increases the risk of adult onset of UFs by creating an inflammatory milieu in the myometrium. Vitamin D3 and Paricalcitol treatment are capable of reversing the effect of DES exposure-induced activation of pro-inflammatory pathway in MTECs, suggesting that vitamin D3 and its analogue as a treatment option could be useful to decrease the incidence of UF.

SUPPORT: NIH RO1 ES028615 and U54 MD007602.

O-245 Wednesday, October 16, 2019 11:45 AM

USE OF CRISPR/cas9 SYSTEM FOR INDUCTION OF MESENCHYMAL STEM CELLS. Sercin Karahuseyinoglu, MD, Ayse Kose, MD, Gizem Nur Sahin, MS, Yagmur Ergun, MS, Student. *Assat. Prof., Istanbul, Turkey; **MS, Istanbul, Turkey; ***MS, Student, Istanbul, Turkey.

OBJECTIVE: The objective of this study is to use CRISPR/cas9 gene edition technology in order to increase gene activation for induction of differentiation of mesenchymal stem cells obtained from human umbilical cord matrix.

DESIGN: Human umbilical cord mesenchymal stem cell line was used for differentiation via chemical induction or CRISPR/cas9 genome activation system. Osteogenic, adipogenic, and neurogenic differentiations were established. The experiments were designed as three biological replicated and three technical replicates for each biological replicates. The efficiency of differentiation capacity was evaluated by qPCR, Western blotting and super resolution microscopy.

MATERIALS AND METHODS: Human umbilical cord mesenchymal stromal cells (hUCMSCs) (Cell line: PSCS05000/1ATCC) was first differentiated to osteocytes, adipocytes and neurons via use of chemicals. Dexamethasone, glycerol-3-phosphate, ascorbic acid in DMEM with 10% FBS were used for osteogenic induction. Dexamethasone, insulin, indomethacin, isobutyl xantine in DMEM with 10% FBS were used for adipogenic induction. Valproic acid, potassium Chloride, butylated hydroxyanisole in DMEM with 10% FBS were used for neurogenic induction. The inductions lasted for 28 days.

RESULTS: In other group of MSCs were induced via use of Cas9 viral transduction. In order to induce differentiation related transcriptional/or activator factors were activated via use of dCas9-SAM (SynergisticActivation Mediator) system. Guide RNAs (gRNAs) for PPAR-gamma, RUNX2 and SOX were designed to target the area of 0 to -200 basepair according to TSS (transcription starting site). For 48 hours gRNAs were transduced to MSCs via lentiviruses that holds the plasmids and gRNAs. At the end of induction period (28 days after chemical and 2 days after CRISPR/cas9 induction) MSCs were assessed for morphological and biochemical changes. Osteopontin and alizarin red were used for osteogenic; oil red o and adipo- nectin were used for adipogenic and MAP2, Neun, beta-III-tubulin were used for evaluation of neurogenic induction, qPCR, IF, and WB were used.

RESULTS: The induction of MSCs via CRISPR/cas9 showed significantly efficient results in terms of both phenotypical and biochemical changes. 35% for adipogenic induction, 45% for osteogenic induction, and 25% for neurogenic induction (p<0.05) as depicted by qPCR analysis. Superresolution microscopy evidently elaborated the changed morphology of cells with positive stainings for osteopontin in osteogenic cells, lipid granules in adipogenic cells. The neurogenic cells showed long dendrite-like extensions that reach out to each other. These cells were positive for Neun, beta-III-tubulin and MAP2.

CONCLUSIONS: CRISPR/cas9-SAM activation system was significantly more efficient for differentiation of human umbilical cord MSCs into different lineages. The differentiation was more rapid, did not need constant use of induction medium and did not reverse by time.

O-246 Wednesday, October 16, 2019 12:00 PM

POST-MEIOiotic MALE GERM CELL DIFFERENTIATION OF MOUSE EMBRYONIC STEM CELLS BY EXPOSURE TO CONDITIONED MEDIUM. Aysha Trout, B.A., Philip Xie, B.S., David A. Kelly; Aysha Trout, M.Sc., Zeyn Rosewaks, M.D., Gianpietro D. Palermo, M.D., Ph.D., The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To determine whether the exposure of mouse embryonic stem cells (mESCs) to medium conditioned by adult pertubular or neonatal germinal epithelial cells that efficiently increases differentiation into primordial germ cell–like cells (PGC-LCs) and induces meiosis.

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DESIGN: We tested a novel culture system utilizing a mesh interphase system to initiate meiotic differentiation of mESCs under media conditioned by adult peritubular cells consisting mainly of Leydig cells, or by neonatal germinal epithelial cells containing pre-Sertoli cells, which are adapted to provide intercellular crosstalk. mESCs without exposure of these cells served as a control.

MATERIALS AND METHODS: Over a 6-month period, mESCs were differentiated into epiblast-like cells (EpiLCs) and PGCCLCs. Peritubular cells derived from adult mouse testes were isolated by differential plating; germ-line cells from neonatal mice were isolated by trypsinization of testes and placed on the mesh. After 7 passages, 1.2 x 10^6 mESCs were plated on each well with MEFs and cultured in the mesh interphase system. Continued expression of Oct4 (>95%) and Nanog (45%) indicated the successful differentiation of mESCs into epiblast-like cells (EpiLCs) and PGCCLCs. Peritubular interstitial cells had greater expression of DAZL and VASA than those interstitial cells cultured in media conditioned by adult interstitial cells. The option was determined to be a 1:5 ratio of adult cells to mESCs. DAZL and VASA expression was negative in the control group, suggesting the important role of the medium conditioned by testicular cells.

RESULTS: As day 3 of differentiating mESCs in mesh interphase–conditioned medium containing Activin A, bFGF, and KSR, decreased positivity of Nanog (45%) indicated the successful differentiation of mESCs into EpiLCs. Continued expression of Oct4 (>95%) was detected in the cells at day 3, suggesting the retention of stemness. Cytoplasmic DAZL positivity at day 5 demonstrated early meiotic differentiation into spermatocyte lineage. On day 8, approximately 30% expressed VASA positivity, indicating further progression into meiosis. Cells cultured in media conditioned by adult interstitial cells had greater expression of DAZL and VASA than those cultured with neonatal interstitial cells. The optimal condition was determined to be a 1:5 ratio of adult cells to mESCs. DAZL and VASA expression were negative in the control group, suggesting the important role of the medium conditioned by testicular cells.

CONCLUSIONS: These results indicate that our novel culture system can promote differentiation of mESCs into PGCCLCs and further meiotic differentiation. Initiation of neospermatogenesis using mESCs can be optimized in the presence of factors secreted from Leydig cells derived from adult mouse testes. Reproducing spermatogenesis in vitro may provide valuable information on overcoming male infertility due to spermatogenic arrest or germ cell aplasia.

REPRODUCTIVE ENDOCRINOLOGY

O-247 Wednesday, October 16, 2019 10:45 AM

VARYING LEVELS OF SERUM ESTRADIOL DO NOT ALTER THE TIMING OF THE EARLY ENDOMETRIAL SECRETORY TRANSFORMATION. Emily K. Osman, MD,a Tianren Wang, MD, Ph.D.,b Min Yang, PhD,c Yiping Zhan, Ph.D.,d Caroline R. Juncadell, MD,e Scott J. Morin, MD,f Emre Seli, M.D.,* Richard Thomas Scott, Jr., MD,a Jason M. Fransasiak, MD. *IVI-RMA New Jersey, Basking Ridge, NJ; bFoundation for Embryonic Competence, Basking Ridge, NJ; cAudubon Fertility, New Orleans, LA; dIVI-RMA Northern California, San Francisco, CA.

OBJECTIVE: Endometrial receptivity is induced by the systematic exposure of estradiol (E2) followed by progesterone (P4). There has been concern that the exaggerated E2 levels seen in stimulated cycles may attenuate the impact of P4 rise and initiation of secretory transformation, ultimately altering the window of receptivity. This study aimed to determine if supra-physiologic E2 levels in the ranges attained during normal and high response superovulation cycles can modify the onset of secretory transformation.

DESIGN: Prospective, randomized, paired.

MATERIALS AND METHODS: A total of 30 biopsies were collected from 10 volunteers that were enrolled and randomized to the order in which they completed 3 different uterine stimulation cycles: physiologic (approximately 180 pg/mL), moderately supraphysiologic (600-800 pg/mL) or supra-physiologic (2000 pg/mL) ranges in order to approximate natural, controlled ovarian stimulation, and in vitro fertilization (IVF) cycles. E2 valerate, selected for consistent levels that more accurately simulate conditions during the proliferative phase, was administered in physician adjusted doses for 12 days. Intramuscular P4 in oil 10 mg/day, a dose known to mimic the P4 rise seen prior to the onset of secretory transformation, was administered and after two completed days of P4 exposure, an endometrial biopsy was performed. DNA was isolated from the specimens and bisulfite sequencing was performed to construct a methylation array. Differential methylation and RNAseq analyses were performed to compare the relative methylation changes in individual patients within the low, moderate, and supraphysiologic groups in an interpatient analysis.

RESULTS: The mean peak E2 level in the physiologic group was 275 pg/mL, moderate group was 909.7 pg/mL, and 2043.4 pg/mL in the supraphysiologic group. Principal component analysis of 834,913 CpG sites was performed on M-values of individual patients within the low, moderate, and supraphysiologic conditions in a paired approach. There were no differences in genome-wide methylation within individual patients across E2 groups. A paired analysis revealed that gene expression profiles did not differ within the same individual at each of the three E2 levels. No significant alterations in gene expression were identified between the low, moderate and supraphysiologic groups in an interpatient analysis.

CONCLUSIONS: Highly supraphysiologic E2 levels do not alter the ability of physiologic levels of P4 to induce secretory transformation. These data suggest that the diminution in implantation seen in stimulated cycles results from embryonic-endometrial dys synchrony following early P4 elevations or slowly blastulating embryos, which may be independent of the magnitude of the E2 rise.

O-248 Wednesday, October 16, 2019 11:00 AM

DISRUPTION OF MITOCHONDRIAL DYNAMICS IN OOCYTES RESULTS IN INFERTILITY AND DIMINISHED OVARIAN RESERVE. Man Zhang, M.D., Ph.D.;a Muhammed Burak Bener, B.S.;b Zongliang Jiang, Ph.D.;b Tianren Wang, M.D., Ph.D.;b Ecem Esencan, M.D.,c Richard Scott, III, B.S.;b Emre Seli, M.D.;d *Yale School of Medicine, New Haven, CT; bLouisiana State University, Baton Rouge, LA; cFoundation for Embryonic Competence, Basking Ridge, NJ; dFoundation of Embryo Competence, Basking Ridge, NJ.

OBJECTIVE: Mitochondrial fusion and fission (collectively referred to as mitochondrial dynamics) allow mitochondria to adapt to changes in their metabolic milieu and to respond to environmental stressors. Mitofusin-1 (Mfn1) regulates mitochondrial dynamics by promoting mitochondrial fusion. The aim of the current study was to determine the role of Mfn1 in female reproductive competence using a mouse model with oocyte-specific deletion of Mfn1.

DESIGN: Experimental study.

MATERIALS AND METHODS: Mfn1-/-;Zp3-Cre mice were crossed with Zp3-Cre mice to produce mice with oocyte-specific Mfn1 deletion (Mfn1-/-). Fertility was assessed by mating 2-month-old Mfn1-/- and wild type (WT) female mice (n=7 per group) with WT fertile males for 12 weeks. Follicle development was assessed by staining serial ovarian sections with hematoxylin and eosin. Ability to generate oocytes (germinal vesicle [GV] and metaphase II [MII]) was assessed after injection with PMSG (5IU) or PMSG and hCG (5IU). RNA sequencing analysis was performed using pooled Mfn1-/- and WT secondary follicle-enclosed oocytes (n=3 mice per group). Protein and mRNA expression were assessed using immunofluorescence and qRT-PCR, respectively.

RESULTS: Mfn1-/- female mice were infertile and did not produce any pups. Mfn1-/- mice (8-weeks-old) ovaries had similar number of primordial, primary, and secondary follicles compared to WT, but no antral follicles. They also did not produce mature (MII) oocytes (p<0.001), and generated a significantly lower number of immature oocytes (17±3.6 vs 40±3.0, p<0.01). When changes in follicular pool was assessed across mouse reproductive lifespan, Mfn1-/- mice were found to have significantly lower number of primordial and primary follicles compared to WT at 6 months, and depletion of follicles of all stages at 12 months (p<0.01 for all comparisons). RNA-seq analysis revealed a total of 982 genes that were differentially regulated in Mfn1-/- oocytes with a number of affected pathways including cell death (apoptosis) signaling and ceramide biosynthesis (p<0.01). As suggested by RNAseq analysis, caspase 6 (mediator of apoptosis) and ceramide levels were elevated in Mfn1-/- secondary follicle-enclosed oocytes compared to WT (p<0.01). Because elevated intracellular ceramide may induce apoptosis, we tested whether decreasing ceramide levels in Mfn1-/- mice would rescue reproductive phenotype. Indeed, treatment with ceramide synthesis inhibitor myriocin (1.5 mg/kg daily injection for 21 consecutive days) rescued follicular defects in Mfn1-/- mice and resulted in development of antral follicles.

CONCLUSIONS: Absence of Mfn1 in oocytes results in infertility and diminished ovarian follicular reserve. Importantly, the mechanism of Mfn1 in oocytes may be exploited to improve human reproductive efficiency will need to be further investigated.
O-249 Wednesday, October 16, 2019 11:15 AM

CELL TYPE SPECIFIC EFFECTS OF HYPERLIPIDEMIA AND HYPERINSULINEMIA, CHARACTERISTIC OF REPROMETABOLIC SYNDROME, ON PITUITARY FUNCTION. Rosemary McDonald, BS, Katherine Kuhn, MS, Andrew P. Bradford, PhD, Nanette Santoro, M.D. University of Colorado Anschutz Medical Campus, Aurora, CO; University of Colorado School of Medicine, Aurora, CO.

OBJECTIVE: Obesity has a profound impact on reproductive function, reducing fertility and increasing the risk of pregnancy complications and birth defects. Obesity in women is associated with hyperlipidemia, hyperinsulinemia, and decreased basal and GnRH-stimulated FSH and LH secretion from gonadotrope cells in the pituitary. We have termed this phenotype “Reprometabolic Syndrome.” We have previously shown that acute infusions of lipids and insulin into healthy human women reduce circulating LH and FSH concentrations and downregulate the reprometabolic phenotype of obesity. However, the underlying mechanisms are not understood. We sought to confirm that the decreased FSH and LH were not attributable to differential hemodilution, and investigated if the effects of lipid/insulin infusions were confined to gonadotropes or impacted other anterior pituitary cell types.

DESIGN: 8 normal weight, regularly cycling women underwent 6-hour visits with either a saline and heparin (control) infusion, or a hyperinsulinemic-euglycemic clamp with heparin and Liposyn (Abbott laboratories). GnRH stimulation was applied at 240 minutes.

MATERIALS AND METHODS: Frequent blood sampling (q10 min) was conducted at each visit, which occurred in random order, between days 2-5 in sequential menstrual cycles. Anterior pituitary hormones TSH and prolactin (PRL), cortisol, follicle-stimulating hormone (FSH), luteinizing hormone (LH), thyroid stimulating hormone (TSH), total T3, total T4, and cortisol were measured in serum samples. TSH was measured in pooled samples q30 min. PRL, FT4, total T3, and cortisol samples were pooled to measure approximately 0, 30, 160, and 360 min time points. Lastly, creatinine was measured hourly in pooled samples.

RESULTS: In contrast to the decrease in gonadotropins, TSH increased in the lipid/insulin-treated samples, with the most dramatic percent change after 160 minutes (28.2% increase), significantly different from TSH levels in the saline-infusions (p<0.0005), which slightly increased (+11%). Thyroid hormones (FT4 and total T3), PRL, cortisol, and serum creatinine did not differ between saline or lipid/insulin infusion conditions.

CONCLUSIONS: Lack of change in serum creatinine showed there was no hemodilution due to variable infusion volumes. FT4 and total T3 were unchanged, suggesting that the increase in TSH was a thyrotrope cell response to lipid/insulin and not a result of altered thyroid function. Cortisol, an inhibitor of TSH production, was unaffected by infusion condition. Levels of the lactotroph hormone PRL were not impacted by lipid/insulin, confirming that effects on the pituitary are both complex and cell type specific. Our results imply that the impact of obesity on the hypothalamic-pituitary-gonadal axis is not simply suppression, and extends beyond reproductive functions. Further research is needed to elucidate mechanisms underlying the selective modulation of pituitary trophic hormones in response to changes in diet and metabolism.

O-250 Wednesday, October 16, 2019 11:30 AM

CHRONIC EXPOSURE TO AMH MAY ACCELERATE GROWTH OF FOLLICLES VIA DOWNREGULATION OF AMHRII. Limor Man, M.D. M.Med.Sc., Eleni Kallinos, B.S., Daylon James, PhD, Zev Rosenwaks, M.D. Assistant Professor of research, NKC, NY; NY, NY. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: Anti-Müllerian hormone (AMH) has been suggested to exert a repressive input on activation and growth during folliculogenesis. We have previously shown that direct paracrine delivery of AMH via engineered endothelial cells (ECs) reduces premature follicular mobilization and growth in short-term human ovarian tissue xenografts (Man et al., 2017). Others, using continuous administration of AMH via an osmotic pump or intraperitoneal injection of lentivirally encoded AMH in a murine model, have shown similar results (Kano et al., 2017). Here, we investigated the influence of AMH-producing ECs on follicle growth in long-term grafts.

DESIGN: Xenograft of human ovarian tissue into NOD scid gamma (NSG) mice with co-transplantation of control ECs or ECs that constitutively secrete human AMH.

MATERIALS AND METHODS: We used lentiviral vectors encoding both a fluorescent reporter and human AMH to modify ECs. We obtained a large volume of ovarian tissue from a 26-year-old organ donor to serve as a source of patient-matched material for study. We co-transplanted cortical fragments from this donor with AMH-expressing or control ECs to establish xenografts in oophorectomized NSG mice. We recovered xenografts at 2 (CTRL, n=7; AMH, n=7), 8 (CTRL, n=6; AMH, n=8), and 14 (CTRL, n=7; AMH, n=6) weeks. We assessed the ratio of primordial to growing follicles in each treatment in histologic sections using H&E staining and light microscopy. Antral follicles at 14 weeks were stained for AMH type II receptor (AMHRII), and the level of expression was quantified by measuring the ratio of area of AMHRII-positive staining to the total nuclear area using a confocal microscope.

RESULTS: In contrast to short-term grafts (2 weeks), in which AMH-ECs promoted quiescence (primordial: growing follicles ratio: CTRL 0.32 vs. AMH-ECs 1.39, P<0.01), the AMH group in long-term grafts revealed a shift in the follicular pool toward accelerated growth (primordial: growing follicle ratio: 8 weeks - CTRL 0.55 vs. AMH ECs 0.19, P=0.06; and 14 weeks - CTRL 0.29 vs. AMH 0.12, P=0.05). Notably, at 14 weeks, antral follicles from the AMH group exhibited 3-fold larger diameter than antral follicles in the CTRL group (CTRL median diameter 0.5 mm vs. AMH-ECs 1.5 mm, P<0.01). Lastly, measurement of AMHRII protein level revealed a median ratio of 22.4 in the CTRL compared to 1.15 in the AMH group.

CONCLUSIONS: As autotransplantation of ovarian tissue becomes more widely practiced, resolving the mechanisms mediating follicular activation and growth is increasingly relevant. Our unexpected finding, given previous results indicating a suppressive input of AMH, suggests that a chronic AMH stimulus of theca may initially suppress activation but ultimately induces a rebound effect, in part, via negative feedback and downregulation of AMHRII.


O-251 Wednesday, October 16, 2019 11:45 AM

ANDROGEN HORMONES AND SEXUAL FUNCTION AMONG CANCER SURVIVORS: SHORT AND LONG-TERM TREATMENT EFFECTS. Leigh A. Humphries, MD, Katherine E. Cameron, MD, MBE, Mary D. Sammel, ScD, Clarisa R. Gracia, MD, MSCE. "Hospital of the University of Pennsylvania, Philadelphia, PA; University of Pennsylvania, Philadelphia, PA; Department of Biostatistics, Epidemiology and Informatics, University of Pennsylvania, Philadelphia, PA.

OBJECTIVE: Sexual function is a critical component of quality of life for many cancer survivors. Given the importance of androgen production in sexual health, we sought to characterize circulating androgen levels before and after cancer therapy as well as sexual function.

MATERIALS AND METHODS: Prospective cohort study.

RESULTS: In adjusted models, women with a new cancer diagnosis (median age 27) had significantly lower testosterone and DHEAS levels than similar-aged controls, even prior to the start of therapy (median testosterone 0.35 ng/mL vs 0.49 ng/mL, p<0.01; DHEAS 0.79 µg/mL vs 1.3 µg/mL, p<0.01); with no difference in AMH levels pre-treatment. After cancer therapy, testosterone levels were further suppressed, with a median within-person decrease of 62% (p<0.01) at 2 months and 39% (p<0.01) at 6 months after treatment end. By 12 months after treatment, testosterone levels among cancer patients exhibited some recovery, at a rate of 6% per month (p<0.01).

Reported sexual dysfunction before and after treatment was prevalent regardless of testosterone levels, with 41% of sexually active participants reporting decreased libido at their pre-treatment visit and 42% at 6 months post-treatment.

O-252 Wednesday, October 16, 2019 1:00 PM

LATE TREATMENT EFFECTS OF CANCER THERAPY ON ANDROGEN LEVELS IN YOUNG ADULT CANCER SURVIVORS. Cynthia A. Helzlsouer, PhD, MS, Tanya M. Silbergeld, DrPH, MPH, MBBS, UMD, Baltimore, MD; Cancer Prevention Research Program, Fred Hutchinson Cancer Research Center, Seattle, WA; Department of Epidemiology, University of Washington, Seattle, WA.
In long-term survivors, women (median age 24) remote from therapy (median 8.2 years) had significantly lower testosterone and DHEAS levels compared to similar-aged controls (p=0.01 and p<0.01, respectively), though higher than late-reproductive age controls (median age 47), (p=0.02 for testosterone, p<0.01 for DHEAS). However, sexual dysfunction did not differ from controls (20% in survivors, 16% in similar-aged controls, 17% in late reproductive-aged controls, p=0.83), and symptom prevalence was not associated with androgen levels.

CONCLUSIONS: Prior to chemotherapy, women with a new cancer diagnosis have lower androgen levels than controls, possibly due to pre-existing suppression of the hypothalamic pituitary ovarian axis. Androgen levels drop further after therapy. While there is some recovery, long-term levels remain lower than controls. Sexual dysfunction is prevalent immediately post-therapy; yet, in long-term survivors, androgen levels do not correlate with self-reported sexual dysfunction, and thus androgens may not play a major role in sexual functioning in this population. More studies investigating sexual function and quality of life in cancer survivors, particularly immediately post-therapy, may help guide counseling for these women.

O-252 Wednesday, October 16, 2019 12:00 PM
ETHNIC DISCORDANCE IN SERUM MÜLLERIAN HORMONE (AMH) IN HEALTHY WOMEN; POPULATION STUDY FROM CHINA AND EUROPE. Scott M. Nelson, MD, PhD, Gemma L. Clayton, PhD, Abigail Fraser, PhD, Sun Aijun, PhD. University of Glasgow, Glasgow, United Kingdom; University of Bristol, Bristol; University of Bristol, Bristol, United Kingdom; Peking Union Medical College Hospital, Beijing, China.

OBJECTIVE: Chinese women are known to have an earlier age at natural menopause than their European counterparts, whether they also have a lower functional ovarian reserve is unknown. This study was designed to assess whether there are ethnic differences in Anti-Müllerian Hormone (AMH) in women of reproductive age.

DESIGN: Non-select cohort of women in the Netherlands and China.

MATERIALS AND METHODS: Women with regular menstrual cycles, not on hormonal contraception or with any medical history of note, were recruited to provide a day 2-5 early follicular sample in China and Europe. AMH was determined using the Roche Elecsys assay. AMH decline was modelled with a linear, quadratic and quadratic with interaction on age equation to assess the impact of ethnicity.

RESULTS: 1348 subjects met the inclusion criteria and participated in the study; 887 European and 461 Chinese women. Despite the Chinese population being slightly younger 34.07 ± 8.38 years than their European counterparts 34.75 ± 8.87 years, their median AMH was lower 1.87 (IQR 0.73, 3.64) as compared to 2.11 (IQR 0.37, 3.96), with evidence of increasing discordance from age 25 years. In all regression models of the AMH age-related decline, there was evidence of a difference between Chinese and European women. On average AMH was 16% geometric mean ratio=0.49 (95% CI 0.44 to 0.55) lower in the Chinese population compared to the European population.

CONCLUSIONS: There were independent effects of age and ethnicity on serum AMH concentrations, with Chinese women having a substantially lower AMH in adult life than their European counterparts from age 25 onwards.

SUPPORT: None.

REPRODUCTIVE IMMUNOLOGY

O-253 Wednesday, October 16, 2019 10:45 AM
INTERFERON GAMMA-INDUCED PROTEIN 10 (IP-10) IS SIGNIFICANTLY LOWER AT EARLY IMPLANTATION IN TWIN VERSUS SINGLETON PREGNANCIES. Samantha Simpson, MD, Janina Kaisasuo, MD, PhD, Gang Peng, PhD, Paulomi Aldo, MS, Michael Paidas, MD, Seth Guller, PhD, Gil Mor, MD, PhD, Lubna Pal, MBBS. Yale University, New Haven, CT; Affiliation not provided.

OBJECTIVE: To determine if pro-inflammatory cytokines in maternal serum differ between twin and singleton gestations in the implantation phase.

DESIGN: A prospective longitudinal cohort of women.

MATERIALS AND METHODS: Women with an initial positive β-hcg serum blood draw after a double or single embryo transfer following in vitro fertilization (IVF) were eligible to participate. Patients were selected for analysis based on healthy term singleton (n=21) or healthy term dichorionic diamniotic (di/di) twin (n=6) delivery. Cytokines tumor necrosis factor alpha (TNFα) and interferon gamma-induced protein 10 (IP-10) were analyzed in triplicates in serial samples (n=94) from day 9-15 after blastocyst day ivf transfer using the SimplePlex immunoassay platform. Samples were compared throughout the sample period using t-tests and Cohen’s D.

RESULTS: TNFα and IP-10 were detected in all sera samples. From day 9-15, IP-10 was significantly lower in di/di twin gestations than in singleton gestations (day 9-11, 8.45 ± 2.85 v 129.1 ± 67 pg/mL, p=0.01; day 12-13, 93.8 ± 29.2 v 120.8 ± 40.7 pg/mL, p<0.05; day 14-15, 102.7 ± 19.9 v 145.6 ± 63.7 pg/mL, p=0.01). Looking at the overall trend, Cohen’s D was -0.59, indicating that IP-10 was significantly lower in days 9-15 in twin pregnancies (95% confidence interval -1.15 to -0.04). During this same time frame, TNFα showed no significant difference (day 9-11, 5.3 ± 1.7 v 6.2 ± 1.5 pg/mL; day 12-13, 5.2 ± 1.4 v 5.8 ± 1.4 pg/mL; day 14-15, 5.4 ± 1.2 v 6.4 ± 2.2 pg/mL). Cohen’s D for TNFα also was not significantly different (-0.29, 95% confidence interval -0.83 to 0.26).

CONCLUSIONS: This is the first report describing IP-10 in serum in the early implantation phase, and the first report comparing pro-inflammatory cytokines between patients with singletons and di/di twins. We demonstrate that serial IP-10 concentrations are significantly lower throughout the early implantation phase in di/di twin pregnancies when compared to normal singleton pregnancies, while TNFα concentrations are not. This strengthens the inhibitory roles ascribed to IP-10 regarding angiogenesis in pregnancy, as increased angiogenesis would be expected in a di/di twin pregnancy.

SUPPORT: Prelate Fertility - Scientific Advisory Board Grant.

O-254 Wednesday, October 16, 2019 11:00 AM
SUPEROVULATION ALTERS THE HUMAN UTERINE NATURAL KILLER CELL REPERTOIRE DURING THE WINDOW OF IMPLANTATION. Anna Sokalska, MD, PhD, Scott Gordon, MD, PhD, Snea Mani, PhD, Charikleia Kalliouri, MD, Monica Mainigi, MD. University of Pennsylvania, Philadelphia, PA; Children’s Hospital of Philadelphia, Division of Neonatology, Philadelphia, PA.

OBJECTIVE: Adverse perinatal outcomes associated with fresh IVF, including pre-eclampsia and growth restriction, have been at least partially attributed to abnormal placental secondary to the maternal hormonal environment following superovulation. Trophoblast invasion and uterine vascular remodeling is regulated in part by maternal immune cells, with multiple abnormal pregnancy outcomes associated with disturbances in the immune cell populations. A recent study defined three subtypes of natural killer (NK) cells (NK1, NK2, NK3) in the endometrium that may play a role in human placentation. This study is the first to evaluate the effect of superovulation on human endometrial immune cell distribution during the window of implantation.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Endometrial biopsies and peripheral blood samples were collected from 25 subjects: 16 samples obtained in natural cycle, and 9 obtained after a positive pregnancy test. All participants obtained 7 days after egg retrieval in gonadotropin stimulated IVF cycles. All participants had regular menstrual cycles, no known history of endometriosis or autoimmune disorders and were free of hormonal and chronic anti-inflammatory treatment prior to their biopsies. Immune cell populations were analyzed using flow cytometry. Serum estradiol (E2) and progesterone (P4) levels were measured by chemiluminescent competitive immunoassay. Student t-test or Mann-Whitney U-test was used to evaluate between-group differences.

RESULTS: Baseline characteristics were comparable for both groups. As expected, serum E2 levels on the day of biopsy were significantly higher in patients following gonadotropin stimulation. No differences in serum P4 levels were noted. Characterization of the total leucocyte population (CD45+ cells) revealed a statistically significant reduction in CD56bright endometrial NK cells in stimulated cycles compared to natural cycles (24.54 ± 3.62 vs. 37.23 ± 2.63 % of total CD45+ cells, p=0.009). When NK cell subtypes were analyzed, there was a significant increase in endometrial NK1 subpopulation as a proportion of all NK cells (19.14 ± 5.04 vs. 9.48 ± 2.28 % of total CD56bright cells, p=0.008) and a decrease of endometrial NK3 subpopulation (28.8 ± 3.3 vs. 49.29 ± 3.88 % of total CD56dim cells, p=0.043) in the stimulated cycles compared to natural cycles. The fraction of NK2 cells as a proportion of all NK cells was unchanged. No changes were seen in the percentage of endometrial CD14+ monocytes/macrophages. There were no differences in the immune cell populations in peripheral blood on the day of biopsy.
CONCLUSIONS: These findings demonstrate that superovulation affects the distribution of NK cells in the endometrium during the window of implantation. Uterine NK cell, specifically NK3 cells, based on marker expression and cytokine production, appear to function in regulating trophoblast invasion during early implantation. These data provide a potential mechanism by which alterations in the maternal hormonal environment may lead to an increased risk of disorders of placentation and adverse perinatal outcomes.

O-255 Wednesday, October 16, 2019 11:15 AM

UNRAVELLING THE IMMUNOGENETICS OF PREGNANCY: PARENTAL HLA-C ALLOTYPES ARE PREDICTIVE OF PREGNANCY LOSS AFTER SINGLE EUPLOID EMBRYO TRANSFERS.

Diego Marin, M.S.,a Xin Tao, Ph.D.,b Li Sun, Ph.D.,b Richard Thomas Scott, Jr., MD. a IVI-RMA New Jersey, Basking Ridge, NJ; bFoundation for Embryonic Competence, Basking Ridge, NJ.

OBJECTIVE: Uterine natural killer cells (uNK) orchestrate correct placentation through cellular responses mediated by their killer cell immunoglobulin-like receptors (KIR) and the HLA-C ligands (C1 or C2) presented by trophoblast cells. It has been reported that when patients have KIR AA genotypes (inhibitory) and their embryos are homozygous for the HLA-C2 allele, the risk of miscarriage increases significantly compared to other combinations. Since it is not always feasible to know the embryonic HLA-C ligands before a transfer, this study aimed to evaluate if parental HLA-C genotypes are predictive of clinical outcomes in a context of euploid single embryo transfer (SET).

METHODS: Patients undergoing a euploid SET with own eggs were included in the study. Only the first SET per couple and SETs that resulted in a positive B-hCG were included in the analysis since the effect of KIR-HLA interactions occurs after implantation. Maternal KIR and parental HLA-C genotyping was performed using quantitative PCR. The variable “nC2” was created to score each couple based on the number of their C2 alleles. Next, the number of maternal C2s was subtracted from the paternal ones (PC2-MC2) so as to assess if a higher HLA-C2 load from either parent is associated with outcomes. Primary endpoints were ongoing pregnancy and clinical loss rates. Logistic regressions and the Fisher’s exact test were computed when appropriate.

RESULTS: 790 euploid SETs were included in the analysis. Mean maternal age was 35.96 ± 3.74 years. The overall frequency of maternal KIR AA and Bx genotypes was 28.7% and 71.3% respectively. For parental HLA-C allele combinations, the frequencies were: C1C1 37.4%, C1C2 46.6% and C2C2 16%. Overall ongoing pregnancy rate was 77.59% (95% CI 74.52-80.45) and remained statistically unchanged irrespective of parental HLA-C or maternal KIR. However, clinical pregnancy loss was positively dependent of parental nC2 in KIR AA patients only (β = 0.73, p = 0.0027), reaching 33.33% when both parents were homozygous C2C2. Regarding each parent’s C2 load, a higher parental C2 load was significantly associated with lower risk of pregnancy loss in patients only (β = -0.41, p = 0.0074), which also showed that a higher paternal C1 load is associated with a higher risk of clinical loss in this group. In fact, when there were more C1 alleles from father than mother per couple (PC1 > MC1) the risk of clinical loss was significantly increased in the Bx population (OR: 2.37, 95% CI: 1.33 – 4.18).

CONCLUSIONS: The risk of miscarriage increased significantly in relation to parental C2 alleles in KIR AA patients. Notably, when the parental origin of HLA-C alleles was investigated, a higher paternal C1 load increased the risk of clinical loss in patients with activating KIR (Bx), a finding in alignment with the theory of immunological memory of uNK cells with maternal HLA-C allelotypes. This data also suggests that parental KIR-HLA-C genotyping could be useful for counselling patients undergoing euploid SET in cases where HLA-C-based embryo selection is not feasible.

O-256 Wednesday, October 16, 2019 11:30 AM

EFFICIENCY OF IMMUNOMODULATION OF ENDOMETRIUM WITH MIXED PATERNAL AND MATERNAL PERIPHERAL MONONUCLEAR CELLS IN REPEATED IMPLANTATION FAILURES.

Hassen Elloumi, Dr Khadeed Mahmoud, Dr Sonia Mnallah, Dr, Mariem ben Khelifa, Phd, Fathi Zhioua, Dr, Khadeed Terras, Dr, Mohamed Khrouf, Dr clinique la rose, centre FERTILLIA, Tunis, Tunisia.

OBJECTIVE: To date, implantation is the rate-limiting step for the success of IVF. The process of implantation is a complicated process that requires the orchestration of a series of events involving both the embryo and the endometrium. Recently, accumulating evidence has suggested that local immune cells at the implantation site have actively contributed to embryo implantation. Some studies suggested the role of endometrium immune-modulation with maternally activated peripheral mononuclear cells (PBMCs) in implantation success. However, the effect of intra uterine insemination of mixed paternal and maternal activated PBMCs before embryo transfer in RIF cases has not been studied enough. In this direction, the aim of our work is to examine the influence of the type and the number of intrauterine peripheral blood mononuclear cells application on embryo implantation rates for infertile patients.

DESIGN: Prospective study conducted between February 2018 and February 2019. Forty one couples with RIF were included. The patients were categorized into two groups with regard to their treatment type, autologous PBMC: group A (n = 18) and co-cultured maternal and paternal PBMC; group B (n = 26). Subgroups were defined according to the number of PBMC inseminated: < 2 millions (Group A1 (n = 8) and group B1 (n = 10); ≥ 2 millions (Group A2 (n = 11) and group B2 (n = 13)).

MATERIALS AND METHODS: Mononuclear cells were isolated from patient’s peripheral blood by density gradient centrifugation using commercially available lymphocyte preparation and then cultured for 3 days and transferred into the endometrial cavity prior to embryo transfer. All patients were selected on the following inclusion criteria: failure to achieve a pregnancy following a minimum of three IVF/ICSI cycles in which more than 5 high-grade embryos were transferred, age > 40 years old, primary infertility and absence of uterine pathology.

RESULTS: Baseline clinical parameters and number of embryos transferred were found to be comparable in all groups. Our study demonstrates that activated PBMC promote clinical pregnancy rates (CPR) (39 %). The CPR were significantly higher when at least 2 millions of co-cultured maternal and paternal PBMC were inseminated, group B2, (62%) in comparison respectively to group A1, A2 and B1 (38%; 37%; 10%); (p < 0.005). The implantation rate was also significantly higher in group B2 (35.5%) in comparison respectively to group A1, A2 and B1 ((19%; 22%; 8.3%); (p < 0.005).

CONCLUSIONS: In conclusion, we provide for the first time the effect of the adjuvant of paternal activates PBMC to immune modulate endometrium. Intra Uterine insemination of paternal cultured-activated PBMC 48h prior embryo transfer can provide biological signals specifically paternal antigen and cytokines that can exerts a considerable influence on female reproductive tract physiology by inducing pro inflammatory cytokines, chemokines and cytokines profiles changes to mediate maternal immune tolerance of the embryo at implantation. The precise mechanism of PBMCs action still unclear and both in vitro and in vivo experiments are needed in order to clarify the mechanism.
lymphocyte counts obtained from a Beckman Coulter LH500 analyzer. A level greater than 30% of total endometrial lymphocyte population was adjudged the criteria for administering intravenous intralipid infusion of 20% as bolus dose, when optimal endometrium (thickness ≥ 8 mm and Applebaum Zone 3–4 vascularity) was observed by transvaginal ultrasonography. Sample size calculation was based on to achieve 80% power to detect a difference of proportion of 0.2 of clinical pregnancy rate between the groups. The test statistic used was the two-sided Z test with pooled variance. The significance level of the test was targeted at 0.05.

RESULTS: Receiver operator curve analysis shows that an elevated uterine NK cell level of 30–38% (at a sensitivity of 60.7% and specificity of 52.2%) as a surrogate for T cell activation.

CONCLUSIONS: Uterine NK cell activity of 30–38% in RIF patients, minimal benefit of intralipid therapy was discernible. However, there seems to be no significant increase in the pregnancy outcome with Intralipids.

SUPPORT: NIL.
SUBDERMAL HORMONE IMPLANT AS TREATMENT FOR THE IMPROVEMENT OF MENOPAUSAL SYMPTOMS IN A PRIVATE FERTILITY CENTER. Arnoldo Gonzalez, M.D., Pasquale Patrizio, M.D., Julio C. Rosales, M.D., Guillermo Russell, M.D., Salomon Alvarado, M.D., Roberto Santos, M.D. *IECH, Monterrey, NL, Mexico; 1Yale Fertility Center, New Haven, CT.

OBJECTIVE: To evaluate the effect of testosterone subdermal implants on improvement of menopausal symptoms.

METHODS AND MATERIALS: A total of 96 consecutive patients who attended the menopause clinic from August 2017 to December 2018 were prospectively enrolled. Symptoms evaluation was performed with the Menopause Rating Scale (MRS), a specific scoring scale of menopausal symptoms. It is composed of 11 points or items of symptoms that are grouped into three subscales or dimensions: 1) Somatic-vegetative. 2) Psychological. 3) Urogenital. Higher MRS scores are associated with increased deterioration in the quality of life.

Subcutaneous testosterone (2 mg/kg) implants were applied for symptoms relief in all patients and MRS scores assessed before and after. The application of testosterone was carried out in the office under local anesthesia, in the subcutaneous tissue of the gluteal or abdominal regions. The time of effect of the implant was 6 months and no patients required implant removal. The follow-up questionnaire was performed 12 weeks after initial placement. Paired Student t tests were performed to compare variables.

RESULTS: The mean age of the 96 patients was 51 years ± 6.51 and the onset of menopausal symptoms was less than 5 years in all. The mean MRS score (31.93 ± 7.46) had a significant decline (12.37 ± 7.4, P < 0.001) once the implant was applied. Patients experienced the most improvements in Hot flashes (P <0.001), Cardiac palpitations (P <0.001), Sleep disorders (P <0.001), Mood (P <0.001), Irritability (P <0.001), Tiredness (P <0.001), Vaginal Dryness (P <0.001).

CONCLUSIONS: Testosterone hormone subdermal implants represent a valid alternative to hormone replacement therapy, effectively improving major menopausal symptoms. Further studies and follow-ups are required to evaluate continuous efficacy, tolerability and safety of testosterone implants.
A 5-YEAR ANALYSIS OF DEMOGRAPHICS, CYCLE CHARACTERISTICS AND REPRODUCTIVE OUTCOMES OF 907 EGG FREEZING CYCLES IN PATIENTS WITH DIMINISHED OVARIAN RESERVE AND AGE-RELATED FERTILITY DECLINE. Aylin P. Cil, M.D., Remzi Abali, M.D., Ayse Boza, M.D., Lale S. Karakis, M.D., Mehmet Ceyhan, M.D., Ece Akkasal, M.D., Ipek Keles, Ms, Ozgur Oktem, M.D., Mustafa Barsa Ata, M.D., Mustafa Bahceci, M.D., Ph.D., Bulent Urman, M.D. American Hospital, Istanbul, Turkey; Bahceci Health Group-Fulya IVF Centre, Istanbul, Turkey; Koc University School of Medicine, Istanbul, Turkey.

OBJECTIVE: Since the adoption of new regulations on ART procedures in 2014, non-medical oocyte cryopreservation has been legalized in Turkey for childless women with diminished ovarian reserve (DOR). As older women face age related fertility decline regardless of their ovarian reserve, they also benefit from egg freezing under this regulation. Since there are no studies to date addressing the cycle characteristics and reproductive outcomes of egg freezing cycles in patients with DOR, we aim to evaluate cycle characteristics and reproductive outcomes of women with DOR and those undergoing egg freezing in older women facing age-related fertility decline.

DESIGN: Retrospective data analysis.

MATERIALS AND METHODS: Electronic databases or charts of patients who underwent egg freezing in 3 IVF centers in Istanbul between 2014 and 2019 were retrospectively reviewed. Egg freezing cycles of patients with DOR (DOR group) or patients who were ≥38 years with normal/high ovarian reserve according to their age (NR-Aged group) were included into the study. This study reviewed 907 egg freezing cycles of 586 patients. Sixteen percent of women were <35 years old, whereas 66% were over the age of 38. 517 patients with DOR underwent 825 egg freezing cycles and 69 NR-Aged patients underwent 82 egg freezing cycles. In the DOR group, 76 cycles (9%) were cancelled due to inadequate follicular development, premature ovulation, no oocyte or no mature oocytes collected. The mean age and AMH of the DOR group at the time of freezing were 37.4±5.2 years and 0.6±0.4ng/dl, respectively. Mean number of frozen MII oocytes per cycle was 3.4±2.3. The average number of egg freezing cycles per patient was 1.6±1.1 resulting in a total frozen MII oocyte number of 5.3±3.7 per patient. In the NR-Aged group the mean AMH level was 2.2±1.4 and the mean number of frozen MII oocytes was 11.8±4.1. A total of 20 patients returned to use their frozen oocytes. None of the three patients returned in the NR-Aged group who had more than 12 frozen oocytes got pregnant. Of the 17 patients in the DOR group, 6 patients did not have embryo transfers and only 5 patients had live births (17.6%), of the two from thawed oocytes (11.7%). However, the third patient got pregnant in the following fresh cycle after thawed oocytes could not be fertilized. In order to increase the number of oocytes, 7 thawing cycles were combined with fresh cycles.

CONCLUSIONS: To our knowledge, this is the first reported analysis of egg freezing cycles of patients with DOR. Young women with DOR is the most important group who will benefit from preventive egg freezing. Since the cycle cancellation rate is high and reproductive outcomes of these patients are very low, these patients should be counseled accordingly about the risks and expectations, and advised to have higher number of oocytes.

Objectives: While clinical outcomes from in vitro fertilization (IVF) cycles performed using surgically extracted sperm and ejaculated sperm have been reported to be similar, men requiring surgical sperm extraction represent a unique patient population (1,2). Additionally, the relationship between paternal age and assisted reproductive technology (ART) outcomes is a controversial topic which is often confounded by factors arising from the female partner. This study sought to determine whether increasing paternal age is associated with adverse outcomes in the setting of a single embryo transfer (SET) of a euploid embryo created with surgically extracted sperm. Preimplantation genetic testing for aneuploidy (PGT-A) was utilized to minimize the potential effects of aneuploidy.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: This study was performed at a large fertility practice. Couples were included if they underwent a first cycle of IVF between 2012 and 2019 with surgically extracted sperm and then underwent intracytoplasmic sperm injection (ICSI) and PGT-A followed by SET of a euploid embryo. Wilcoxon rank sum test, Chi-square analysis, Fisher’s exact test, logistic regression models, and linear regression models were utilized to assess the relationship between paternal age and rates of implantation, delivery, biochemical loss, and clinical loss. An analysis of the relationship between paternal age and fertilization rate, blastulation rate, and euploid rate was also performed.

RESULTS: 207 couples met inclusion criteria. Mean male partner age was 37.2±7.5 years, with 69 male patients age 40 or older. Mean female partner age was 33.8±4.7 years. Among couples undergoing SET of a PGT-A tested embryo with surgical sperm, implantation rate was 84.5%, delivery rate was 58.8%, biochemical loss rate was 12.0%, and clinical loss rate was 6.5%. Adjusting for female age, there was no statistically significant association between male partner age and implantation rate (p=0.34), delivery rate (p=0.07), or biochemical loss rate (p=0.092). In a sub-group analysis of men age 40 or above compared to men younger than 40, there was no significant association observed between paternal age and fertilization rate (p=0.11), blastulation rate (p=0.07), or euploid rate (p=0.43) while adjusting for female age.

CONCLUSIONS: When a couple undergoes SET of a euploid embryo using sperm obtained via surgical extraction techniques, increasing paternal age does not appear to affect pregnancy outcomes (implantation rate, delivery rate, biochemical loss rate, and clinical loss rate). Furthermore, no relationship was demonstrated between paternal age and the embryologic outcomes of fertilization rate, blastulation rate, and euploid rate. While multiple factors undoubtedly contribute to the overall health and development of an early pregnancy, the role of paternal age is unlikely to be significant if surgically extracted sperm is utilized.


SUPORT: None.
P-1 Tuesday, October 15, 2019 6:30 AM

DOES AN INSURANCE MANDATE TO COVER INFERTILITY TREATMENT INCREASE ACCESS TO IN VITRO FERTILIZATION? Kelly Payne, B.A.,* Nannan Thirumavalavan, M.D.,* Jabez Gondokusumo, B.S.,* Adithya Balasubramanian, BA,*, Michael Lehner, B.S.,* Jason Scovell, Ph.D.,* J. Scott Gabrielsen, M.D., Ph.D.,* Dolores J. Lamb, Ph.D.,* Larry I. Lipshultz, M.D.* Baylor College of Medicine, Houston, TX; University Hospitals Urology Institute/Case Western Reserve University, Cleveland, OH; University of Texas McGovern Medical School, Houston, TX; Weill Cornell Medical College, New York, NY.

OBJECTIVE: Financial constraints limit many patients from being able to access infertility care, especially assisted reproductive technologies (ART) such as in vitro fertilization/intracytoplasmic sperm injection (IVF/ICSI). We sought to determine the impact of state insurance mandates for infertility care on the utilization of IVF within each state.

DESIGN: Retrospective analysis of publicly available data.

MATERIALS AND METHODS: All IVF centers in the United States in 2017, their zip code, and number of cycles performed were extracted from CDC data. Using US census data, the median salaries for zip code and state were extracted. The number of IVF centers and number of IVF cycles between states with and without infertility coverage insurance mandates were compared. ASSOC: The association between geographic region, income and the number of IVF cycles was evaluated. IVF centers in mandate and non-mandate states were sequentally sorted by the median household income of the zip code they are located in and grouped into successive increments of $10,000 of median household income. Total number of cycles per successive $10,000 income bracket were compared in mandate and non-mandate states. Paired and unpaired Student’s T-tests were performed for continuous variables.

RESULTS: Fifteen states mandate some degree of infertility coverage. States with insurance mandates for infertility coverage had a greater number of yearly IVF cycles per 100,000 residents compared to states without infertility coverage mandates (104 cycles vs 57 cycles per 100,000 p = 0.029). However, there was no difference between the number of IVF centers per person between states with and without infertility coverage mandates (0.16 vs 0.13 per 100,000 residents, p = 0.058). On average, IVF centers were located in zip codes with greater median incomes than their respective states ($73,325.17 vs $62,607.53, p < .0001). This relationship held true for both states with infertility insurance mandates ($79,894.00 vs $66,820.87, p < .0001) and without infertility insurance mandates ($65,813.11 vs $57,759.77, p < .0001). There was no significant difference between number of cycles in mandate and non-mandate states at IVF centers located in median household income brackets below $80,000. In centers located in median household income brackets greater than $80,000, the total number of cycles performed was significantly greater in mandate states vs. non-mandate states (p = 0.0461).

CONCLUSIONS: States with insurance mandates for infertility coverage have a greater number of IVF cycles per 100,000 residents, but surprisingly do not have a greater number of IVF centers carrying out these cycles. On the whole, IVF centers are located in relatively wealthier zip codes in both mandate and non-mandate states. Only at IVF centers in zip codes with median household income greater than $80,000 do mandate states have a greater number of IVF cycles than non-mandate states. This suggests that state insurance mandates for infertility coverage may not be making IVF more accessible for all but may be selectively benefitting wealthier geographic regions.

P-2 Tuesday, October 15, 2019 6:30 AM

DEFINING INFERTILITY: HOW THE LANGUAGE USED TO DESCRIBE INFERTILITY SHAPES PUBLIC PERCEPTION AND POLICY. Abigail C. Mancuso, MD, Karen M. Summers, MPH CHES, Rebecca K. Chung, MD, Aaron Scherer, PhD, Ginny L. Ryan, MD, MA, University of Iowa Carver College of Medicine, Iowa City, IA.

OBJECTIVE: To investigate if the label associated with infertility has a causal impact on public perceptions of infertility and infertility treatment.

DESIGN: Cross-sectional study.

P-3 Tuesday, October 15, 2019 6:30 AM

PATIENT ACCESS AND UNTAPPED POTENTIAL: CAN NEW DATA DRIVE PROGRESS? Howard Tasker, BA, Patty Stull, BS, Andrew F. Khair, PhD, MBA, Gaurang S. Daftary, MD, MBA, Fertility Dynamics, Washington, DC; Ferring Pharmaceuticals, Inc, Parsippany, NJ.

OBJECTIVE: Determine gaps and factors that cause a discrepancy between the potential for, and utilization of, infertility care in the U.S.

DESIGN: Multivariate models to determine potential number of patients for, and actual numbers receiving, treatment in all Nielsen designated U.S. Market Areas (DMAs).

MATERIALS AND METHODS: The number of women receiving treatment by a reproductive endocrinologist was calculated using fresh cycle data reported by the CDC, combined with an estimate of IUI-only patients based on state insurance mandate. A multivariate prediction model was created using >20 variables including insurance mandate, age, gender and psycho-demographics in 115 DMAs to predict numbers of patients receiving treatment. Variable coefficients related to treatment potential (defined as need and predisposed) were separated from those impacting...
utilization (e.g., doctors, locations and distance) to construct a sub-model to identify numbers of potential patients. Accuracy was determined using R² coefficient. Analysis was used to obtain results for all 211 DMAs by zip code.

RESULTS: The multivariate model predicted the number of patients being treated with a $R^2 > .93$ (p < 0.001) among 115 DMAs with fertility clinics. Of the 330,200 women determined to have potential for treatment (need and pre-disposition), only 137,000 are estimated to be receiving it (41% utilization) with a gap of 193,200 who would receive treatment if it were more accessible. Although insurance requirements and affluence were significant factors, other variables such as psycho-demographics were even more so. The number of patients with potential for treatment vs. utilization varied significantly among and within DMAs. Of all DMAs, 47 had high incidence (>mean 23%) of potential patients; of these 30 had high utilization levels (>mean 41%) whereas 17 had low utilization levels (<mean 41%), resulting in a mean of 3,202 underserved patients per DMA. If just the 17 low-use DMAs increased use to match the high-utilization DMAs, patient access would increase by 11% nationally. Similar access opportunities exist in every DMA.

CONCLUSIONS: Intuition rather than objectivity have often guided efforts to improve patient access by factoring variables such as wealth and proximity to medical centers. New data identifies and quantifies populations who need and are predisposed to treatment by incorporating provider and patient based variables that impact treatment utilization. This data can be used to expand geographic access to care and optimize patient outreach.

<table>
<thead>
<tr>
<th>Potential (Predisposed)</th>
<th>Low</th>
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<tbody>
<tr>
<td># DMAs</td>
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<tr>
<td>Potential as % of Need</td>
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<td>33%</td>
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<td>High % Util</td>
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<tr>
<td>Low % Util</td>
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<td>34%</td>
</tr>
<tr>
<td>Underserved per DMA</td>
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<td>3,202</td>
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</table>

P-4 Tuesday, October 15, 2019 6:30 AM

GENDER AND FERTILITY STATUS AFFECT PERCEPTIONS OF INFERTILITY AND SUPPORT FOR ACCESS TO CARE: A CROSS SECTIONAL STUDY. Rebecca K. Chang, MD, Karen M. Summers, MPH CHES, Abigail C. Mancuso, MD, Aaron Scherer, PhD, Ginny L. Ryan, MD, MA, University of Iowa Hospitals and Clinics, Iowa City, IA.

OBJECTIVE: To determine if gender and fertility status impact perceptions of infertility and support for treatment access. DESIGN: Cross sectional study. MATERIALS AND METHODS: Subjects aged 18 years and over were recruited to complete an online survey, and quotas were used to reflect gender, age, and race/ethnicity national rates. Exclusion criteria included transgender, non-binary, those who identified themselves as “other,” as well as any missing gender data. Respondents were surveyed about their attitudes towards infertility treatment-related health insurance coverage, fertility preservation, public awareness campaigns, sex education, public assistance programs, sex selection, embryo disposition and other related beliefs.

RESULTS: Of the 1221 subjects recruited, 1157 were included based on our criteria. A total of 54 out of 564 (9.6%) females reported infertility, and 49 of 593 (8.6%) males reported infertility. Overall, females with infertility were more likely to support public assistance programs for infertility treatments (p = .001; see Table 1), especially for persons unable to afford treatment or will undergo cancer treatment that may cause infertility. They were also more supportive of infertility public awareness campaigns (p = .015). They were least likely to support the use of IVF to choose the sex of their desired child (p = .027). Males with infertility were most likely to support the use of IVF both in people with and with infertility to choose the sex of their child (p = .027 and p < .001, respectively) and as well as government regulation to limit the number of embryos transferred to avoid twins (p < .001) and triplets or greater (p < .034). They were also more likely to have negative infertility beliefs (p < .001) and agree that if someone is unable to have children, they were “not meant to have children”, “it is the will of God,” they “did something to become infertile,” and “they just need to relax and they will get pregnant.”

CONCLUSIONS: Males and females with infertility were more likely to support greater access to care with coverage of treatment through insurance and public assistance programs. However, males with infertility were most likely to have negative beliefs regarding infertility.

<table>
<thead>
<tr>
<th>TABLE 1. Perceptions of infertility by gender and fertility status</th>
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<tbody>
<tr>
<td>Infertility status</td>
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<tr>
<td>--------------------</td>
</tr>
<tr>
<td>Support for infertility insurance coverage</td>
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<tr>
<td>Support for fertility preservation insurance coverage</td>
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<td>Support for infertility public awareness campaigns</td>
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<tr>
<td>Support for public assistance programs for infertility treatments</td>
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<tr>
<td>Negative fertility beliefs</td>
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P-5 Tuesday, October 15, 2019 6:30 AM

VARIATION IN AVAILABILITY OF FERTILITY CARE TREATMENTS ACROSS US REGIONS. Leslie B. Ramirez, PhD, Alexa R. Adler, BS, Bat-Sheva L. Maslow, MD, MScTR, Joshua U. Klein, MD, Urbano L. Franca, PhD. *Extend Fertility, New York, NY; "Boston Children's Hospital / Harvard Medical School, Boston, MA.

OBJECTIVE: Across the US, the number of patients being cared for in fertility centers has grown considerably over the last years. However, the differential access to infertility care in the regions of the country remains to be understood. Taking into consideration population growth, this study describes and quantifies the evolution and regional variation of the utilization of assisted reproduction (AR) treatment in the US over five years.

DESIGN: Retrospective study. MATERIALS AND METHODS: We used the publicly available Society for Assisted Reproductive Technology (SART) dataset to measure utilization of AR services in the US between 2011 and 2015. Clinics were grouped into states and into the 4 US census regions. The number of clinics per million (Clinics/1M) and cycles per thousand (Cycles/1k) per region was standardized using the US Census data on the number of females of reproductive age (20–44 years). Trends were assessed using Mann-Kendall test and statistical significance set at P < 0.05.

RESULTS: There were 958,231 cycles performed in the US during the study period. On average, there were 8.7 fertility clinics per million females, ranging from an average of 7.6 per million in the South to 10.5 per million in the Northeast. Contrary to the absolute number of cycles, which increased in all regions, the number of cycles per thousand females only increased significantly in the West and Midwest, remaining stable in the Northeast and South (Table). The results for states can be visualized at http://bit.ly/asrm19var.

CONCLUSIONS: The number of cycles in the US increased significantly over the last five years, but the population-standardized rate remained stable in two of the US regions. In association with the unchanging number of clinics, this suggests that in some regions the expansion of fertility services is driven by the female population growth and not by an increasing fraction of this population seeking infertility care. Further research is needed to evaluate the reasons for these variations and their impact on outcomes. These results should be considered when evaluating policies aimed at...
expanding access to fertility care and the allocation of resources by new fertility centers.

SUPPORT: None.

P-6 Tuesday, October 15, 2019 6:30 AM

NATIONWIDE SURVEY OF ACCESS TO CARE INITIATIVES IN REI PRACTICES ASSOCIATED WITH OB/GYN RESIDENCY PROGRAMS. Tia Jackson-Bey, MD MPH,1 Holly Mehr, MD MSe,2 Jacqueline Ho, MD MS,3 Lasine Aghajanova, MD PhD,3 Molly M. Quinn, MD,4 Jacquelyn Rose Hoffman, BA,5 Christopher N. Herndon, MD,4 University of Illinois at Chicago, College of Medicine, Chicago, IL;6 University of California, Los Angeles, Los Angeles, CA;7 University of Southern California, Los Angeles, CA;8 Stanford University School of Medicine, Stanford, CA;9 University of Arizona College of Medicine - Tucson, Tucson, AZ;10 University of Washington, Seattle, WA.

OBJECTIVE: To survey practice patterns designed to increase access to infertility care among REI practices associated OB/GYN residency programs in the United States.

DESIGN: Cross-sectional survey.

MATERIALS AND METHODS: A total of 281 ACGME certified OB/GYN residency programs were identified. Contact information was found for 270 programs, which were contacted via email and asked to have their REI division director or REI resident rotation director complete an anonymous online survey. The survey included 28 questions on demographics of the residency program, associated REI practice, and presence of initiatives at the institution to expand access to infertility care. Responses were analyzed with logistic regression analysis using STATA software, with significance as p<0.05.

RESULTS: A total of 80 responses were received for a 30% response rate. Of these, 41% (n=33) of REI practices associated with OB/GYN residency programs identified as academic, 24% (n=19) private practice, 26% (n=21) hybrid academic/private, 4% (n=3) military practices and 5% (n=4) other. Responses were received in all US geographic regions with 22% (n=17) located in the Northeast, 33% (n=26) South, 29% (n=23) Midwest, and 16% (n=13) West. In regards to practice size, 20% (n=16) of practices had 1-2 REI providers, 40% (n=32) had 3-5 providers, and 31% (n=25) had 6 or more providers. Eighty eight percent (n=70) of practices offered IVF and of those 78% (n=55) reported utilizing an onsite embryology lab. Thirty eight percent (n=30) of practices reported having an REI fellowship. Of clinical initiatives to expand access to infertility care, lower income patients, respondents reported offering discounted infertility services (38%, n=30), utilization of a low-cost IVF program (28%, n=22), and utilizing a resident and/or fellow staffed clinic to provide infertility care (39%, n=31). The most commonly discounted infertility services included IVF (73%, n=22), clinical consultation (70%, n=21), and IU1 (53%, n=16). The provision of discounted prices for infertility services was correlated with increasing practice size (OR 2.29, 95% CI 1.23, 4.24, p=0.01) and number of ART cycles performed annually (OR 3.65, 95% CI 1.48, 9.02, p=0.05). Academic REI practices (OR 3.6, 95% CI 0.98, 13.25, p=0.05) tended to be more likely to have a low-cost IVF program although sample size was low. The lower costs were achieved through use of mild stimulation (50%, n=11), less lab draws and/or ultrasound during cycle monitoring (32%, n=7), institutional based discounts or write-offs (41%, n=9), and pharmaceutical company based medication discount programs (36%, n=8). Of practices with a low-cost IVF program, 40.9% (n=9) were developed within the past five years.

CONCLUSIONS: To our knowledge, this study of REI practices associated with OB/GYN residency programs is among the first to broadly survey clinical access to infertility care initiatives across the United States. Our findings demonstrate utilization of diverse approaches to expand access to care. Larger practices and academic REI programs were more likely to have clinical initiatives to increase access to care.

CANCER

P-7 Tuesday, October 15, 2019 6:30 AM

ONCOLOGIC OOCYTE CRYOPRESERVATION FOR FERTILITY PRESERVATION: NATIONAL TRENDS AND COMPARISON OF CYCLE CHARACTERISTICS BETWEEN WOMEN WITH AND WITHOUT CANCER. Jennifer F. Kawwass, MD,a Lisa M. Shandley, MD, MS,c Sheree L. Boulet, DrPH,c Heather S. Hipp, MDa Emory University, Atlanta, GA; bAffiliation not provided; cEmory University School of Medicine, Atlanta, GA.

OBJECTIVE: To compare trends, cycle characteristics, and outcomes between women freezing oocytes for fertility preservation due to cancer diagnosis versus elective social reasons. We also compared cancer-related oocyte cryopreservation (OC) outcomes to those for other medical or fertility-related diagnoses.

DESIGN: Retrospective cohort study using national surveillance data reported to the Society for Assisted Reproductive Technology Clinical Outcomes Reporting System from 2012-2016 in the United States.

MATERIALS AND METHODS: Cycles were divided into 4 distinct groups: 1. cancer only, 2. elective only, 3. medically-indicated, 4. infertility-indicated. Trends in absolute number and proportion of cycles within each group were calculated. Multiple imputation was used to characterize cycles with a missing indication (32.3%), race/ethnicity (47.2%), and body mass index (22.0%). Cycle and outcome characteristics were compared between the 4 groups. We used multivariable log-binomial models to estimate pooled adjusted risk ratios (aRRs) and 95% confidence intervals (CIs) for associations between reason for cryopreservation and hyperstimulation, gonadotropin dose, and cycle cancellation. Poisson regression models were used to estimate oocyte yield. Models controlled for age, body mass index, stimulation protocol, geographic region, gonadotropin dose, and race/ethnicity.

RESULTS: Between 2012-2016, 29,631 autologous OC cycles were reported to SARTCORS. The total number of cycles performed for a cancer-related indication increased from 2,925 to 8,828 cycles from 2012 to 2016 and comprised a similar proportion (range 5.6-6.1% annually) of all OC cycles performed in the United States. Compared to purely elective OC cycles, cycles completed for a cancer diagnosis were more likely to be performed among women under 35 years old, with a higher BMI, living in the South, and were more likely to use an antagonist protocol. Compared to purely elective OC, gonadotropin dose (aRR 0.89, [CI] 0.80-0.99), cycle cancellation (aRR 0.90, 95% CI 0.70-1.14), and hyperstimulation (aRR 1.46, 95% CI 0.77-2.29) were not clinically different for cancer-related cycles. Average oocyte yield (approximately 16) and percent maturity (approximately 80%) were comparable in both groups. Oocyte

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cryopreservation performed for medical indications was associated with higher gonadotropin dose (aRR 1.22, 95% CI 1.12-1.33) and higher likelihood of cancellation (aRR 1.68, 95% CI 1.46-1.92) compared to elective OC.

CONCLUSIONS: The number of OC cycles among women with a cancer diagnosis has increased over the past 5 years; however the percentage OC cycles for cancer has remained stable. While patient demographic characteristics were different among those freezing eggs for fertility preservation due to cancer, the cycle outcomes were comparable to elective OC after controlling for potential confounding. Women freezing eggs for oncologic reasons can be reassured that their cycle outcomes are comparable to those freezing eggs electively. The outcomes of the subsequent egg thaw, fertilization, and transfer cycles remain unknown.

SUPPORT: N/A.

P-9 Tuesday, October 15, 2019 6:30 AM

UTILIZATION OF GONADOTROPIN-RELEASING HORMONE AGONISTS FOR PRESERVATION OF OVARIAN FUNCTION IN WOMEN WITH BREAST CANCER RECEIVING CHEMOTHERAPY. Sally F. Vitez, MD, Ling Chen, MD MPH, Paula C. Brady, MD, Jason D. Wright, MD, Columbia University Medical Center, New York, NY.

OBJECTIVE: To determine the use and predictors of GnRH (gonadotropin-releasing hormone) agonists for ovarian conservation in young, reproductive age women with newly diagnosed breast cancer undergoing chemotherapy.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The MarketScan database was used to identify women 15-45 years of age with newly diagnosed breast cancer from 2008-2017. All patients who underwent cancer directed surgery (lumpectomy, mastectomy, biopsy or lymph node evaluation) and received cytotoxic chemotherapy within three months before or after surgery. Patients were considered to have received GnRH agonist therapy if they had one claim for a GnRH agonist in the same period. All women with history of oophorectomy before or during the study period were excluded from the study. Trends and predictors of GnRH agonist use were described and compared using Cochran-Armitage trend test and Chi-square tests.

RESULTS: We identified a total of 13,634 women with breast cancer who underwent treatment with chemotherapy. The median age was 39 years with 755 women <30 (5.5%) years of age and 12,879 >30 (94.5%) years old. GnRH agonists were administered to 112 (0.8%, 95% CI 0.7-1.0%) women. The rate of GnRH agonist use was higher in women age 15-30 years compared to women age 30-45 (2.8% vs 0.7%) (P < 0.001). During the study period, the utilization of GnRH agonists increased from 0.3% in 2008 to 1.3% in 2017 (P < 0.001). Use of GnRH agonists was higher in the Northeast (2.0%) compared to the north central (0.7%), southern (0.6%) and western (0.5%) U.S. (P < 0.001).

CONCLUSIONS: The utilization of GnRH agonists among reproductive age women with breast cancer undergoing chemotherapy is extremely low.

P-10 Tuesday, October 15, 2019 6:30 AM

EVIDENCE THAT ALKYLATING CHEMOTHERAPY IS NOT RELATED TO CLINICAL INFERTILITY IN ADOLESCENT AND YOUNG ADULT (AYA) CANCER SURVIVORS. Kelsey Pinson, MD, Christina Lam, MD, Alexa CO Medica, MD, Brian W. Whitcomb, PhD, Ksenya Shliakhitsitsava, MD, H. Irene Su, MD, M.S.C.E.*, University of California, San Diego, La Jolla, CA; *UCSD resident, San Diego, CA; †University of Massachusetts, Amherst, Amherst, MA; ‡UT Southwestern, Dallas, TX; §University of California San Diego, La Jolla, CA.

OBJECTIVE: Gonadotoxic cancer treatments adversely impact ovarian reserve, but it is unknown if they are related to clinical infertility in AYA cancer survivors. We tested the hypothesis that alkylating chemotherapy (AC) and abdomino-pelvic radiation (RT) increase risks of infertility after cancer.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Female AYA survivors who were ages 21-40 at enrollment, 15-35 at cancer diagnosis, and completed primary cancer treatment, were recruited to the parent Reproductive Window Study on ovarian function. Survivors completed an enrollment questionnaire which included demographic, cancer, and reproductive characteristics, including infertility, pregnancy attempts, and pregnancies. Primary medical records were abstracted for cancer treatments. This analysis included the first episode of pregnancy attempt after cancer (N=200). Primary exposures were AC and RT. The primary outcome was clinical infertility (no pregnancy after 12 months of trying). Chi-square, Fischer’s Exact, and log binomial regression were used to estimate associations between patient characteristics and infertility.

RESULTS: Mean age at time of cancer diagnosis was 26 +/- 5.5 years, 72% were Caucasian, and 17% were Hispanic. The most common cancers were lymphoma (27%), breast (24%), and thyroid (22%). Mean age at pregnancy attempt was 30 (15% age <25 yr, 35% 25-30 yr, 37% 30-35, 14% >35yr). 47% of participants received AC while only 3% received RT. In the first pregnancy attempt, 156 survivors (78%) achieved a pregnancy, 78% by 6 months, 88% by 12 months, and 12% after 12 months. RT was significantly associated with infertility RR 3.75 (95% CI 2.4-5.9). However, alkylating chemotherapy exposure (RR 1.03, CI 0.6-1.7) post- and cyclophosphamide dose by tertile (tertile 2 vs 1, RR 1.5 (95% CI 1.0-9.9); tertile 3
vs 1, RR 0.6 (95% CI 0.1-5.3)) were not associated with infertility. The composite cyclophosphamide equivalent dose (CED) showed no dose dependent association with infertility (< 4 g/m² vs. none, RR 0.86 (95% CI 0.5-1.7); 4-8 g/m² vs. none, RR 0.56 (95% CI 0.15-2.1); > 8 g/m² vs. none, RR 1.1 (0.4-2.9)).

CONCLUSIONS: Abdominopelvic irradiation was associated with a 3-fold higher rate of infertility. Exposure to alkylating chemotherapy, cyclophosphamide, and CED were not associated with infertility in AYA survivors. While these agents are known to decrease ovarian reserve, our novel time to pregnancy data suggests no association with infertility, which is consistent with childhood cancer survivor data that did not observe lower rates of ever pregnancy with alkylating chemotherapy exposure. Although this sample size is relatively small, there is no signal suggesting an association between alkylating chemotherapy and infertility. These data suggest no worse prognosis for becoming pregnant after cancer even with high dose alkylating exposure.

SUPPORT: NIH HD080952-05.

P-11 Tuesday, October 15, 2019 6:30 AM

REPRODUCTIVE POTENTIAL OF VITRIFIED OO-CYTES AND EMBRYOS PRODUCED FROM IN VITRO MATURATION CYCLES OF CANCER PATIENTS FOR FERTILITY PRESERVATION. Weon-Young Son, Ph.D, Helene Creux, M.D., Sara Henderson, M.Sc, Shaoguang Jin, Ph.D., Jin-Tae Chung, M.Sc., William Buckett, M.D. Division of Reproductive Endocrinology and Infertility, McGill University Health Care Centre, Montreal, QC, Canada.

OBJECTIVE: Few clinical options for fertility preservation (PF) are available to women with cancer. Although vitrification of oocytes/embryos obtained from IVF cycles has been used successfully in the PF program, controlled ovarian stimulation (COH) is contraindicated for patients with certain forms of cancer. In addition, many cancer patients have limited time to do COH before therapy. In these cases, immature oocyte collection followed by in vitro maturation (IVM) can be an alternative. This vitrification technique has also been applied to cryopreserve oocytes/embryos obtained from IVM program, but data about embryological and clinical outcomes is limited. The aim of this study was to evaluate post-thawing outcomes of immature oocytes collected by transvaginal aspiration in a fertility preservation program for women with cancer.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: IVM treatment for cancer patients was performed on the basis of the menstrual cycle. IVM oocyte retrieval was performed 38 h after an administration of 10,000 IU hCG. Immature oocytes obtained were cultured in vitro until 48 hours. The matured oocytes were cryopreserved using vitrification method either mature stage or cleavage stage after fertilization with partner sperm. We conducted study of cancer patients treated in a university based IVF center for 16 years (2003-2018). We reviewed the records of 213 cancer patients who underwent IVM cycles (n=237) for PF for cancer. All embryos and oocytes that were vitrified and warmed were included in the study. Post-warming embryological and clinical outcomes were evaluated.

RESULTS: Most frequent cancer for PF in our IVM program was breast cancer (67.6%) followed by hematological cancer (17.8%). The median time lapse before returning to attempt pregnancy was 6.0 (4–13) years for IVM oocyte and 5.5 [4–13] years for IVM embryo cryopreservation. Thirty-four cycles (14.1%) and 33 cycles (13.9%) were transferred. Three patients became clinically pregnant (25.0% per cycle), resulting in the normal delivery of a healthy baby, one ongoing for 34 weeks and one miscarriage. Live birth/ongoing pregnancy rate per patient was 25.0% (2/8). In the IVM oocyte cryopreservation, 77 oocytes were warmed from 8 patients (9 cycles), survival rate per oocyte was 71.6 %, 56.8 % normal fertilization and cleavage rate per embryo was 68.1%. Two cycles of embryo transfers were canceled due to no cleavage. Out of 7 ET cycles, there were 2 biochemical pregnancies, but no clinical pregnancy.

CONCLUSIONS: IVM embryos can be stored with a reasonable result for cancer patients. However, cryopreservation of oocytes collected from IVM program seems to have poor reproductive potential. Therefore, more studies are urgently required to improve IVM- and vitrification method to successfully preserve oocytes collected from cancer patients.

P-12 Tuesday, October 15, 2019 6:30 AM

FEASIBILITY OF FERTILITY PRESERVATION IN PRE-PUBERTAL MALES SCHEDULED TO RECEIVE CHEMOTHERAPY. Helen Levey Bernie, DO MPH, Elizabeth Schofield, MPH, Nicole Benfante, BS, John P. Mulhall, MD MSc FECSM FACS Memorial Sloan Kettering Cancer Center, New York, NY.

OBJECTIVE: Overall incidence rates of childhood cancer vary between 50-200/million children across the world. Childhood cancer survival rates are high, as are the late effects of gonadotoxic agents, such as infertility, in cancer survivors. While cryopreservation of sperm in adults is widely used, cryopreservation of testicular tissue in pre-puberal boys has only recently been applied as a means to help preserve future fertility in pre-puberal boys with cancer. The objective of this study is to present our experience with pre-puberal pre-chemo fertility preservation.

DESIGN: We reviewed all pre-puberal patients who underwent pre-chemo fertility preservation at a large cancer center for feasibility and safety.

MATERIALS AND METHODS: All pre-puberal pre-chemotherapy patients who underwent fertility preservation using testicular sperm extraction (TESE) were analyzed. Parents were informed that: the procedure was experimental, given that it is unknown if the tissue will be of use in the future; the procedure had to be performed under an anesthetic; for another procedure (infusion port, bone marrow aspiration); the procedure would not be covered by insurance. A unilateral technique was utilized as most patients were to undergo chemotherapy within 48 hours of TESE. Safety data including rates of infection, hematoma development or delay in chemotherapy initiation were recorded.

RESULTS: A total of 22 pre-puberal males had a mean age of 7.613 years constituted the study population. Mean FSH level was 6.9±1.6 (range 0.3-15.4) IU/ml. Most (71%) were Tanner stage 1, mean testicular volume 3.6±1.9. The most common childhood cancers in this cohort were sarcomas (55%), immune deficiencies (23%), and leukemias (14%). The procedure took an average of 22 . The tissue was sent to the sperm bank where it was cryopreserved. Viability testing on the first 10 specimens revealed healthy testicular tissue. No wound infections or scrotal hematomas occurred postoperatively. All patients were able to commence chemotherapy on schedule, usually within 24 hours or less of the fertility procedure.

CONCLUSIONS: Fertility preservation in pre-puberal pre-chemotherapy patients is a safe and feasible operation.

SUPPORT: None.

P-13 Tuesday, October 15, 2019 6:30 AM

FERTILITY PRESERVATION DISCUSSION IN CANCER PATIENTS IS UNDERUTILIZED AND VARIES BASED ON AGE. Peter N. Dietrich, MD, G Luke Machen, MD, Pranav Dadhich, MD, Johnathan Doolittle, MD, Elizabeth Schofield, MPH, Nicole Benfante, BS, Jay I. Sandlow, MD Medical College of Wisconsin, Milwaukee, WI.

OBJECTIVE: The American Society of Clinical Oncology recommends that all patients with a cancer diagnosis be counseled on the impact of their disease and treatment on fertility. Despite this, onc fertility is often omitted in pretreatment discussion and planning. The reason for lack of adequate counseling and referrals for fertility preservation is unclear. This study seeks to evaluate the prevalence of cryopreservation discussions.

DESIGN: A retrospective review was performed on 3133 male patients aged 18-60 years with a cancer diagnosis at a single institution. Patient’s charts were queried for “vasectomy”, “semen”, “sperm”, “fertility” and “preservation”.

MATERIALS AND METHODS: Patients were excluded if they had a vasectomy or sperm banking prior to their cancer diagnosis, as well as if they had no treatment for their cancer diagnosis. Data was collected for cryopreservation discussion, discussion prior to treatment, discussion before chemotherapy, and if cryopreservation of sperm was performed. Age, race, cancer location, primary treatment, and chemotherapy status was also recorded.

RESULTS: A total of 2504 patients were included for analysis. Mean age was 49 years. There was documentation of counseling on cryopreservation in 353 (14.1%)—280 (79.3%) before primary treatment and 298 (84.4%) before chemotherapy. 126 (5.0%) patients underwent cryopreservation. A logistic regression indicated a significant effect of age, race, site of cancer, primary treatment, and chemotherapy treatment on whether cryopreservation was discussed (chi²<0.001, pseudo R²=0.29). Chemotherapy at any time of treatment (OR 0.69, p<0.001) was significantly associated with cryopreservation counseling. Testicular and prostate cancer patients were significantly more
likely to be offered cryopreservation (p<0.001 and p=0.005, respectively). Patients aged 30-39, 40-49, and 50-60 were significantly less likely to receive counseling when compared to patients aged 18-29 while controlling for other variables (OR 0.41, 0.12 and 0.05 respectively, p<0.001 for all 3 groups).

CONCLUSIONS: Reproductive side effects are not as commonly discussed as other systemic side effects when a patient receives a cancer diagnosis or when they start treatment. Our study indicates that cryopreservation is vastly underdiscussed. Younger patients, those undergoing chemotherapy during their treatment period, and a diagnosis of testicular and prostate cancer were more likely to receive cryopreservation counseling. As assisted reproductive techniques have become more successful and readily available, it is important to include options and counseling for all patients.

P-14 Tuesday, October 15, 2019 6:30 AM

FERTILITY-SAVING TREATMENT (FST) AND ASSISTED REPRODUCTIVE TECHNOLOGY (ART) IN PATIENTS WITH ENDOMETRIAL CARCINOMA (EMCA) AND ENDOMETROL INTRAEPITHELIAL NEOPLASIA (EIN): PREGNANCY OUTCOMES AFTER EMBRYO TRANSFER (ET). Hilary Friedlander, MD,1 Jennifer K. Blakemore, MD,1 David H. McCulloh, Ph.D.2 Mary Elizabeth Fino, MD,3 NYU School of Medicine, New York, NY;3 NYU Langone School of Medicine, New York, NY;3 NYU Langone Health, New York, NY;3 NYU Langone Fertility Center, New York, NY.

OBJECTIVE: Non-surgical management for patients desiring future fertility with EMCA and its’ precursor, EIN, has the goal of clearance of affected tissue and reversion to normal endometrial function (1). Only approximately 15% of these patients will have a livebirth (LB) without the need for ART (2). Despite this low number, little information exists on the pregnancy outcomes for patients who will go on to utilize ART. We investigated the pregnancy outcomes for patients who underwent ET after FST.

DESIGN: Retrospective cohort study of all patients who underwent ET after FST for EMCA or EIN at a single center between 1/2003 and 12/2018.

MATERIALS AND METHODS: An analysis of all patients and ET outcomes after FST was performed. Patients who utilized ART but did not yet return for ET were excluded. Descriptive data are presented as mean ± SD. Observed ET outcomes were sub-grouped into 1) LB + ongoing pregnancy (OP) and 2) spontaneous abortion (SAB) + not pregnant (NP). Observed outcomes were compared to expected outcomes matched for age and type of transfer [fresh or frozen, number of embryos transferred, and with or without pre-implantation genetic testing (PGT)] at our center with a Wilcoxon Signed-Rank Test, p < 0.05 considered significant.

RESULTS: 14 patients, 3 with EMCA and 11 with EIN, met criteria for inclusion for a combined total of 40 ETs. The mean age at initiation of ART following FST was 35.14 ± 4.77 (range 28 to 44) and includes two patients, aged 40 and 44, who ultimately used donor eggs. The average BMI at diagnosis was 26.51 ± 4.17. FSTs prior to ET included megestrol acetate (n=7), oral progesterone (n=5), levonorgestrel intrauterine device (n=1), and polycystectomy (n=1). The average time from diagnosis to first ET was 1.62 ± 1.52 years. The average number of ETs per patient was 2.86 ± 2.03, with a range of 1 to 9. Of 40 ETs, 10 transfers were fresh ETs with an average of 2.70 ± 1.06 embryos transferred per cycle. Three ETs were untested donor eggs, each with a single embryo transferred per cycle. Twelve were frozen untested ETs, with an average of 1.77 ± 0.81 embryos transferred per cycle. Six patients elected to use PGT [Array Comparative Genomic Hybridization (aCGH) and Next Generation Sequencing (NGS)] for 14 ETs. Of 40 and 21 ETs, with an average of 1.69 ± 0.97 embryos transferred per cycle. Outcomes for all ETs included 7 LB, 1 OP, 8 SAB, and 24 NP. An analysis of observed outcomes by sub-group, compared to the expected from matched controls (age, ET type and number, and PGT as described above) showed that patients with EMCA/EIN after FST had a significantly lower LB/OP rate than expected, Z = -5.04, df = 39, p < 0.001. A sub-group analysis of the 14 euploid ETs (7 single by NGS, 4 single by aCGH, 3 double by aCGH) resulted in a LB/OP rate of 21.4% compared to an expected rate of 62.8% (Z = -3.32, df = 13, p < 0.001).

CONCLUSIONS: Patients who have undergone FST for EMCA/EIN have significantly poorer outcomes than expected after ET. Further evaluation of the impact of the diagnosis, treatment and repeated cavity instrumentation for EMCA/EIN is necessary to create an individualized and optimized approach for this unique patient population.


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OVARIAN STIMULATION IN CANCER PATIENTS: RANDOM VERSUS CONVENTIONAL START. Andrea Natalia Coscia, MD,1 Mariana Miguens, M.D.,1 Mariana Cecilia Calvo, MD,1 Rocio Belén Anría, M.D.,1 Milfra Espinal, M.D.,2 Elayne Margarita Vasquez, M.D.,2 Sergio D. Papier, Sr., M.D.3 CEGYR, Ciudad Autonoma de Buenos Aires, Argentina;3 Cegyr, Buenos Aires, Argentina.

OBJECTIVE: To determine if random start ovarian stimulation in cancer patients provides similar results compared to conventional stimulation starting in follicular phase.

DESIGN: Retrospective data analysis at a single center (CEGYR).

MATERIALS AND METHODS: All patients undergoing oocyte cryopreservation for fertility preservation due to recent cancer diagnosis were ruffled from 2012 to 2018. Patients were grouped according to random start or conventional start of the ovarian stimulation. Conventional start was defined as scheduled in early follicular phase initiation of gonadotrophins; random start was initiated at any other moment of the menstrual cycle.

The analyzed variables were: number of oocytes, number of mature oocytes (metaphase II), and cycle length.

RESULTS: 71 cycles met inclusion criteria.

Oocytes were collected of 23 (33%) patients on the random start group and 48 (67%) from the conventional one.

Mean age was 33.8 years old in the conventional and 33.25 years old in the random start groups. (p=0.65 IC95%, 2.04-3.23).

The mean number of oocytes collected were similar 11.9 (conventional) versus 10.4 (random) (p=0.47 IC95%, 2.65-5.66) and mean number of mature oocytes vitrified was also similar (metaphase II): 9.30 (conventional) vs 7.6 (random) (p=0.34 IC95%, 1.81-5.13).

The cycle duration was different, being the conventional shorter (9.7 days) than the random group (11.3 days) (p=0.0019 IC95%, 0.61-2.58).

CONCLUSIONS: Random start stimulation cycles for cancer patients has comparable results and allows patients to start gonadotrophin stimulation irrespective of menstrual cycle phase, with no impairment of oocyte yield and only a small increase of cycle duration.

Random start is a good opportunity for patients who are run out of time and face a fertility threatening medical condition.

P-16 Tuesday, October 15, 2019 6:30 AM

ADDED BENEFIT OF IMMATURE OOCYTE MATURATION FOR FERTILITY PRESERVATION IN WOMEN WITH MALIGNANCY. Samer Tannus, M.D., a Alexander Volodarsky-Perel, M.D.1, Weon-Young Son, Ph.D.1, Togas Tulandi, M.D.2, William Buckett, M.D.1 "Reproductive center- IVF unit. Tel Aviv Sourasky Medical Center, Tel Aviv, Israel." Division of Reproductive Endocrinology and Infertility, McGill University Health Care Centre, Montreal, QC, Canada.

OBJECTIVE: To assess the added value of maturing immature oocytes collected during fertility preservation treatments in women with malignancy.

DESIGN: A retrospective case control study conducted at a tertiary academic IVF unit.

MATERIALS AND METHODS: Patients: 327 cancer patients undergoing fertility preservation treatment from 2009 to 2017. We compared oocyte maturation rates and cycle parameters from 3 types of fertility preservation treatments: 1. Stimulated IVF cycle (n=143), 2. Non-stimulated IVF cycle (n=158), 3. Follicle aspiration and oocyte collection from ovarian tissue prepared for ovarian tissue cryopreservation followed by in vitro maturation of the immature oocytes (n=48). The primary outcome measure was the maturation rate and the number of mature oocytes. The secondary outcomes were oocyte fertilization and embryo development rates.

RESULTS: The mean maturation rate in IVF cycles was 38% and in the non-stimulated IVF cycles was 55%. In women who chose to cryopreserve their embryos, similar fertilization and embryo cleavage rates were found in oocytes that matured after stimulated IVF cycles compared to non-stimulated
IVM cycles. Gonadotropin releasing hormone agonist triggering, treatment with aromatase inhibitor or oral contraceptives use before the cycle, did not affect the maturation rate.

CONCLUSIONS: Although the maturation rate of immature oocytes collected in IVF cycles is low, it is still a viable source of oocytes that can be used to improve the efficacy of fertility preservation treatments by increasing the number of mature oocytes available for freezing or fertilization.

P-17 Tuesday, October 15, 2019 6:30 AM
ACCESS TO FERTILITY-SPARING TREATMENT OF ENDOMETRIAL INTRAEPITHELIAL NEOPLASIA: REPRODUCTIVE OUTCOMES AND PATIENT SATISFACTION. Matthew Shear, MD,1 Alice Kennedy, BS,2 Hannah Stack-Dumbill, BS,2 Emily A. Seidler, MD,2 Michele Hacker, ScD, MPhE,1 Katherine M. Esselen, MD, MBA,2 “Beth Israel Deaconess Medical Center, Boston, MA;2Boston IVF, Waltham, MA;3Harvard Medical School, Boston, MA.

OBJECTIVE: Endometrial intraepithelial neoplasia (EIN) is the precursor to type 1 endometrioid adenocarcinoma, which is caused by unopposed estrogenic proliferation of the endometrium. Hysterectomy is curative in up to 98% of cases, but women desiring fertility preservation now have access to hormonotherapy as a treatment option. Our objective was to characterize patient satisfaction and subsequent reproductive outcomes among patients with EIN or grade 1 endometrial adenocarcinoma who elected fertility-sparing treatment. DESIGN: Retrospective cohort, survey.

MATERIALS AND METHODS: We performed a retrospective medical record review for all patients seen in consultation for EIN or grade 1 endometrial adenocarcinoma from a single gynecologic oncology practice at a tertiary care hospital from 2007 through 2016. The abstracted data included patient characteristics, fertility treatment, and reproductive outcomes. We also invited patients to complete a survey, either online or via telephone, to understand patient experiences with fertility-sparing management of EIN and type 1 endometrioid adenocarcinoma. Reported data are from a combination of the medical record review and the survey.

RESULTS: There were 64 eligible patients, and 41 (64%) completed the survey. Among the 64 patients, the majority (77%) had EIN. Initial treatment included a progestin-containing intratubine device for 61%, an oral progesterin for 33%, and both for 1%; initial treatment was unknown for 5%. Complete regression was documented in 69% of patients, and 26% underwent hysterectomy. Roughly half of patients (56%) had a documented infertility consultation, and 36% pursued treatment with ovulation induction or stimulation, intrauterine insemination and/or in vitro fertilization. Of the 24 patients who we know attempted pregnancy after fertility-sparing treatment, 11 (46%) had a total of 16 pregnancies and 8 patients had at least one live birth. Among the survey respondents, 87% agreed or strongly agreed that they were pleased with the advice they received about treatment options, and 92% felt they had a choice about their treatment. Most respondents (68%) agreed that their initial treatment was helpful in treating their cancer. Nearly all respondents (91%) agreed or strongly agreed they would make the same decision to try hormonal treatment.

CONCLUSIONS: The majority of patients with EIN or grade 1 endometrial adenocarcinoma who elected fertility-sparing treatment subsequently pursued consultation with an infertility specialist and many underwent infertility treatment. Among those who we know attempted pregnancy, one third had a live birth. Overall, patients were very satisfied with their fertility-sparing treatment, and nearly all expressed that they would make a similar choice again. In future studies, we aim to further elucidate the unique aspects of fertility treatment in patients with EIN who elect fertility-sparing treatment.

P-18 Tuesday, October 15, 2019 6:30 AM
LETROZOLE AND FERTILITY PRESERVATION IN PATIENTS WITH BREAST CANCER. Marouen Brahmi, Sr., Associate professor, Sarah Amari, Medical Degree,1 Khadija Feriel Kacem Berjeb, Associate professor,2 Haithem Khalil, Sr., Doctorate in Medicine,3 Manel Hamdoun, Medical Degree,1 Mounir Ben Meftah, Sr., Medical Degree,1 Habiba Essoussi, Medical Degree,1 Olfa Bahri, Sr., Professor, Anis Fadheliaoui, Associate Professor,2 Fethi Zhioua, Pr,4 Aziza Othmana University hospital, Tunis, Tunisia;3Gynecology, Obstetric and Reproductive Medicine Department. Aziza Othmana University Hospital, Tunis, Tunisia;2Reproductive Medicine Laboratory. Aziza Othmana University Hospital, Tunis, Tunisia;4Biochemistry Department. Aziza Othmana University hospital., Tunis, Tunisia.

OBJECTIVE: Ovarian stimulation with exogenous gonadotropins leads to a significant rise in circulating estrogen levels which could aggravate the spread of breast cancer. The use of anti aromatase agents such as letrozole could prevent this elevation. But is it safe and effective in fertility preservation?

DESIGN: We conducted a prospective comparative study.

MATERIALS AND METHODS: A total of 171 patients were referred to our FP consult. Only 143 patients underwent fertility preservation (oocyte/embryo vitrification) and 75 amongst them had breast cancer. A FP consultation is provided by both a gynecologist and a biologist of the department. A complete physical examination is performed. An informed consent is signed before starting the procedure. The evaluation of the ovarian reserve is done by Antral Follicle Count (AFC) ultrasound and AMH dosage.

The stimulation is conducted according to a random-start antagonist protocol using GnRH agonist triggering. For patients with breast cancer, the adjunction of letrozole 5mg/day was started the first day of ovarian stimulation and continued 7 days after oocyte pick up, while closely monitoring estrogen levels during COS.

We compared the number of mature oocytes obtained between patients with breast cancer (Group 1) and patients diagnosed with other types of cancer (group 2).

RESULTS: The average age of our patients (years) in group 1 was 30.3 +/- 3.7 and 26.9 +/- 6.7 in group 2; with no significant statistical difference (p=0.73). The evaluation of ovarian reserve using AFC (12.3 +/- 6.2 vs 13.9 +/- 6.4; p = 0.7) and serum AMH levels (2.43 +/- 2.3 ng/ml vs 2.8 +/- 2.45 ng/ml; p = 0.5) showed similar results in both groups.

The duration of the ovarian stimulation was not significantly different between both two groups: 10.2 +/- 2.3 days vs 11.8 +/- 3.1 days; (p = 0.5).

Estradiol level on the day of ovulation triggering was 479 +/- 323 pg/ml in the breast cancer group versus 1701 +/- 682 pg/ml in the other group (p = 0.02).

The number of CCOs obtained in the breast cancer group was 10.76 +/- 8.39 compared with 9.11 +/- 6.81 in the group 2 and the difference was not significant (p=1.83).

The mean number of mature metaphase II oocytes collected in the breast cancer group was 7.38 +/- 6.11 oocytes versus 6.09 +/- 4.72 oocytes in group 2. The difference was not statistically significant either (p=1.33).

CONCLUSIONS: Breast cancer is one of the most frequent malignancies in women worldwide and the demand for fertility preservation is on the rise. Letrozole would provide much ease and safety during emergency controlled ovarian stimulation, without negatively impacting its outcome.

CYPRESERATION

P-19 Tuesday, October 15, 2019 6:30 AM
OOCYTE YIELD WITH IMMEDIATE SUBSEQUENT OOCYTE CRYOPRESERVATION (OC) CYCLES COMPARED TO INTERVAL CYCLES. Bat-Sheva L. Maslow, MD, MSCTR, Dayna Hemmey, MSN, NP-C, Michael M. Guarinacci, MD, MPH, Leslie B. Ramirez, PhD, Joshua U. Klein, MD Extend Fertility, New York, NY.

OBJECTIVE: Women undergoing OC cycles often desire multiple cycles to increase oocyte yield. Traditionally, an interval of 1 menstrual cycle (MC) or more was advised. However, data supporting this recommendation are limited. The aim of this study is to evaluate the difference in oocyte yield between 1st and 2nd retrievals in women undergoing immediate subsequent cycle compared to those with an interval of 1 or more MC, and to evaluate whether interval length is associated with 2nd cycle oocyte yield.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All women undergoing 2nd OC cycles at Extend Fertility Medical Practice from 4/2016-12/2018 were included in the study. Demographic and cycle data were abstracted from the electronic medical record. Difference in days and MII cryopreserved oocytes between retrievals were calculated and categorized. Subjects were also categorized by whether they yielded more, equal, or fewer oocytes in 2nd cycle compared to 1st cycle. Comparisons between groups were made utilizing Mann-Whitney-U, Kruskal-Wallis or X2, where appropriate. A multinomial logistic regression was performed to assess the association between retrieval interval and 2nd cycle oocyte yield, while controlling for age and AMH.

RESULTS: 399 subjects with 2nd retrievals were included in the study. For the cohort, mean age was 36.5 +/- 3.0 years, median AMH was...
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P-20 Tuesday, October 15, 2019 6:30 AM

INITIAL VALIDATION OF AN AUTOMATED CRYOSTORAGE AND INVENTORY MANAGEMENT SYSTEM. Timothy Allen Sharp, B.S., a William N. Garbarini, Jr., MBA, a Chad A. Johnson, PhD, a Ann Watson, B.A., a Rachel Greenberg, B.A., a Kathryn J. Go, PhD, a TMRW Life Sciences, New York, NY; bTMRW Life Sciences, Inc., New York, NY.

OBJECTIVE: To validate an automated and robotic liquid nitrogen vapor-based storage tank for cryopreserved embryos and gametes.

DESIGN: Experimental study.

MATERIALS AND METHODS: Cryopreserved mouse embryos (2PN-stage) in straws (Embryotech. Haverhill, MA) were distributed into platform-specific containers and either robotically uploaded into the automated tank (Group A) or transferred to a liquid nitrogen-filled dewar (Group B). Five days of storage ensued after which the embryos were robotically or manually retrieved from the tank or dewar, respectively, for warming. In each group, post-warming survival was evaluated and embryos were randomly allocated to culture in groups of 10 for incubation at 37°C in an atmosphere of 5%CO2/5%O2 for 96 hours. At the end of the incubation period, blastocyst formation rate (#blastocysts/#2PN) was assessed. One-way ANOVA was applied for statistical analysis.

RESULTS: In both Groups A and B, post-warming survival of 2PN was 100%. Blastocyst formation rates were 93.2±7.9% (S.D.) (97/104) in Group A and 91.3±8.5% (95/104) in Group B. One-way ANOVA indicated no statistical difference (p=0.575).

CONCLUSIONS: This initial validation study suggests that application of a robotic, liquid nitrogen vapor-based tank for storage of cryopreserved mammalian embryos is feasible. Although studies utilizing human embryos and gametes remain to be done, this proof of concept study provides grounds to similar between the groups.

CONCLUSIONS: In an egg-sharing donation program, embryo developmental competence and implantation potential are reduced when vitrified oocytes are injected with frozen sperm. Reference: NA. SUPPORT: None.

P-22 Tuesday, October 15, 2019 6:30 AM

AUTOMATED VITRIFICATION FOR EMBRYO CRYOPRESERVATION: PRELIMINARY COMPARATIVE RESULTS AND FIRST LIVE BIRTH IN EUROPE. Mariabeatrice Dal Canto, BSc, PhD, a Clarissa Moutier, BSc, a Fausta Brambillasca, BSc, PhD, b Maria Cristina Guglielmo, BSc, PhD, a Alessandro Bartolacci, BSc, a Mario Mignini Renzini, MD, a Rubens Fadini, MD, a Jose Buratini, DVM, PhD, a Biogenesi Reproductive Medicine Centre, Monza, Italy; bBiogenesi Reproductive technology, Monza, Italy.

OBJECTIVE: Automated vitrification has been made available recently, but its clinical efficiency has not been properly addressed in relation to manual vitrification. Therefore, the objective of this ongoing study is to compare clinical outcomes following automated embryo vitrification with those achieved after manual vitrification.

DESIGN: In June 2018 we began a study in which, so far, we have vitrified 924 stage embryos and 181 blastocyst using the automated vitrification system (Gavi®-Genea Biomedx), and 203 cleavage stage embryos and 255 blastocysts using the universally accepted/gold-standard system for manual vitrification (Kitazato Vitrification - Cryotop® Kit). This study is still in progress.

MATERIALS AND METHODS: Participants are couples undergoing embryo transfer following vitrification from June 2018 in our fertility centre. Embryos were cryopreserved using Gavi® according to manufacturer’s

P-21 Tuesday, October 15, 2019 6:30 AM

CRYOPRESERVATION OF BOTH MALE AND FEMALE GAMETES LEADS TO REDUCED EMBRYO DEVELOPMENT AND IMPLANTATION POTENTIAL. Assumppto Iaconelli, Jr., MD, a Amanda Souza Setti, MSc, a Daniela Paes de Almeida Ferreira Braga, PhD, a Matheus de Castro Azevedo, BSc, a Edison Borges, Jr., PhD, a Fertility Medical Group / Sapientiae Institute, Sao Paulo, Brazil; bFertility Medical Group, Sao Paulo, Brazil.

OBJECTIVE: Egg-sharing is an effective way to speed up the waiting time for recipients and to provide treatment for infertile patients who need help funding their own treatment. The impact of egg and sperm cryopreservation on the outcomes of recipients’ cycles is uncertain. The objective of this study was to investigate the influence of oocyte and sperm cryopreservation on donated eggs in terms of laboratory and clinical outcomes of intracytoplasmic sperm injection (ICSI) cycles.

DESIGN: Historical cohort study.

MATERIALS AND METHODS: Data analyzed in this study were obtained via chart review of 115 oocyte donor ICSI cycles (age range 21-34 years), and 122 oocyte recipients (age range 31-48) undergoing 152 oocyte recipient ICSI cycles, participating in an egg-sharing donation program, from 2016 to 2018, in a private university-affiliated IVF center. The sample size calculation suggested that 148 cycles would be enough to demonstrate a 20% effect with 80% power and 5% significance level considering as primary outcome implantation rate. Cycles were split into four groups according to the origin of oocytes and semen, as follows: Fresh O/S Group, recipients in which fresh oocytes were injected with fresh sperm (n=19); Fresh O / Cryo S Group, recipients in which fresh oocytes were injected with cryopreserved sperm (n=14); Cryo O / Fresh S Group, recipients in which cryopreserved oocytes were injected with fresh sperm (n=85); and Cryo O/S Group, recipients in which cryopreserved oocytes were injected with cryopreserved sperm (n=34). The impact of oocyte and semen cryopreservation on recipients’ ICSI outcomes was investigated by using General Mixed Models fit by restricted maximum likelihood, followed by Bonferroni post hoc test for the comparison of means amongst the four groups. The model was generated using covariates as fixed effects and egg-donors and egg-recipients as random effects, with unstructured covariance structure, adjusted for potential confounders.

RESULTS: Normal cleavage speed rate on day 3 was significantly lower in Cryo O/S Group (55.5%) compared to all other groups (Fresh O/S Group: 76.4%, Fresh O / Cryo S Group: 75.7%, and Cryo O / Fresh S Group: 62.4%). Blastocyst development rate was also significantly lower in Cryo O/S Group (24.0%) compared to all other groups (Fresh O/S Group: 32.9%, Fresh O / Cryo S Group: 41.1%, and Cryo O / Fresh S Group: 30.0%). A statistically significant gradual decline was observed in implantation rate (Fresh O/S Group: 36.7%, Fresh O / Cryo S Group: 32.9%, and Cryo O / Fresh S Group: 29.5%, Cryo O/S Group: 14.5%). The rates of fertilization, high quality embryos on days 2 and 3, normal cleavage speed on day 2, high-quality blastocyst, clinical pregnancy, and miscarriage were similar between the groups.

CONCLUSIONS: In an egg-sharing donation program, embryo developmental competence and implantation potential are reduced when vitrified oocytes are injected with frozen sperm.

Reference: NA. SUPPORT: None.

P-18 Tuesday, October 15, 2019 6:30 AM

INFLUENCE OF OVA RETRIEVAL INTERVAL ON OOCYTE YIELD. Amanda Souza Setti, MSc, a Daniela Paes de Almeida Ferreira Braga, PhD, a Fertility Medical Group / Sapientiae Institute, Sao Paulo, Brazil; bFertility Medical Group, Sao Paulo, Brazil.

OBJECTIVE: Egg-sharing is an effective way to speed up the waiting time for recipients and to provide treatment for infertile patients who need help funding their own treatment. The impact of egg and sperm cryopreservation on the outcomes of recipients’ cycles is uncertain. The objective of this study was to investigate the influence of oocyte and sperm cryopreservation on donated eggs in terms of laboratory and clinical outcomes of intracytoplasmic sperm injection (ICSI) cycles.

DESIGN: Historical cohort study.

MATERIALS AND METHODS: Data analyzed in this study were obtained via chart review of 115 oocyte donor ICSI cycles (age range 21-34 years), and 122 oocyte recipients (age range 31-48) undergoing 152 oocyte recipient ICSI cycles, participating in an egg-sharing donation program, from 2016 to 2018, in a private university-affiliated IVF center. The sample size calculation suggested that 148 cycles would be enough to demonstrate a 20% effect with 80% power and 5% significance level considering as primary outcome implantation rate. Cycles were split into four groups according to the origin of oocytes and semen, as follows: Fresh O/S Group, recipients in which fresh oocytes were injected with fresh sperm (n=19); Fresh O / Cryo S Group, recipients in which fresh oocytes were injected with cryopreserved sperm (n=14); Cryo O / Fresh S Group, recipients in which cryopreserved oocytes were injected with fresh sperm (n=85); and Cryo O/S Group, recipients in which cryopreserved oocytes were injected with cryopreserved sperm (n=34). The impact of oocyte and semen cryopreservation on recipients’ ICSI outcomes was investigated by using General Mixed Models fit by restricted maximum likelihood, followed by Bonferroni post hoc test for the comparison of means amongst the four groups. The model was generated using covariates as fixed effects and egg-donors and egg-recipients as random effects, with unstructured covariance structure, adjusted for potential confounders.

RESULTS: Normal cleavage speed rate on day 3 was significantly lower in Cryo O/S Group (55.5%) compared to all other groups (Fresh O/S Group: 76.4%, Fresh O / Cryo S Group: 75.7%, and Cryo O / Fresh S Group: 62.4%). Blastocyst development rate was also significantly lower in Cryo O/S Group (24.0%) compared to all other groups (Fresh O/S Group: 32.9%, Fresh O / Cryo S Group: 41.1%, and Cryo O / Fresh S Group: 30.0%). A statistically significant gradual decline was observed in implantation rate (Fresh O/S Group: 36.7%, Fresh O / Cryo S Group: 32.9%, and Cryo O / Fresh S Group: 29.5%, Cryo O/S Group: 14.5%). The rates of fertilization, high quality embryos on days 2 and 3, normal cleavage speed on day 2, high-quality blastocyst, clinical pregnancy, and miscarriage were similar between the groups.

CONCLUSIONS: In an egg-sharing donation program, embryo developmental competence and implantation potential are reduced when vitrified oocytes are injected with frozen sperm.

Reference: NA. SUPPORT: None.
instructions or with Cryotop®. Embryo quality, number of transferred embryos and patient age have been balanced in both groups. Embryos were thawed according to the manufacturer’s instructions and transferred in double (cleavage stage embryos) or single transfers (blastocysts). The clinical end-point for the comparative analysis is clinical pregnancy rate. Clinical pregnancy has been diagnosed by ultrasound examination 7 weeks after transfer, following a positive β-hCG test.

RESULTS: So far, we thawed 30 cleavage stage embryos vitrified with Gavi®, which were utilised in 15 double embryo transfers. During the same period, 66 cleavage stage embryos vitrified with Cryotop® were also double transferred (33 DET). So far, clinical pregnancy rates after automated and manual vitrification of cleavage stage embryos are 26.7% (4/15) and 33.3% (11/33), respectively. In parallel, we thawed 36 blastocysts after automated vitrification and 77 blastocysts after manual vitrification, all of them utilised in single stage transfers, except for 1 blastocyst from the manual vitrification group which was classified as degenerated after thawing. So far, clinical pregnancy rates after automated and manual vitrification of blastocysts are 44.4% (16/36) and 32.9% (25/76), respectively. No miscarriages have been observed so far after automated vitrification of cleavage stage embryos (0/4), whereas the abortion rate following manual vitrification of cleavage stage embryos is 27.3% (3/11) so far. For cryopreserved blastocysts, abortion rates are 12.0% (3/25) and 12.5% (2/16) with manual and automated vitrification, respectively, so far. Theses results resulted in the first twenty pregnancies following automated embryo vitrification in Europe. At the time this abstract was written, one live birth, the first in Europe, had already occurred.

CONCLUSIONS: These data suggest that automated vitrification is technically efficient and may benefit the consistency of clinical outcomes following vitrification, as well as the logistics of the fertility centres.

P-23 Tuesday, October 15, 2019 6:30 AM
PROLONGED SEMEN CRYOPRESERVATION DECREASES MOTILE CONCENTRATION.
Rhodel Simbulan, MS, Emani Harris, BS, Fleurlieza Rabara, BS, CLS, Sean Pae, BS, MS, Fang Xie, PhD, Liza Jalalian, BS, CLS, Mitchell P. Rosen, MD, HCLD, University of California San Francisco, San Francisco, CA.

OBJECTIVE: There is a paucity of data regarding the viability of cryopreserved sperm. Good laboratory practice involving cryopreservation include QA/QC, equipment maintenance and stable temperatures of -196°C. These ensure tissues remain viable for later use. However, cryopreservation has been shown to alter the structure and function of stored spermatozoa. This study aims to determine if sperm viability is affected by long-term storage.

DESIGN: Before-After Study.

MATERIALS AND METHODS: Patients sperm samples that were abandoned over the years of 1995-2014 (average 14.5 years) were thawed and analyzed before discard. Samples were considered abandoned if patients couldn’t be contacted within the past 5 years to continue storage. Prior to initial freeze, semen analyses were performed. Semen samples were stored in a 1:1 mixture of test yolk buffer, aliquoted into 1.5 ml cryovial and suspended in nitrogen vapor for 30 minutes prior to being plunged into liquid nitrogen. Vials were thawed by placing cryovials into 37°C heat blocks for 20 minutes. Post-thaw survival of sperm was determined by calculating sperm concentration, motility and progression. Pre and post analyses were analyzed using regression analyses with a cluster analysis to account for pair-wise comparisons.

RESULTS: 131 patient semen samples were grouped into four categories listed in Table 1. Age, initial sperm concentration and motility were not different between groups. Overall there is a significant decline in sperm motility with years of storage as vials stored for 20 years and longer show a 70% decrease compared to 10 years and less (p<0.0012). The patient age or initial sperm concentration at the time of freeze has no impact on sperm survival.

CONCLUSIONS: Despite appropriate measures to maintain specimen in storage, it appears that prolonged storage in liquid nitrogen may impact sperm survival. This result warrants further study as viability of tissues may be affected over time and reduce the success of fertility outcomes.

P-24 Tuesday, October 15, 2019 6:30 AM
EMBRYOS FROZEN WITHIN A SHORT TIME OF REACHING THE EXPANDED BLASTOCYTS FROM THE EARLY BLASTOCYSTS HAVE HIGH VIABILITY: TIME-LAPSE INVESTIGATION OF 5177 BLASTOCYSTS.

OBJECTIVE: Morphological grading of blastocysts is in widespread use; however, morphokinetic grading by time-lapse monitoring is much less commonly applied. As PGS is not permitted in Japan, a method for estimating the potential viability of embryos using morphokinetic evaluation is required. It is known that Day5 blastocysts have higher viability than Day6 blastocysts. However, it is less understood whether an interval between early blastocysts and expanded blastocysts affects the embryo fertility.

DESIGN: The data was obtained in a retrospective study of 4097 cycles (mean patient age 38.2 years old) in the period 2013–2017.

MATERIALS AND METHODS: In total, 7283 embryos derived from IVF or ICSI were monitored using a time-lapse system (EmbryoScope, Vitrolife, Denmark) and the time from reaching the blastocysts to freezing the expanded blastocysts was recorded. The blastocysts selected for freezing had an ICM and inner diameter of more than 160 μm. 5177 blastocysts were subsequently thawed for transfer. The survival rate at thawing, the pregnancy rate after single embryo transfer, and the live birth rate were determined. These three metrics were compared among embryos classified by the time between reaching the blastocysts and freezing the expanded blastocysts.

RESULTS: Three groups of thawed embryos were compared: 0–20 hours (3083), 21–40 hours (1111), and 41 hours or more (889) from blastocoel formation to expanded blastocysts frozen-thawed. Survival rates at thawing were 97.6% (3010/3083), 95.0% (1091/1111), and 92.8% (778/889), respectively, in these groups; the rate was significantly higher in the 0–20 hour group compared to the other 2 groups. Pregnancy rates of 58.8% (1767/3083), 42.9% (819/1907), and 14.3% (11/77) were obtained; the rate in the 0–20 hour group was significantly higher than the other 2 groups. Live birth rates were 68.6% (1212/1767), 62.6% (513/819), and 54.5% (11/77) respectively, in these groups; the rate was significantly higher in the 0–20 hour group.

CONCLUSIONS: As the viability of the thawed embryos with a short interval between reaching blastocysts and freezing expanded blastocysts was higher than in embryos with longer intervals, we suggest that patients with multiple blastocysts should be preferentially transplanted with those frozen a short time of developing expanded blastocysts.

Reference: None.

SUPPORT: None.

TABLE 1. Summary of difference between initial and post-thaw motile concentrations

<table>
<thead>
<tr>
<th>Years Stored</th>
<th>n</th>
<th>Pt Age</th>
<th>Initial Motile Concentration (M/ml)</th>
<th>Post-Thaw Motile Concentration (M/ml)</th>
<th>Δ</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;10</td>
<td>20</td>
<td>38.8±4.9</td>
<td>37.6±33.5</td>
<td>19.6±29.8</td>
<td>0.26±0.26</td>
</tr>
<tr>
<td>10-14</td>
<td>36</td>
<td>37.7±7.5</td>
<td>28.2±29.3</td>
<td>16.6±22</td>
<td>0.28±0.18</td>
</tr>
<tr>
<td>15-19</td>
<td>36</td>
<td>38.7±7.7</td>
<td>68.8±36</td>
<td>10.1±21.9</td>
<td>0.18±0.21</td>
</tr>
<tr>
<td>&gt;20</td>
<td>29</td>
<td>34.7±8.7</td>
<td>45±58.2</td>
<td>11.7±24.1</td>
<td>0.09±0.13*</td>
</tr>
</tbody>
</table>

*p<0.05
THE TWO-STEP ASYNCHRONOUS VITRIFIED-THAWED BLASTOCYST EMBRYO TRANSFER STRATEGY: THE IMPACT ON MULTIPLE PREGNANCY RATE. Viktor Veselovskyy, MD Nadiya Clinic, Kyiv, Ukraine.

OBJECTIVE: To compare clinical and multiple pregnancy rate among women who underwent two-step asynchronous blastocyst embryo transfer (TSABET) versus DET in the frozen embryo transfer (FET) cycle with patients who had at least two vitrified blastocysts.

DESIGN: Retrospective single-center cohort study.

MATERIALS AND METHODS: All patients (534 consecutive IVF/ICSI cycles) at NADIYA Clinic from 6/30/2015-12/31/2018 who met such criteria as age <38, good quality day 5-6 blastocysts, and at least 2 remaining cryopreserved blastocysts and subsequently underwent FET, were included in this study. Exclusion criteria were preimplantation genetic testing (PGT) cycles and donor oocyte cycles.

Primary outcomes were clinical pregnancy rate per transfer and multiple pregnancy rate. Secondary outcomes were miscarriage rate, ectopic pregnancy rate.

All women received estradiol for the preparation of the endometrium. The administration of progesterone (50 mg in oil, daily) was initiated when endometrium thickness exceeded 8 mm. In the DET group (433 cycles), on day 6 (P+6) or 7 (P+7) after the initiation (P+1) of progesterone treatment, two blastocysts were transferred. In the TSABET (101 cycles), on day P+6 and day P+9 the blastocysts were transferred twice.

The results between the DET and the TSABET cycles were compared (see Table below).

Clinical pregnancy 247 (57.0%) 71 (70.3%) 0.015
Multiple pregnancy 109 (44.1%) 7 (9.9%) <0.001
Ectopic pregnancy 2 (0.8%) 1 (1.4%) 0.664
Miscarriages <20w 48 (19.4%) 12 (16.9%) 0.631

CONCLUSIONS: To our knowledge, this is the first study of using two-step vitrified-thawed blastocyst transfer strategy with 72h interval between transfers. In the group of good prognosis patients TSABET strategy resulted in a higher clinical pregnancy rate than DET, but also was associated with a much lower multiple pregnancy rate. When deciding on the two embryos to transfer in this group, TSABET strategy should be preferable.
IS THE INCREASE IN EGG FREEZING CYCLES RELATED TO INCREASED NUMBERS OF SINGLE
WOMEN IN THE UNITED STATES?  Alexandra Peyser, M.D., Avner Hershlag, M.D., Northwell
Health Fertility, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: In 2017, the United States Census reported 110.6 million unmarried persons over the age of 18, 53.2% of which were women. At the same time, the number of women choosing to freeze their eggs has increased over the last decade. The objective of this study was to determine whether there is an association between the rise in egg freezing and the number of single women in the United States.

DESIGN: Retrospective Cohort.

MATERIALS AND METHODS: Data on oocyte banking for fertility preservation from the SART database from 2014-2017 was analyzed. In addition, data from the United States Census Bureau on marital status of single women was obtained for the same years. The total number of single women reported was compared with the number of oocyte banking cycles. The Pearson correlation test was used to investigate associations between the number of egg freezing cycles and single women. Significance was defined as p<.05.

RESULTS: Between 2014-2017, a total of 33,324 egg freezing cycles were recorded from the SART database. Over this time frame, the number of cycles has increased by 79% while the total number of single women reported has increased 5% (Table 1). We found a high correlation between the increasing number of egg freezing cycles in the USA and the increasing numbers of single women nationwide. However, it did not reach statistical significance (coeff=.87, p=.13).

<table>
<thead>
<tr>
<th>Year</th>
<th>Number of egg freezing cycles (n)</th>
<th>Single (n)</th>
<th>Married (n)</th>
<th>Total(n)</th>
<th>Percentage single (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014</td>
<td>6090</td>
<td>37,311,000</td>
<td>66,732,000</td>
<td>129,871,000</td>
<td>28.73</td>
</tr>
<tr>
<td>2015</td>
<td>7591</td>
<td>37,394,000</td>
<td>67,217,000</td>
<td>131,395,000</td>
<td>28.46</td>
</tr>
<tr>
<td>2016</td>
<td>8707</td>
<td>38,995,000</td>
<td>67,450,000</td>
<td>132,662,000</td>
<td>29.39</td>
</tr>
<tr>
<td>2017</td>
<td>10,936</td>
<td>39,087,000</td>
<td>68,082,000</td>
<td>133,403,000</td>
<td>29.30</td>
</tr>
</tbody>
</table>

CONCLUSIONS: 1. In just 4 years, egg freezing has seen an exponential rise of 79%.
2. During the same period, the number of single women in the USA increased by 5%.
3. These two observations are highly correlated, yet did not reach statistical significance. We suggest that an increase in the numbers of years of egg freezing cycles reported could reach significance.
4. Likely, the sharp rise in egg freezing is also related to improvements in egg freezing technique and results, increased awareness of reproductive ageing, the impact of social media and advertising and more. These factors cannot be enumerated and, might have diluted impact of the increase rate of single women over the same time period.
5. Last but not least: the relationship between egg freezing statistics and the number of single women may have already shifted from uni-directional to bi-directional. How many women delay marriage because egg freezing is readily available and increasingly more reliable?.

THE IMPACT OF THE SHORT-TERM HUMAN SPERM STORAGE IN THE CRYOPROTECTANT-FREE MEDIUM ON SPERM MOTILITY AND VITALITY.  Nabil Sayme, Dr. med., Marija Kljajic, Master of Biology Science, Thomas Krebs, Biology, Dieter Maas, Prof. Dr. med. Team Kinderwunsch Hannover, Hannover, Germany; Saarland University Medical Center, Homburg, Germany.

OBJECTIVE: Slow freezing is currently the most commonly used technique for sperm cryopreservation since the vitrification of spermatozoa is still a rather unexplored methodology. Storage sperm at +4 C is a relatively new technique and in the aim of reach better recovery rates, many studies confirmed that freezing/store sperm without cryoprotectants gives better results. The purpose of the study was to investigate does it the sperm storage in the cryoprotectant-free medium a good alternative for short-time preservation (up to 4 weeks) compare to the conventional slow freezing, as well as the impact of the short-term human sperm storage on sperm motility and vitality.

MATERIALS AND METHODS: After slow freezing two straws of each sample were preserved into liquid nitrogen for a period of one and four weeks. Samples treated with Sperm Preserve were divided as well into two straws and stored in fridge at 4 C degrees for the same period. After this period samples were thawed with Sperm Active (GM501 Sperm store, Gynemed, Germany) or sperm preserve medium (Sperm Preserve, Gynemed, Germany) and motility and vitality after these two freezing procedures were compared. For statistical analysis, a One-Way ANOVA was used.

RESULTS: After one week of slow freezing and storage in liquid nitrogen, 24.9±11.22% of spermatozoa regained their motility compared to samples which were stored on 4 C where recovery rate was 32.75±11.02%. One-Way ANOVA confirmed that there is a significant difference between these two groups (p=0.31). The sperm motility rate after four weeks was slightly lower 20.4±6.87% in the slow freezing sample group, compared to 28.05±9.81% after storage at 4 C but still, further statistical analysis confirmed a significant difference between these two groups (p=0.005). Asthenozoospermic samples stored at 4 C had better motility recovery rate after one week 28.8±11.6% vs 13.6±2.96% (p=0.02) than after four weeks 24.2±14% vs 12.8±4.7% where the difference between these two groups was not statistically significant as well as neither between teratozoospermic samples. Vitality was one of the characteristics which we analyzed as well and the difference was significant especially after one week (p=0.0001) where survival rate after slow freezing was 40.5±11.80% compared to the storage sample where that number was 54.25±13.20 %. After four weeks as well, a higher percentage of sperm survive in the storage group 39.75±7.88% compared to the 30.7±6.78% of slow frozen samples (p=0.001).

CONCLUSIONS: The cryoprotectant-free sperm storage protocol tested in this study renders considerably better recovery rates (motility and vitality) of the sperm compared to slow freezing.

SUPPORT: Gynemed.
**DONOR GAMETES**

**P-30** Tuesday, October 15, 2019 6:30 AM

**CHANGES IN U.S. UTILIZATION OF DONOR EGG IVF CYCLES AT DIFFERENT FEMALE AGES BETWEEN 2005-2016.** Norbert Gleicher, MD, Sarah K. Darmon, PhD, David F. Albertini, PhD, David H. Barad, MD, MS. Center for Human Reproduction, New York, NY.

**OBJECTIVE:** To investigate as part of a larger study of changing U.S. practice patterns in IVF, how the utilization of third-party donor eggs has changed between 2005-2016.

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** IVF outcome data are generated annually under Congressional mandate by the Center for Disease Control and Prevention (CDC), including almost all (in 2016, 463/502) of the nation’s IVF centers, and are publicly reported with approximately two-and-a-half years delay. Most recent available data are, therefore, in the 2016 Annual Assisted Reproduction Summary Report from the CDC. We here report on CDC outcome reports longitudinally between years 2005-2016, with years 2005, 2010, 2015 and 2016 serving as index years.

**RESULTS:** With advancing female age, third-party donor egg cycles universally increased in all years as a subgroup of all IVF cycles until around 2010, when they peaked, representing 37% of all cycles. By 2015 they were only 34% and by 2016 only 33% of all cycles at ages 43-44; at ages above 44 years, they in 2010 represented as much as 73% of all cycles but by 2015 only 71% and by 2016 only 65%. We also observed a dramatic switch from use of fresh to frozen donor eggs, also starting in 2010, gaining ground much quicker especially above age 42. Above age 42 in 2005, 36% of donor cycles utilized frozen eggs, by 2010 38% of 43-44 year-olds and 45% of women above age 44 utilized frozen oocytes; by 2015 those numbers had further risen to 65% of 43-44 year-olds and 70% of women above age 44 years.

**CONCLUSIONS:** These data reveal a welcome decline in third party donor egg cycles after 2010, suggesting that more IVF centers are offering older patients the chance of pregnancy and delivery with use of own eggs. They, however, also raise concern about the rapid switch from use of fresh to frozen donor oocytes since 2010, likely caused by growth in commercial frozen egg banks, since frozen donor eggs produce ca.10% lower birth rates than fresh eggs.1 These developments, therefore, may adversely affect live birth rates with third-party donors.


**SUPPORT:** Intramural funds from The Center for Human Reproduction and grants from The Foundation for Reproductive Medicine.

**P-31** Tuesday, October 15, 2019 6:30 AM

**DONOR OOCYTE PREGNANCIES AND FETAL FRACTION: MANAGING PATIENT EXPECTATIONS AND PROVIDING ACCURATE INFORMATION.** Melissa K. Maisenbacher, MS, Georgia Goldberg, MS, Wendy DiNonno, MS, Allison Ryan, PhD Natera, San Carlos, CA.

**OBJECTIVE:** Determine if differences in fetal fraction (FF) are observed in donor oocyte pregnancies compared to the general population.

**DESIGN:** Retrospective analysis

**MATERIALS AND METHODS:** Noninvasive prenatal testing (NIPT) samples from singleton pregnancies were analyzed at a single reference lab. NIPT was performed using a SNP-based method with FF measured as previously described.1 FF from 1611 donor oocytes was analyzed and compared to a large set of reference cases matched for maternal weight (MW) and gestational age (GA). A z-score was calculated for each donor oocyte compared to its reference data. If no impact to FF from the use of donor or IVF, the average z-score is expected to be zero.

Statistical analysis was performed using a z-test to establish if this was the case.

**RESULTS:** For donor cases the average z-score was -0.4. A z-test determined this deviation from normal to be significant (p < 0.00001), showing that donor cases have lower FF than their corresponding reference data. The average MW was 154.3 lbs. (range 79.2-370.4 lbs.), average GA was 12.9 weeks (range 9-33 weeks) and average FF was 8.4%.

**CONCLUSIONS:** The adoption of NIPT over other screening and diagnostic methods continues to grow, especially among women using donor oocyte/IVF. This population’s preference for NIPT may stem from increased anxiety, higher false positive rates with traditional serum screening and avoidance of diagnostic procedures carrying miscarriage risk. Therefore, understanding the differences in FF in this population is critical.2,3

**Previous studies have reported lower FF in patients undergoing IVF and in donor oocyte populations.**4,5 Lower FF has also been associated with increased MW, early GA, certain maternal health conditions, and abnormal fetal results (T18/T13/triploidy).6,8,9 Our results reveal statistically significant lower FF in donor oocyte pregnancies compared to matched reference data.

It is unknown why FF is lower in donor oocyte/IVF pregnancies. Hormone treatment and higher rates of abnormal cord insertion among IVF pregnancies and a high degree of antigenic dissimilarity among donor oocyte pregnancies suggest that the IVF process may impair implantation.2,5,6,8,9 However, lower fetal fractions are also associated with increased risk for chromosome abnormalities. Thus, choosing a NIPT lab with high FF accuracy will reduce the risk of false negatives for this vulnerable population.

Identifying factors that affect FF can optimize NIPT algorithms for various populations and be useful during genetic counseling. Women choosing NIPT after donor oocyte/IVF cycles should be informed of risks for lower FF and higher test failure rates which are associated with increased risks of adverse perinatal outcomes and obstetric complications.

Future analysis should determine the effect on FF of donor oocyte versus non-donor IVF cycles, of various IVF techniques (ICSI, fresh vs. frozen embryo) used to achieve pregnancy and of different etiologies of infertility.

**References:** 1. Zimmerman et al., Noninvasive prenatal aneuploidy testing of chromosomes 13, 18, 21, X, and Y, using targeted sequencing of polymorphic loci. Prenatal Diagnosis 2012; 32: 1-9


7. van der Hoon ML et al., Clinical and immunologic aspects of egg donation pregnancies: a systematic review. Hum Reprod Update. 2010;16(6):704-12


**SUPPORT:** Natera, Inc.

**P-32** Tuesday, October 15, 2019 6:30 AM

**FRESH OOCYTE CYCLES YIELD IMPROVED EMBRYO QUALITY AND SURPLUS EMBRYO CRYOPRESSION RATES COMPARED TO FROZEN OOCYTE CYCLES IN AN EGG-SHARING DONATION PROGRAMME.** Amanda Souza Setti, MSc, Daniela Pues de Almeida Ferreira Braga, PhD, Matheus de Castro Azevedo, BSc, Assumpto Iaconelli, Jr., MD, Edson Borges, Jr., PhD Fertility Medical Group / Sapienitae Institute, Sao Paulo, Brazil; Fertility Medical Group, Sao Paulo, Brazil.

**OBJECTIVE:** To investigate as part of a larger study of changing U.S. practice patterns in IVF, how the utilization of third-party donor eggs has changed between 2005-2016.
OBJECTIVE: An egg-sharing programme provides a good opportunity for recipients and donors to achieve motherhood. At present, there are no evidences to ensure that the cryopreservation of shared eggs is not detrimental to recipients’ treatment outcomes. The objective of this study was to investigate the reasons for cryopreservation on donated eggs in terms of laboratorial and clinical outcomes of intracytoplasmic sperm injection (ICSI) cycles.

DESIGN: Historical cohort study.

MATERIALS AND METHODS: Data analyzed in this study were obtained via chart review of 267 oocyte donor ICSI cycles (age range 19-34 years), and 320 oocyte recipients (age range 26-48) undergoing 307 vitrified and 119 fresh oocyte recipient ICSI cycles, participating in an egg-sharing donation program, from 2015 to 2018, in a private university-affiliated IVF center. The sample size calculation suggested that 199 cycles would be enough to demonstrate a 20% effect with 80% power and 5% significance level considering as primary outcome blastocyst development rate. The impact of oocyte cryopreservation on recipients’ ICSI outcomes was investigated using General Mixed Models fit by restricted maximum likelihood, followed by Bonferroni post hoc test for the comparison of means between fresh and warm oocyte donation groups. The model was generated using co-variables as fixed effects and egg-donors and egg-recipients as random effects, with unstructured covariance structure, adjusted for oocyte dysmorphisms and other potential confounders.

RESULTS: The fertilization rate (80.7% vs. 75.8%, p = 0.034), high quality embryos rate on days 2 (70.3% vs. 57.8%, p = 0.047) and 3 (50.2% vs. 34.6%, p = 0.003), normal cleavage speed rate on days 2 (90.6% vs. 77.2%, p = 0.027) and 3 (50.2% vs. 0.001), and blastocyst rate (47.1% vs. 19.8%, p < 0.001) were significantly higher on fresh oocyte donation cycles compared to warmed oocyte donation cycles. There were no statistically significant differences between fresh and warmed oocyte donation cycles in terms of high-quality blastocyst rate (71.2% vs. 62.0%, p = 0.328), implantation rate (35.7% vs. 25.7%, p = 0.182), clinical pregnancy rate (54.1% vs. 42.9%, p = 0.313), and miscarriage rate (12% vs. 15.9%, p = 0.745). The surplus embryos cryopreservation rate was significantly higher on fresh cycles compared to warmed cycles (65.4% vs. 24.1%, p = 0.015).

CONCLUSIONS: In an egg-sharing donation program, fertilization and embryo developmental competence are reduced when vitrified oocytes are used for ICSI compared to fresh oocytes. Despite no statistical significant differences were observed in terms of pregnancy outcomes, cycles using fresh oocytes had higher rates of surplus embryo cryopreservation, which is interesting for those patients with a negative pregnancy outcome, allowing them to resort to warmed embryo transfer instead of a new cycle of oocyte donation. Efforts must be made so donor-recipient matching makes it possible to receive fresh eggs.

References: NA.

SUPPORT: None.

P-33 Tuesday, October 15, 2019 6:30 AM

DONOR PHALLOLOGIE: A CROSS-SECTIONAL ASSESSMENT OF LONG-TERM MEDICAL AND PSYCHOLOGICAL HEALTH STATUS AFTER ELECTIVE OOCYTE DONATION. Jennifer K. Blakemore, MD, a Paxton E. Voigt, BA, b Mindy R. Schiffman, PhD, b Shelley Lee, PhD, b Mary Elizabeth Fino, MD, c NYU Langone School of Medicine, New York, NY; *NYU School of Medicine, New York, NY; NYU Langone Fertility Center, New York, NY.

OBJECTIVE: There is an inverse relationship between the use of elective oocyte donation and the understanding of long-term potential impact. We sought to assess the long-term medical and psychological health status of all elective oocyte donors (anonymous, directed, agency) at a single institution.

DESIGN: Anonymous quantitative and qualitative survey.

MATERIALS AND METHODS: An anonymous survey was emailed to all donors with a working email who donated between 2008 – 2019 (n = 161). RESULTS: 36 donors completed the survey (response rate 22.4%). The majority identified as Caucasian (77.1%). Most identified as not religious (33.3%), atheist (19.4%) or spiritual (16.7%). 44.4% reported they are currently single and 33.3% as currently married. 41.6% had at least a Bachelors degree, 30.9% Masters and 16.7% a doctorate. 60.5% reported high altruistic/half financial motivations, 14.3% reported pure altruism and another 14.3% purely financial. Most (54.3%) were between 25-30 years old at time of first donation. 40.0% donated between 2-5 years ago and another 34.3% 5-10 years ago. 40.0% of respondents donated once, 17.1% twice, 17.1% three times, and 25.7% 4 or more times. Most reported no post-op complications (34.3%) or minor symptoms only (51.4%). 30.6% reported at least 1 pregnancy but 57.1% hadn’t tried or were not interested. Of donors reporting pregnancies, none required Assisted Reproductive Technology for conception but 13.3% reported >2 losses. Of donors with living biological children, 75.5% reported their children had no medical problems. A directed donor reported her niece has Schaff-Yang syndrome. 80% reported no update in their medical history; 2 reported new allergies, 1 epilepsy, 1 anemia, 1 collagenous colitis, 1 fibrocytic breasts, and 1 reported a keratocanthoma removal. 1 respondent each reported a diagnosis of ovulatory dysfunction, blocked fallopian tubes, unexplained infertility and fibroids respectively. Over half of donors reported being treated for or having ever experienced symptoms of depression or anxiety. Birth control was the most reported new medication. 63.0% reported no update in their family history; 2 reported new cancers in grandmothers (breast, cervical) and 3 reported a family death (depression, colon cancer, old age). 31.3% reported they knew children were born from their oocytes and all wrote positive comments about the knowledge of livebirth. 80.6% reported that they would make the same choice to donate and 58.1% reported they would recommend donation.

62.5% would still have donated under open donation or ID disclosure models. 81.3% were interested in maintaining contact for future updates.

CONCLUSIONS: Most donors did not have major medical history updates. The majority felt positively about donation but also reported a high rate of depression/anxiety, which could be related. Donors felt positively about open disclosure and maintaining contact with recipients. Continued long-term follow up will help provide better counseling about the medical and psychological benefits of donation. Moving toward an open donation disclosure may expand the psychological benefits for both donor and recipient.

References: None.

SUPPORT: None.
RESULTS: Young women who donated oocyte to our program give oocytes to 3 partners as an average. Pregnancy was not associated to paternal age (see table 1). Additionally, number of oocytes, fertilization rate, donor oocyte recipient age and insemination technique (ICSI or FIV) were not related to clinical pregnancy. Interestingly, blastulation rate and the embryo quality were the only parameters associated to pregnancy.

CONCLUSIONS: The strength of the present study was that the same donors give oocytes to different partners. Our results suggest that paternal age does not influence the clinical pregnancy. Although, prospective studies are need by using sibling oocytes.

SUPPORT: None

EMBRYO CULTURE

P-35 Tuesday, October 15, 2019 6:30 AM

PROSPECTIVE RANDOMIZED MULTICENTER STUDY ON CULTURE OF SIBLING HUMAN OOCYTES IN A SEQUENTIAL MEDIA SYSTEM WITH AND WITHOUT ANTIOXIDANTS: THE EFFECT OF FEMALE AGE. Shigetoshi Mizumoto, Ph.D., a Atsumi Yoshida, M.D., Ph.D., MBA,b Takeshi Kuramoto, M.D., Ph.D., a Miho Tanaka, M.Sc., b Markus HM. Montag, Ph.D., a David Gardner, Ph.D. a,b Kuramoto Women’s Clinic, Fukuoka, Japan; bKiba Park Clinic, Tokyo, Japan; bIliabcomm GmbH, Eisenach, Germany; aSchool of Biosciences, University of Melbourne, Melbourne, VIC, Australia.

OBJECTIVE: To investigate the combined effect of three antioxidants Acetyl-L-Carnitine (ALC), N-Acetyl-L-Cysteine (NAC) and α-Lipoic Acid (ALA) in a sequential culture media system on human embryo development and clinical outcome in relation to maternal age

DESIGN: Prospective randomized sibling oocyte multicenter study

MATERIALS AND METHODS: This study included couples intending to undergo IVF or ICSI, with female age < 40 years old and at least eight cumulus-oocyte-complexes after retrieval. Cycles involving PGT, split IVF/ICSI and surgically retrieved sperm were excluded. Human oocytes were randomly distributed to Vitrolife G-Series with or without a combination of three antioxidants ALC/10 /NAC /ALA (A3). IVF/ICSI and embryo culture were conducted in 5% oxygen. Embryo quality on day 3 and day 5/6 and clinical outcome were assessed in relation to maternal age (<35 versus >35). Good embryo quality on day 3 was defined as 8 to 10-cells with even cells and low fragmentation; good quality blastocysts as equal or greater than 3BB. Clinical outcome was assessed in either fresh or vitrified-warmed embryo transfer cycles. The study was registered with clinicaltrials.gov (NCT02999958).

RESULTS: A total of 133 patients participated in the study. The mean female age was 33.8 ± 3.1 years. 1783 oocytes were collected of which 890 were allocated to G-Series media with A3 and 893 to standard G-Series media. When analyzing for age groups in G-Series with A3 compared to standard G-Seriers, the following results were obtained:

- Good quality Day 3 embryo development was significantly higher in the younger age group in G-Series with A3 (<35: 50.2 % vs 38.2 %, P < 0.05; ≥ 35: 48.6 % vs 41.1 %, n.s.)
- The overall blastocyst rate on Day 5 + 6 was higher in both age groups in G-Series with A3 (<35: 61.3 % vs 56.6 %; ≥ 35: 66.2 % vs 60.7 %) but not significant.
- The GQB rate on Day 5 + 6 was higher in both age groups in G-Series with A3 (<35: 57.5 % vs 23.5 %, 50.0 % vs 26.5 % and 50.0 % vs 25.8 %, respectively).

CONCLUSIONS: The strength of the present study was that the same donors give oocytes to different partners. Our results suggest that paternal age does not influence the clinical pregnancy. Although, prospective studies are need by using sibling oocytes.

SUPPORT: None

EMBRYO CULTURE

P-36 Tuesday, October 15, 2019 6:30 AM

MODELING OF AIRBORNE EMBRYOTOXIC VOLATILE ORGANIC COMPOUNDS (VOCs) IN THE IVF CULTURE ENVIRONMENT – THEIR CONCOMITANT CYTOTOXIC CONCENTRATION WITHIN THE GROWTH MEDIA AND EMBRYO. Kathryn Colonna Worrilow, Ph.D., a Alicia R. Urrutia, B.S., a Huey T. Huynh, M.S., a John T. Fox, Ph.D., b LifeAire Systems, Allentown, PA; bLehigh University, Bethlehem, PA.

OBJECTIVE: VOCs are a common component of laboratory ambient air. VOCs are unique in their polarity, molecular weight and structure and play a critical role in preimplantation toxicology and epigenetic processes. This study sought to define the mechanisms of cytotoxicity associated with VOCs found in the IVF culture environment. The concomitant concentrations of VOCs common to IVF laboratories were modeled with Henry’s Law (HL) from the gaseous to aqueous phase, and the final resulting concentration within the embryo was modeled with octanol water partitioning coefficients (OWPC).

DESIGN: HL was used to model VOC mass transfer from the air to the water/media phase. This model uses the air-water partitioning coefficient and the definition that the ratio between the liquid and air phase concentration is defined and unique for each organic compound. The OWPC was used for each compound to correlate the mass transfer from the water/media phase to the embryo using the ratio between the organic phase and water phase concentration.

MATERIALS AND METHODS: Evaluation of over 40 IVF laboratories identified the mean total VOC (TVOC) levels and 6 most common VOCs. HL and OWPC calculations determined the concomitant VOC concentrations in the culture media, embryo in culture, and time required to reach equilibrium for each compound. Research has shown that TVOC concentrations greater than or equal to 500 ppb in the media is embryotoxic and exerts a statistically significant impact on blastocyst conversion rates. Air phase VOC concentrations were compared to known embryotoxic VOC levels in cell culture media to determine if typical VOC levels in IVF laboratories are embryotoxic.

RESULTS: The concentration of each VOC within the embryo (Cembryo) was modeled based on airbone VOC levels measured. This modeled Cembryo was defined as 8 to 10-cells with even cells and low fragmentation; good quality Day 3 embryo development was significantly higher in the younger age group in G-Series with A3 (<35: 50.2 % vs 38.2 %, P < 0.05; ≥ 35: 48.6 % vs 41.1 %, n.s.)

More blastocyst were used for cryopreservation and transfer on Day 5 + 6 in G-Series with A3 in both age groups (<35: 41.2 % vs 37.2 %; ≥ 35: 43.5 % vs 38.8 %).

We noted no difference between G-Series with A3 vs G-Series in the younger age group for implantation per fertil sac, per fertil heart and for the ongoing pregnancy rate (<35: 50.6 % vs 55.3 %, 48.2 % vs 52.6 % and 48.1 % vs 52.6 %, respectively). A significant difference (P < 0.05) was found for the same parameters in the older age group for G-Series with A3 (≥35: 57.5 % vs 23.5 %, 50.0 % vs 26.5 % and 50.0 % vs 25.8 %, respectively).

CONCLUSIONS: In general the presence of antioxidants during IVF and embryo culture imparts significant benefits on day 3 embryo quality and a trend to better day 5 embryo quality and utilization rate. Implantation rates and ongoing pregnancy rates are significantly higher in media with A3 in patients with advanced maternal age but not in younger patients, but cumulative pregnancies could increase as more embryos were cryopreserved. Supplementation of antioxidants to culture media may improve the viability of human embryos in ART; plausibly through the reduction of oxidative stress, and improve clinical outcomes in certain age groups.

SUPPORT: Vitrolife sponsored part of the media for the study.
was compared to the embryotrophic level when embryos were cultured in an aqueous environment of 500 ppb VOCs. Levels of acetone, formaldehyde and isopropanol measured in IVF laboratories resulted in cytotoxic cellular levels.

CONCLUSIONS: Airborne VOCs are driven to reach equilibrium and can be magnified in concentration as they partition from the air to the cell culture media, and ultimately, into the embryo. Once cellular, the VOCs exert a negative influence on blastocyst conversion, implantation, and clinical pregnancy rates. This study related the measured concentration of airborne VOCs to the modeled concentration within the embryo. This novel study further defines the mechanisms of cytotoxicity of VOCs by defining their partition from the gaseous to aqueous phase, and most importantly, to the cellular phase. This data furthers our understanding of the role of VOCs in epigenetic variation and cytotoxicity.

P-37 Tuesday, October 15, 2019 6:30 AM

RANDOMIZED STUDY OF EMBRYO COMPETENCE AND DEVELOPMENTAL POTENTIAL IN GLOBAL BLASTOCYST MEDIUM AND G-TL MEDIUM, DESIGNED FOR TIME LAPSE. Nina Desai, Ph.D., HCLD, a Jeffrey M. Goldberg, M.D., b Rebecca Flyckt, MD, a Marjan Attaran, M.D., a Julie Tantibhedhyangkul, M.D., a Cynthia M. Austin, M.D. a aCleveland Clinic, Beachwood, OH; bCleveland Clinic, Cleveland, OH.

OBJECTIVE: Continuous uninterrupted culture of embryos to the blastocyst stage requires that the medium be able to support growth to day 6 without refreshment. Global Blastocyst (GB) medium initially formulated for conventional culture with medium exchange on day 3 has been used successfully in time-lapse (TL) chambers. Our study objective was to compare zygote performance in G-TL medium, designed for continuous culture to Global Blastocyst medium.

DESIGN: Randomization of sibling zygotes between culture media and retrospective analysis of embryo morphokinetic and outcome data

MATERIALS AND METHODS: A total of 7331 zygotes from consecutive non-PGS patients undergoing IVF from 2016 thru December 2018 were cultured in the Embryoscope TL chamber. G-TL (with human serum albumen-HSA) and GB medium with 10% added HSA protein supplement with globulins (SPS) were placed in the Embryoscope slide (6 wells per medium). Sibling zygotes were randomly distributed amongst wells and cultured at 37 °C with 6% CO2 /6% O2. Time lapse videos were annotated daily for cell divisions and dysmorphisms. The following kinetic markers were assessed: tSyn (syngamy), t2 (time to 2c), t3, t4, t5, t8, tM (fully compacted morula), tSB (start of blastulation), tBL (time of blastulation), tEBL (胚胎 compactation) for cryopreservation was calculated for each medium. Embryonic competence based on implantation (sac, fetal heart-FHT) in fresh and frozen SET cycles. Reprod Biol Endocrinology 12:54 (20 June 2014).A

RESULTS: With G-TL, 80% of blastocysts were BG3/4 as compared to 77% of GB blastocysts (p=0.003) but ICM/TE scores did not differ. Multinucleation was higher in GB vs G-TL (44 % vs 40%, respectively; p=0.009). Hatching process was faster in 3D gyration than the regular platform. There is no differences between the RPM or angle fit of 3D gyration. Also there is no differences between medium drop sizes from 0.01 to 0.6ml on 3D gyration. There is no differences between the RPM or angle fit of 3D gyration. Also there is no differences between medium drop sizes from 0.01 to 0.6ml on 3D gyration. ICM/TE count in day 5 blastocysts were not different. From real time-PCR, ZO-1 alpha gene was expressed in 3D gyration than the regular platform. According to these results, mouse embryo culture on 3D gyration rockers accomplished higher blastocyst and further hatched embryos.

CONCLUSIONS: The shear stress by 3D gyration rocker may induced mechanical stimuli and auto/paracrine effectors and improve the embryo development. This research was supported by NRF-017R1D1A1B03028155.

SUPPORT: This research was supported by NRF-017R1D1A1B03028155.

P-39 Tuesday, October 15, 2019 6:30 AM

GROUP EMBRYO CULTURE STRATEGIES AFFECT THE OXIDATIVE STATUS OF THE SPENT CULTURE MEDIA AND EMBRYO DEVELOPMENT. Lorena Bori, PhD, a Raquel Del Gallego, PhD, b Lucia Alegre, PhD, a Silvia Azafia, MSc, c Tamara Vitoria, PhD, a Marcos Meseguer, PhD, a IVIRMA Global, Valencia, Spain; bIVIRMA Global, Valencia, Spain, Tel Aviv, Israel.

OBJECTIVE: To describe the impact of the group embryo culture over the oxidative profile of the medium and over the fertilization and the blastocyst rates in two types of culture dishes from two time-lapse incubators.

DESIGN: A retrospective analysis, including 299 IVF cycles from May 2017 to December 2018, was conducted. Culture media from 413 groups

<table>
<thead>
<tr>
<th>GB</th>
<th>GT-L</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cultured zygotes (n)</td>
<td>3859</td>
<td>3472</td>
</tr>
<tr>
<td>Blasts (c)</td>
<td>2592 (67%)</td>
<td>2218 (64%)</td>
</tr>
<tr>
<td>Expanded blastocysts (%)</td>
<td>2390 (52%)</td>
<td>1722 (30%)</td>
</tr>
<tr>
<td>Embryo utilization (%)</td>
<td>2273 (59%)</td>
<td>1889 (34%)</td>
</tr>
<tr>
<td>GQE-Frozen (%)</td>
<td>1851 (48%)</td>
<td>1599 (46%)</td>
</tr>
<tr>
<td>Transfers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fresh SET IR-Sac (%)</td>
<td>82/142 (58%)</td>
<td>91/126 (62%)</td>
</tr>
<tr>
<td>Fresh SET IR-FHT (%)</td>
<td>80/142 (56%)</td>
<td>94/80 (62%)</td>
</tr>
<tr>
<td>Frozen SET IR-Sac (%)</td>
<td>81/124 (65%)</td>
<td>76/126 (60%)</td>
</tr>
<tr>
<td>Frozen SET IR-FHT (%)</td>
<td>77/124 (62%)</td>
<td>69/126 (54%)</td>
</tr>
</tbody>
</table>


Desai N, Goldberg I, Austin C, and Falcone T. Are cleavage anomalies, multinucleation, or specific cell cycle kinetics observed with time-lapse imaging predictive of embryo developmental capacity or ploidy? Fertil Steril 2018 109 (4A) 665-674

SUPPORT: None
of embryos (15 μl group) monitored with EmbryoScope Plus® (ES+) and Geri Plus® were analysed by the Thermochemiluminescence (TCL) AnalyzerTM (Carmel Diagnostics, Israel).

MATERIALS AND METHODS: A total of 299 spent embryo culture media from ES+ and 114 from Geri were analyzed. Sequential medium was used in 227 embryo groups and single-step medium in 186. The TCL AnalyzerTM consists on the heat-induced oxidation of biological fluids, leading to the production of light energy counted as photons emitted per second (cps). The oxidative parameters were obtained after 55 sec. (H1), 155 sec. (H2) and 255 sec. (H3). A smoothing algorithm (sm) was used to normalize data. Data were analyzed with ANOVA and Chi-squared tests (SPSS software).

RESULTS: Higher fertilization rates were found as the number of oocytes increased in the same group. However, blastocyst rate and the number of good quality blastocysts decreased when the number of embryos per group increased: 73.6±30.3% for ≤6 embryos, 69.0±23.7% for 7-8 embryos, 67.4±23.1% for 9-12 embryos and 64.9±23.2% for ≥13 embryos. The comparison between two time-lapse incubators with this kind of embryo culture showed significantly (p<0.05) higher fertilization rates for Geri (78.9±17.3% for Geri vs. 73.7±20.6% for ES+) and higher blastocyst rates for ES+ (70.6±26.7% for ES+ vs. 65.7±22.6% for Geri). According to our data, sequential culture medium worked significantly better (p<0.05) than single-step medium in terms of blastocyst rate (72.1±24.5% for sequential medium vs. 65.7±26.6% for single-step medium). In addition, oxidative stress level of the medium the fifth day post ICSI was significantly higher as more oocytes were successfully fertilized (Table). Table: Mean and standard deviation of the TCL parameters according to the number of successfully fertilized oocytes.

<table>
<thead>
<tr>
<th>Oocytes fertilized</th>
<th>N (Groups)</th>
<th>H1 (cps)</th>
<th>H2 (cps)</th>
<th>H3 (cps)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤4</td>
<td>117</td>
<td>88.7 ± 32.8</td>
<td>91.5 ± 34.9</td>
<td>98.3 ± 39.4</td>
</tr>
<tr>
<td>5-6</td>
<td>108</td>
<td>83.6 ± 35.9</td>
<td>85.8 ± 37.5</td>
<td>92.9 ± 41.5</td>
</tr>
<tr>
<td>7-8</td>
<td>93</td>
<td>103.3 ± 49.2</td>
<td>108.0 ± 54.5</td>
<td>117.1 ± 63.8</td>
</tr>
<tr>
<td>≥9</td>
<td>95</td>
<td>105.1 ± 32.3</td>
<td>109.9 ± 32.6</td>
<td>121.3 ± 37.1</td>
</tr>
<tr>
<td>P Values</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
</tr>
</tbody>
</table>

CONCLUSIONS: Group embryo culture strategies affect embryo development results: as the number of oocytes cultured per group increased fertilization rates were improved, but not blastocyst rates, which were higher when medium was replaced. Moreover, media’s oxidative stress level was higher when more fertilized oocytes were cultured per group.

P-41 Tuesday, October 15, 2019 6:30 AM

THE Efficacy of the new embryo culture medium which designed from the components of human tubal fluid: Prospective randomized trial. Takefumi Usunomiya, M.D., Ph.D., Yoko Kumasako, PhD, Eiko Otsu, PhD, Yufuko Kai, M.D., Ph.D., Yuichi Furukawa, M.D., Ph.D., Hiroko Itoh, M.D., Ph.D. St.Luke Clinic, Oita, Japan.

OBJECTIVE: Single and sequential step media are the most widely used for embryo cultures in IVF. There is no medium which designed from human oviductal fluid. Almost all media that available to use at present are derived and arranged from previous somatic cell culture media. In 2017, the medium (HiGROW OVT; Fuso Pharma, Japan) composed of amino acid concentrations by the data of human oviductal fluid became available to use in Japan, which contained different concentrations of amino acids from previous media. In this study, we examined the clinical availability of the new media in terms of utilization of embryos and giving birth to healthy baby in IVF.

DESIGN: Prospective randomized trial.

MATERIALS AND METHODS: Human oviductal fluid was aspirated laparoscopically from 28 women aged 26–39 years with no major intraepithelial abnormality to formulate new embryo culture medium. Liquid chromatography with tandem quadruple mass spectrometry and ion chromatography were used to analyze 31 components of the oviductal fluid sample. We conducted an RCT to evaluate the medium using 3,418 embryos obtained from 674 cycles of patients who underwent IVF or intracytoplasmic sperm injection (ICSI) between September 2017 and March 2019. Before fertilization, the oocytes were divided into two groups: cultures using the new medium composed of human oviductal amino acid (OVT); and cultures using current medium (Medium A). The embryo grade during culture period to the blastocyst stage and clinical outcome after embryo transfer were compared between the OVT group and the Medium A group.

RESULTS: Between the two groups, patient characteristics were not significantly different. The number of embryos in the OVT group on day 3 which showed “8-cell 2-grade” by Veeck’s criterion, was larger (18.6% (318/1,709)) than in the Medium A group (14.1% (241/1,709)); P<0.01. The OVT group showed significantly higher rates of blastocyst development (62.4% (1,024/1,641)) than the Medium A group (58.5% (961/1,643); P<0.05). The number of embryos which were elected for ET or cryopreserved was larger in the OVT group (44.4% (759/1,709)) compared with the Medium A group (37.2% (636/1,709)); P<0.01. Furthermore, in the OVT group had higher implantation rates (28.1% (124/442)) after ET than that in the Medium A group (25.5% (94/368); the difference was not statistically different. Birth weight of the OVT group was 3,179.2±473.3 grams (n=39) and the Medium A group was 3,087.1±409.1 grams (n=28). The ratio of male to female was 20:19 in the OVT group (n=39), and 10:16 in the Medium A group (n=26). One trisomic nascentium child was confirmed in the OVT group and one congenital ear fistula child was confirmed in the Medium A group.

CONCLUSIONS: Medium composed of human oviductal amino acids enhances embryonic ability more than the current single step medium, and it may make a contribution to clinical success in IVF treatment. References: none

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A NOVEL ZONA-FREE CULTURE SYSTEM FOR SEVERE CYTOPLASMIC FRAGMENTATION CASES: A PILOT STUDY USING 3PN EMBRYOS AND TIME-LAPSE CINEMATOGRAPHY. Keitaro Yumoto, M.D., Toko Shimura, B.S., Minako Sugishima, B.S., Yasuyuki Mio, MD. PHD “Mio Fertility Clinic, Yonago, Japan; ’Japan.

OBJECTIVE: A study in 2017 observed perivitelline threads in more than 50% of cleavage-stage human embryos using time-lapse imaging, and the rate of cytoplasmic fragmentation (at the first cleavage) was significantly decreased in embryos without perivitelline threads (P < 0.001). While it is proposed that perivitelline threads play an important role in crosslinking the cumulus cells and oocyte during maturation, the mechanism underlying such a role remains unclear. It is also unknown whether the threads still function in mature MII oocytes. Therefore, in this study, zona pellucida of abnormally-fertilized oocytes which were donated by patients was removed at pronuclear stage. Those zona-free oocytes were observed in time-lapse culturing system in order to examine developmental morphology.

DESIGN: Prospective study.

MATERIALS AND METHODS: This study used 57 abnormally fertilized (3PN) embryos (n=51, ICSI: n=6) donated by assisted reproduction technology patients in our clinic with informed consent since 2017. After confirming the three pronuclei, we removed the ZP from each 3PN embryo using a laser, and the resultant zona-free embryos were cultured and observed in an incubator equipped with a time-lapse imaging system. For ZP removal, 3PN embryos were placed in drops of 0.125M sucrose-containing HEPES media that had been covered with mineral oil and warmed to 37°C. Despite a small reduction in ooplasm size, half of the ZP was removed by laser (Satur n; Origos, Lykos; Hamilton Thorne). Subsequently, the ooplasm were completely separated from their ZPs by pipetting, and these zona-free 3PN embryos were cultured continuously for 5 days with time-lapse imaging.

RESULTS: Of 58 zona-free embryos in total, 54 (94.7%) were cleaved, and there was no significant decrease in cleavage rate compared to 2PN embryos (98%) used routinely in our clinic. Furthermore, 28 of the 54 embryos (51.9%) developed to the morula stage after third cleavage, and 18 embryos (33.3%) formed a blastocoele and became blastocysts. Thus, removing the ZP before cleavage did not adversely affect the embryo development. In terms of the amount of fragmentation, based on the modified Veeck’s criteria, 36 of 54 zona-free 3PN embryos (66.7%) showed less than 20% of the volume in fragments compared to the total volume of cytoplasm at the first cleavage (Grade 1 and 2), 14 (25.9%) showed 20-40% fragments (Grade 3), and only 4 (7.4%) showed > 40% fragments (Grade 4). These results suggested that the rate of fragmentation was decreased by ZP removal before the first cleavage.

CONCLUSIONS: This study revealed that the ZP is not always necessary for normal development after the pronuclear stage because the zona-free
embryos studied herein developed normally, maintained their cell adhesion well, and showed a decreased rate of fragmentation. This innovative culture system might provide the major breakthrough needed for patients who have difficulty obtaining good-quality embryos.

**SUPPORT:** None

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**TYPE OF CULTURE MEDIUM IS ASSOCIATED WITH PREIMPLANTATION EMBRYO DEVELOPMENT.** Linette van Duijn, MD, MElek Roussian, MD, PhD, Eva S. van Marion, MD, PhD, Joep S. E. Laven, MD, PhD, Régine P. M. Steegers-Theunissen, MD, PhD, Esther B. Baart, PhD.

- **Erasmus University Medical Centre, Rotterdam, Netherlands.**
- **Erasmus MC University Medical Centre, Rotterdam, Netherlands.**

**OBJECTIVE:** Previous research has demonstrated several influences of the periconception maternal environment on health later in life. The culture medium used in IVF/ICSI treatment, however, can be considered as an artificial environment for the preimplantation embryo. Since the introduction of the EmbryoScope™ time-lapse incubator preimplantation embryo development can be closely observed. The aim of this study is to investigate the influence of two commercially available culture media on the developmental kinetics of the pre-implantation embryo, and IVF/ICSI treatment outcome.

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** Data were obtained between 2012-2017 of 545 women undergoing their first IVF/ICSI treatment at the Erasmus MC. In this period Vitrolife G1 (n=225) and Sage 1-Step (n=220) culture media were used subsequently. Embryos were cultured until day 3 of development in the EmbryoScope™ time-lapse incubator and morphokinetic parameters of all transferred and frozen embryos were retrospectively annotated and not used for embryo selection. Treatment and patient characteristics were retrieved from medical records. Crude and adjusted associations between culture media and morphokinetic parameters were investigated using linear mixed models. Differences in treatment outcome were assessed by logistic regression.

**RESULTS:** Embryos cultured in Sage 1-Step medium show faster development over all developmental stages (from fading of pronuclei to 8-cell stage) compared to Vitrolife G1. For example, embryos cultured in Sage 1-Step reach the 2-cell stage 2.08 (95%CI 1.57-2.60) and 8-cell stage 3.61 (95%CI 1.78-5.44) hours faster, respectively. After adjustment for female age, fertilisation method, type of ovarian stimulation, lowered oxygen culture and overall embryonic improvement over time, embryos cultured in Sage 1-Step reach the 2-cell stage 3.07 (95%CI 1.18-5.62) and 8-cell stage 9.89 (95%CI 2.80-16.99) hours faster. After adjustment for female age, fertilisation method and type of ovarian stimulation, embryos cultured in Vitrolife G1 demonstrated similar odds for positive β-hCG-test, fetal heartbeat and liveborn, when compared with embryos cultured in Sage 1-Step medium.

**CONCLUSIONS:** When compared to embryos cultured in Vitrolife G1, embryos cultured in Sage 1-Step culture medium are associated with faster development, however ongoing pregnancy rate is not significantly different. Our statistical approach enables analysis of the whole cohort of usable embryos per patient for an association between the type of culture medium and developmental kinetics. As embryo kinetics are likely to reflect embryo metabolism, the type of culture medium may impact embryo metabolism but not implantation potential. Further prospectively collected data is needed to unravel the relation between pre-implantation embryo kinetics and post-implantation development.

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**EMBRYO CULTURE IN TIME-LAPSE SYSTEM PROVIDES BETTER RATES OF BLASTOCYST FORMATION, DECREASES EMBRYO DEVELOPMENT ARREST RATE COMPARED TO TRADITIONAL TRIPLE-GAS CULTURE SYSTEM.** Mariana Niccolini, BSc, Catherine Jacobs, BSc, Andrea Belo, BSc, Ana Paula Reis, BSc, Renata Erberelli, BSc, Fabiana Mendez, BSc, Marina Fanelli, BSc, Livia Cremonesi, BSc, Paulo Cesar Serafini, MD, Phd, Eduardo LA. Motta, MD, PhD, Aline R. Lorenzo, PhD, Jose Roberto Alegetti, MSc "Huntington Medicina Reprodutiva, Sao Paulo, Brazil; "Huntington Medicina Reprodutiva, Clinical Department, Sao Paulo, Brazil; "Scientific Coordinator, Huntington Medicina Reprodutiva, Sao Paulo, Brazil.

**OBJECTIVE:** Evaluate rates of blastocyst formation and embryo development arrest between uninterrupted (time-lapse) and triple-gas (90% N2, 5% CO2, 5% O2) systems.
DESIGN: This is a cohort study analyzing laboratory data between January 2018 and March 2019 at Huntington Medicina Reproductiva Clinic in São Paulo, SP, Brazil.

MATERIALS AND METHODS: A total of 1,276 cycles of IVF were evaluated. Single-step culture media formed the traditional triple-gas system (90% N₂ / 5% CO₂ / 5% O₂). Mean age 37.56±3.59 years old and embryos were externally evaluated on days 1, 3, 5 and 7, if applicable. In the time-lapse group (EmbryoScope®), 595 cycles, mean age 37.54±3.47 years old, were cultured uninterrupted. Blastocyst formation rate (no. blastocysts/no. 2PN), blastocyst mean number formed per cycle, and cycle cancellation rate due to embryo development arrest were compared.

RESULTS: A total of 9,482 mature oocytes followed in vitro fertilization. 4,936 in the triple-gas group and 4,546 in the time-lapse group, being fertilized 3,565 (72.23%) and 3,473 (75.30%) oocytes, respectively. From those, 1,791 blastocysts were formed in the traditional incubator group and 1,942 in the time-lapse group (50.2% versus 56.7%, p = 0.001, chi-square test). Blastocyst mean number formed in the time-lapse group were generally higher than the control group (3.4±2.8 versus 2.7±2.8 p < 0.0001, t-test). When maternal age was considered in analysis, ages between 35 and 42 years old showed gains in blastocysts mean number formed in time-lapse group: a) 34 years or less, no difference (4.1±3.1 versus 3.9±3.3, p = 0.34); b) 35 to 37 years, higher in time-lapse group (3.8±3.2 versus 3.0±2.7, p = 0.02); c) 38 to 40 years, higher in time-lapse group (3.2±2.6 versus 2.4±2.5; p = 0.0003); d) 41 to 42 years, higher in time-lapse group (2.6±2.2 versus 1.8±2.3; p = 0.001) and e) 43 years or older, no difference (1.7±1.4 versus 1.4±1.4, p > 0.05). Embryo developmental arrest rate was also lower in the time-lapse group (11% versus 15%, respectively; p = 0.05, chi-square test).

CONCLUSIONS: The uninterrupted culture available at the time-lapse system produced better blastocyst formation rates, especially between 35 and 42 years old, lower embryo arrest rate and mainly with the ability to produce approximately 01 (one) extra blastocyst per cycle, which could increase the cumulative pregnancy rates. Considering younger (<34 yo) or older women (>43 yo) no benefits were shown from time-lapse to traditional culture systems, possibly due to a better or worst oocyte quality. Our results indicate that uninterrupted systems are important to enhance blastocyst formation and may play a fundamental aspect for cumulative pregnancy rate producing an extra embryo.

EMBRYO PHYSIOLOGY

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INHIBITION OF LINE-1 TRANSCRIPTION BLOCKS TELOMERE ELONGATION AND DOWNREGULATES TOTIPOTENCY GENES DURING MOUSE EMBRYO DEVELOPMENT. Isaac J. Chamani, B.A., Fang Wang, PhD, Danxia Luo, MD, Paula Andorra Navarro, MD, Vanessa Lynn Cortes, B.A., David L. Keefe, M.D. New York University School of Medicine, New York, NY. New York University School of Medicine, Department of Obstetrics and Gynecology, New York, NY.

OBJECTIVE: During preimplantation embryo development, the telomere aging clock resets and 2-cell genes establish totipotency. Like most long-lived cells, oocytes have short telomeres, but telomeres elongate markedly during early embryo development, even in the absence of telomerase. Recent studies report that the retrotransposon, LINE-1, is activated after fertilization, when telomeres elongate. Retrotransposons protect chromosome ends in many species, so we hypothesized that inhibiting retrotransposition of LINE-1 during mouse early embryos would disrupt telomere elongation. This suggests that 2-cell genes are activated at synthesis phase of the 2-cell stage. Moreover, LINE-1 synthesis by AZT blocks telomere elongation. AZT also inhibits the 2-cell genes, DUX and Zscan4d, suggesting that LINE-1 is essential not only for telomere reprogramming but also for the establishment of totipotency during early development.


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HYPERGLYCOLYSED HUMAN CHORIONIC GONADOTROPIN IN BLASTOCYST CULTURE MEDIUM OF MALE AND FEMALE HUMAN EMBRYOS. Georgi Stamenov Stamenov, MD/PhD, Kristina Nikolova, MSc, Magdalena Vasileva, MSc, Iwayo Rangelov, MSc, Rumiana Ganeva, MSc, Maria Pancheva, MSc, Maria Serafimova, MSc, Rada Staneva, MD, PhD, Savina Hadjidekova, MD/PhD, Fabio Scarpellini, MD, Dimitar Parvanov, PhD, Nadezhda Women’s Health Hospital, Sofia, Bulgaria; Department of Medical Genetics, Medical University of Sofia, Sofia, Bulgaria; Centre for Endocrinology and Reproductive Medicine, Rome, Italy.

OBJECTIVE: The hyperglycosylated human chorionic gonadotropin (hCG-H) is considered a good marker of early trophoblast invasion. However, little is known about its production and secretion during the first five days of embryo development. The aim of this study is to compare the levels of hCG-H in culture media from male and female human embryos.

DESIGN: Observational study.

MATERIALS AND METHODS: Single-step culture media samples from 78 good quality embryos, derived from good prognosis patients undergoing intracytoplasmic sperm injection (ICSI), were collected on the fifth day of embryo cultivation. All embryos were tested by next-generation sequencing (NGS) technique and only the balanced ones were used for analysis. hCG-H levels in the culture media were evaluated by ELISA kit (Cusabio Biotech, CBS-E15803h) according to the manufacturer’s instructions. The absorption was measured on a microplate reader (Beckman Coulter DTX 880 Multimode detector) at 450 nm. Data analysis was performed using SPSS v21 (IBM Corp., Armonk, NY, USA). Descriptive parameters and patients’ characteristics were reported as mean ± SD. P<0.05 was considered statistically significant.

RESULTS: The NGS analysis revealed that 37% of the embryos (n=29) were balanced, 48% (n=14) of them were female (XX) and 52% (n=15) were male (XY). The presence of hCG-H was confirmed in all embryo culture media samples. When comparing culture media samples from male versus female embryos hCG-H levels were not significantly different (0.09 ± 0.01 mIU/ml vs. 0.10 ± 0.03 mIU/ml; P = 0.37, respectively). However, the variety in hCG-H concentration was significantly lower in the samples from male embryos compared to female ones (Levene’s Test for Equality of Variances, p = 0.004).

CONCLUSIONS: Our results suggest that the chromosomal sex of human embryos could have an effect on the secretion of hCG-H. The female embryos produce more variable quantities of hCG-H compared to the male ones.

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STUDY ON THE RELATIONSHIP BETWEEN PRONUCLEAR PROXIMITY IN ZYGOTE AND MULTINUCLEATION OF EARLY CLEAVAGE EMBRYOS IN HUMAN USING TIME-LAPSE SYSTEM. So Young Kim, M.S., Sojung Kwon, PhD, Soyoung Bang, M.S., Wonyun Choi, PhD, Jin Hee Eum, Ph.D, Hyunjin Kim, M.D., Han Moie Park, M.D.Ph.D, Jin Young Kim, M.D. Ph.D, Eun Mi Chang.
OBJECTIVE: It has recently been reported that two separate bipolar spindles aligned their poles before anaphase keeping the parental genomes apart during the first cleavage in mammalian zygote including mouse and human. In mouse, the failure of spindle alignment by increasing the distance between the two pronuclei, which led to a larger gap between the spindles, gives rise to multinucleated two-cell embryos phenocopying frequently observed errors in IVF clinics. The purpose of our study is to examine the relationship between pronuclear (PN) proximity in zygote and multinucleation (MN) of early cleavage embryos in human using time-lapse system (TLS).

RESULTS: The incidence of gap between PN was considerably low (G; 31.2% vs. J; 92.3%). The average of PN distance was significantly different between two groups (G: n=17) and group Juxtaposition [J; n=203]). The number of MN in 2-cell and 4-cell embryo was checked then the embryos were divided into three groups (No MN, MN, and N/A; not available due to abnormal division). Embryo development was checked up to day 3. The quantitative variables were expressed as mean ± SD and statistically analyzed with Student t test. p <0.05 was considered to be statistically significant.

RESULTS: The incidence of gap between PN was considered low (G; 7.7% vs. J; 92.3%). The average of PN distance was significantly different between two groups (G; 31.2 ± 5.1 μm vs. J; 21 ± 4.9 μm, * p < 0.05). The rate of No MN (23.5%[2C] and 52.9%[4C]) was highly decreased but the rate of MN (41.4%[2C] and 5.9%[4C]) and N/A (35.3%[2C] and 41.4%[4C]) was increased in the Group compared with Juxtaposition group (49.8%[2C]/4C, 38.4%[5%/2C]/4C, and 11.8%[21.7%[2C]/4C]). Also the rate of 3D good quality embryo is slightly decreased in Group J (82.4% vs. J; 89.7%).

CONCLUSIONS: This study suggests that the PN proximity is also one of the applicable explanations for the MN in early cleavage embryos of human due to the failure of zygotic spindle alignment as other mammalian embryos such as mouse. As the occurrence of MN in human embryos, especially during the first and second mitotic divisions, is generally considered to be abnormal, our study on the relationship between PN proximity and MN combined with TLS could be used as a noninvasive technique to enhance selection of competent embryos likely to have the greatest potential of development. This may be of particular benefit to patients desiring elective single embryo transfer without PGS screening.

MATERIALS AND METHODS: We assessed the PN proximity, distance, MN, and development of early cleavage embryos using EmbryoScope® Vi-trolight. Gothenburg, Sweden. Drawing tool was used to measure the distance from a PN center to another PN center in the same focal plane before PN fade. Zygotes were divided into two groups according to the proximity (group Gap [G; n=17] and group Juxtaposition [J; n=203]). The number of MN in 2-cell and 4-cell embryo was checked then the embryos were divided into three groups (No MN, MN, and N/A; not available due to abnormal division). Embryo development was checked up to day 3. The quantitative variables were expressed as mean ± SD and statistically analyzed with Student t test. p <0.05 was considered to be statistically significant.

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FERTILITY & STERILITY®

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OXIDATIVE STRESS IN HUMAN TESTICULAR TISSUE BEFORE AND AFTER CRYOPRESERVATION: A COMPARATIVE STUDY. Alaa Moubasher, MD, a Hanan Mory, MD, b Ay Hassan Younis, MD, b Mikel Effat, MD, c Emad Taha, MD d Assiut University, Assiut, Egypt; Affiliation not provided; e Assiut University, Biochemistry department, Assiut, Egypt.

OBJECTIVE: To compare oxidative stress in human testicular tissue in both cases of obstructive(OA) and non-obstructive or functional azoospermia (NOA) before and after cryopreservation.

RESULTS: The study included 21 OA (group A), 16 positive NOA (group B) and 21 negative NOA (group C) with negative sperm retrieval. Mean CAT activity in positive and negative NOA groups (151.90 ± 122.32 U/gm protein) and (146.00 ± 121.7U/gm protein respectively), were significantly higher than OA group (65.67 ± 72.99 U/gm protein respectively), (P=0.017, P=0.018 respectively). MDA level was also significantly higher in positive and negative NOA (31.50 ± 15.81nmol/gm) compared with OA (20.33 ± 9.61nmol/gm) (P=0.043, P=0.0000 respectively).CAT activity and MDA level correlated negatively with mean number of retrieved sperms in groups with positive sperm retrieval A&B (r= -0.261, P= 0.048, r= -0.402, P=0.002 respectively). After thaw there was significant increase in CAT activity in OA only (213.67 ± 160.36 v 65.67 ± 72.99 U/gm protein) (P=0.000), while there was no significant difference in MDA level in both OA and positive NOA. However, after thawing mean MDA level was still significantly higher in NOA than OA (26.94 ± 11.21 vs 24.19 ± 15.97 nmol/gm) (P= 0.049).

CONCLUSIONS: Men with NOA seem to have increased basal testicular oxidative stress compared to those with OA as indicated by increased CAT activity and MDA level in fresh testicular samples. These markers of oxidative stress correlated negatively with spermatogenic activity. Furthermore, OA seem to resist oxidative injury induced by cryopreservation by enhancing CAT activity more efficiently than NOA.

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SELF-CORRECTION OF ANEUPLOIDY IN HUMAN BLASTOCYSTS AND SELF-ORGANIZING GASTRULOIDs. Tiago Rito, PhD, b Jeff Naftaly, BA, b Norbert Gleicher, MD, c Ali H. Brivanlou, PhD, d Rockefeller University, New York, NY; e Center for Human Reproduction, New York, NY.

OBJECTIVE: Finding of aneuploid cells in trophoderm biopsies at blastocyst stage is currently considered cause for disposal of embryos. Degree of tolerated aneuploidy and whether embryos self-correct downstream have, however, become one of the most controversial issues in reproductive medicine. Objective of this study was, therefore, investigation of degree of self-correction of aneuploidy in human blastocyst-stage embryos and in an in vitro model of early human gastrulation - gastruloids.

METHODS: We tracked aneuploidy in pre-implantation human embryos using single-cell RNA-seq data and conducted prospective in vitro studies on the impact of aneuploidy on human gastrulation.

MATERIALS AND METHODS: We induced aneuploidy in human embryonic stem cells by treatment with reversine, an inhibitor of MPS1, crucial for the spindle assembly checkpoint and the error correction pathway during cell division. Aneuploid and euploid cells were mixed to generate chimeric human gastruloids and their developmental outcomes were measured using a highly quantitative micropatterning platform. To provide in vivo relevance, we used a computational approach to track aneuploidy in pre-implantation human embryos using single-cell RNA-seq data.

RESULTS: Aneuploid colonies did not affect maintenance of pluripotency, albeit displaying increased TP53. Chimeric euploid-aneuploid differentiated gastruloids showed differential cell death. This was particularly acute in the ectodermal (SOX2+) and mesendodermal (BRAA+, SOX17+) lineages, without affecting extra-embryonic (GATA3+CDX2+) tissue. Using bioinformatics, we showed the presence of wide-spread but selective chromosomal instability in human blastocysts. The gene expression signature of aneuploid cells was closely associated to that of euploid cells and, consistent with the above noted gastruloid studies. Originally high levels of aneuploidy (up to 50%) gradually corrected themselves with time.

CONCLUSIONS: Similarly to the mouse, aneuploidy is tolerated in human embryos in extra-embryonic tissue but not in cells contributing to the embryo proper. Altogether, these results strongly suggest that presence of aneuploidy in human trophectoderm is not an indicator of embryo quality to be used for embryo selection in human IVF.

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EMBRYO RESPIRATION TO EVALUATE THE EMBRYO QUALITY AND VIABILITY, AND ITS CLINICAL OUTCOME. Atsushi Fukui, MD, PhD, Yuji Ukita, MD, Ryo Takeyama, MD, Toru Kato, MD, Hiroaki Shibahara, MD, PhD. Hyogo College of Medicine, Nishinomiya, Hyogo, IL, Japan.

OBJECTIVE: Earlier prediction of the quality and viability of in vitro developing embryo is very important. The measurement of embryo oxygen consumption, that is embryo respiration may be one of the objective methods to know the embryo quality and viability. Oxygen consumption is an ideal indicator of overall metabolic activity because ATP is generated
RESULTS: Human preimplantation embryos show endogenous DNA damage, demonstrated by γH2AX, RPA and abnormal nucleation. Cleavage embryos had significantly greater foci and micronucleation vs blastocysts (γH2AX cleavage mean 2.3 vs blastocyst 1.0, p <0.0001; RPA cleavage mean 1.7 s.c. 1.3, p<0.0001; abnormal nucleation cleavage mean 15.9% vs blastocyst 4.2%, p<0.0001). DNA damage foci coincided with RPAS33, indicating RPA phosphorylation by G2 checkpoint kinase ATR, Rad51, indicating repair by homologous recombination, and 53BP1, indicating unpaired DNA is passed to daughter cells.

Aphidicolin-induced replication delay resulted in DNA damage (γH2AX and RPA), and RPAS33, indicating an ATR-dependent G2 checkpoint. Additional DNA repair mechanisms included Rad51 and 53BP1, similar to human embryos. Though some unreplicated DNA is tolerated in mitosis and compatible with euploidy, aphidicolin-induced under replication in the first cell cycle precipitated instability in later cell cycles, leading to decreased blastulation (45% after 8h aphidicolin vs 91.8% control, p<0.0001), and poor quality embryos as evidenced by significantly fewer total cells and inner cell mass with significantly greater DNA damage and micronucleation with increasing duration of aphidicolin exposure compared to controls.

CONCLUSIONS: DNA damage responses to incomplete replication in G2 (ATR and Rad51), and the G1 response to unreplicated DNA (53BP1) mirror endogenous repair activity in human preimplantation embryos. Developmental consequences of replication stress likely persist beyond the preimplantation stage and may contribute to failed implantation or miscarriage. The murine model of genomic instability enables further study of these processes and the development of targeted therapeutics.


SUPPORT: New York Stem Cell Foundation (NYSCF), New York State Stem Cell Science Program (NYSTEM).

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OBJECTIVE: During in vitro fertilization (IVF), variations in zona pellucida (ZP) thickness are frequently observed in retrieved oocytes. It is possible that these variations in ZP appearance are caused by the alteration of patterning glycoprotein matrix, which may be associated with oocyte cytoplasmic competence for embryonic development. In the present study, a large cohort of 1,664 oocytes was evaluated to understand the relationship between ZP thickness and embryonic outcomes.

DESIGN: This was a retrospective, single-center, cohort study.

MATERIALS AND METHODS: A retrospective study on 1,664 oocytes from 978 cycles (827 patients, mean age: 40.7 ±0.1 years) was conducted from August 2018 to January 2019 in a single center. All patients underwent clomiphene citrate-only minimal stimulation IVF cycles. Maturation status of oocytes was confirmed by the appearance of meiotic spindles and oocytes were inseminated by intracytoplasmic sperm injection (ICSI). The ZP thickness was measured relative to a line drawn along the major axis of the oocyte. Two ZP thickness measurements were taken at opposite sides of the line and values were averaged. Spearman’s correlation coefficient was used to evaluate the relationship between the age of the female and ZP thickness. Multivariable logistic regression analysis, which included all significant confounding factors, yielding adjusted odds ratios (ORs) and 95% confidence intervals (CIs), was used to evaluate the correlation of ZP thickness to embryonic outcomes. Values were considered statistically significant when p-values were <0.05.

RESULTS: The mean ZP thickness was 19.0±1.1 μm. A significant negative correlation was observed between ZP thickness and age of the female (Spearman’s correlation coefficient, r = -0.0656, p =0.0078). Fertilization, cleavage, blastocyst formation, and blastocyst utilization rates in this cohort were 45.6%, 14.3% (1,439/10,064), 76.6% (1,439/1,940), 67.4%, and 42.7% (709/1,664), respectively. Multivariable logistic regression analysis revealed that there were no statistically significant associations between ZP thickness and fertilization (adjusted OR: 1.011, 95% CI: 0.960-1.065, p =0.6725), cleavage (adjusted OR: 0.991, 95% CI: 0.942-1.042, p =0.7303), blastocyst formation (adjusted OR: 0.974, 95% CI: 0.940-
1.011, p=0.1637), and blastocyst utilization (adjusted OR: 0.003, 95% CI: 0.957-1.031, p=0.7168).

CONCLUSIONS: The properties of ZP have been considered to reflect the history of oocyte cytoplasmic maturation. Our results demonstrate that ZP thickness has no relation with embryonic outcomes, suggesting that variations in ZP thickness do not influence oocyte cytoplasmic competence for embryonic development.

SUPPORT: None

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IDENTIFICATION OF NUCLEOLAR CHANNEL SYSTEMS (NCSs) IN ENDOMETRIAL SECRETIONS AT THE TIME OF FROZEN EMBRYO TRANSFER IN ARTIFICIAL CYCLES WITH SUCCESSFUL IMPLANTATION: Rachel S. Gerber, MD,a Erkan Buyuk, MD,a Harry Lieman, MD,a U. Thomas Meier, Ph.D,a,b Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY; bDept. of Anatomy & Structural Biology, Albert Einstein College of Medicine, Bronx, NY.

OBJECTIVE: NCSs are histological markers of the window of implantation in natural and controlled ovarian hyperstimulation cycles. Thus far, NCSs have not been detected in frozen embryo transfer artificial (FET-A) cycles. This study aims to detect NCSs in endometrial aspirations obtained immediately prior to embryo transfer during blastocyst FET-A cycles without affecting implantation.

CONCLUSION: Prospective study at a single university-affiliated site

MATERIALS AND METHODS: Patients undergoing FET-A using estradiol and progesterone for endometrial preparation are consented for a lower uterine segment aspiration using an open tip embryo transfer catheter during a mock embryo transfer performed immediately prior to the actual embryo transfer. The aspirated endometrial secretions containing endometrial cells are then analyzed for the presence of NCSs using indirect immunofluorescence. Based on a prior study, positive NCS status was defined as the presence of NCSs in at least 3 endometrial epithelial cells (EECs). Pregnancy outcomes are monitored to ensure that there is no effect of the aspiration on implantation rates.

RESULTS: Uterine secretions were obtained from 5 patients immediately prior to embryo transfer. The average age of women was 37.2 ± 4.2 years. NCSs were detected in exfoliated EECs of uterine secretions in 4 of 5 (80%) samples and could not be unequivocally identified in 1 of 5 (20%), which was designated as indeterminate. Implantation as evidenced by a positive BHC immunostaining was seen in 5 of 5 (100%) of the patients who underwent aspiration with a clinical pregnancy rate of 40% and an ongoing pregnancy rate of 20%.

CONCLUSIONS: This is the first report of NCS detection in FET-A cycles in the absence of follicular development and ovulation. NCS status can be determined in exfoliated EECs of uterine secretions obtained at the time of embryo transfer while maintaining implantation. Our study provides proof of principle to determine endometrial receptivity through individualized point of care testing of NCS status during frozen embryo transfer in artificial cycles.

SUPPORT: This study was supported by a grant from the NIH (HD949293 to U.T.M.).

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SINGLE-CELL MITOCHONDRIAL STAINING OF HUMAN BLASTOCYSTS: Taraneh Gharib Nazem, MD,a Kristin Beaumont, PhD,a,b Christine Briton-Jones, PhD, HCLD,b Joseph A. Lee, BA,a Robert P. Sebra, PhD,a Alan B. Copperman, MD.a 1Institute of Reproductive Medicine at Mount Sinai, New York, NY; 2Reproductive Medicine Associates of New York, New York, NY; 3Sema, a Mount Sinai Venture, Stamford, CT.

OBJECTIVE: Physicians are looking beyond chromosomal copy number to understand why some euploid embryos fail to implant. Studies investigating the contribution of mitochondrial (mt) DNA levels on implantation have shown some association between mt and embryonic competence, but these studies are limited, as DNA count has been estimated based on limited sampling of trophectoderm (TE). As mt are the primary energy source of embryonic cells, characterization of mt activity rather than DNA copy number might offer insight into embryonic competence. This study aimed to characterize mt activity on the single cell level in human blastocysts as a marker of embryonic quality.

CONCLUSION: Mitochondrial activity (MT) was measured by Cytopainter staining, a method that combines restriction digestion and bisulfite sequencing to enrich for cytosine residues and guides differentiation during embryonic development. As its accuracy and efficiency is essential for embryo viability, DNA methylation (DNAme) has been used to detect these epigenetic changes on the single cell level to gain insight into genomic markers and drivers of embryonic development and competence.

SUPPORT: None

P-55 Tuesday, October 15, 2019 6:30 AM
COMPARATIVE ANALYSIS OF DNA METHYLATION IN EUPLOID AND ANEUPLOID HUMAN EMBRYOS USING REDUCED REPRESENTATION BISULFITE SEQUENCING: Xin Tao, Ph.D.a Yiping Zhan, Ph.D.b Katherine Scott, MS,a Richard Thomas Scott, Jr., MD,a Emre Seli, M.D.a “The Foundation for Embryonic Competence, Basking Ridge, NJ; bFoundation for Embryonic Competence, Basking Ridge, NJ; cIVI-RMA Southern California, Los Angeles, CA; dIVI-RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: DNA methylation (DNAme) is a fundamental epigenetic control mechanism that occurs by the addition of methyl (CH3) groups to cytosine residues and guides differentiation during embryonic development. As its accuracy and efficiency is essential for embryo viability, DNAme has the potential to be a marker for embryonic reproductive competence. Reduced representation bisulfite sequencing (RRBS) is a high-throughput technique that combines restriction digestion and bisulfite sequencing to enrich for highly methylated regions of the genome, allowing analysis of genomewide methylation profiles on a single nucleotide level. In this study, we used RBBS to characterize differences in DNAme profiles of euploid and aneuploid human blastocysts.

SUPPORT: None

MATERIALS AND METHODS: Two trophoectoderm (TE) biopsycs from each of the 10 previously diagnosed euploid and 10 aneuploid embryos were analyzed. The libraries were prepared with cell lysis, MspI digestion, end repair/AdA-T tailing, adapter ligation, bisulfite conversion, and amplification, then sequenced using Illumina HiSeq 2500 with paired-end 150 bp reads. The sequencing reads were trimmed to remove the adapter read through and filtered to eliminate the reads without the MspI recognition sites, then aligned to the reference using Bismark software. Unconverted reads were filtered. The methylation profiles at the GC-rich regions were compared in euploid and aneuploid human embryos.

RESULTS: The overall whole genome CpG coverage of the TE biopsies was 5-10%, which was the expected as RRBS detects 1-2 million CpG sites
of whole genome (28.7 million CpG sites). The average DNAme level was 15%. Aneuploid embryos showed significantly lower DNAme levels compared to euploid embryos (p<0.0001). Increased patient age was corre-
lated with elevated DNAme levels in blastocysts (p=0.04). Blastocyst cry-
opreserved on day 6 had significantly lower DNAme compared to those that were cryopreserved on day 5 (p=0.001). Whole chromosomal aneuploidy predicted by calculating the fraction of read count from each chromosome showed 100% consistence with previous diagnosis. The chromosomes involved in monosomy embryos (-4,-13,-16, and -18) showed reduced methylation rates compared to the other chromosomes.

CONCLUSIONS: DNAme levels detected by RRBS in trophoectoderm biopsies from human blastocysts is associated with ploidy status, maternal age, and embryo growth characteristics. This novel tool could provide a foundation for the development of epigenetic biomarkers of reproductive competence.

P-56 Tuesday, October 15, 2019 6:30 AM
MATERNAL AGE AND BLASTOCYST QUALITY DO NOT INFLUENCE THE EMBRYO PRODUCTION OF HYPERGLUCOSYLATED HUMAN CHORIONIC GONADOTROPIN. Dimitar Parvanov, Ph.D., Dragomira Nikolova, Ph.D., Rumiana Ganeva, MSc, Kristina Nikolova, MSc, Magdalena Vasileva, MSc, Ivaylo Rangelov, MSc, Fabio Scarpellini, MD, Giorgi Stamenov Stamenov, MD/PhD, Nadezhdra Women’s Health Hospital, Sofia, Bulgaria; Department of Medical Ge-

etics, Medical Faculty, Medical University – Sofia, Sofia, Bulgaria; Centre for Endocrinology and Reproductive Medicine, Rome, Italy.

OBJECTIVE: The purpose of the study was to evaluate the associations between the human embryo quality, maternal age and the amount of human chorionic gonadotropin (hCG-H) in the secretome of in-vitro cultured em-

bryos.

DESIGN: Observational study.

MATERIALS AND METHODS: Individual embryos from 49 women were cultured to the blastocyst stage in 25 μL of single-step culture medium in the EmbryoScope. Media samples (n=54) were collected on day 5 from wells containing good, fair or poor quality blastocysts, respectively. Media from wells without an embryo were also collected as controls. The quality of the embryos was assessed morphologically. Measurement of hCG-H concentra-
tion in culture media is performed with ELISA kit (Cusabio Biotech, CBS-E15803h) according to the manufacturer’s instructions. The absorption of each media sample was measured at 450 nm. SPSS v.21 is used for the statistical analysis (IBM Corp., Armonk, NY, USA). P<0.05 indicates the statistical significance between the compared groups.

RESULTS: The mean age of the patients included in the study was 38.08 ± 4.28 years. The number of observed Day 5 good, fair and poor quality blastoc-
tocysts was 26, 22 and 6, respectively. The presence of hCG-H was confirmed in both culture media samples but was absent in the controls. Compar-
ison between poor, good and excellent quality embryos was made by Mann-
Whitney U test as parameters were not normally distributed. The measured mean hCG-H levels were not significantly different between poor, fair and good quality embryos (0.095 μIU/mL vs. 0.095 μIU/mL vs. 0.08 μIU/mL; p=0.91, respectively). In addition, there was a lack of significant correlation between women’s age and the level of hCG-H, produced by embryos (R=−0.17, p=0.23).

CONCLUSIONS: Our results suggest that the embryo’s secretion of hCG-
H is not influenced by maternal age and morphological quality of human blastocysts.

P-57 Tuesday, October 15, 2019 6:30 AM
EVALUATING THE ABILITY OF AN OOCYTE TO REPAIR FRAGMENTED SPERM CHROMATIN. Derek Keating, B.A., Alessandra Parrella, M.Sc., Zev Rosenwaks, M.D., Gianpietro D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To evaluate the ability of oocyte DNA repair mechanisms to detect and fix deficiencies in sperm chromatin integrity and support embryo implantation.

DESIGN: From 2006-2017, ejaculates from 127 men were assessed for sperm chromatin fragmentation (SCF). Intracytoplasmic sperm injection (ICSI) clinical outcomes were divided into groups according to the SCF level of the male partner and the proportion of mature oocytes obtained at retrieval. Proportional oocyte nuclear maturity was considered an indirect marker for presumed cytoplasmic readiness of the oocyte, suggesting its ability to repair the male chromatin during late oocyte maturation.

MATERIALS AND METHODS: Samples from consenting couples were screened for SCF levels by terminal deoxynucleotidyl dUTP nick-end label-
ing (TUNEL) utilizing a commercially available kit. A minimum of 500 sper-
matozoa were assessed per patient, and an SCF of 15% or below was consid-
ered normal. From the retrieved cohort, the proportion of meta-
phase-II oocytes at the time of ICSI was recorded and used for this assess-
ment. ICSI was performed in the standard fashion. Female partners were limited to ≤35 years of age to control for eventual confounding female fac-
tors.

RESULTS: A total of 127 couples underwent 191 ICSI cycles. Of them, 84 couples in which the male partner had a normal SCF level (9.8±13%) under-
went 125 ICSI cycles; conversely, 43 couples in which the male partner had an abnormal SCF level (24.1±11%; P < 0.0001) underwent 67 ICSI cycles.

When the proportion of mature oocytes was over 80% at the time of re-
trieval, there was no difference in the ICSI clinical outcome between coup-
les with normal and abnormal SCF levels, indicating that a mature ooplas-
matic dysmaturity, occurring with a suboptimal MII cohort, may not effi-
ciently overcome compromised sperm chromatin integrity.

P-58 Tuesday, October 15, 2019 6:30 AM
THE MITOCHONDRIAL DNA QUANTIFICATION IN CUMULUS CELLS AND IMPLANTATION POTENTIAL OF EMBRYOS. Anna Korolkova, MD, Nona Mishieva, PhD, Bella Martazanova, PhD, Yulia Kiseleva, PhD, Evgeniya Kovalskaya, MSc, Olga Burmenskaya, PhD, Aydar Abubakirov, PhD, Tatiana Kodyleva, MSc Reproductive endocri-
nology, Moscow, Russian Federation; Embryologist, Moscow, Russian Federation; Genetic, biology, Moscow, Russian Federation.

OBJECTIVE: Recent studies have suggested that age-related decreased competence of oocytes may be due to low quantity of mitochondrial DNA (mtDNA) copy number. Moreover, quantification of mtDNA in the oocyte-
cumulus-cell complexes (OCCCs) may serve as a predictor of blastocysty,

ability. The purpose of this study was to investigate relative levels of mtDNA
in the OCCCs in association with female age, ovarian reserve, embryo mor-
phology, ploidy and blastocyst implantation rate.

DESIGN: Prospective clinical study performed on 470 OCCCs retrieved from 72 advanced reproductive age patients undergoing ART treatment with intracytoplasmic sperm injection (ICSI) and preimplantation genetic testing for aneuploidy. Inclusion criteria: age 35-45 years; BMI: 18 - 29 kg/m2; FSH ≤ 15 IU/mL; normal female/male karyotype; non-smokers. Exclusion
criteria: genetic endometriosis III-IV; severe extragenital pathology; polycystic ovary syndrome; chronic endometritis; > 96% of sperm with abnormal morphology according to WHO criteria. The morphological assessment of em-

bryos was carried out according to the Gardner classification. Out of the 130
obtained blastocysts 56 embryos were diagnosed as aneuploid, and 74 as euploid. Presently, 51 frozen euploid embryos were transferred (FET). All transferred euploid blastocysts (n=51) divided into 2 groups: 1 group (n=21) - implanted embryos, 2 group (n=30) - non-implanted.

MATERIALS AND METHODS: Cumulus cells (CCs) were removed from OCCCs using fine needles. Collected CCs were placed into the Eppen-
dorf tube and frozen at ~80 °C for subsequent DNA analysis. MIDNA was assessed by using a quantitative real-time polymerase chain reaction tech-
nique. DNA from the trophectoderm samples were amplified and subjected to quantitative real-time polymerase chain reaction technology, Moscow, Russian Federation; bEmbryologist, Moscow, Russian Federation; cReproductive endocri-
nology, Moscow, Russian Federation; dGenetic, biology, Moscow, Russian Federation.

OBJECTIVE: The purpose of the study was to evaluate the ability of oocyte DNA repair mechanisms to detect and fix deficiencies in sperm chromatin integrity and support embryo implantation.

DESIGN: From 2006-2017, ejaculates from 127 men were assessed for sperm chromatin fragmentation (SCF). Intracytoplasmic sperm injection (ICSI) clinical outcomes were divided into groups according to the SCF level of the male partner and the proportion of mature oocytes obtained at retrieval. Proportional oocyte nuclear maturity was considered an indirect marker for presumed cytoplasmic readiness of the oocyte, suggesting its ability to repair the male chromatin during late oocyte maturation.

MATERIALS AND METHODS: Samples from consenting couples were screened for SCF levels by terminal deoxynucleotidyl dUTP nick-end label-
ing (TUNEL) utilizing a commercially available kit. A minimum of 500 sper-
matozoa were assessed per patient, and an SCF of 15% or below was consid-
ered normal. From the retrieved cohort, the proportion of meta-
phase-II oocytes at the time of ICSI was recorded and used for this assess-
ment. ICSI was performed in the standard fashion. Female partners were limited to ≤35 years of age to control for eventual confounding female fac-
tors.

RESULTS: A total of 127 couples underwent 191 ICSI cycles. Of them, 84 couples in which the male partner had a normal SCF level (9.8±13%) under-
went 125 ICSI cycles; conversely, 43 couples in which the male partner had an abnormal SCF level (24.1±11%; P < 0.0001) underwent 67 ICSI cycles.

When the proportion of mature oocytes was over 80% at the time of re-
trieval, there was no difference in the ICSI clinical outcome between coup-
les with normal and abnormal SCF levels, indicating that a mature ooplas-
matic dysmaturity, occurring with a suboptimal MII cohort, may not effi-
ciently overcome compromised sperm chromatin integrity.
mass index was 22.3±1.5. A positive correlation of the relative level of mtDNA in the CCs with the patients’ age (p = 0.008) and AMH levels (p = 0.003) was revealed. There was no statistically significant correlation between mtDNA copy number and embryo morphology on day 5 (p=0.7). There was a tendency to increase mtDNA copy number in group 1 vs. group 2, 390 and 299, respectively (p >0.05). In this study we didn’t find relationship between median mtDNA content of CCs and embryos ploidy (356 vs. 325, in euploid (n=74) and aneuploid (n=56) blastocyst, respectively, p >0.05).

CONCLUSIONS: mtDNA content in CCs correlated with female age and AMH level. However, the determination of mtDNA copy number in CCs don’t predict embryos implantation potential.

P-59 Tuesday, October 15, 2019 6:30 AM

DYNAMIC AND VIABILITY OF HUMAN DAY-6 TROPHODERM CELLS DURING 141 DAYS OF CELL CULTURE. Oscar Perez, Ph.D.,1 Hannalie Adriassena, BS,4 Breana Tilley, MSc,2 Gabriella Navarrete, BS,2 Ravi Gada, MD,3 Laura Lawrence, MD,3 Mika R. Thomas, MD,3 Karen Lee, MD,3 Samuel Chantilis, MD1 Dallas Fertility Center, Dallas, TX; 1Dallas Fort Worth Fertility Associates, Dallas, TX.

OBIJECTIVE: To determine the dynamic and viability of derived human trophoderm cells (TE) in vitro cultured for 141 days.

DESIGN: Research ongoing study.

MATERIALS AND METHODS: Study trophoderm cells were obtained from day-6 blastocysts determined to be non-viable after undergoing in vitro fertilization. This study was conducted in accordance with an IRB. Biopsied mass of approximately 25 TE cells was placed in three individual wells in a central depression with a diameter of 200 μm. TE cells were settled at the bottom of three samples. TE cells responded with aggressive expansion and growth during the first 30 days of culture and then remained in a plateau growth pattern during the rest of the cell culture time. TE cells were video monitoring in the 10-minute cycle time with seven focal planes for 141 days. TE cells from the same well were counted (using a cell counter) three times to obtain the average number. A sample of 5 μl aliquot of cells was taken for each well and analyzed by Veriseq (high-resolution Next Generation Sequencing) to confirm the viability and the chromosomal analysis of the TE cells. Genetic testing was performed by Reprogenetics Recombine Genetics (Cooper Genomics). The remaining cells were discarded.

RESULTS: Dynamic reproduction of TE cells was observed in all biopsied samples. TE cells responded with aggressive expansion and growth during the first 30 days of culture and then remained in a plateau growth pattern during the rest of the cell culture time. The number of cells was an estimated average, but it could be inaccurate due to the size of the cells and the focal plane of the video picture. The viability of the cells was determined by the genetic information outcome, color, and integrity of the cells.

CONCLUSIONS: Deriving TE cells from human day-6 blastocysts is possible. This outcome opens the opportunity to explore new trophoderm cell culture conditions. Increment in trophoderm cells might offer new alternatives to improve our knowledge of this type of cells on IVF patients with a poor number of trophoderm cells on day-6 embryos.

P-60 Tuesday, October 15, 2019 6:30 AM

IS LOW MITOCHONDRIAL DNA (mtDNA) CONTENT AFTER FERTILIZATION FAILURE DUE TO OOCYTE AGING IN CULTURE? Marta Perez, phd, student,1 Amparo Mercader, PhD,6 Diana Beltrán, Master,1 Arantza Delgado, PhD,1 Laura Escrich, phd,6 Antonio Pellicer, MD, PhD,1 Carmen Vidal, M.D., Ph.D.1, Ma José de los Santos, PhD.1 IVI foundation, Instituto de Investigación Sanitaria la Fe, Valencia, Spain; 2IVIRMA Valencia, Valencia, Spain; 3IVIRMA ROMA, Roma, Italy.

OBJECTIVE: Low mitochondrial DNA (mtDNA) content in oocytes has been correlated with oocyte fertilization failures. However, all the studies with failed-fertilization oocytes have been performed in in-vitro aged oocytes. As the results have relevant clinical implications on understanding oocyte competence, the aim of the study was to evaluate the effect of in vitro aging in mtDNA content in failed-fertilized oocytes.

DESIGN: A prospective cohort study was performed with 101 samples consisting on 36 “fresh” non-inseminated MII donated oocytes, 31 in-vitro aged failed-fertilized oocytes, 17 “fresh” failed-fertilized oocytes from patients and another 17 from donors.

MATERIALS AND METHODS: Samples were collected in PCR tubes the same day of follicle aspiration in the case of donated MII oocytes, after 19-22 hours post-ICSI for “fresh” failed-fertilized oocytes and after 5-6 days of culture in the case of in vitro aged failed-fertilized oocytes. Q-PCR was performed with SurePlex DNA Amplification System (Illumina) using specific primers for the ATP8 gene to assess the total mtDNA copy number. Data was analyzed by ANOVA test with Scheffé multiple comparison.

RESULTS: Significant higher mtDNA content was found in “fresh” non-inseminated MII oocytes comparing with “fresh” and failed-fertilized ones (P<0.05) in both patients and donors. Besides, there were no significant differences in terms of mtDNA content between “fresh” and in-vitro aged failed-fertilized oocytes (P>0.05).

CONCLUSIONS: As it appears in literature, we have observed a significant decrease in mtDNA content associated with failed-fertilized oocytes compared to “fresh” non-inseminated MII oocytes. Such decrease occurs regardless of the in vitro aging. In addition, we observed that the decrease of mtDNA content in failed-fertilized oocytes is independent of the maternal age. Furthermore, it seems that the decrease of mtDNA content observed in failed-fertilized oocytes compared to non-fertilized oocytes is due to the fail of fertilization itself and not because of the mtDNA degradation in culture, since when we compare fresh failed-fertilized oocytes and failed-fertilized oocytes that were sampled after 5 or 6 days after ICSI, we do not observe significant differences. Therefore, we can conclude that the fail of fertilization is related to oocytes with an unusually low mtDNA content and this finding supports the importance of the mtDNA content in oocytes as a biomarker for embryo viability.

<table>
<thead>
<tr>
<th>Biopsied Specimen</th>
<th>Initial Number of TE Cells (Average)</th>
<th>Number of TE Cells at 30 Days of Cell Culture (Average of 3 Counts)</th>
<th>Number of TE Cells at 141 Days of Cell Culture (Average of 3 Counts)</th>
<th>Genetic Screening at 141 days of Cell Culture (Next Generation Sequencing)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>25</td>
<td>1200</td>
<td>5000</td>
<td>Aneuploid</td>
</tr>
<tr>
<td>2</td>
<td>25</td>
<td>2300</td>
<td>6000</td>
<td>Euploid</td>
</tr>
<tr>
<td>3</td>
<td>25</td>
<td>3500</td>
<td>8000</td>
<td>Euploid</td>
</tr>
</tbody>
</table>

CONCLUSIONS: As it appears in literature, we have observed a significant decrease in mtDNA content associated with failed-fertilized oocytes compared to “fresh” non-inseminated MII oocytes. Such decrease occurs regardless of the in vitro aging.

SUPPORT: This work was funded by a grant from the Generalitat Valenciana (Spain).
suggested that male embryos grow faster than female embryos and as a result embryologists are more likely to select a male embryo for transfer. The objective of this study is to assess whether an embryo’s sex and/or chromosomal normalcy may be related to their rate of development.

DESIGN: A retrospective study of PGT-A results obtained between 2016 and 2018.

MATERIALS AND METHODS: Information was derived from PGT-A results of 151 patients (691 embryos; 21 uncounted due to being beyond parameters or missing information). We determined the ratios of day-5 XY to XX, labeling this as group A, day-6 XY to XX as group B, day-5 euploid (N) to aneuploid (AN) as group C, and day-6 N to AN as group D. These ratios were then tested to determine whether embryo growth exhibited any significant patterns.

RESULTS:

A chi-square test for independence was performed on the ratios of four groups: A, B, C, and D. The former three groups’ ratios yielded no significant differences, with group B and C possessing ratios very close to an even split 50/50, which is consistent with the average prediction of embryo development. However, the latter group yielded a significant difference with 92:128 euploid to aneuploid ratio (p = 0.015).

CONCLUSIONS: Our results do not support the notion that male embryos grow faster than female embryos. The was a significant difference in the rate of aneuploidy seen when comparing day 6 blastocysts to those that reached the blastocyst stage on day 5.

References: n/a

SUPPORT: n/a

P-62 Tuesday, October 15, 2019 6:30 AM

TROPHOECTODERM CELL DEVELOPMENT FROM DAY-6 HUMAN BLASTOCYSTS. IS IT POSSIBLE TO REPRODUCE THEM IN VITRO?. Oscar Perez, Ph.D., a
Hannalie Adriaanse, BS, a Breanna Tilley, MSc, a
Gabriella Navarrete, BS, a Linda Lay, BS, a Lucille M. Little, BS, a
Ravi Gada, MD, a Laura Lawrence, MD, a Karen Lee, MD, a
Mika R. Thomas, MD, a Samuel Chantilis, MD, b
Hannalie Adriaanse, BS, a Linda Lay, BS, a Lucille M. Little, BS, a
Ravi Gada, MD, a Laura Lawrence, MD, a Karen Lee, MD, a
Mika R. Thomas, MD, a Samuel Chantilis, MD, b Dallas Fertility Center, Dallas, TX; bDallas Fertility Institute, Chicago, IL.

OBJECTIVE: To create trophoderm cells (TE) in vitro from discarded day-6 blastocysts.

DESIGN: Research ongoing study

MATERIALS AND METHODS: Trophoderm cells from non-viable, discarded, day-6 blastocysts were selected for this study. Specimens were derived from unused cells obtained from in vitro fertilization patients who had consented to have these discarded cells used for this IRB-approved research study. Three biopsied cell masses were cultured in RPMI 1640 medium supplemented with 20% HSA. TE cells were cultured with human fibroblast growth factor (VEGF), and on the changes in the metabolic pathway in the endometrium.

The aim of this study is to investigate the effects of hypoxic stress on the regulation of HIF-1α and vascular endothelial growth factor (VEGF), and on the changes in the metabolic pathway in the endometrium.

RESULTS: Trophoderm cell derivation started after initial cell culture. Proliferated TE cells resulted in smaller cells of approximately 2-5 μm. Some of these smaller cells grew and reached the same size as the original TE cell source. The number of cells was an estimate number, but it could be inaccurate due to the size of the cells and the focal plane of the video picture.

CONCLUSIONS: Developing trophoderm cells in vitro is possible. Although some of the derived cells resembled the same origin, the growth pattern of most cells was prolonged. Moreover, most of the resulted TE cells were smaller than 5 μm. These smaller TE cells might need different culture protocols and growth factors to express similar characteristics as the original TE cells from day-6 blastocysts.

P-63 Tuesday, October 15, 2019 6:30 AM

CAN GROWTH HORMONE REALLY IMPACT ANEUPLOIDY RATES? Ruchi Kaushik Amin, MD, a
Lauren Grimm, MA, b Elisabeth Rosen, BS, MA, b
Angelina Beltsos, MD, a Roohi Jeelani, MD, b Wayne State University, Detroit, MI; bVios Fertility Institute, Chicago, IL.

OBJECTIVE: To specifically look at the effect of growth hormone (GH) on preimplantation genetic testing for aneuploidy (PGT-A).

DESIGN: Retrospective chart review at a private infertility center.

MATERIALS AND METHODS: All patients enrolled in poor-responder in-vitro fertilization (IVF) protocols from 2016-2018 were included in this study. Cycles, in which GH was administered, were analyzed for PGT-A results, when available, and compared to the results of other poor responder IVF protocols without the use of GH. A two sample t-test was used to analyze the data using Stata 14.0 (StataCorp LLC., College Station, TX, USA).

RESULTS: A total of 171 cases that utilized PGT-A were identified. The euploidy rate in the GH group was 28.4% compared to 23.3% in the age-matched control group. Although not statistically significant, this study shows that addition of GH in patients with poor oocyte quality may lead to a successful pregnancy and lower chances of miscarriage (p=0.256).

CONCLUSIONS: Historically, GH has been implemented for the improvement of oocyte quality. Previous literature has shown that the addition of GH improves clinical pregnancy rates and decreases miscarriage rates, which is consistent with the fact that PGT-A also decreases miscarriage rate. Although, not statistically significant, our results demonstrate that GH not only improves oocyte quality, but helps improve euploidy rates in patients with diminished ovarian reserve. We stipulate that the mechanism of action of GH is to decrease aneuploidy, thereby improving clinical pregnancy rates.

ENDOMETRIAL PHYSIOLOGY

P-64 Tuesday, October 15, 2019 6:30 AM

THE INFLUENCE OF HYPOXIA ON ANGIOGENESIS AND METABOLISM IN HUMAN ENDOMETRIAL STROMAL CELLS. Hidetaka Okada, MD Takeharu Kido, MD. Kansai Medical University, Hirakata, Japan.

OBJECTIVE: Hypoxia is a physiological event that occurs in the endometrial tissues during the premenstrual period and implantation. Hypoxia-inducible factor-1 (HIF-1) is the master regulator of the cellular response to hypoxia. HIF-1α activation by the hypoxic microenvironment is involved in angiogenesis and metabolism. The aim of this study is to investigate the effects of hypoxic stress on the regulation of HIF-1α and vascular endothelial growth factor (VEGF), and on the changes in the metabolic pathway in the endometrium.

DESIGN: Prospective in vitro studies using human primary endometrial stromal cell cultures.

Development of trophoderm cells in vitro

<table>
<thead>
<tr>
<th>Time of Cell Culture</th>
<th>Specimen 1</th>
<th>Specimen 1</th>
<th>Specimen 2</th>
<th>Specimen 2</th>
<th>Specimen 3</th>
<th>Specimen 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TE Cells ≥ 10</td>
<td>TE Cells ≤ 10</td>
<td>TE Cells ≥ 10</td>
<td>TE Cells ≤ 10</td>
<td>TE Cells ≥ 10</td>
<td>TE Cells ≤ 10</td>
</tr>
<tr>
<td>0 hours</td>
<td>25 (n)</td>
<td>0 (n)</td>
<td>25 (n)</td>
<td>0 (n)</td>
<td>25 (n)</td>
<td>0 (n)</td>
</tr>
<tr>
<td>500 hours</td>
<td>200 (n)</td>
<td>1000 (n)</td>
<td>300 (n)</td>
<td>2000 (n)</td>
<td>250 (n)</td>
<td>2500 (n)</td>
</tr>
</tbody>
</table>
MATERIALS AND METHODS: Human endometrial tissues were obtained from 21 patients aged 32–46 years undergoing hysterectomy for benign reasons with regular menstrual cycles. The human endometrial stromal cells (ESCs) were purified by the standard enzyme digestion method. ESCs were cultured under hypoxic (2% O2) or normoxic (20% O2) conditions with echinomycin, a small-molecule inhibitor of HIF-1α. The mRNA levels and production of VEGF were assessed by real-time PCR and ELISA, respectively. The HIF-1α protein levels were measured using western blot analysis. Metabolome analysis was measured by capillary electrophoresis electrospray ionization time-of-flight mass spectrometry and capillary electrophoresis-triple quadrupole mass spectrometry. Differences in the measured parameters across the different groups were statistically assessed using ANOVA followed by Dunnett’s test and a level of P < 0.05 was considered statistically significant.

RESULTS: Real-time PCR analysis demonstrated that hypoxia caused a significant increase in the levels of VEGF mRNA expression (P < 0.01). Hypoxia caused a significant increase of VEGF production after 6 h of culture with normoxia (P < 0.01), and this effect continued to increase until the end of the study at 48 h. Hypoxic stress significantly induced the expression of HIF-1α protein (P < 0.05), and its highest expression was observed at 6 h. Echinomycin inhibited hypoxia-induced VEGF production without affecting the HIF-1α protein level. These results suggest that hypoxia acts to increase VEGF via HIF-1α-dependent manner. A total of 116 metabolites were analyzed. Hypoxia significantly increased glucose 6-phosphate and fructose 6-phosphate in the glycolytic pathway (P < 0.05). However, while hypoxia suppressed cis-aconitic acid, isocitric acid, and citric acid in the tricarboxylic acid cycle, the decrease only reached the borderline of significance (P = 0.08).

CONCLUSIONS: These results indicate a potential mechanism for the action of hypoxic conditions that could influence angiogenesis and metabolism in the human endometrium.

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DOES THE ENDOMETRIUM HAVE A ROLE IN SELECTING EMBRYO GENDER?: Javier Herreros, Sr., MSc, Hector Huete Ferriz, MSc, Mireia Florensa, MSc, Marga Esbert, PhD IVI RMA Barcelona, Barcelona, Spain.

OBJECTIVE: It is still unknown if the endometrium can select the embryo depending on the gender. To date, it has been thought that the gender of the newborn children depends on the spermatozoa which fertilized the oocyte carried of Y or X chromosome. Nevertheless it is possible that the endometrium could have an important role on this event. The aim of our study is to prove if the endometrial receptivity could change depending on the gender of the transferred embryo.

DESIGN: Retrospective study.

MATERIALS AND METHODS: This retrospective study includes 2237 IVF cycles performed in our center between January 2004 and May 2018. Patients were divided into 2 different branches:

Branch 1: study the gender percentage of the newborn children in couples who have undergone DET (double embryo transfer) in one cycle, obtaining all the possible combinations: male-male, female-female and male-female.

Branch 2: compare if there is any tendency towards the embryo’s implantation depending on whether the replaced embryo has the same sex as the previous children or not in couples with two or more newborn children resulting from cycles at IVI Barcelona.

We have analyzed our data with a Chi-squared test.

RESULTS: Depending on the embryo gender of the newborn children, we have classified the different combinations in 10 groups: 6 male-male, 5 female-female and male-female. There were no differences between the gender of the transferred embryo and the outcome of the PGT-A cycles. Nonetheless, the correlation between these aging biomarkers and embryo aneuploidy rate in ART cycles is not clear.

CONCLUSIONS: Our findings suggest that having a first newborn child has no influence on the gender of the following newborn children irrespective of the number of embryos replaced or the number of cycles performed. Therefore, according to our results, the endometrium does not play a role in selecting the embryo gender.

EUPLOID EMBRYO PREDICTORS

P-66 Tuesday, October 15, 2019 6:30 AM

THE ASSOCIATION OF AGING MARKERS IN LUTEINIZED GRANULOSA CELLS AND EMBRYO ANEUPLOIDY RATE IN PREIMPLANTATION GENETIC TEST FOR ANEUPLOIDY CYCLES. Tsung-Hsien Lee, MD, PhD,1 En-Hui Cheng, PhD,1 Maw-Sheng Lee, MD, PhD,1 “Chung Shan Medical University Hospital, Taichung, Taiwan; 2Lee Women’s Hospital, Taipeh, Taiwan; 3Chung Shan Medical University, Taichung, Taiwan.

OBJECTIVE: The ovarian aging is associated with poor quality oocytes, especially increasing aneuploidy rate. In addition to chronological age, several biomarkers could represent the aging status of individual person, such as telomere length and mitochondrial copy number in somatic cells. Nonetheless, the correlation between these aging biomarkers and embryo aneuploidy rate in ART cycles is not clear.

DESIGN: This prospective cohort study was performed for the patients for preimplantation genetic test for aneuploidy (PGT-A) programs in a single reproductive center in Taiwan.

MATERIALS AND METHODS: The telomere length and mitochondria copy number in leucocytes and luteinized granulosa cells were measured as aging biomarkers. The association among these aging biomarkers was explored. The correlation between these aging biomarkers and embryo aneuploidy rate was investigated with Spearman correlation test and linear regression model.

RESULTS: A total of 110 PGT-A cycles were recruited for this study. The telomere length and the mitochondria copy number are intimately correlated.

### TABLE 1. Correlation between biomarkers of aging (Spearman correlation test)

<table>
<thead>
<tr>
<th>Biomarkers</th>
<th>Leukocyte telomere length</th>
<th>Granulosa cell telomere length</th>
<th>Leukocyte mitochondrial copy number</th>
<th>Granulosa cell mitochondrial copy number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.093</td>
<td>-0.186</td>
<td>-0.069</td>
<td>-0.019</td>
</tr>
<tr>
<td>AMH</td>
<td>-0.015</td>
<td>0.385</td>
<td>0.006</td>
<td>0.261</td>
</tr>
<tr>
<td>Leukocyte telomere length</td>
<td>0.003</td>
<td>0.003</td>
<td>0.074</td>
<td>0.095</td>
</tr>
<tr>
<td>Granulosa cell telomere length</td>
<td>0.008</td>
<td>1.000</td>
<td>-0.075</td>
<td>0.361</td>
</tr>
<tr>
<td>Leukocyte mitochondrial copy number</td>
<td>0.477</td>
<td>0.093</td>
<td>0.437</td>
<td>-0.020</td>
</tr>
<tr>
<td>Granulosa cell mitochondrial copy number</td>
<td>0.095</td>
<td>0.361</td>
<td>-0.020</td>
<td>1.000</td>
</tr>
</tbody>
</table>
with each other within leukocytes or granulosa cells, but not correlated between leukocytes and granulosa cells. In addition, serum anti-Mullerian hormone (AMH) is closely correlated with telomere length and mitochondrial copy number in granulosa cells, but not those in leukocytes. Linear regression model revealed that chronological age is the sole aging biomarker associated with aneuploidy rate of embryos in ART cycles.

CONCLUSIONS: Although the serum AMH, telomere length of granulosa cells, mitochondrial copy number in granulosa cells are closely correlated with each other, the chronological age is the main factor to affect aneuploidy rate of embryos in PGT-A cycles. The results suggest that the main source of aneuploidy is oocyte meiosis, especially if the oocyte stayed at metaphase stage for a long period of time.

SUPPORT: The study was supported by a grant from Ministry of Science and Technology for Maw-Sheng Lee (MOST 106-3114-B-040-001).

P-67 Tuesday, October 15, 2019 6:30 AM

BLASTOCYST PLOIDY IS NOT RELATED TO THE NUMBER OF EMBRYOS GENERATED NOR TO THE TYPE OF OVARIAN STIMULATION. Sandro C. Esteves, M.D., Ph.D., a Peter Humaidan, M.D., Ph.D., a José F. Carvalho, Ph.D., a Danilo Cimadomo, Ph.D., a,1 Alberto Vairelli, M.D., a Hakan Yarali, M.D., a,1 Irem Y. Ozbek, Ph.D., a Thor Haahr, MD, a Alessandro Conforti, MD, a Carlo Alviggi, MD, Ph.D., b Filippo Maria Ubaldi, MD, Ph.D., a,2 Medical Director, Campinas, Brazil; a The Fertility Clinic, Skive Regional Hospital, Skive, Denmark; 1 Statistica Consulting, Campinas, Brazil; a GENERA, Center for Reproductive Medicine, Rome, Italy; 1 Anatolia IVF, Ankara, Turkey; a Department of Neuroscience, University of Naples Federico II, Naples, Italy.

OBJECTIVE: More than half of human embryos are aneuploid which is the main reason for the decreased live birth rates among advanced maternal age (AMA) patients undergoing Assisted Reproductive Technology (ART). However, concerns were raised regarding a putative detrimental effect of ovarian stimulation (OS) regimens on embryo ploidy status. We aimed to investigate whether euploidy is related neither to the number of blastocysts generated nor to the intensity of ovarian stimulation

DESIGN: Multicenter retrospective analysis of 3,108 trophectoderm biopsies from 1,109 infertile couples undergoing ICSI and preimplantation genetic testing for aneuploidy (PGT-A) between 2016 and 2017.

MATERIALS AND METHODS: Ovarian stimulation regimens included conventional OS using GnRH antagonist co-treatment (n=1,011 patients) and minimal OS (n=98 patients). PGT-A was indicated due to AMA, severe male factor, recurrent miscarriage, repeated implantation failure, and due to concerns about their embryonic ploidy status. Biopsied trophectoderm cells were analyzed by next-generation sequencing analysis (NGS) or real-time quantitative polymerase chain reaction (qPCR). Logistic regression was applied to the dataset. The dependent variable was blastocyst genetic status (euploid/aneuploid) whereas the independent variables were female age, the number of blastocysts biopsied, and type of OS (conventional versus minimal). Mosaic blastocysts detected by NGS (5.7% of biopsied blastocysts) were excluded from the analysis. Computations were performed using JMP 13 (www.jmp.com).

RESULTS: The mean female age was 39.0 years (95% confidence interval [CI]: 34.8-43.0 years), and the mean number of blastocysts available for PGT-A per patient was 3.0 (95% CI: 1.0-5.0). Overall, the percentage of euploid embryos in our cohort was 42.0% whereas the mean number of blastocysts available for biopsy (Estimate: 0.03; 95% CI: -0.00; 0.06) and type of OS (Estimate: 0.06; 95% CI: -0.39; 0.73) were not significant. The logistic model generated the probability, 'p', as an output (where 'p' is the probability that a biopsied cell would be euploid) as a function of blastocyst cohort size and type of OS, adjusted by female age. There was a significant (p < 0.001) decrease in the probability of a blastocyst being euploid with every year of female age. However, this probability was not significantly associated with the blastocyst cohort size and type of OS. Introduction of the clinic into the regression model essentially did not change the estimates.

CONCLUSIONS: The probability of a blastocyst being euploid decreases with female age but is not affected by blastocyst cohort size and type of OS. This information might aid clinicians counseling patients undergoing ART about their chances of producing euploid blastocysts according to the treatment regimen and the age of the female.

SUPPORT: None

TABLE 1.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Unadjusted OR [95% CI]/p-value</th>
<th>Adjusted OR [95% CI]/p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;35</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>[35, 38]</td>
<td>0.586 [0.399 0.861]/0.007</td>
<td>0.665 [0.447 0.989]/0.044</td>
</tr>
<tr>
<td>[38, 41]</td>
<td>0.382 [0.265 0.550]/&lt;0.001</td>
<td>0.371 [0.254 0.541]/&lt;0.001</td>
</tr>
<tr>
<td>[41, 43]</td>
<td>0.158 [0.107 0.233]/&lt;0.001</td>
<td>0.172 [0.114 0.258]/&lt;0.001</td>
</tr>
<tr>
<td>43+</td>
<td>0.051 [0.030 0.087]/&lt;0.001</td>
<td>0.067 [0.039 0.117]/&lt;0.001</td>
</tr>
<tr>
<td>Folicle size</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum</td>
<td>1.003 [0.991 1.015]/0.609</td>
<td></td>
</tr>
<tr>
<td>Top 5 average</td>
<td>1.002 [0.996 1.007]/0.584</td>
<td></td>
</tr>
<tr>
<td>Top 5 sd</td>
<td>1.129 [1.046 1.219]/0.002</td>
<td></td>
</tr>
<tr>
<td>Top 5 sum</td>
<td>1.034 [1.022 1.046]/&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Simulation days</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>[10, 12]</td>
<td>1.050 [0.785 1.405]/0.741</td>
<td></td>
</tr>
<tr>
<td>12+</td>
<td>0.876 [0.653 1.207]/0.417</td>
<td></td>
</tr>
<tr>
<td>MATUER EGGs Retrieved</td>
<td>1.150 [1.124 1.178]/&lt;0.001</td>
<td>0.976 [0.907 1.051]/0.526</td>
</tr>
</tbody>
</table>

P-68 Tuesday, October 15, 2019 6:30 AM

THE IMPACT OF LEAND FOLLICLE SIZE AND DURATION OF STIMULATION ON THE PROBABILITY OF EUPLOYDIC EMBRYOS. Denis Schapira Wajman, MD, a David L. Keefe, M.D., b David H. McCulloh, Ph.D., c James A. Grifo, MD, PhD, c Cheungeon Oh, PhD, c "NYU Langone, New York, NY; c New York University School of Medicine, Department of Obstetrics and Gynecology, New York, NY; c NYU Langone Fertility Center, New York, NY.

OBJECTIVE: Clinical guidelines on the optimal duration of controlled ovarian stimulation and ideal follicle size were developed for fresh embryo transfer cycles. Whether these apply to freeze all cycles remain unclear. We evaluated the impact of lead follicle size and duration of stimulation on the probability of euploid embryos in women undergoing IVF/PGT-A

DESIGN: Cross-sectional study

MATERIALS AND METHODS: Data from 721 patients undergoing at least two cycles of COS for IVF with preimplantation genetic testing for aneuploidy (PGT-A) via Next Generation Sequencing (NGS) (1859 cycles). Mixed-effect logistic regression, which can account for correlations among repeated outcomes within sample patients, was used to evaluate the association between independent variables and probability of achieving euploid embryos. We first conducted a mixed-effect logistic regression in a univariate manner. All variables then were evaluated in a multivariate model to control for confounding effects. Significant variables to p<0.05 were retained in the final model. p-values <0.05 were considered significant. Statistical analyses were performed using "lme" and "lme4" package from R project. Results are reported as odds ratios (OR) with 95% confidence intervals (CI).

RESULTS: Increasing sum (1.034 [1.022 1.046]/p<0.001) and mean diameter (1.129 [1.046 1.219]/p=0.002) of the 5 largest follicles increased the probability of forming euploid embryos. Increasing days of stimulation showed a non-significant trend toward lower chance of forming euploid embryos (0.976 [0.923 1.031]/p=0.382) (Table 1).

CONCLUSIONS: Allowing the lead follicles to exceed 18mm in increases the total number of euploid embryos formed per cycle, presumably by enabling retrieval of additional mature oocytes. Evidence of a detrimental effect of excessive follicle size was not evident in our study, though the number of cycles with follicles exceeding 24 mm was limited. The non-significant trend toward decreased euploid embryos following prolonged stimulation may reflect the effects of poor responders.

REFERENCE

V. Vol. 112, No. 3, Supplement, September 2019
EXOGENOUS GONADOTROPIN USE NOT ASSOCIATED WITH INCREASE IN ANEUPLOIDY OF IN VIVO RECOVERED BLASTOCYSTS. Steven T. Nakajima, MD,a Sam Najmabadi, MD,b Santiago Munne, PhD,c Alex Nadal, BA,a Kajal Choudhary, PhD,a John E. Buster, MD,b 1Stanford University School of Medicine, Stanford, CA; 2Punta Mita Hospital, Punta Mita Fertility Center/Center for Reproductive Health and Gynecology, Punta de Mita, NA, Mexico; 3Overture Life, Madrid, Spain; 4Previvo Genetics Inc., San Carlos, CA.

OBJECTIVE: Does exogenous gonadotropin stimulation increase the risk of aneuploidy for in vivo blastocysts?

DESIGN: We performed 134 stimulated uterine lavage cycles to evaluate the safety and efficacy of a new lavage system (Previvo Genetics, Inc., San Carlos, CA). Patients gave their written informed consent. All lavages were performed in Punta Mita, Mexico from August 2017 to June 2018. Subjects were stratified according to age, euploid rate was increased in hGH cycles in both <37 years (8.75% vs. 53.9%, p = 0.001) and >38 years (12.7% vs. 26.7%, p = 0.03).

RESULTS: In 134 uterine lavage cycles, 46 (34%) resulted in recovery of one blastocyst. Mean age and BMI of the sub-group were 35.1 years and 24.2 kg/m², respectively. Subjects were stratified for an average of 9.4 days with a mean total gonadotropin dosage of 1789 IU, mean total hMG dose of 888 IU. At the time of trigger, subjects had a mean maximum E2 of 2613 pg/mL (range 394-6377 pg/mL) and 9.6 follicles 16mm.

A total of 96 blastocysts were recovered and biopsied. After the initial biopsy, 37% (33/89) were euploid, 63% (56/89) aneuploid, and 7 blastocysts had no determination. Due to the high rate of aneuploidy, a second biopsy was performed in 64% (61/96) of the blastocysts (10 euploid, 48 aneuploid, 3 no determination). The second biopsy result was used to determine the euploid status of the blastocysts for this analysis resulting in a euploid rate of 53% (49/92), 47% (43/92) aneuploid, and no determinations. In 8.2% (11/134) of the cycles, the positive hCG was present 13 days after IUI. The hCG levels in all cycles resolved spontaneously, or after curettage with or without methotrexate.

A logistical regression was performed to determine whether there was any correlation between covariates (days of stimulation, mean total gonadotropins, mean total hMG, mean maximum estradiol and follicles 16mm at trigger) and euploid status. No significant associations were found between any of the variables and euploid status.

CONCLUSIONS: This study reinforces existing IVF data that imply gonadotropin stimulation is not associated with higher rates of aneuploidy but now shows a significant increase in number of biopsied blastocysts but no difference in number of euploid embryos/eploid rate. In women classified as non-POR, there were significant improvements in all cycle parameters. When the data was stratified according to age, euploid rate was increased in hGH cycles in both <37 years (8.75% vs. 53.9%, p = 0.001) and >38 years (12.7% vs. 26.7%, p = 0.03).

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CONCLUSIONS: This study reinforces existing IVF data that imply gonadotropin stimulation is not associated with higher rates of aneuploidy but now performed in an in vivo data set. These findings support the continued use of stimulation in the process of uterine lavage. However, the sample size is small, and the lavage system is not fully optimized to recover all embryos.

SUPPORT: Previvo Genetics, Inc.

P-70 Tuesday, October 15, 2019 6:30 AM

ADJUVANT GROWTH HORMONE USE IMPROVES EUPLOID RATE IN WOMEN UNDERGOING IVF/PGT-A WHO ARE NOT POOR RESPONDERS. Whitney A. Leonard, MD - PGY2,a Winifred Mak, MD, Ph.D,b Amanda Skillern, MD, FACOG,c Jordyn Pike, MPH,a1University of Texas Dell Medical School, Dept of Women’s Health, Austin, TX; 2University of Texas Dell Medical School, Women’s Health, Austin, TX; 3Aspire Austin, Austin, TX; 4University of Texas Dell Medical School, Women’s Health, Austin, TX.

OBJECTIVE: To determine the effect of adjuvant human growth hormone (hGH) during IVF/PGT-A cycles on euploid embryo rate in women with and without poor ovarian response (POR).

DESIGN: Retrospective non-randomized cross over study MATERIALS AND METHODS: The study was carried out at a single clinic site from 2014-2018. Inclusion criteria: women who underwent one cycle of IVF/PGT-A and at least one consecutive IVF/PGT-A cycle with hGH within a 1-year period. hGH (1.45 mg) was started on the first day of ovarian stimulation and continued until trigger. Patients were stratified as POR by Bologna criteria. Women without POR were offered hGH if prior cycles had a suboptimal response or suboptimal blastocyst development as predicted by age/antil follicle count/AMH. Using a two-tailed paired t-test, sample size of 34 was sufficient to detect an effect size of 0.5 or greater at 0.8 power. Paired t-test analysis was performed with GraphPad Prism 8.0 to detect statistical significance of p = 0.05.

RESULTS: 51 patients underwent 79 cycles during the study period and met inclusion criteria. Table 1 shows cycle outcomes for POR women compared to non-POR. Interestingly, in POR patients there was a small but statistical increase in number of biopsied blastocysts but no difference in number of euploid embryos/eploid rate. In women classified as non-POR, there were significant improvements in all cycle parameters. When the data was stratified according to age, euploid rate was increased in hGH cycles in both <37 years (8.75% vs. 53.9%, p = 0.001) and >38 years (12.7% vs. 26.7%, p = 0.03).

However, when stratified by AMH, women with AMH >1 did not show a significant increase in euploid rate (5.26% vs. 11.8%, p=0.4), whereas women AMH <1 did show a significant benefit (14.5% vs. 40%, p=0.0003).

CONCLUSIONS: Prior studies have focused on use of hGH in poor responder women during IVF, but little is known about the utility in non-POR. This study shows that hGH significantly increases the number of euploid embryos/eploid rate in women who are not poor responders but had suboptimal response or poor embryo development. Interestingly, this study shows that in POR patients, all cycle outcomes are significantly improved by hGH except euploid rate. In conclusion, our study shows the use of hGH should be considered in non-POR women to improve IVF cycle outcomes.

Table 1: IVF/PGT-A cycle outcomes in women with and without adjunct use of hGH: Mean (SD)
same incubator for embryogenesis. Fertilization was assessed on Day 1 and resulting embryos were cultured until Days 5, 6 and 7 for blastocyst tropho
toderm biopsy. Biopsied samples were PGT-A analyzed by Next Generation Sequencing. The total number of euploid embryos were compared between the two males in each couple. The male partner with the higher number of euploid embryos was denoted as Male A; and the other male with an equal or fewer number of euploid embryos was denoted Male B. The data was analyzed using Chi-square analysis with a significance set at p<0.05. RESULTS: The data from eight same-sex male couples was analyzed, with a total of 187 mature oocytes inseminated; 94 and 93 oocytes for Males A and B, respectively. There was a total of 35 euploid embryos (57.4% of those biopsied). 22 for Male A and 13 for Male B, demonstrating a statistically significant
difference (p<0.05) in euploid rates among the groups analyzed. CONCLUSIONS: This study demonstrates that same-sex male couples desiring to generate embryos equally using the same oocyte donor at the time of a single IVF cycle, do not yield an equivalent number of euploid em-
bryos even when both males are normospermic and under the same exact cul-
ture conditions. This study indicates that there is likely an underlying sperm factor that impacts euploidy rates even in fertile normospermic males. More research is needed to elucidate the cause of this observation in order to help clinicians in counseling same-sex male couples.

P-72 Tuesday, October 15, 2019 6:30 AM
ANEUPLOIDY RATE IN BRCA CARRIERS IS SIMILAR TO AGE-MATCHED INFERTILE WOMEN. Maria Facadiso Antero, MD, 1,2 Mindy S. Christianson, MD, 3 William G. Kears, MD, PhD,4 1John Hopkins University School of Medicine, Lutherville, MD; 2John Hopkins University School of Medicine, Lutherville, OR; 3Johns Hopkins University School of Medicine, Advenqix, 9430 Key West Hwy, Suite 130, MD.

OBJECTIVE: BRCA 1 and BRCA 2 are tumor suppressor genes involved in DNA mismatch repair. Studies have shown that ovarian aging is acceler-
ated in women with BRCA mutations secondary to diminished ovarian reserve and accumulation of DNA damage in the oocytes of primordial fol-
icles.[i] It is unclear whether this DNA damage seen in primordial follicles translates to a higher aneuploidy rate. This study sought out to compare aneup-
loidy rates between BRCA1 and BRCA2 mutation carriers undergoing in vi-
tro fertilization (IVF) and preimplantation genetic testing for monogenic condition (PGT-M) and for aneuploidy (PGT-A) with age-matched control women with infertility undergoing IVF/PGT-A. DESIGN: Retrospective analysis of an anonymous database at a commer-
cial genetics laboratory. MATERIALS AND METHODS: This study included BRCA 1/2 mutation carriers undergoing IVF with PGT-M for BRCA 1/2 mutations and PGT-A from 2018-2019. Infertile, non-carriers undergoing IVF with PGT-A during the same period were included as controls. All embryos were biopsied at the blastocyst stage. PGT-A for both groups was performed by Next Generation Sequencing (NGS). The primary outcome of this study was to compare the aneuploidy rates between BRCA carriers and age-matched controls. For both cases and controls the aneuploidy rates were stratified into four age cat-
tegories: <35, 35-37, 38-40 years old. Chi square test was used to compare the aneuploidy rates between BRCA carriers and non-carriers in the different age groups. RESULTS: A total of 73 BRCA 1/2 mutation carriers were included in this study. There were 584 embryos tested in the carrier group with a mean num-
buer of embryos tested per cycle of 8 (range 4-11). Of the em-
bryos tested, 268 (46%) did not have a pathogenic BRCA mutation. A total of 24,850 embryos were tested in the control group. No information regarding incidence of diminished ovarian reserve was available for either group. There was no statistical difference between carriers and non-carriers in all age categories: <35-year-old 42% vs 49% (p=0.117), 35-37-year-old 47% vs 54% (p=0.16), 38-40-year-old 51% vs 63% (p=0.063) respectively. CONCLUSIONS: Aneuploidy rates in BRCA carriers were similar to infertile controls of the same age. As BRCA carriers become older, the in-
crease in aneuploidy rate is similar to that observed in the general infertile population. BRCA carrier status does not appear to affect aneuploidy rates how-
ever further studies including non-infertile controls may provide further in-

P-73 Tuesday, October 15, 2019 6:30 AM
SUBOPTIMAL STIMULATION IS PREDICTIVE OF INCREASED ANEUPLOIDY AND REDUCED PREGNANCIES PER CYCLE START. John B. Whitney, BS,1 Robert E. Anderson, MD,8 Mitchel C. Schiewe, MS, PhD4 O-
vation Fertility, Newport Beach, CA; 8SCRM, Newport Beach, CA.

OBJECTIVE: To correlate a measurable stimulation outcome parameter to its effect on blastocyst (BL) development, aneuploidy and pregnancy out-
comes, and determine if oocyte cohort maturity effects the implantation poten-
tial of a euploid BL? DESIGN: Oocyte quality is difficult to independently quantify, while the percent of metaphase II (i.e., mature) oocytes within a cohort of cumulus oocyte complexes (COC) retrieved can be used to assess overall stimulation effectiveness. A 5-year (2014-2018) retrospective analysis was conducted on 1,817 spontaneous cycles using PGT-A and 796 vitrified-warmed euploid BL transfers. Cycle cohort maturity was subdivided into patients with >=70% mature eggs (Group 1) or <70% (Group 2).

MATERIALS AND METHODS: Single physician clinic stimulated 1046 patients for 1264 cycles. Oocyte maturity was evaluated, and all fertilized zy-
gotes were grown to BL for biopsy/PGT-A and vitrification all cycles. Only first transfer attempts were compared in the per cycle analysis. Stimulation protocols were predominantly antagonist based. Oocytes were retrieved 35.5h post-hCG trigger. COC denuded 2-3h-post-retrieval before ICSI and the % mature oocytes calculated. Comparisons using t-test and chi-square were performed for cycles failing to produce a BL, cycles resulting normal embryos, aneuploidy and implantation.

RESULTS: Average patient age was 37 and 38 years old for Groups 1 and 2 respectively. Mean patient age (p<0.01) and mean % mature oocytes (p<0.01) between carriers and non-carriers for carriers undergoing IVF/PGT-A. Group 1 had a higher (p<0.01) mean BL yield of 2.4 blastocysts per cycle compared to 5.2 per Group 1 cycle. Yet, % BL production per cycle was not significant. Group 2 BL had a higher (p<0.01) aneuploidy rate (63 vs 56%) and more cycles failed to yield a normal embryo (52 vs 33%). Implantation of euploid BL was derived from either group was not statistically different averaging 7%. While our overall live birth rate, independent of age, exceed 65% per euploid ET, the overall clinical pregnancy rate per cycle start was lower for Group 2 (35%) than Group 1 (52%). CONCLUSIONS: It is well understood that multiple factors influence stimulation and oocyte maturity. Nonetheless, after a half decade of data collection, this study has identified a measureable outcome, oocyte cohort maturity, which predicts an increased risk of aneuploidy, a decreased euploid cycle outcome and embryos with a reduced implantation potential. Cohort maturity is influenced by several factors, including age, AMH, FSH, stimula-
tion protocol, and endocrine/ovarian conditions. When those factors pro-
duce suboptimal maturity, cycles are adversely affected, likely due to incomplete cytoplasmatic maturation of fertilized zygotides. A further under-
standing of the genetic regulation/omics, oocyte in-vivo genetics and basic cell biology is needed to better identify why suboptimal cycle maturity negatively effects the developmental potential of the pending BL as-
essed by PGT-A. SUPPORT: None

FERTILITY PRESERVATION

P-74 Tuesday, October 15, 2019 6:30 AM
ESTIMATES OF INFERTILITY IN AN ERA OF INCREASING STI RATES, 2002-2015. Morgan Snow, BA,1 Tyler McClung, BS, MS, 2 Maria Trent, MD, MPH, 3 Jamie Perin, PhD 4Johns Hopkins School of Medicine, Balti-
more, MD; 3Johns Hopkins University, Baltimore, MD.

OBJECTIVE: Has the decline in infertility remained uniform across sub-
groups? How do factors like PID and status of STI care affect infertility? DESIGN: Pelvic inflammatory disease (PID) has declined in an era of increasing sexually transmitted infection (STI) rates. Meanwhile, access to sexual and reproductive health (SRH) services remains tenuous for young and low-income women. This study aims to estimate the changes in infertility from 2002 to 2015 and explain the impact of PID and receipt of SRH services on fertility in the United States.

MATERIALS AND METHODS: Periodic data from the 2002, 2010, 2013, and 2015 cycles of the National Survey for Family Growth (NSFG) were
and the average storage time was 2.8 days.

RESULTS: The decline in infertility among married and cohabiting women from 7.0% in 2002 to 5.8% in 2010 is significant; the increases to 6.3% and 7.0% in 2013 and 2015 respectively, however, are not. This trend was present across nearly all subgroups. The multivariate model showed that women who were nulliparous, had fewer years of education, or were not receiving SRH services were more likely to be infertile.

CONCLUSIONS: This study confirms that parity and education level continue to impact infertility. Further, the results demonstrate that access to SRH services plays an important role in infertility. In contrast to previous studies, infertility in the United States is no longer on the decline, and age, race, and ethnicity did not have significant impacts on infertility. Given the rise of STIs and the persistent lack of access to SRH services, particularly among already vulnerable groups, the connection between access to care and infertility is ripe for further investigation.

P-75 Tuesday, October 15, 2019 6:30 AM

FERTILITY PRESERVATION FOR SOCIAL REASONS IN A POPULATION OF OLDER WOMEN: MYTH OR REALITY? Raymond Joseph Ocs, MD, Alberto Valcarcel, PhD, Marisa Tiveron, MS, Mercedes Leticia Guidobono, MS, Macarena Felici, MS, Soledad Bouzas, MS, Alberto Kenny, MD, IFER Ciudad Autónoma de Buenos Aires, Argentina.

OBJECTIVE: Oocyte cryopreservation for social reasons in older women is increasingly being performed in Argentina. Reproductive outcomes derived from such approach remain controversial. The aim of this study was to evaluate the reproductive performance of our oocyte vitrification program in this older population that chose fertility preservation for social reasons.

DESIGN: Retrospective descriptive study.

MATERIALS AND METHODS: The results of our Anticipated Gamete Exhaustion (AGE banking) program during the 2008-2017 year-period are presented. A total of 490 women were included in our study. Of these, 80.8% were 36 years old (396/490): 265 were between 36-39 and 131 ≥ 40 years old at the time of vitrification.

RESULTS: The average age of the patients at the time of oocyte vitrification was 37.6 ± 3.5 years old, and the number of vitrified MII oocytes was 6.2 ± 4.9. Only 32 women (6.5%) used their oocytes stored to date. In the subgroup of women at the age of 40 and above, the average age at cryopreservation was 39.1 ± 2.9 years and the average storage time was 2.8 ± 1.8 years. The average age at the time of thawing was 41.9 ± 3.4 years old. The average number of vitrified oocytes was 5.2 ± 3.1 with a survival rate of 96.5 ± 9.0%. The average number of injected oocytes was 5.0 ± 3.0 and 3.5 ± 2.2 achieved fertilization. Fertilization rate was 70.7 ± 27.8%. The average number of cleaved embryos was 3.2 ± 2.0 and the average number of day-3 embryos that went to day-5 blastocysts was 1.0. Seventy-nine percent of women who thawed their vitrified oocytes used sperm samples belonging to their male partners (24/32) while 25% (8/32) used donor sperm at the time of the procedure. A total of 36 ICSI procedures were performed in 32 women and 34 embryo transfers were done; two of the patients had no embryos for transfer. A total of 79 embryos were transferred. Clinical pregnancy rate was 29.4% (10/34), implantation rate was 12.6% (10/79), abortion rate 20% (2/10) and live birth rate was 23.5% (8/34). The live birth/cryopreserved oocyte rate was 5.1% (8/158). Of the 8 births recorded, 3 corresponded to women who vitrified their oocytes at 40 years of age, 2 at 41 years, 1 at 37 years, 1 at 38 years and 1 at 42 years.

CONCLUSIONS: According to our results, it is a myth that cryopreservation of any number of oocytes at any age in patients who choose to postpone their motherhood for social reasons ensures future biological motherhood. For that matter, it is a reality that a clear advice, based on the number of oocytes retrieved and the age of the patient at the time of cryopreservation, should be given regarding the real possibilities of becoming a biological mother when later using the cryopreserved material. Nonetheless, the ready availability of this reproductive strategy in this older age group offers, perhaps, the only chance of having their own genetic children in the future.

P-76 Tuesday, October 15, 2019 6:30 AM

THIS MYTH OR REALITY? Oocyte Cryopreservation for Social Reasons in Older Women: Transplantation. Yodo Sugishita, M.D., Ph.D.a Yuki Suzuki, M.D., Ph.D.a Sandy Nishimura, M.S.,b Meng Lingbo, M.B., Atsushi Uekawa, Ph.D., Akiko Tozawa, M.D., Ph.D.b Nao Suzuki, M.D., Ph.D.a St.Marianna University, School of Medicine, Kawasaki, Kanagawa, Japan; St. Marianna University, Kanagawa, Japan.

OBJECTIVE: Ovarian tissue cryopreservation for cancer patients has been gradually increasing in numbers. Though the standard method for ovarian tissue cryopreservation is slow freezing, the simple and feasible vitrification method has been gaining popularity, especially after the reports of live births using vitrification. Since vitrification uses high concentration of cryoprotectant, the safety concerning the residual cryoprotectant in thawed tissues should be verified.

DESIGN: This study quantified the residual cryoprotectant in thawed ovarian tissue and demonstrated the minimal culturing time needed before transplantation.

MATERIALS AND METHODS: Bovine ovaries were used to make ovarian tissue pieces (10x10x1mm) for slow freezing (DMSO 1.5M and PrOH 1.5M) and vitrification (EG 35%). One week later, the frozen ovarian tissue was thawed/warmed in media for either 60 minutes or 120 minutes. Then, the amount of residual cryoprotectant in the thawed ovarian tissue were measured by gas chromatography.

RESULTS: Before thawing, DMSO and PrOH concentration were 8.77±0.19% and 7.77±0.75% in slow frozen ovarian tissues, respectively, and EG concentration was 27.9±1.63% in vitrified ovarian tissues. Immediately after thawing, DMSO and PrOH concentration dropped to 0.71±0.18% and 0.66±0.08%, respectively; however, EG concentration remained relatively high (3.17±0.13%). After 60 minutes media culturing, DMSO, PrOH and EG concentrations were measured at 0.0072±0.0027%, 0.025±0.012% and 0.038±0.011%, respectively. When doubling the media culturing time to 120 minutes DMSO, PrOH and EG concentration to minimal at 0.00078±0.00046%, 0.0038±0.0016% and 0.0093±0.0069%, respectively.

CONCLUSIONS: The ovarian tissues, cryopreserved either by slow freezing or vitrification, needs to be thawed/warmed for at least 120 minutes in media to completely remove the cryoprotectants from the thawed ovaries. The concentration of cryoprotectants is removed by free diffusion. This research demonstrated the safety of thawed ovarian tissue for transplantation.


SUPPORT: Grant-in-Aid for Scientific Research(B), Nao Suzuki.

P-77 Tuesday, October 15, 2019 6:30 AM

EMPLOYER-BASED INSURANCE COVERAGE DRAMATICALLY INCREASES UTILIZATION OF PLANNED OOCYTE CYROPROTECTION. Arielle S. Yeshua, MD, Christine Mullin, M.D., Avner Hershlag, M.D., Tomer Singer, MD, Randi H. Goldman, M.D. Northwell Health Fertility, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: Planned oocyte cryopreservation (OC) is gaining recognition in the public and medical communities as a viable option for fertility preservation. However, cost is a significant barrier to planned OC utilization for many women, and most insurance plans do not include this benefit.

Beginning in 2018, our tertiary care academic medical center initiated coverage for planned OC. The purpose of this study is to determine the impact on planned OC utilization at our center in the year immediately prior to and the year of insurance coverage commencement for employees.

DESIGN: Retrospective Cohort Study

MATERIALS AND METHODS: Planned OC cycles from 2017 and 2018 were analyzed. Patient demographics and cycle outcomes were compared.
between cycles occurring in 2017 vs. 2018 according to insurance coverage and insurance type, maternal age, number of oocytes retrieved, and number of oocytes frozen. Only a patient’s first cycle was included in the final analysis. Two-tailed Fisher’s exact tests were performed; p<0.05 determined significance.

RESULTS: Between January 2017 and December 2018, 123 unique patients presented to our fertility clinic and underwent planned oocyte cryopreservation. Patient age ranged from 23 to 43 years and the mean age did not significantly differ between 2017 and 2018 (34.9 vs. 35.2, respectively). There was a 12% overall increase in planned OC utilization from 2017 (N=58) to 2018 (N=65). Significantly more patients had any insurance coverage in 2018 vs. 2017 (71.9% vs. 40.4%, p<0.001), a 78% increase. From 2017 to 2018, the number of patients undergoing planned OC who were employed with hospital-based insurance coverage increased by a factor of 9 (5% to 41.5%, p<0.001). In contrast, the number of self-pay patients significantly decreased from 2017 to 2018 (p=0.001). No significant differences were found regarding cycle outcomes, including number of oocytes cryopreserved.

<table>
<thead>
<tr>
<th>Variable</th>
<th>2017</th>
<th>2018</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
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<td>40.4</td>
<td>0.001</td>
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<tr>
<td>% employees</td>
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<td>35.2</td>
<td>NS</td>
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<td>AMH (ng/mL)</td>
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<td>3.13</td>
<td>NS</td>
</tr>
<tr>
<td>Number oocytes retrieved</td>
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<td>16.2</td>
<td>NS</td>
</tr>
<tr>
<td>Number oocytes cryopreserved</td>
<td>11.6</td>
<td>12.5</td>
<td>NS</td>
</tr>
</tbody>
</table>

CONCLUSIONS: A greater proportion of women seeking planned OC at our facility had insurance coverage for treatment in 2018 vs. 2017. Employer-based insurance coverage for planned OC yielded a significant increase in planned OC utilization by hospital employees. This data underscores the impact insurance coverage has on planned OC utilization rates. As awareness of coverage increases and other employers begin to expand benefits, we expect planned OC utilization rates to continue to rise.

P-78 Tuesday, October 15, 2019 6:30 AM

OOCYTE VITRIFICATION FOR ANTICIPATED GAMETE EXHAUSTION (AGE -BANKING) - A SYSTEMATIC REVIEW AND META-ANALYSIS OF SOCIAL TRENDS AND EFFICACY, Shira Baram, MD, a Noga Fuchs - Weitzman, MD, a Janice Montbriand, Ph.D., a Clifford Lawrence Librach, MD, a, b CreAte Fertility Centre, Toronto, ON, Canada; c Department of Obstetrical Anesthesia, Sunnybrook Health Sciences Centre, Toronto, ON, Canada.

OBJECTIVE: To explore current trends in attitudes and knowledge of oocyte vitrification freezing (VF) for fertility preservation, as well as to provide an update on the efficacy of the process.

DESIGN: A systematic review and meta-analysis.

MATERIALS AND METHODS: We conducted a systematic search using PubMed/MEDLINE, EMBASE, the Cochrane Database and PsychINFO, using appropriate controlled vocabulary, to identify all relevant studies published from Jan 2007 to Nov 2018. The review protocol followed PRISMA guidelines in PECO format, and was registered with PROSPERO (#CRD42019128268). The protocol was comprised of two parts; the first addressed attitudes and knowledge regarding AGE-banking, the second focused on evaluating AGE-banking efficacy and outcomes while comparing these metrics with efficacy and outcomes in vitrified donor oocytes and in cases of supernumerary oocytes vitrified following infertility treatments. Only original articles published in peer-reviewed journals written in English were included.

RESULTS: The literature search yielded 8038 articles of which 58 were included in the meta-analysis: 20 in the section exploring attitudes towards AGE-banking, and 38 in the section exploring its efficacy. Most respondents were aware of AGE-banking, mainly from online sources, and believed the ideal timing for AGE-banking is before women turn 35y/o. Only 40% of respondents answered correctly, when asked about the procedure and its associated risks and anticipated success rates. While two-thirds endorse AGE-banking for others, only a third would consider it for themselves. The main factors affecting the decision whether or not to perform AGE-banking in declining order were: 1. being wary of potential health implications, 2. perceived low success rate of the procedure, 3. financial considerations, and 4. time commitment. The results of AGE-banked vitrified oocytes, were favorable and approached those obtained utilizing donor oocytes, with a post-thaw survival of 84%, fertilization rate of 74%, cleavage rate of 89%, implantation rate of 41%, clinical pregnancy rate of 50%, and live birth rate of 32%. Results obtained by utilizing supernumerary vitrified oocytes lagged behind. Currently there is no available data regarding blastulation rate and embryo quality for embryos derived from AGE-banked oocytes.

CONCLUSIONS: AGE-banking provides a reasonable and adequate method for preserving fertility, yet gaps in attitudes and knowledge, as well as affordability, result in under-utilization. This review points to a general lack of awareness regarding the process, its efficacy, and the ideal time to pursue AGE banking. Future research should include large scale cohort studies to further evaluate changes in attitudes and knowledge. There is also a need for establishing international registries for AGE-banking that would provide information on the efficacy of the process as well as on related health implications.

SUPPORT: Create Fertility Centre

P-79 Tuesday, October 15, 2019 6:30 AM

FERTILITY PRESERVATION: FROZEN IN TIME? Stephanie R. Baum, MD,a Randi H. Goldman, M.D., a Tomer Singer, M.D., b Christine Mullin, M.D., c Lenox Hill Hospital - Northwell Health, New York, NY; d Northwell Health Fertility, Manhasset, NY; e Northwell Health Fertility, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: There has been an increase in the number of patients opting to undergo oocyte and embryo banking since removal of the “experimental” egg freezing label. However, to date, relatively few women have returned to use frozen gametes. The purpose of this study is to examine the relationship between number of oocyte and embryo banking cycles and use of previously banked oocytes and embryos.

DESIGN: Retrospective study of select SART-affiliated clinics

MATERIALS AND METHODS: A total of 179,982 cycles from 69 SART-affiliated clinics from four states (Georgia, Illinois, Massachusetts, and New York) were included; 10 clinics were excluded due to missing SART data. Information on number of oocyte and embryo banking cycles as well as number of cycles from previously frozen oocytes and embryos was collected from the years 2015-2017. The ratio between number of new oocyte and embryo banking cycles to cycles utilizing previously banked oocytes and embryos was calculated.

RESULTS: From 2015 to 2017, there was an increase in the total number of cycles from 54,540 to 65,138, representing an increase of approximately 19%. The number of embryo banking cycles was largely unchanged in this time frame, ranging from 918 to 1,007, approximately 1.5-1.7% of the total number of cycles. The number of oocyte banking cycles increased linearly from 2,563 to 3,185, representing an increase of 19.5%. In 2015, 2016, and 2017, the number of embryo banking cycles converted from fertility preservation was 25%, 18%, and 20% of the total number of embryo banking cycles, respectively. The number of oocyte banking cycles converted from fertility preservation was only about 1-1.5% of the number of oocyte banking cycles.

CONCLUSIONS: Fertility preservation continues to be a major focus of reproductive health and utilization of planned oocyte cryopreservation is increasing. In this select population, the number of embryo banking cycles converted from fertility preservation cycles is approximately 20-25% of the number of embryo banking cycles, but the number of oocyte banking cycles converted from fertility preservation remains a small percentage of the number of oocyte banking cycles. To date, relatively few women have returned to use their frozen gametes. We expect this percentage to rise.

References: None

SUPPORT: None
OBJECTIVE: Fertility preservation counseling is recommended for all patients undergoing fertility impacting cancer treatments. Although multiple options exist, patients face significant barriers to fertility preservation including knowledge deficits, access issues, possible treatment delays, psychologic stress and high cost. Our fertility division has partnered with a non-profit foundation to provide fully funded fertility preservation to patients undergoing cancer treatment. The goal of this project is to explore referral patterns and follow up for fertility preservation when all options are provided within the patient's ability.

DESIGN: Retrospective chart review

MATERIALS AND METHODS: All female patients ages 15-39, with cancer or precancerous diagnoses, who were referred for outpatient fertility preservation between 2010-2018. All procedure and monitoring costs were covered by the foundation for patients who did not have insurance coverage for fertility preservation and the met the income criteria. Data on demographics, cancer treatment and fertility preservation were collected from medical records. Outcomes included age, insurance status, fertility preservation treatment offered, and acceptance and follow-through of fertility preservation services.

RESULTS: 122 women met the inclusion criteria with a mean age of 28 at the initial visit. 90.2% (n=110) of patients presented for the scheduled appointment. Of those scheduled, 26.7% had public insurance, 66.7% had private insurance, 5.0% were uninsured and 1.6% had no insurance data available for review. 95.5% (n=110) of patients were offered oocyte or embryo cryopreservation. 66% (n=69) of those patients who were offered fertility preservation followed through with cryopreservation. 40% of uninsured patients and 56% of those with public insurance underwent oocyte/embryo cryopreservation.

CONCLUSIONS: Fertility preservation counseling is essential in the care of adolescent and reproductive-aged patients with cancer. However, fertility preservation can be expensive and is often not covered by insurance. Our fertility division has partnered with a non-profit foundation to provide fully funded fertility preservation. The majority of patients in this study not only presented for their appointment but also followed through with treatment when offered in the setting of a cost-covering grant. This type of non-profit foundation could serve as a model for others practicing in states without broad insurance coverage for fertility preservation.

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All patients provided written informed consent prior to their participation. The study design was approved by the institutional review board of our facility.

RESULTS: A total of 217 patients were referred and attempted sperm cryopreservation in Yokohama City University Medical Center from January 2012 to September 2017. Of those, 12 patients (5.5%) were in status peri-treatment of non-malignant diseases at the time of consultation.

The median age was 29.5 years (range: 18–51 years). Breakdown of original diseases was aplastic anemia (3), interstitial pneumonia (2), eosinophilic granulomatosis with polyangiitis (2), and others (5: collagen disease etc). Breakdown of therapeutic regimen was cyclophosphamide with hematopoietic stem cell transplantation (9), cyclosporine (4), and methotrexate (8). Mean sperm concentration was significantly higher than that of patients with malignancies (58.26±42.53 vs. 27.13±29.08 million/ml, P < 0.001).

And in all cases, sperm cryopreservation was successfully carried out. Of the 5 cases referred from our own institution, 3 were still in maintenance, and in 2 cases, samples were discarded on their request. On the other hand, of 7 cases referred from other institutions, 5 patients have not visited our hospital.

CONCLUSIONS: For patients with non-malignant diseases, pretreatment sperm cryopreservation should be carried out before gonadotoxic treatment.

In addition, establishing a network that encourages patients to visit us for maintenance of cryopreservation is thought to be essential because patients from other facilities did not visit for maintenance at a higher rate.

P-82 Tuesday, October 15, 2019 6:30 AM

EQUALLY OPPORTUNITY FOR ALL? AN ANALYSIS OF RACE AND ETHNICITY IN FERTILITY PRESERVATION (FP) IN A MAJOR AMERICAN CITY.

Paxton E. Voigt, BA,1 Jennifer K. Blakemore, MD,2 Teppei Takeshima, M.D, Shinnosuke Kuroda, M.D, Yasushi Yamura, Ph.D,Yokohama City University, Medical Center, Yokohama, Japan.

OBJECTIVE: It has been suggested that socio-demographic factors may affect access to FP opportunities.1 In one of America’s most racially diverse cities, we sought to compare the racial make-up of patients with cancer (Ca) who completed FP against the overall racial diversity (including Hispanic origin) identified in the incidence of Ca in women of reproductive age in our city.

DESIGN: A retrospective cohort study and cross-sectional comparison of all medical embryo banking (Em) and egg freezing (Eg) cycles from 1/2017-12/2018 at our center.

MATERIALS AND METHODS: All patients who completed at least one medical Em or Eg cycle were reviewed. Race was self-reported at time of recent Ca incidence data by race2 and available city census data by race, age and gender.3 Statistical analysis included chi square goodness of fit and test for independence where appropriate, with p < 0.05 considered statistically significant.

RESULTS: 107 patients who completed medical FP were included. Overall, 55 (51.4%) identified as White, 3 (2.8%) as Black, 13 (12.2%) as Asian, 6 (5.6%) as Hispanic, 3 (2.8%) as other and 27 (25.2%) did not report.

40.2% of patients were diagnosed with Breast Ca, 15.0% Gynecologic Ca, 15.0% Hematologic Ca, 5.6% Neurologic Ca, 4.7% GI Ca, 4.7% Sarcoma, 3.7% Endocrine Ca, 2.8% other Ca and 7.5% tested BRCAX with scheduled BSO. There was no significant difference in racial distribution by Ca type (p=0.255). A subgroup analysis excluding the BRCAX+ patients and those races not reported by the census3 (n=69) was then performed to compare the racial distribution of patients who completed medical FP at our center with the racial distribution of women of reproductive age who were diagnosed with Ca in our city. Based on the calculated frequency of race within the incidence of Ca in women of reproductive age (42% White, 21% Black, 10% Hispanic, 21% Asian, 8% Other), an expected number of FP cases for each race was calculated and compared. Results show that there is a statistically significant difference between observed (O) and expected (E) cases of FP by race at our center; White 470/29E, Black 30/15E, Asian 60/19E, Hispanic 60/17E (X2=16.07, df 3, p < 0.001). This FP subgroup was further analyzed by FP type [Em (n=31, 44.9%) vs Eg (n=38, 55.1%)]. A statistically significant difference in racial distribution by FP type was observed; White 66.0% Eg vs 34.0% Em, Black 33.3% Eg vs 66.7% Em, Asian 46.2% Eg vs 53.8% Em and Hispanic 0% Eg vs 100% Em (X2=10.60, df 3, p < 0.014).
CONCLUSIONS: There is a difference in the observed versus expected racial distribution of patients completing medical FP at our clinic, as well as a difference in the racial distribution between procedure types (Eg vs Em). Black and Hispanic patients were underrepresented in FP and White patients had a higher incidence of Eg, while non-White patients had a higher incidence of Em. Further studies are needed to determine if these differences generalize beyond our clinic and to identify modifiable factors that can improve equal opportunity to all patients.


P-83 Tuesday, October 15, 2019 6:30 AM

WHAT IS IMPORTANT TO WOMEN CONSIDERING FERTILITY PRESERVATION BEFORE CANCER TREATMENT? COMPARING DECISION-MAKING VALUES WITH AND WITHOUT USING THE PATHWAYS PATIENT DECISION AID WEBSITE. Sukkhampal Campbell, MD, Aubri Hoffman, PhD, June Weston, Sr Research Coordinator, Laura Covarrubias Crocker, MSPH, Deborah Holman, CRNP, Ashley Houston, MSCI, OTD, Robert Volk, PhD, Terri Woodard, MD, Baylor College of Medicine, Houston, TX; The University of Texas MD Anderson Cancer Center, Houston, TX.

OBJECTIVE: Deciding whether to undergo fertility preservation treatment prior to initiating cancer treatment is a complex personal decision. Patient decision aids have been proposed to help women navigate these decisions by providing up-to-date, balanced information and helping women clarify how they value key factors in their decision. The objective of this study was to compare female cancer patients’ decision-making values (i.e., the importance of 10 key factors) and treatment preferences with and without the use of the Pathways patient decision aid website.

DESIGN: Randomized Controlled Trial

MATERIALS AND METHODS: Pathways – a fertility preservation patient decision aid website for women with cancer explains the risk of cancer-related infertility and describes fertility preservation treatments (tailored by cancer type) and other family-building options. It also provides structured decision-making activities to help women personalize the information and prepare to discuss the options with their providers. Thirty newly-diagnosed reproductive-age women were randomized to view Pathways or standard educational brochures, then rate how important 10 factors were in their decision (“Not Sure”, or from 0 = Not Important to 10 = Very Important) and to indicate their treatment preferences. At 2 months, women indicated whether they had completed a fertility preservation treatment.

RESULTS: Among the 10 factors, women rated Avoiding regret about my decision, Starting my cancer treatment as soon as possible, and Being able to genetically screen my future child for cancer as most important in their decision-making (9.4, 9.2, and 7.5 out of 10). As expected, decision-making values were highly individual and no systematic differences were observed between groups. Women who viewed the patient decision aid were more confident in their treatment preferences (9.3 versus 8.2 out of 10). All of the women in the control group indicated they were Not Sure or would Wait and See, while half of the women who viewed Pathways chose egg or embryo freezing. However, only 11 women were able to complete the study and only one woman had chosen fertility preservation at 2 months.

CONCLUSIONS: Interacting with an interactive patient decision aid may help women become more clear and confident in their fertility preservation decisions. It may also help providers assess patients’ values and preferences. However, addressing dissemination challenges may be key in providing timely care for all women.

P-84 Tuesday, October 15, 2019 6:30 AM

ELECTIVE OOCYTE CRYOPRESERVATION COUNSELING TOOL BASED ON NEXT GENERATION SEQUENCING RESULTS. Mariana Miguens, M.D., Andrea Natalia Coscia, MD, Daniela Lorenzi, B.Sc, Melina Elena Bilinski, B.Sc, Mariana Cecilia Calvo, MD, Rocío Belén Anria, M.D., Milfra Espinal, MD, Sergio D. Papier, Sr., M.D, ”CEGYR, Ciudad Autonoma de Buenos Aires, Argentina; “NOVA-GEN, Ciudad Autonoma de Buenos Aires, Argentina.

OBJECTIVE: The aim of this study was to determine the appropriate age for counseling and referral in fertility preservation, based on the number of mature oocytes (MII) needed to achieve an euploid embryo. We consider that age is the main variable that determines the quantity and quality of oocytes as well as the average and euploidy of embryos obtained.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: 150 patients who performed preimplantation genetic testing of aneuploidies (PGT-A) cycles from 2016 to 2018 at a private IVF practice were included for this study. The molecular analysis was performed by Next-generation sequencing (Veriseg-PSG, Illumina).

The age range was between 27 and 46 years. Patients were arbitrarily divided into four groups: <35, 35-37, 38-40 and >40 years.

The variables analyzed per cycle were: the number of metaphase II oocytes (MII), the number of euploid blastocysts, the number of MII required to obtain an euploid blastocyst. Statistical analysis was performed by ANOVA results.

CONCLUSIONS: Oocyte cryopreservation by social reasons represents a legitimate exercise of women reproductive autonomy. One of its main advantages is that oocytes can be stored for a long time without this implying a quality detriment. There is a worldwide tendency to postpone motherhood. As a woman ages, the chance of having an aneuploid embryo increases.

PGT-A is an alternative to perform in advanced maternal age.

Based on our results, we can infer that oocyte recovery is lower after the age of 35, affecting mainly patients older than 37 years old. Aneuploidy increases after 38 years old. The most relevant data for counseling is the number of MII oocytes required to obtain an euploid embryo. Also, we can conclude that up to 35 years old, patients would have enough oocytes to have at least two euploid embryos in a single cycle. Between 35-37 years old patients would only achieve one euploid embryo per cycle. After 38 years, between two to four cycles would be needed to have an euploid embryo.

Women age has a great impact on her reproductive capacity. We recommend assessment on fertility preservation between 30-34 years as the first approach and a second assessment between 35-37 years old.

Our conclusions emerge from an indirect analysis of the embryonic euploidy and there is still a need for comprehensive studies to develop an accurate clinical counseling tool.

<table>
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<th>Age group</th>
<th>Number of cycles</th>
<th>MII average / cycle</th>
<th>Euploid blastocysts average / cycle</th>
<th>MII required to achieve at least one euploid blastocyst</th>
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<td>1.89 7.02 (CI95%: 4.08-9.03) *</td>
<td>7.02 (C95%: 4.08-9.03) *</td>
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<td>35-37</td>
<td>33</td>
<td>9.42 (Min:2 Max: 26)</td>
<td>1.15 8.19 (CI95%: 6.59-10.07)*</td>
<td>8.19 (CI95%: 6.59-10.07)*</td>
</tr>
<tr>
<td>38-40</td>
<td>55</td>
<td>8.15 (Min:3 Max: 22)</td>
<td>0.53 15.38 (CI95%: 14.16-16.75)*</td>
<td>15.38 (CI95%: 14.16-16.75)*</td>
</tr>
<tr>
<td>&gt;40</td>
<td>44</td>
<td>8.18 (Min:1 Max: 24)</td>
<td>0.29 28.2 (C95%: 26.83-29.6)*</td>
<td>28.2 (C95%: 26.83-29.6)*</td>
</tr>
</tbody>
</table>

(*p<0.05, min: minimum, max: maximum)
OBJECTIVE: Oocyte In-vitro maturation (IVM) is a technique aimed to maximize reproductive potential for patients undergoing fertility preservation. Patients who suffer from compromised ovarian reserve, poor oocyte quality, or low number of MII oocytes at retrieval may benefit from employing IVM prior to cryopreservation. Over the past decade, optimization of oocyte maturation and cryopreservation techniques has enhanced cellular survival rates. More recent studies have suggested clinical utility of vitrified/thawed IVM oocytes (1), but data remains limited within the literature regarding reproductive potential. This study aims to assess the reproductive potential and genomic composition of blastocysts derived from vitrified/thawed IVM oocytes.

DESIGN: Retrospective cohort analysis.

MATERIALS AND METHODS: The study included all patients who underwent an elective oocyte vitrification cycle(s) with subsequent thawing and fertilization from 2010 and 2019. After oocyte retrieval, immature oocytes (Metaphase I and Germinal Vesicle stages) were cultured and were first assessed for maturity after 6 hours: Early-IVM (E-IVM). A second assessment was performed after 24 hours in culture: Late-IVM (L-IVM) as described by Escrich L et al. Matured oocytes were vitrified/thawed, underwent ICSI, and cultured sequentially to blastocyst stage. Cohorts were segregated into 2 groups: E-IVM and L-IVM oocytes. Fertilization, blastulation, and euploid rates were compared among cohorts. XI2, T-test, and logistic regression analyses were performed, significance was considered at (p<0.05).

RESULTS: 292 IVM oocytes obtained from 105 patients were thawed over the course of the study. 203 oocytes were E-IVM, while 89 oocytes were L-IVM. No differences were found in survival rates (81.2%, 80.8%, p=0.94), fertilization rate (53.9%, 56.9%, p=0.67), percentage of zygotes reaching cleavage stage (87.6%, 90.2%, p=0.93), and blastulation rate (49.4%, 40.2%, p=0.24). Utilizable blasts number was similar among groups (E-IVM: 38.6%, L-IVM: 37.9%, p=0.95), though a difference was found in the percentage of good quality blastocysts among groups: (70.5%, 9%, p=0.0004). Biopsied blast per group (34%, 27.5%, p=0.56) and euploidy rates (25%, 37.5%, p=0.53) were similar among cohorts. After adjusting for age, BMI, AMH, and total number of eggs retrieved per cycle, no association was found between the time to maturation and the odds of aneuploidy (OR 0.6, 95% CI 0.05-7.85, p=0.74) or the odds of developing a good quality embryo (OR 0.18, 95% CI 0.02-1.4, p=0.11).

CONCLUSIONS: Formerly, the culture of embryos derived from cryopreserved IVM oocytes was perceived as having low survival rates, suboptimal maturation, and an increased risk of aneuploidy. Our study demonstrated that IVM oocytes can be successfully cultured to the blastocyst stage and could be used for clinical treatment for infertile patients. By employing IVM, we can optimize the reproductive potential per oocyte retrieve. Moreover, implementation of IVM in ART centers may increase the number of transferable euploid blastocysts and enhance patients’ ability to build a healthy family.

REFERENCES:

SUPPORT: None.

OBJECTIVE: Patients of an advanced maternal age who have sometimes shown unsynchronized follicle growth often receive ovarian stimulation. In those cases, immature oocytes are collected from smaller follicles. Even immature oocytes are valuable for those patients, but it is necessary for those immature oocytes to be allowed to effectively mature in vitro. The aim of the present study was to evaluate whether supplementing culture media with human follicular fluid (HFF) could improve the maturation and subsequent embryonic development of immature mouse oocytes.

DESIGN: This was an experimental study. Mouse germinal vesicle (GV) oocytes derived from 8-10 week-old female B6D2F1 mice were divided into three groups according to their concentration of HFF supplementation: The first group used 100% HFF (all-FF group), the second group used culture media with 50% HFF (50%/C15/half-FF group), and the third group used only culture media (non-FF group).

MATERIALS AND METHODS: After obtaining informed consent, HFF obtained from the first puncture of a follicle during oocyte retrieval without blood contamination was used in this study. The culture media for in-vitro maturation (IVM) involved conventional media (Universal IVF media®) for human IVF treatment in addition to recombinant FSH (0.075 IU/ml) and hCG (0.1 IU/ml). The maturation rates of GV oocytes and the blastocyst formation rates were evaluated among the three groups. Maturation was defined as confirmation of MII stage chromosomes via staining Hoechst solution under fluorescence microscopy. The mature oocytes after IVM were inseminated and fertilized oocytes were additionally extended to the blastocyst stage (up to 124 hours).

RESULTS: The maturation rate following IVM in the half-FF group was 100%, which was significantly higher than that of the non-FF group (67.0%, p<0.05), but was similar to the all-FF group (92.0%). The fertilization rates of the all-FF, half-FF and non-FF groups were 78.1, 56.2 and 21.9%, respectively, which showed a significant increase in accordance with the inclusion of HFF. The blastocyst formation rates of the all-FF and half-FF groups were 61.1 and 63.3%, respectively, whereas that in the non-FF group (16.7%) was significantly lower (p<0.05).

CONCLUSIONS: Supplementing the culture media with HFF during IVM significantly improves the maturation rate of immature mouse oocytes, and the mature oocytes derived from IVM media with HFF possessed higher developmental potential for blastocyst formation. Supplementing IVM culture media with HFF could be useful option for the IVM of human immature oocytes.

OBJECTIVE: In vitro maturation (IVM), while successful in domestic and laboratory species, has not been widely adopted in human ART. This is due in part to low oocyte maturation in vitro, as well as the widespread success of stimulation protocols that include administration of hCG to induce ovulation followed by retrieval of mature oocytes. However, some patients are susceptible to ovarian hyper-stimulation (OHSS) using this approach. Retrieval of immature oocytes after minimal ovarian stimulation without an ovulation trigger would alleviate this concern. The objective of this IRB approved clinical trial is to evaluate the efficacy of a newly developed IVM system as a clinical treatment for infertile patients.

DESIGN: Prospective cohort study

MATERIALS AND METHODS: Beginning on D2 until D5 of the cycle, patients received 150 IU Menopur at 2 PM. Patients had an ultrasound and moved into IVM medium for 27-30 hr. Following IVM, cumulus cells were removed and eggs assessed for maturity. Mature (MII) oocytes underwent ICSI; immature oocytes were returned to IVM medium for an additional 18 hr, when any mature oocytes underwent ICSI. Zygotes (2PN) were cultured in sequential culture medium and good quality blastocysts vitrified on days 5, 6, and 7. All blastocysts were biopsied for PGT-A.
RESULTS: To date (January-April, 2019), 8 patients have participated in the clinical study. Four patients were diagnosed with PCOS, two patients with PCO and recurrent pregnancy loss, one patient with fibroids and unexplained infertility, and one patient with DOR and poor embryo quality. Average patient age (49.0±5.3 years) included: Age, 31.5±y; AMH 7.0 ng/mL; D3 FSH 6.3 mlU/mL; AFC, 45.1; and BMI 28.5. On the day of retrieval, average E2 was 248 pg/mL, and the average size of the largest follicle was 9.1 mm. In total, 234 immature oocytes were retrieved (average 29.3 oocytes per patient, range 5–55), of which 27 were atretic (11.5%). After pre-IVM and IVM, 114 (55.1%) oocytes matured; an additional 41 oocytes matured the following day for a total maturation percentage of 74.9% (155/207). After ICSI, 81/155 (52.3%) of eggs fertilized normally. Following culture, 6 good quality blastocysts (7.4%) were produced on D5, and 16 (19.8%) overall. Five of the eight patients (62.5%) produced at least 1 good quality blastocyst; all of these were PCO/PCOS patients. Ten of the 16 blastocysts produced were euploid (62.5%). To date, 2 patients have undergone FET; one has an ongoing pregnancy. CONCLUSIONS: IVM is successful in a clinical setting, and is logistically feasible in the typical IVF laboratory work flow. This aligns alleviates concerns of hyper-stimulation, and drastically reduces medication costs and injections. Thus, IVM is a realistic alternative ART approach for PCOS patients.

SUPPORT: None.

P-88 Tuesday, October 15, 2019 6:30 AM

THE TIMING OF THE RELEASE OF THE FIRST POLAR BODY PREDICTS THE CLEAVAGE RATE AFTER PARTHENOGENETIC ACTIVATION FOR HUMAN OO-CYTES OBTAINED BY IN VITRO MATURATION. Hiroimitsu Shirasawa, Ph.D. M.D., Yukiko Kumazawa, Ph.D., M.D., Wataru Sato, Ph.D., M.D., Kazumasa Takahashi, Ph.D., Yukihiro Terada, Ph.D., M.D. Akita University Hospital, Akita, Japan.

OBJECTIVE: Human parthenogenetic blastocysts (HPB) are important materials for making parthenogenetic human embryonic stem cells (pHESC) and so on. Though, the efficient method for making HPB considering the progress of time-lapse imaging (TLI) during in vitro maturation (IVM) has not been established. The objectives were to clarify the behavior of oocytes obtained by IVM during parthenogenetic activation (PA) and to characterize the features of TLI of cleaved embryos by focusing on the first polar body (PB) releases during IVM.

DESIGN: Basic research study.

MATERIALS AND METHODS: 55 immature oocytes were collected from resected ovaries of the 5 patients with endometrioid adenocarcinoma. These oocytes were assigned to either early or late groups based on the results of 24 hour IVM. Oocytes that released PB within 24 hours were defined as the early group, and underwent PA. On the other hand, oocytes that did not release PB after 24 hour IVM were subjected to an additional 24 hours of IVM, and the oocytes that subsequently released the PB were defined as the late group and underwent PA. PA; was carried out using calcium ionophore and 6-dimethylamínopurine, and subsequently oocytes were cultured in single step medium with observation by TLI. Based on the data from TLI of PA, the duration of pronucleus (PN) formation and oocytes cleavage rate were analyzed. Oct4 and Cdx2 of cleavage embryos were detected by immunofluorescence staining.

RESULTS: Oocytes were collected from five patients with a mean age of 36.0 ± 4.0 years, and IVM was performed on 50 oocytes. 15 oocytes were assigned to the early group and 13 to the late group. The rate of the oocytes which released PB was 56.0%. The duration of PN formation was significantly longer in the early group (60.2 ± 13.0 hours) than in the late group (23.9 ± 8.4 hours) (p=0.045). The over all cleavage rate was 39.3%, and the results was summarized in table 1. The rate of cleavage to 8 or more cells were significantly higher in the late group than in the early group. The overall rate of cleavage to morula was 7.1%. Revers cleavage was observed in 54.5% (early group 80.0%, late group 15.4%) of all cleaved embryos, and these did not all cleaved to morula. Oct4 was detected in the HPB in late group.

CONCLUSIONS: The timing of release of PB within IVM may related to the results of PA. This finding is an important point in creating an efficient pHESC, which we have clarified for the first time. It is probable that the time difference between nuclear maturation and cytoplasmic maturation is related, though the impact of the duration of PN formation is unknown at this time, and should be investigated in the future.

Financial support was provided by JSPS KAKENHI Grant Number 19K19320 (H.S.).

SUPPORT: This study was supported by A Kanzawa Medical Research Foundation.

P-89 Tuesday, October 15, 2019 6:30 AM

EMBRYOLOGIST FRIENDLY PROGRAMMED IVM WITH DELAYED BLASTOCYST TRANSFER. Bruce I. Rose, MD, PhD. Kevin Nguyen, MS, Samuel Brown, MD. Brown Fertility LLC, Jacksonville, FL.

OBJECTIVE: To design an approach to IVM (in vitro maturation) which can be easily integrated into a busy IVF laboratory and which results in oocytes with a high maturation rate, a good blastocyst production rate, and a reasonable pregnancy rate.

DESIGN: Our IVM protocol uses a programmed approach to enable scheduling cases and requires only laboratory techniques already used by the embryologist. Retrieval is designed to improve environmental conditions for oocytes. Embryos are transferred back in a subsequent FET cycle.

MATERIALS AND METHODS: Patients with a PCO pattern in their ovaries were recruited. Oral contraceptives were used to plan prospectively for a day for retrieval. Letrozole was started on day 5 after stopping oral contraceptives (SOC). FSH (25 to 75U/day) was started on the 7 after SOC. Ovulation was confirmed on day 11 or 12 after SOC. Oocyte retrieval was on day 13 or 14 after SOC. Cycles were cancelled if all follicles were less than 8 mm or if one follicle was greater than 13 mm.

On the day of retrieval we used a 5 cm 19g needle to enable flushing and limit dead space in the oocyte collection system to 0.000004 ml. This needle is constructed from a 5 cm 19g needle attached to a 17g needle with fluid entering at the junction of these two needles. Flush fluid is simultaneously pushed into both the 19g and 17g needles. Aspiration while flushing is used to empty the 17g needle into the collection tube. Our objective was to get the oocyte into the laboratory as soon as possible after it was aspirated from the follicle. The large volume of flush also enabled the embryologist to use routine oocyte retrieval laboratory techniques to locate oocytes in the aspirate.

Sage IVM maturation media with 10% heat inactivated maternal serum and 75 mIU FSH/ml was used. Oocytes were visually evaluated for maturity at retrieval and twice a day until 48 hours after retrieval. Mature oocytes were fertilized using ICSI. Zygotes were cultured to blastocysts. Blastocysts were vitrified on day 5 or 6 after ICSI. Oral contraceptives were used as patients transitioned into our routine FET program.

RESULTS: Twenty patients were recruited. Two cycles were canceled for follicles that were too large. The average number of oocytes retrieved was 11. The average maturation rate was 85%. The average fertilization rate per mature oocyte was 86%. Two patients had an oocyte aspiration, which did not produce blastocysts. Thus 89% of results resulted in blastocysts with an average of 3 blastocysts per patient and with 36% of fertilized oocytes becoming blastocysts. After one FET cycle, 50% of patients had a clinical pregnancy, and 38% had an ongoing or delivered pregnancy.

CONCLUSIONS: IVM can be adapted to not disrupt a clinical IVF lab. Better treatment of oocytes during retrieval resulted in better maturity and blastocyst production.

IVF OUTCOME PREDICTORS - AGE

P-90 Tuesday, October 15, 2019 6:30 AM

INCREASED PATERNAL AGE IS ASSOCIATED WITH DECREASED BLASTULATION AND EUPLOID RATES BUT NOT PREGNANCY OUTCOMES IN THE SETTING OF A EUPOLOID SINGLE EMBRYO TRANSFER. Brent M. Hanson, MD,a Julia G. Kim, MD, MPH,a Emily K. Osman, MD,a Ashley W. Tieg,a Shelby A. Neal, MD,a Ruth B. Lathi, MD,a Richard Thomas Scott, Jr., MD, Jason M. Franasiak, MD,a IVI-RMA New Jersey, Basking Ridge, NJ; Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA; aStanford Fertility and Reproductive Medicine Center, Sunnyvale, CA.

OBJECTIVE: The relationship between paternal age and assisted reproductive technology (ART) outcomes is often confounded by factors arising from the female partner. In order to minimize these effects, this study utilized...
preimplantation genetic testing for aneuploidy (PGT-A). To date, the role of paternal age on ART outcomes remains controversial. This study sought to determine whether increasing paternal age is associated with adverse outcomes in the setting of a single embryo transfer (SET) of a euploid embryo.

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** This study was performed at a large fertility practice. Included couples underwent a first cycle of in vitro fertilization (IVF) using ejaculated sperm and then underwent intracytoplasmic sperm injection (ICSI) and PGT-A followed by SET of a euploid embryo. Kruskal-Wallis testing, Chi-square analysis, and linear regression models were utilized to assess the relationship between paternal age and rates of implantation, delivery, biochemical loss, and clinical loss. The relationship between paternal age and fertilization rate, blastulation rate, and euploid rate was also analyzed.

**RESULTS:** 4367 couples met inclusion criteria. Mean male partner age was 37.1 ± 5.5 years, with 87 male patients over age 50. Mean female partner age was 34.9 ± 4.0 years. Among couples undergoing SET of a PGT-A tested embryo, implantation rate was 82.1% (3566/4367 embryos transferred), delivery rate was 56.8% (2480/4367 embryos transferred), biochemical loss rate was 8.8% (385/4367 embryos transferred), and clinical loss rate was 7.2% (313/4367 embryos transferred). Adjusting for female age, there was no statistically significant association between male partner age and implantation rate (p = 0.40), delivery rate (p = 0.48), biochemical loss rate (p = 0.18), or clinical loss rate (p = 0.19). A sub-group analysis evaluating men over age 50 (n = 877) also failed to demonstrate a relationship between paternal age and implantation rate (p = 0.32), delivery rate (p = 0.19), biochemical loss rate (p = 0.08), or clinical loss rate (p = 0.42).

For men over age 50, there was a significant association observed between paternal age and blastulation rate (p = 0.01) as well as euploid rate (p = 0.03) but no significant association between age and fertilization rate (p = 0.92).

When using 40 years as a cutoff point, the relationship between paternal age and blastulation rate remained significant (p = 0.0006) but there was no association between age and euploid rate (p = 0.86) or fertilization rate (p = 0.70).

**CONCLUSIONS:** When couples undergo SET of a euploid embryo, increasing paternal age does not appear to detrimentally impact pregnancy outcomes, including implantation rate, delivery rate, biochemical loss rate, and clinical loss rate. However, paternal age greater than 50 negatively affected blastulation and euploid rates. Poorer blastulation was also seen in men over age 40. If a single euploid embryo is transferred, the role of paternal age is unlikely to be significant, but increasing paternal age may negatively impact a couple’s ability to create a euploid embryo and thus cumulative pregnancy rate.

**SUPPORT:** None.

**P-92 Tuesday, October 15, 2019 6:30 AM**

**CLINICAL PREGNANCY OUTCOME ACCORDING TO AGE OF PATIENTS WITH HIGH PROPORTION OF FAILED OOCYTE MATURATION IN ICSI**

**OBJECTIVE:** The purpose of this study was to compare the clinical pregnancy outcomes according to age of patients with high proportion of maturational arrest oocytes in ICSI cases.

**DESIGN:** Retrospective cohort study. This study was conducted on patients with ICSI cases who had transferred embryos. Clinical outcomes were analyzed by dividing the maturational arrest rate (under 40%/over 40%) and the age of 38yrs (under 38yrs/over 38yrs).

**MATERIALS AND METHODS:** From June 2011 to December 2018, a total of 2495 cycles were analyzed in this study. All the patients underwent ICSI cycle followed by fresh embryo transfer. Inclusion criteria: female age between 23 and 48yrs, use of fresh or cryopreserved sperm. Exclusion criteria: surgically retrieved sperm.

These patients were divided into group A (maturational arrest rate <40%, Age <38yrs), group B (maturational arrest rate ≥40%, Age <38yrs), group C (maturational arrest rate <40%, Age ≥38yrs) and group D (maturational arrest rate ≥40%, Age ≥38yrs). The pregnancy outcomes were compared among these 4 groups.

**RESULTS:** A total of 2495 cycles were included (group A = 1355, group B (n) = 90, group C (n) = 960 and group D (n) = 54). There was no significant differences in fertilization rate between groups (group A vs. B: 80.7% ± 20.0 vs 81.0% ± 24.1, P=0.958 and group C vs. D: 83.2% ± 20.1 vs 83.4% ± 19.6, P=0.743). But there was a significant difference in implantation rate, pregnancy rate, and miscarriage rate. More than 40% of oocyte maturation failure group had lower levels of embryo quality. There was significant difference in at least one good quality embryo transfer cycle rate (group A vs. B: 69.4% vs 64.7%, P<0.001) and group C vs. D: 63.1% vs 55.6%, P<0.001. And more than 40% of oocyte maturation failure group had lower clinical pregnancy rate (group A vs. B: 41.6% vs 20.0%, P<0.001 and group C vs D: 25.7% vs 7.4%, P<0.0001) and ongoing pregnancy rate (group A vs. B: 35.9% vs 14.4%, P<0.001 and group C vs D: 17.0% vs. 1.9%, P<0.001).

**CONCLUSIONS:** According to our study, high rate of oocyte maturation failure group had lower embryo quality, pregnancy rate and higher miscarriage rate. However, there was no effect on in fertilization rate. There was a similar
Objective: To compare assisted reproductive technique (ART) outcomes after frozen-thawed cleavage stage embryo transfer between embryos transferred 2 to 5 hours and transferred 18 to 24 hours after thaw.

Design: Double-blinded, randomized, controlled trial (ClinicalTrials.com NCT03581001).

Materials and Methods: A total of 388 patients submitted to ART treatment who had their embryos frozen on day-2 had their data analysed. All embryos were cryopreserved using the same vitrification protocol (open system) and all patients received the same endometrial priming with estradiol valerate, at 6 mg/d, taken orally, followed by vaginal progesterone started on day-0. Randomization was performed using sealed envelopes. We calculated that 286 subjects would provide 80% power for detecting over 10% absolute difference in pregnancy rate with α = 0.05. The study was performed from May 2017 until December 2018.

Results: A total of 179 patients had embryos transferred 2-5 hours after thaw (Group D2) and 209 patients had embryos transferred 18-24 hours after thaw (Group D3). The mean age in Group D2 was 36±4.4 and 36±5.4 in group D3. Forthel D2 group vs. D3 group, respectively, the clinical pregnancy rate was 30.7% and 36.8% (p<0.2) and ongoing pregnancy rate was 28% and 33.5% (p = 0.2).

Conclusions: ART outcomes were similar after transfer of frozen-thawed cleavage stage embryos that were kept in culture either for 2 to 5 hours or 18 to 24 hours after thaw. These results suggest that increasing the culture time of embryos in one day to improve selection before transfer does not increase pregnancy rate. More studies are necessary to confirm our results.

Reference: None.

Support: Grant form CNPq (Brazilian research council) to Selmo Geber.
showed that both maternal age and oxygen tension in extended embryo culture affect blastocyst formation rate, and that both maternal age and embryo quality on day 3 also affect usable blastocyst rate (p<0.0001). Blastocyst formation rate was significantly higher in the 2% O2 group (58.3%) than in the 5% O2 group (55%), p<0.005. The extended culture under ultra-low O2 tension improved for 35-37 year of age group both blastocyst formation rate: 61.1% vs 53.4% in the 2% O2 and 5% O2 groups respectively, p<0.001; and usable blastocyst rate: 38.7% vs 31.8% in the 2% O2 and 5% O2 groups respectively, p<0.005. Maternal age impacts negatively on blastocyst formation rate as well as usable blastocyst rate in each group of day 3 embryo quality.

CONCLUSIONS: Blastocyst and usable blastocyst formation rates on day 5/6 both significantly decrease with maternal age. Beyond the age of 37, blastocyst rate is reduced by 28%. Therefore, this study leads us to question the relevance of extended culture beyond that age. Nevertheless, 2% O2 tension in extended culture is associated with better blastocyst yield. In 35-37 years of age group, it also improves usable blastocyst rate. This data supports the idea that maternal age and embryo quality on day 3 are crucial criteria to be considered for the choice of extended culture strategy.

**P-96** Tuesday, October 15, 2019 6:30 AM
THE EFFECTS OF CO-CULTURE WITH AUTOLOGOUS CUMULUS CELL ON PREGNANCY OUTCOMES BY MATERNAL AGE. Daehan Kim, Master, Jeong-Ho Cha, Ph.D., Sun-Hee Shin, Master, Yun-Jung Kim, Master, Seul-Ki Lee, Master, Ji-Hae Kim, Master, Hwa-Yeong Kim, Master, Seung-Hyun Back, Master, Ji-Hyun Ahn, M.D., Hye-Young Kim, M.D., Kyung-Ah Pak, M.D., Ji-Sung Yoon, M.D., Seo-Young Park, M.D. Agaon fertility clinic, seoul, Korea, Republic of (South).

OBJECTIVE: It is known that the incidence of apoptosis in cumulus cells is associated with women age. In this study, we aimed to evaluate the influence of autologous cumulus cell co-culture on pregnancy outcomes by maternal age.

DESIGN: A retrospective study was performed from January 2014 to December 2018.

MATERIALS AND METHODS: A total of 588 cycles which underwent GnRH long or antagonist protocol with fresh embryo transfer were analyzed. The cycles with severe male factor and single embryo transfer were excluded. The cycles were divided into two groups according to maternal age: 32–36 years (Group 1), ≥37 years (Group 2). Each group had embryos cultured in defined medium with autologous cumulus cell (ACC) or without autologous cumulus cell (No ACC). The ACC was dissected from the patient’s oocyte-cumulus complexes using two 29-gauge needles and washed twice. The collected ACC was directly put into the culture medium without hyaluronidase treatment. We compared the rates of clinical pregnancy, ongoing pregnancy, and implantation rate as well as usable blastocyst rate in each group of day 3 embryo quality.

RESULTS: The woman age, man age, and Day 3 good quality embryo rate were similar in the two groups. In the Group 1 cultured with ACC, the pregnancy rates were significantly increased compared to ACC (Clinical Pregnancy, 49.4% vs. 37.2%, P < 0.05). Ongoing Pregnancy: 45.6% vs. 31.0%, P < 0.05. Implantation: 32.1% vs. 22.1%, P < 0.05). The clinical pregnancy and ongoing pregnancy rates were not statistically different between ACC and No ACC in Group 2 (Clinical Pregnancy: 16.5% vs. 26.3%, P = 0.06). Ongoing Pregnancy: 13.4% vs. 19.4%, P = 0.21). However, implantation rate was significantly decreased in ACC (9.0% vs. 15.8%, P < 0.05).

CONCLUSIONS: The age of women might influence the pregnancy outcomes. These results suggested that co-culture with autologous cumulus cell is not recommended to patients over 37 years old for the improvement of pregnancy rate. Further studies are needed to measure the incidence of apoptosis in autologous cumulus cells to compare the correlation between woman age and the incidence of apoptosis.

**IVF OUTCOME PREDICTORS - EMBRYO TRANSFER**

**P-97** Tuesday, October 15, 2019 6:30 AM
LIVE BIRTH RATES AFTER BLASTOCYST TRANSFERS PERFORMED BY FELLOWS. Dana B. McQueen, M.D., M.A.S, Jared C. Robins, MD, John Zhang, PhD, Eve C. Feinberg, M.D. Northwestern University, Chicago, IL.

OBJECTIVE: To evaluate live birth rates following embryo transfer performed Reproductive Endocrinology and Infertility fellows compared to attending physicians.

DESIGN: Retrospective Cohort Study.

MATERIALS AND METHODS: Institutional Review Board approval was obtained. Women undergoing blastocyst transfer between 1/2015 and 1/2018 were reviewed. Cycle characteristics and outcomes were compared between embryo transfers performed by fellows and attending physicians. A sample size of 750 embryo transfers was required to detect a 10% difference between groups, with 80% power and alpha of 0.05.

RESULTS: A total of 940 blastocyst transfers were included; 254 performed by five fellows and 686 performed by ten attending physicians. There were no differences in the mean age, anti-mullerian hormone (AMH) levels and rate of preimplantation genetic testing for aneuploidy (PGT-A) testing between groups (Table). The afterload technique was utilized more frequently by fellows, 95.2% (242/254) vs. 87.5% (602/686), P = 0.0004. A stylet was used less frequently by fellows, 0.4% (1/254) vs. 4.5% (31/686), P = 0.0008. The pregnancy rate in the fellow group was not significantly different from the pregnancy rate in the attending group: 72.8% (185/254) among fellows versus 67.6% (461/686) among attending physicians, p = 0.27. There were also no significant differences in the live birth rate between groups, 51.6% (131/254) versus 49.4% (339/686) respectively, p = 0.61. After controlling for embryo transfer technique and stylet use, there remained no difference in pregnancy outcomes. The average pregnancy rate among fellows performing their first 20 embryo transfers was 67.4% (58/86), and was no different from the average pregnancy rate among attending physicians, 67.6% (461/686) P = 1.0.

**TABLE 1. Group Characteristics (N=940 transfers)**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Fellow ET (N=254)</th>
<th>Attending ET (N=686)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (SD), yr</td>
<td>34.1 (3.4)</td>
<td>34.1 (3.6)</td>
<td>1.00</td>
</tr>
<tr>
<td>AMH (SD), ng/mL</td>
<td>3.9 (3.1)</td>
<td>3.8 (3.3)</td>
<td>0.68</td>
</tr>
<tr>
<td>% PGS testing</td>
<td>22.0% (56/254)</td>
<td>22.6% (155/686)</td>
<td>0.93</td>
</tr>
<tr>
<td>% Fresh Transfer</td>
<td>41.3% (105/254)</td>
<td>34.4% (236/686)</td>
<td>0.06</td>
</tr>
<tr>
<td>Afterload technique</td>
<td>95.2% (242/254)</td>
<td>87.8% (602/686)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Stylet</td>
<td>0.4% (1/254)</td>
<td>4.5% (31/686)</td>
<td>0.0008</td>
</tr>
<tr>
<td>Blood on catheter tip</td>
<td>4.3% (11/254)</td>
<td>6.8% (47/686)</td>
<td>0.17</td>
</tr>
<tr>
<td>Embryo Retained</td>
<td>0% (0/254)</td>
<td>0.3% (2/686)</td>
<td>1.0</td>
</tr>
<tr>
<td># Embryos</td>
<td>1.2 (0.5)</td>
<td>1.3 (0.5)</td>
<td>0.1</td>
</tr>
<tr>
<td>Transferred (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy Rate</td>
<td>72.8% (182/254)</td>
<td>67.6% (464/686)</td>
<td>0.27</td>
</tr>
<tr>
<td>Miscarriage Rate</td>
<td>18.9% (48/254)</td>
<td>16.8% (115/686)</td>
<td>0.44</td>
</tr>
<tr>
<td>Live Birth Rate</td>
<td>51.6% (131/254)</td>
<td>49.4% (339/686)</td>
<td>0.61</td>
</tr>
</tbody>
</table>

**TABLE 1. Comparison of pregnancy outcomes between ACC and No ACC according to the age of patient.**

<table>
<thead>
<tr>
<th>Group (Age)</th>
<th>Cycle (n)</th>
<th>Clinical Pregnancies (%)</th>
<th>Ongoing Pregnancies (%)</th>
<th>Implantation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 (32-36)</td>
<td>79</td>
<td>39 (49.4)</td>
<td>36 (45.6)</td>
<td>54/168 (32.1)</td>
</tr>
<tr>
<td>Group 2 (≥37)</td>
<td>97</td>
<td>16 (16.5)</td>
<td>13 (13.4)</td>
<td>20/223 (9.0)*</td>
</tr>
<tr>
<td>Group 1 (32-36)</td>
<td>226</td>
<td>84 (37.2)*</td>
<td>70 (31.0)*</td>
<td>104/471 (22.1)*</td>
</tr>
<tr>
<td>Group 2 (≥37)</td>
<td>186</td>
<td>49 (26.3)</td>
<td>36 (19.4)</td>
<td>63/399 (15.8)</td>
</tr>
</tbody>
</table>

* P < 0.05

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e145
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PREGNANCY OUTCOME AFTER BED REST VERSUS EARLY AMBULATION FOLLOWING EMBRYO TRANSFER DURING IVF/ICSI CYCLES—A RANDOMISED CONTROLLED STUDY. Neena Malhotra, MD FRCOG, 1 Plabani Sarkar, MD, 2, 3 All India Institute of Medical Sciences, New Delhi, India; 2Member AOGD, NEW DELHI, India.

OBJECTIVE: Embryo transfer (ET) is the final and most critical step in an ART cycle. Strategies that improve success include avoidance of uterine contractility, use of soft catheters, getting rid of cervical mucus and ultrasound-guided placement of embryos in mid cavity to optimise outcomes. Bed rest and immobilisation after ET has been practiced for long with the intention to improve pregnancy outcomes, however this is a subject of debate. Recent studies suggest that contrary to the belief bed rest does not alter pregnancy outcome after ET. Our hypothesis was that immediate immobilisation after ET improves the outcome of IVF treatment. The objectives of the study were to compare pregnancy outcomes between bed rest or early ambulation after embryo transfer (ET) in women undergoing IVF/ICSI cycles.

DESIGN: Prospective randomised controlled trial.

MATERIALS AND METHODS: Women undergoing fresh IVF/ICSI cycles with age 25-38 years, BMI 18-28 kg/m2, normal endometrial cavity, and willing to participate were included in the study. Women undergoing frozen thawed ET, any factor disturbing implantation such as uterine fibroid, adenomyosis of uterus, unilateral or bilateral hydrosalpinx not treated surgically, or poor endometrium, <6 mm at time of ET were excluded from the study. A prior sample size was calculated after reviewing literature (1). Anticipating a 20% increase in live birth rate after early ambulation with 80% power and an alpha error of 5% with 95% confidence interval the sample size calculated was 90 in each group. This was done using STATA version 15. One hundred and eighty women, 90 in each group were recruited for the study. Patients fulfilling eligibility criteria were randomised to receive 15 minutes rest after ET (Group A) or early ambulation (Group B). Primary Outcome assessed was Live birth rate; secondary outcome was: Implantation rate, clinical pregnancy rate, miscarriage, ectopic pregnancy and multiple gestation rate.

RESULTS: The live birth rate was 20.0% (95% CI: 11.7-28.31) and 26.4% (95% CI: 17.2-35.7 p value 0.310) in Group A and Group B respectively. The implantation rates were 12.7% for Group A and 13.9% for Group B (p value = 0.554). Clinical pregnancy rates were 23.3% (95% CI: 14.26-32.1) and 28.7% (95% CI: 19.2-38.2) in Group A and Group B respectively (p value 0.41). Secondary outcome measures including miscarriage rates were lower in the early ambulation group however did not reach statistical significance.

CONCLUSIONS: Pregnancy rates were comparable in both the groups even though absolute numbers were higher in the group ambulating early after embryo transfer. There is little advantage of advising bed rest after ET, rather women should be allowed early ambulation to improve pregnancy after ET in IVF cycles.


SUPPORT: None.

P-99 Tuesday, October 15, 2019 6:30 AM

THE CONTINUED PUSH TOWARDS ELIMINATING TWIN PREGNANCY: THE CLINICAL IMPACT OF THE 2017 ASRM EMBRYO TRANSFER GUIDELINES. Allison A. Eubanks, MD,a John M. Csokmay, MD,a Micah J. Hill, DO,a aWalter Reed National Military Medical Center, Bethesda, MD; bEunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD.

OBJECTIVE: To evaluate the differences in twin birth rates before and after implementation of the 2017 ASRM guidelines which limits the number of embryos transferred.

DESIGN: Retrospective cohort study.

CONCLUSIONS: Embryo transfer success rates were not different between fellows and attending physicians. Barriers to fellowship training in embryo transfer should be evaluated and addressed, as there was no compromise in pregnancy rates, even in the first twenty embryo transfers performed.

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HIGHER PREGNANCY RATES ARE OBSERVED AFTER SINGLE EUPLOID FROZEN EMBRYO TRANSFER UTILIZING TIME-LAPSE MONITORING TECHNOLOGY WHEN COMPARED TO TRADITIONAL EMBRYO INCUBATION. Lauren W. Sundheimer, MD, MS,a Zachary Haimowitz, BS, b Alin Lina Akopians, MD, PhD, a Deborah E. Johnson, MA,b Wendy Y. Chang, MD,a Mark W. Surrey, MD,a Hal C. Danzer, MD,a Shahin Ghadir, MD,a Carolyn J. Alexander, MD,a Jason A. Barritt, PhD, b Southern California Reproductive Center, Beverly Hills, CA; aART Reproductive Center, Beverly Hills, CA.

OBJECTIVE: One of the challenges in assisted reproductive technology is to identify and select embryos with the highest developmental potential, with a goal of improving pregnancy and ultimately live birth rates. Preimplantation genetic testing for aneuploidy (PGT-A) with next generation sequencing (NGS) has improved pregnancy rates by transfer of euploid embryos, however room for improvement remains. Time-lapse monitoring (TLM) is a non-invasive system that allows for continuous embryo imaging, maintenance of optimal culture conditions, and detection of developmental events that may lead to improved outcomes. Our objective is to determine whether TLM at the time of embryo development leads to improved pregnancy rates over traditional embryo incubation.

DESIGN: Retrospective cohort study at a large, private fertility center.

MATERIALS AND METHODS: A comprehensive electronic chart review was performed. All patients utilizing the TLM device (EmbryoScope®, Vitrolife, Sweden) at a single IVF center from 2018 through March 2019 were analyzed. All patients who underwent a frozen embryo transfer (FET) of a PGT-A analyzed day 5, 6, or 7 embryo of good or fair quality were included in the study. Statistics were performed using 2-tailed Chi-square analysis where statistical significance was set at p values <0.05.

RESULTS: A total of 952 patients were identified; 83 (8.7%) used the TLM device. Of all patients, 942 (98.9%) had only a single thaw cycle and transfer. Focusing on patients with only a single thaw cycle, thereby isolating the analysis to the best overall embryo(s), the overall pregnancy rate was 644/
494 (68.4%). Of these patients, the pregnancy rate of patients using TLM was significantly higher than those using traditional incubation (59/73, 80.8% versus 585/869, 67.3%; p<0.05). Looking only at patients that had an elective single embryo transfer (eSET), the overall pregnancy rate was 639/869 (73.5%). Pregnancy rates were higher after transfer of embryos created with TLM technology compared to traditional incubation (54/67, 80.6% versus 585/869, 67.3%; p<0.05). Combining patients that had both a single thaw cycle as well as an eSET, the overall pregnancy rate was 636/933 (68.2%) and TLM embryos had a significantly higher pregnancy rate over embryos from traditional incubation (51/64, 79.7% versus 585/869, 67.3%; p<0.05).

CONCLUSIONS: TLM technology at the time of embryo development yields a statistically higher pregnancy rate as compared to embryos created with traditional incubation. This is especially true when the best embryo(s) is/are selected for transfer as well as when only an eSET is performed. Given the significantly improved pregnancy rates, TLM incubation of embryos should be considered as an alternative to traditional incubation.

P-101 Tuesday, October 15, 2019 6:30 AM
DECREASING RATES OF MULTIPLE GESTATION AND NUMBER OF EMBRYOS TRANSFERRED IN GESTATIONAL CARRIER PREGNANCIES: A LONGITUDINAL ANALYSIS. Rachel S. Mandelbaum, MD, Meghan B. Smith, MD, Jacqueline Ho, MD MS, Richard J. Paulson, MD MS, Kristin Bendikson, M.D., University of Southern California, Los Angeles, CA.

OBJECTIVE: The recent national push towards elective single embryo transfer (eSET) has decreased rates of multiple gestations. However, this translates to gestational carrier (GC) pregnancies has not been well established. We sought to evaluate the number of embryos transferred (ET) and the incidence of multiple gestations in GC pregnancies as well as if these metrics have changed over time.

METHODS: A retrospective analysis of all GC deliveries from a single agency between 2008-2019.

RESULTS: Of 836 GC pregnancies, 187 (22.4%) were multiple gestations. Of these, 183 (21.9%) of all pregnancies were twins, 3 (0.4%) triplets, and 1 (0.1%) quadruplet pregnancy. 116 (13.9%) GCs overall had a history of a multiple gestation prior to the current GC pregnancy, of which 53.6% were due to another prior GC pregnancy. There was a similar rate of multiple gestation in the index GC pregnancy when comparing GCs with a history of singleton vs multiple gestations (P = 0.882). There was also no difference between first-time or repeat surrogates in likelihood of having a multiple gestation (P = 0.435). In terms of number of ET, 422 GCs (61.7%) had 2 or more ET, and 14 (1.7%) had four or more. Number of ET was positively correlated with number of infants delivered in the GC pregnancy (r = 0.207, P = 0.001). Number of ET declined significantly over the study period; in 2008-2010, 89% of GCs had ≥2 ET compared to 30.6% in 2017-2019 (P < 0.001). This paralleled a declining incidence of multiple gestations (29.4% in 2008-2010 vs. 11.5% in 2017-2019, P < 0.001). Neither women with a history of twins nor repeat surrogates were more likely to have two or more ET (both P > 0.05).

CONCLUSIONS: In line with trends in autologous transfers, the number of ET and incidence of multiple gestation is declining in GC pregnancies. A GC’s prior obstetric history, specifically a history of multiples or history of surrogacy, does not impact the number of ET or incidence of multiple gestation in the index GC pregnancy. To minimize obstetrical risks to GCs and maximize healthy singleton deliveries for IPs, eSET in appropriate candidates should be encouraged.

Second, the same computer program was utilized to make a quantitative assessment about the likelihood that two embryos transferred concurrently will both implant more often than would be expected by chance alone. This accounts for universal factors that affect all embryos transferred concurrently.

Third, means and standard deviations of outcomes for a test sample of embryo transfers were predicted using the best fit model and random number generation. We tested the model with six groups of multiple embryo transfers (Table 1). The differences between predicted and actual rates of multiple birth were not statistically significant and the standard errors were normally distributed on a quantile-quantile plot.

**RESULTS:** The predicted and actual rates of multiple birth for each of six embryo transfer groups is shown in Table 1. The differences between predicted and actual rates of multiple birth were not statistically significant and the standard errors were normally distributed on a quantile-quantile plot.

**CONCLUSIONS:** Current recommendations for number of embryos to transfer are based on expert opinion. This model can be used with a mobile device application at the point of care for evidence based quantitative prediction of risk of multiple gestation after transfer of multiple embryos.

**TABLE 1.** Predicted and actual rates of multiple birth (multiple deliveries / total deliveries)

<table>
<thead>
<tr>
<th>embryos transferred</th>
<th>less than 38 years</th>
<th>38 years &amp; greater</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 blastocysts</td>
<td>predicted (95% CI)</td>
<td>36% (23-50%)</td>
</tr>
<tr>
<td>actual</td>
<td>30% (p = 0.37)</td>
<td>17% (p = 0.30)</td>
</tr>
<tr>
<td>2 cleavage stage</td>
<td>predicted (95% CI)</td>
<td>9% (0-25%)</td>
</tr>
<tr>
<td>actual</td>
<td>16% (p = 0.31)</td>
<td>16% (5-29%) *</td>
</tr>
<tr>
<td>3 cleavage stage</td>
<td>predicted (95% CI)</td>
<td>34% (18-52%)</td>
</tr>
<tr>
<td>actual</td>
<td>19% (p = 0.59)</td>
<td></td>
</tr>
<tr>
<td>4 or 5 cleavage stage</td>
<td>predicted (95% CI)</td>
<td>n/a</td>
</tr>
<tr>
<td>actual</td>
<td>21% (8-36%)</td>
<td>17% (p = 0.59)</td>
</tr>
</tbody>
</table>

* this group included transfer of 2 or 3 cleavage stage embryos

**P-105 Tuesday, October 15, 2019 6:30 AM**

**REDUCING SIZE OF TRANSFER SYRINGE IS BENEFICIAL FOR IVF PREGNANCY OUTCOMES.** Van Pham, B.S.; Randall Dunn, M.D.; Subodh Chauhan, M.D.; Leah Schenk, M.D.; Rakesh Mangal, M.D.; Ertug Kovanci, M.D.; George M. Granert, M.D.; Wan-Song A Wun, PhD.

OBJECTIVE: Embryo transfer has been emphasized as one of significant factors relates to IVF pregnancy. In addition to non-traumatic technique, fluid dynamic actions during embryo transfer has studied (Ding et al, 2018). In the transfer catheter, embryos encounter sudden increase of pressure (due to push down syringe plunger) then fast decompression when out of catheter. In the mouse model, sudden pressure alteration causes blastomeres apoptosis (Grygoruk et al, 2011, 2012). How the consequence of sudden pressure alteration reflects by the significantly lower implantation and fetal heart beat rates. The results from this study correspond to mouse embryo observations (Grygoruk et al, 2011, 2012). Reducing the size of transfer syringe is beneficial for IVF success.

**MATERIALS AND METHODS:** The study included a total of 3,559 day 5, and 1,740 day 6 vitrified-warmed blastocysts transfers (VBT) in autologous women of 37 years of age and younger recorded between 2004 and 2018. The day 5 group contained 1,857 single (D5sVBT), and 1,702 double (D5dVBT) transfers, whereas the day 6 group contained 680 single (D6sVBT), and 1,060 double (D6dVBT) transfers. The vitrified blastocysts were warmed about 2hrs prior to transfer. Both natural and hormone replacement cycles were used to increase receptivity of the endometrium. Progestrone was supplemented on day 15 of the cycle and blastocysts were warmed on day 5 of progestrone supplementation. Chi-square test was used for statistical analysis of oPR between single and double-vitrified-warmed embryo transfers and according to the day of development (day 5 vs. day 6).

**RESULTS:** The total oPR was significant lower in the day 6 group compared with those in the day 5 group (35.4% vs 51.1%). The oPR was not significantly different between the D5sVBT group and D5dVBT group (49.5 vs 52.8%). However, the oPR was significantly higher in the

**IVF OUTCOME PREDICTORS - EMBRYOS**

**P-105 Tuesday, October 15, 2019 6:30 AM**

**ONGOING PREGNANCY RATE OF VITRIFIED-WARMED BLASTOCYST TRANSFERS IN AUTOLOGOUS PATIENTS: SINGLE VS DOUBLE TRANSFER ACCORDING TO THE DAY OF DEVELOPMENT.** Juergen Liebermann, PhD, HCLD, Sara Sanchez-Julias, BS, Rebecca Brohammer, BS, Janna Schwab, MS, Meike L. Uhler, M.D., Jennifer E. Hirshfeld-Cytron, MD, Christopher Sipe, MD. Fertility Centers of Illinois, Chicago, IL.

OBJECTIVE: Improvement in cryopreservation techniques has led to increasing implantation rates transferring vitrified-warmed embryos. This development has supported the move to recommend single embryo transfers to a greater proportion of patients. Considering the high frequency of day 6 blastocyst formation, the associated lower implantation potential of day 6 blastocyst becomes clinically important. Therefore, in an effort to optimize the pregnancy of transferring growth-delayed day 6 blastocysts, we compared their outcome to normally-developing day 5 blastocysts, and evaluated their efficiency in regards to ongoing (oPR), implantation rate (IR), and Twin pregnancies.

**MATERIALS AND METHODS:** The study included a total of 3,559 day 5, and 1,740 day 6 vitrified-warmed blastocysts transfers (VBT) in autologous women of 37 years of age and younger recorded between 2004 and 2018. The day 5 group contained 1,857 single (D5sVBT), and 1,702 double (D5dVBT) transfers, whereas the day 6 group contained 680 single (D6sVBT), and 1,060 double (D6dVBT) transfers. The vitrified blastocysts were warmed about 2hrs prior to transfer. Both natural and hormone replacement cycles were used to increase receptivity of the endometrium. Progestrone was supplemented on day 15 of the cycle and blastocysts were warmed on day 5 of progesterone supplementation. Chi-square test was used for statistical analysis of oPR between single and double-vitrified-warmed embryo transfers and according to the day of development (day 5 vs. day 6).
D6dVBT group compared with the D6sVBT group (39.4 vs 29.1). The Twin PR was statistically significantly lower in both sVBT groups (1.7% vs. 2.1%) compared to both dVBT groups (42.1% vs 33.1%) regardless of the day of development.

CONCLUSIONS: This study showed that D5sVBT resulted in comparable oPR compared to D5dVBT, while D6dVBT resulted in significantly lower oPR compared to D6dVBT. However, in any VBT the number of embryos transferred should always carefully considered, because transferring 2 blastocysts regardless of day of development always yielded a significantly higher twin rate.

SUPPORT: None.

P-106 Tuesday, October 15, 2019 6:30 AM

RELATIONSHIP OF EMBRYO SEX TO EMBRYO QUALITY, DAY OF BLASTOCYST TRANSFORMATION, AND IVF OUTCOMES. Christopher P. Moutos, MD,1 William G. Kearns, MD, PhD,2 Sarah E. Farmer, MS,2 Jon P. Richards, MS,2 Antonio F. Saad, MD,a John R. Crochet, Jr., MD,c Ma Jose de los Santos, PhD,1 Mar Noahales, PhD,2 Marcos Meseguer, PhD,f Jose Alejandro Remohi, MD, PhD,2 Ana Cobo, PhD,b TVIRMA VALENCIA, VALENCIA, Spain; TVIRMA Valencia, Valencia, Spain; TVIRMA Global, Valencia, Spain, Tel Aviv, Israel; TVIRMA Valencia, Valencia, Spain.

OBJECTIVE: While it has been theorized that the energy required for X chromosome inactivation in female embryos may have an impact on embryo development, conflicting data exists regarding the impact of embryo sex on blastocyst development and quality and subsequent IVF outcomes. The primary objective of this study is to determine if there is a relationship between embryo sex as determined by preimplantation genetic testing for aneuploidy (PGT-A) and blastocyst transformation and quality and the IVF outcomes.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: A retrospective chart review was conducted of patients age 21-47 who underwent PGT-A (N=5708) and subsequent autologous elective single embryo transfer (eSET) (N=539) from June 2007 to December 2018. Primary analyses focused on the relationship of embryo sex to day of blastocyst transformation (day of trophectoderm biopsy) and embryo quality. Secondary analyses examined the relationship of embryo sex to morphological grade, genetic diagnosis, and rates of implantation, clinical pregnancy (CP), ongoing pregnancy (OP), chemical pregnancy, spontaneous abortion, and ectopic pregnancy. Pearson’s chi-squared test was used with P<0.05 being considered significant.

RESULTS: There was no difference in embryo sex and day of blastocyst transformation (P=0.566), embryo grade (P=0.057), or maternal age (P=0.837). Similar results were observed when the analysis was repeated stratified by maternal age and being euploid. Female embryos were more likely than male embryos to be aneuploid (54.6% vs 47.2%, P<0.001). When embryos with sex chromosome aneuploidy were excluded, there was also no correlation between embryo sex and grade (P=0.363) or day of blastocyst transformation (P=0.094). Embryos undergoing blastocyst transformation on day 5 vs day 6 were more likely to result in implantation (71.8% vs 52.6%, P<0.001), CP (69.4% vs 50.9%, P<0.0001) and OP (59.1% vs 44.7%, P=0.018). High-grade embryos were also more likely then mid/low-grade embryos to result in implantation (70.8% vs 60.3%, P=0.018), CP (69.2% vs 56.4%, P=0.005) and OP (59.3% vs 48.1%, P=0.018). Day 6 embryos were more likely to result in a chemical pregnancy (5.1% vs 1.0%, P=0.004). Implantation, CP, and OP rates were not different among sex embryo groups. Unlike male embryos, female embryos undergoing blastocyst transformation on day 5 vs day 6 were more likely to result in a CP (68.8% vs 52.0%, P=0.012) and trended towards being more likely to result in an OP (58.2% vs 45.3%, P=0.062).

CONCLUSIONS: To our knowledge, this is the largest and most comprehensive study to evaluate the potential relationship between embryo sex and quality or development and first to also look at the subsequent IVF outcomes.

Despite not finding a difference between embryo sex and embryo blastocyst development or IVF outcomes, female embryos were more likely to be aneuploid, which is likely due to an increased frequency of X chromosome aneuploidy. In addition, faster developing and higher-grade embryos were more likely to have favorable IVF outcomes.

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IMPACT OF FRESH-EMBRYO PARAMETERS ON SURVIVAL AND IMPLANTATION IN VITRIFIED BLASTOCYST CYCLES: ANALYSIS OF 11936 WARMED BLASTOCYSTS. Aila Coello, Ph.4 Ma Jose de los Santos, Ph.D, 5 Mar Noahales, Ph.D,2 Marcos Meseguer, Ph.D, Jose Alejandro Remohi, MD, PhD, Ana Cobo, PhD, TVIRMA VALENCIA, VALENCIA, Spain; TVIRMA Valencia, Valencia, Spain; TVIRMA Global, Valencia, Spain, Tel Aviv, Israel; TVIRMA Valencia, Valencia, Spain.

OBJECTIVE: To correlate blastocyst features with the predictive potential of survival and successful implantation in vitrified/warmed blastocyst cycles.

DESIGN: Retrospective study.

MATERIALS AND METHODS: The study included 11936 vitrified-warmed blastocysts transferred from January 2017 to December 2018. No PGT-A cycles were included. Pre-vitrification morphological parameters analyzed for all blastocysts were as follows: i) day of vitrification (5 vs 6); ii) blastocyst expansion degree: cavitated (BC), fully expanded (BE) and hatching out of the zona (BH); iii) trofotroctoderm (TE) quality (A, B and C); iv) inner cell mass (ICM) quality (A, B and C); and v) oocyte origin (donor vs. autologous). Survival and implantation rates were analyzed using a logistic regression model. Odds ratios and 95% confident intervals (CI) were calculated. P<0.05 was considered statistically significant.

RESULTS: Logistic regression model estimated that the day of vitrification (5 vs 6) was the strongest predictor of embryo survival (1.71; 95% CI: 1.42 – 2.04; P<0.001). Additionally, the odds of survival increased in blastocysts catalogued as BC with respect to those catalogued as BH (2.05; 95% CI: 1.48 – 2.83; P<0.001), and decreased in blastocysts with TE C compared to those with TE A (1.31; 95% CI: 1.07 – 1.59; P<0.001). However, survival was not affected by the oocyte origin. Regarding implantation, the model showed that TE quality followed by the day of vitrification were the most significant morphological predictors of success. The odds of implantation were doubled for blastocysts with TE graded as A compared to those with TE graded as C (2.03; 95% CI: 1.75 – 2.36; P<0.001), and were cut by half for blastocysts vitrified on day 6 compared to those vitrified on day 5 (0.51; 95% CI: 0.45 – 0.57; P<0.001). The odds of implantation were also increased when transferring hatching blastocysts (1.63; 95%CI: 1.41 – 1.87; P<0.001) and ICM was graded as A (1.35; 95%CI: 1.13 – 1.60; P<0.001).

CONCLUSIONS: Blastocysts vitrified on day 5 with top quality TE should be given priority when warming. The degree of blastocoele expansion when vitrifying is closely related to success: BC embryos showed higher survival but lower implantation rates and should be cultured after warming to allow them to expand prior to the embryo transfer. The possibility of double embryo transfer should be considered in vitrified cycles with blastocysts graded as day 6 and TE C.

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DEVELOPMENT AND PRELIMINARY VALIDATION OF AN AUTOMATED STATIC DIGITAL IMAGE ANALYSIS SYSTEM UTILIZING MACHINE LEARNING FOR BLASTOCYST SELECTION. Alejandro Chavez-Badiola, MD,a Adolfo Flores-Saiffe Farias, MSc, PhD, Gerardo Mendizabal-Ruiz, PhD,a Rodolfo Garcia-Sanchez, MSc,a Andrew J. Drakeley, MD FRCOG,a New Hope Fertility Center Mexico, Mexico City, EM, Mexico;

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OBJECTIVE: To assess an automated static digital image analysis system's capabilities to predict a blastocyst's potential to achieve a pregnancy by analyzing morphometric features extracted from single images and computing these utilizing artificial intelligence.

DESIGN: Retrospective morphometric study to evaluate an automated static digital image-processing algorithm’s predictive capabilities.

MATERIALS AND METHODS: Two balanced and high-quality embryo micrograph databases with pregnancy outcomes from single blastocyst transfers (Database A: 134 images; Database B: 87 images), were used to create a pipeline that extracts relevant morphometric features which, along with metadata, allowed us to predict pregnancy defined as beta hCG >20iu, 7 days following blastocyst transfer. Several classifiers were tested within the pipeline using cross-validation techniques to assess the generalization capabilities of the models: Bayesian, Support Vector Machines, Neural Networks, and Ada Boost. Using artificial intelligence, the probability of achieving pregnancy was then estimated.

RESULTS: A total of 221 images of blastocysts selected for single embryo transfers were included. The developed algorithm was successful at extracting relevant morphological features from every micrograph. Furthermore, it was successfully able to predict a positive pregnancy test in both datasets. With the use of the computed morphological features in combination, it was possible to achieve an F1 score of 0.76; accuracy of 0.75; and sensitivity of 0.77 for database A. For database B we created a predictive model with 0.74 of F1 score; accuracy of 0.67; and sensitivity of 0.78.

CONCLUSIONS: The proposed computational tool based on machine-learning has the capacity to link variables, extracted from single static digital images of blastocysts, to predict pregnancy. By doing so, it allows for a new approach to embryo classification while supporting embryologists towards a more objective and accurate embryo selection process. Different from other approaches, this machine-learning tool doesn’t rely on time-lapse incubators, making it a low cost candidate for easy integration into routine clinical practice. A prospective study on a larger scale is underway to replicate our initial results while, at the same time, aiming to improve predictability capabilities through automated machine-learning.


model using a combination of these parameters to predict euploidy gave an AUC value of 0.70. In FET cycles, a model combining cryopreservation day 5 with TE grade was highly predictive of the euploid embryo’s ability to implant (AUC = 0.69). A day 5 blastocyst was three times as likely to implant (OR 2.95; 95% CI 1.57-5.73; p = 0.0007). Odds of implantation for TE 1 vs TE 3 were 6-fold higher (OR 6.61; 95% CI 2.20-22.89; p = 0.0006) and almost 2.5 fold higher with TE 1 vs TE 2 (OR 2.45; 95% CI 1.24-4.92; p = 0.0097).

CONCLUSIONS: The predictive model described here increases the probability of selecting a chromosomally normal blastocyst. Further study is needed to determine if such a model can increase odds of successful implantation in non-PGS patients.


SUPPORT: None.

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BLASTOCYST GRADE PREDICTS OUTCOME AFTER FROZEN EUPLOID TRANSFER IN PATIENTS WITH RECURRENT PREGNANCY LOSS. Gayathree Murugappan, MD,a Julia G. Kim, MD, MPH, Jonathan D. Kort, MD,b Brent M. Hanson, MD,b Shelby A. Neal, MD,a Ashley W. Tieg, MD,a Emily K. Osman, MD,b Richard Thomas Scott, Jr, MD,a Ruth B. Lathi, MD,a Stanford University Medical Center, Sunnyvale, CA; 3IVF-RMA New Jersey, Basking Ridge, NJ; 4IVI Reproductive Medicine Associates of Northern California, San Francisco, CA; 5Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA.

OBJECTIVE: Trophoblast grade (TE) has been shown to be the most significant predictor of implantation and live birth after fresh untested blastocyst transfer in infertile cohorts. The goal of this study was to determine if TE grade or inner cell mass (ICM) grade are predictive of clinical outcomes in a cohort of RPL patients pursuing PGT-A.

DESIGN: Retrospective cohort study from a single fertility center between 2002 and 2018.

MATERIALS AND METHODS: Patients with 2 or more prior pregnancy losses performing PGT-A with at least one euploid embryo for transfer were included. All patients underwent ICSI and single euploid frozen blastocyst transfer (eFET). Outcome of the first eFET was recorded. Implantation was defined as beta hCG > 5 mIU/mL. Clinical pregnancy was defined as a visualized gestational sac. Pregnancy loss was defined as loss of pregnancy from implantation to twenty weeks gestation. Multivariable logistic regression analysis was used to evaluate the effect of age, TE grade and ICM grade on clinical outcomes.

RESULTS: 660 eFET were included, with clinical outcomes stratified by ICM and TE grade (Table 1). After adjusting for age, ICM grade is not significantly correlated with implantation rate (p=0.12, CI 0.93-1.92), miscarriage rate (p=0.18, CI 0.47-1.16), or pregnancy loss rate (p=0.21, CI 0.56-1.13) but is significantly correlated with live birth rate (p=0.03, CI 1.02-1.81). TE grade is not significantly correlated with implantation rate (p=0.32, CI 0.86-1.56) or miscarriage rate (p=0.11, CI 0.52-1.07) but is significantly correlated with live birth rate (p=0.02, CI 1.06-1.71) and pregnancy loss rate (p=0.04, CI 0.55-0.98). 16 blastocysts were grade CC, with implantation rate 69% (n=11), clinical pregnancy rate 50% (n=8), live birth rate 31% (n=5), clinical miscarriage rate 38% (n=3) and pregnancy loss rate 55% (n=6).

CONCLUSIONS: Compared to embryos with grades A or B, TE and ICM grade C is correlated with lower likelihood of live birth and TE grade C is correlated with higher likelihood of pregnancy loss among RPL patients performing eFET. These results suggest that euploidy pregnancy loss in the setting of RPL is still likely of embryonic origin.


P-111 Tuesday, October 15, 2019 6:30 AM

SURVIVAL BEHAVIOR OF EMBRYO COHORT IN CULTURE IS ASSOCIATED WITH PREGNANCY PERFORMANCE OF A SURVIVING EUPLOID BLASTOCYST AFTER SINGLE EMBRYO TRANSFER (SET): THE CANARIES IN THE COAL MINE? Eleni A. Greenwood, MD, MS,c Rhodel Simbulan, MS,c Charles E. McCalloch, PhD,c Marcelle I. Cedars, MD,c Mitchell P. Rosen, MD, HCLD,c University of California San Francisco, San Francisco, CA; UC SF, San Francisco, CA; University of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA.

OBJECTIVE: Improving metrics for embryo selection is of great interest in the field of assisted reproductive technology. Preimplantation genetic testing for aneuploidy (PGT-A) is one powerful selection tool available today. Our objective was to investigate whether the survival behavior of an embryo cohort in culture associated with 1) euploid rates of biopsied blastocysts produced from that cohort, or 2) pregnancy outcomes after subsequent single euploid embryo transfer.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Trophodectm biopsies for PGT-A at a single academic center between 2010–2019 were reviewed. At our institution, grade BB (Gardner criteria) or better blastocysts are biopsied on day 5 or 6 and subsequently frozen. A “Poor Embryo Survival” (PES) subset of women was defined as those women for whom >70% of normally fertilized embryos (2PNs) did not progress to biopsiable blastocysts (i.e. dropout, corresponding to the ≥75%ile for embryo dropout). Euploid rates (euploid blastocysts / biopsied blastocysts per ovarian stimulation cycle) were compared between the PES women and the remaining 75% (“Controls”), using generalized linear models to control for age of the oocyte and account for the clustered nature of the data. Pregnancy outcomes following single euploid embryo transfer in a subsequent frozen cycle were similarly compared between PES and Control groups.

RESULTS: 1,400 women underwent 2,087 ovarian stimulation cycles yielding 10,087 trophodectm biopsies for review. Average age in PES women was 38.2y vs 37.1y in Controls. Although increasing age was associated with higher embryo dropout, euploid rates from surviving, biopsied blastocysts were no different between PES women (Table) vs Controls after adjusting for age in the model (p=0.23). On the other hand, pregnancy outcomes after euploid SET differed based on embryo cohort survival (Table). A euploid blastocyst from a PES cycle had 37% reduced odds of generating an ongoing pregnancy or live birth vs a euploid blastocyst from a Control cycle (OR 0.63, 95% CI 0.41, 0.95, p=0.03).

TABLE 1.

<table>
<thead>
<tr>
<th>ICM grade</th>
<th>Clinical pregnancy, n (%)</th>
<th>Live birth/ongoing pregnancy, n (%)</th>
<th>Clinical miscarriage, n (%)</th>
<th>Pregnancy loss, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>164 (76%)</td>
<td>145 (67%)</td>
<td>18 (11%)</td>
<td>37 (20%)</td>
</tr>
<tr>
<td>B</td>
<td>293 (72%)</td>
<td>244 (60%)</td>
<td>47 (16%)</td>
<td>78 (24%)</td>
</tr>
<tr>
<td>C</td>
<td>24 (63%)</td>
<td>19 (50%)*</td>
<td>5 (21%)</td>
<td>10 (35%)</td>
</tr>
<tr>
<td>TE grade</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>232 (74%)</td>
<td>203 (65%)</td>
<td>28 (12%)</td>
<td>52 (20%)</td>
</tr>
<tr>
<td>B</td>
<td>205 (75%)</td>
<td>172 (62%)</td>
<td>31 (15%)</td>
<td>53 (23%)</td>
</tr>
<tr>
<td>C</td>
<td>44 (62%)</td>
<td>33 (46%)*</td>
<td>11 (25%)</td>
<td>20 (37%)*</td>
</tr>
</tbody>
</table>

*p<0.05, multivariate regression analysis adjusting for age

FERTILITY & STERILITY®
<table>
<thead>
<tr>
<th>PGT-A result</th>
<th>Biochemical pregnancy</th>
<th>Clinical miscarriage</th>
<th>Ectopic pregnancy</th>
<th>Ongoing pregnancy/ Live birth*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor Embryo Survival (PES)</td>
<td>3.9%</td>
<td>7.9%</td>
<td>0.5%</td>
<td>48.3%</td>
</tr>
<tr>
<td>Control</td>
<td>3.8%</td>
<td>6.2%</td>
<td>0.3%</td>
<td>56.2%</td>
</tr>
</tbody>
</table>

*p<0.05

CONCLUSIONS: Survival rates of embryo cohorts in culture do not appear to correlate with the likelihood of identifying a euploid blastocyst among blastocysts surviving to biopsy, after accounting for age of oocyte. On the other hand, high rates of embryo dropout between fertilization and blastocyst biopsy are associated with reduced odds of live birth or ongoing pregnancy following euploid SET. Embryo cohort behavior in culture may reflect non-genomic pregnancy potential of embryos emerging from these cohorts.


**P-112 Tuesday, October 15, 2019 6:30 AM**

FULLY HATCHED EUPOID BLASTOCYSTS EXHIBIT LOWER PREGNANCY OUTCOMES WHEN COMPARED TO OTHER BLASTOCYST STAGES IN FROZEN SET CYCLES. Ahmad Morsi Abu Maizar, M.Sc.

OBJECTIVE: To determine and compare the clinical outcomes of transferring a trophectoderm biopsied fully hatched blastocyst to other blastocyst stages in Single Embryo Transfer (SET) cycles.

MATERIALS AND METHODS: Pregnancy Rate (PR), Implantation Rate (IR) and Clinical Pregnancy Rate (CPR) of PGT-tested blastocyst SETs during 2017-2018 were analyzed. All fertilized oocytes underwent uninterrupted extended culture until the day of biopsy. Trophectoderm biopsy was performed on culture day 5, 6, or 7 using a single pulse laser breach of the zona pellucida, followed by the insertion of a beveled needle with excision of 3-5 cells. PGT testing was performed utilizing NextGen sequencing. All transfers were performed with vitrified/warmed blastocysts. PR was determined by hCG level of > 5mIU/ml. IR was determined by the number of sacs present at 3 weeks after positive pregnancy, and CPR by the presence of a positive fetal heart beat (FHB) at 7 weeks gestation. Statistical analysis was performed using Chi-square (P <0.05).

RESULTS: Biopsies from 651 transfers utilizing euploid SET were analyzed. Fully hatched blastocysts (n=73) showed a significantly lower PR (42%) when compared to blastocysts with a blastocoeel of more than or equal to half the volume of the embryo (n=168) (58%) (p=0.02), expanded blastocysts (n=260) with a full blastocoeel (60%) (p=0.009) and hatching blastocysts (n=150) (65%) (p=0.001). SETs with fully hatched blastocysts showed the lowest IR (29%) when compared to full blastocysts (51%) (p=0.002), expanded blastocysts (53%) (p=0.0002) and hatching blastocysts (56%) (p=0.0004). Moreover, CPR% was significantly impacted after the transfer of fully hatched blastocysts (27%) when compared to full blastocysts (47%) (p=0.004), expanded blastocysts (53%) (p=0.002), and hatching blastocysts (56%) (p=0.00006). Day of development did not influence the clinical outcomes between the different stages of blastocysts (p=0.18). Also the analysis showed no significant difference among the stages of development within the same category for neither the performing physician nor the transferring embryologist (p=0.94, p=0.65 respectively).

CONCLUSIONS: It has been recently reported that the transfer of fully hatched blastocysts results in significantly lower success rates when compared to other stages of blastocyst development (James, R. M et al, 2018). It has also been suggested that the complete removal of the zona pellucida increases the implantation potential. However, these studies lack evidence to support the hypothesis (Alteri, A et al, 2018). Despite the striking differences in the outcomes, other factors such as age and day of development did not influence the final result. These findings suggest that the zona pellucida confers some level of protection during transfer, and its absence may contribute to lower clinical outcomes.

SUPPORT: None.

**P-113 Tuesday, October 15, 2019 6:30 AM**

BLASTOCYST MORPHOLOGY CORRELATES WITH PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) RESULTS AND MAY FURTHER PRECISE PREGNANCY POTENTIAL AFTER EUPOID SINGLE EMBRYO TRANSFER (SET). Eleni A. Greenwood, MD, MSc. Charles E. McCulloch, PhD. Giovanna Olivera, MS. Wingka Lin, MSc. Fang Xie, PhD. Marcelle I. Cedars, MD. Mitchell P. Rosen, MD. University of California - San Francisco, San Francisco, CA. Affiliation not provided; Ovation Fertility, Austin, TX.

OBJECTIVE: To 1) evaluate the relationship between blastocyst morphology and ploidy via PGT-A, and 2) determine whether morphology might further differentiate pregnancy potential among euploid blastocysts following single embryo transfer (SET)

MATERIALS AND METHODS: PGT-A results from trophectoderm biopsies obtained from 2010-2019 were included. At our institution, Gardner grade BB or better blastocysts were biopsied on day 5 or 6. Expansion stage, inner cell mass (ICM) and trophectoderm grades were investigated as potential predictors of blastocyst ploidy. Euploid biopsy results were coded 1 vs 0; mixed effects generalized linear models with a logit link function used to control for age of oocyte and account for the clustered nature of the data. We used a similar approach to evaluate whether elements of morphologic grading predicted pregnancy outcomes after euploid SET. We also considered day of biopsy (5 vs 6) in the analyses.

RESULTS: Biopsies from 9,667 blasts produced by 1,427 women over 2,134 cycles were reviewed. There was a progressive increase in euploid rates with increasing expansion at biopsy: blastocyst 40.2%, expanded 44.4%, hatching 48.5%, hatched 52.3%, independent of age of oocyte (p=0.001). Grade A ICM blasts were more likely euploid vs grade B (49.4% vs 44.1%; p<0.001). Grade A trophectoderm blasts were more likely euploid vs grade B (56.2% vs 43.0%; p<0.001). Blasts biopsied on day 5 vs 6 were more likely euploid (50.2% vs 41.9% p<0.001). In a model containing all three components of morphology plus day of biopsy, controlled for age, all but ICM grade remained independent predictors of odds of being euploid; hatching expansion was associated with greatest increase in odds of euploid in this model (OR 2.41, 95% CI 1.99, 2.93, p<0.001). Furthermore, morphology grades correlated with pregnancy outcomes after SET of a euploid blastocyst (n=1,101 transfers; Table). When morphologic grading plus day of biopsy were simultaneously considered in the model, Day 5 biopsy (aOR 2.19) and Grade A trophectoderm (aOR 1.47) remained independent predictors of increased odds of live birth or ongoing pregnancy (Table).

CONCLUSIONS: Categorical morphologic grading correlates with ploidy, however grade B blastocysts have reasonable euploid rates. In triaging among surplus euploid blastocysts for transfer, Day 5 biopsy should be prioritized, followed by Grade A trophectoderm, which may reflect non-
The image contains a page from a document discussing the impact of blastocyst-stage transfers on male live-birth rates. The text includes statistical analyses and conclusions regarding the gender ratio of offspring following fresh and frozen-thawed embryos. It also mentions the use of morphological grading and biopsy day as predictors of pregnancy.

### Odds of live birth or ongoing pregnancy after SET of a euploid blastocyst, by morphologic grading and biopsy day

<table>
<thead>
<tr>
<th>Day of biopsy</th>
<th>Univariate OR (95% CI)</th>
<th>p</th>
<th>Multivariate aOR* (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 5</td>
<td>2.34 (1.71, 3.19)</td>
<td>&lt;0.01</td>
<td>2.19 (1.54, 3.12)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Day 6</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>Trophoderm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade A</td>
<td>1.42 (1.00, 2.00)</td>
<td>0.05</td>
<td>1.47 (1.04, 2.08)</td>
<td>0.03</td>
</tr>
<tr>
<td>Grade B</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
<tr>
<td>ICM</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade A</td>
<td>1.56 (1.14, 2.14)</td>
<td>&lt;0.01</td>
<td>1.14 (0.82, 1.59)</td>
<td>0.43</td>
</tr>
<tr>
<td>Grade B</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
<td>Ref</td>
</tr>
</tbody>
</table>

*Multivariate model adjusts for each component in the univariate analyses plus blastocyst expansion.

### Increased Male Live-Birth Rates After Blastocyst-Stage Frozen-Thawed Embryo Transfers Compared With Cleavage Stage: A Society for Assisted Reproductive Technologies Clinical Outcomes Reporting System Study

The study aimed to investigate whether there is a difference in live-birth gender in blastocyst-stage compared with cleavage-stage FETs. The results indicated a statistically significant increase in male live-birth rates following blastocyst-stage FETs compared to cleavage-stage FETs. Design: Retrospective cohort study. Materials and Methods: All IVF cycles reported to the Society for Assisted Reproductive Technology from 2004 to 2013 were evaluated. Results: There was a statistically significant increase in the number of male infants born following a blastocyst-stage FET compared with cleavage-stage FETs. Conclusions: Blastocyst-stage transfers suggest a shift towards males but whether the use of frozen-thawed embryos affects this ratio is not known. The object of this study was to investigate whether there is a difference in live-birth gender in blastocyst-stage compared with cleavage-stage FETs.

### Embryo Selection in Developing Countries: Inner Cell Mass to Blastocyst Dimension Ratio as a Predictor of Pregnancy Outcome

The study assessed the use of morphological grading and biopsy day as predictors of pregnancy outcomes. Design: Retrospective cohort study. Materials and Methods: All IVF cycles reported to the Society for Assisted Reproductive Technology from 2004 to 2013 were evaluated. Results: There was a statistically significant increase in the number of male infants born following a blastocyst-stage FET compared with cleavage-stage FETs. Conclusions: In patients undergoing FETs, blastocyst-stage transfers are associated with higher male gender live-birth rates when compared with cleavage-stage transfers.
DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Groups were classified according to the number of rounds of biopsy and vitrification that the euploid blastocyst (≥ Grade 3BB) underwent prior to FET at a single infertility clinic. Single biopsy (4-6 cells)/Double vitrification (n=93 FETs), and a control group of Single biopsy (4-6 cells)/Single vitrification FETs (n=93 FETs). Standard protocols for a hormone replacement FET were utilized for all patients. Statistical analysis included ANOVA and Chi-square test where appropriate, significance at P<0.05.

RESULTS: Mean maternal age was significantly lower in the Single Biopsy/Double Vitrification group (Table 1; P<0.0001). Blastocyst grade was comparable across the groups. FET reproductive outcomes revealed a significant decrease in clinical pregnancy and live birth rate, with a significant increase in MAB rate when a euploid blastocyst underwent a double biopsy and double vitrification prior to transfer (Table 1; p<0.01). There were no significant differences in reproductive outcomes between the Single Biopsy/Double Vitrification FET group and the control group with Single Biopsy/Single Vitrification (Table 1).

CONCLUSIONS: In conclusion, for transferrable quality, euploid blastocysts a single biopsy, double vitrification had comparable reproductive outcomes as a single biopsy, single vitrification, thereby supporting the efficacy of double vitrification. In contrast, a double biopsy had a significant impact on the developmental potential of a euploid blastocyst with a decreased probability of establishing and sustaining a viable clinical pregnancy. This novel study highlights the adverse impact of removing too many TE cells with a double biopsy for PGT-A.

SUPPORT: None.

TABLE 1.

<table>
<thead>
<tr>
<th></th>
<th>Single Biopsy/Double Vitrification FETs</th>
<th>Double Biopsy/Double Vitrification FET</th>
<th>Single Biopsy/Single Vitrification FET (Control)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal Age</td>
<td>35.1 ±3.7	extsuperscript{a}</td>
<td>37.8 ±3.8	extsuperscript{b}</td>
<td>37.3 ±3.4 \textsuperscript{b}</td>
</tr>
<tr>
<td>Clinical Pregnancy with Fetal Cardiac Activity</td>
<td>63.8%</td>
<td>53.8%*</td>
<td>67.1%</td>
</tr>
<tr>
<td>MAB Rate</td>
<td>5.8%</td>
<td>20.0%*</td>
<td>4.3%</td>
</tr>
<tr>
<td>Live Birth Rate</td>
<td>60.1%</td>
<td>43.0%*</td>
<td>64.3%</td>
</tr>
</tbody>
</table>

\(a\) P<0.0001; \(b\) P<0.01

DEGREE OF RE-EXPANSION FOLLOWING VITRIFICATION/REWARMING OF EUPLOID BLASTOCYSTS IS INVERSELY CORRELATED WITH IMPLANTATION AND CONTINUOUS PREGNANCY/LIVE BIRTH RATES. Sydney Chang, MD, Taraneh Gharib Nazem, MD, Dmitry Gouuko, MA, Marlena Duke, MSc, ELD, Christine Briton-Jones, PhD, HCLD, Alan B. Copperman, MD, Beth McAvney, MD. Icahn School of Medicine at Mount Sinai, New York, NY. Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Routine implementation of blastocyst culture, preimplantation genetic testing, and freeze-all cycles has resulted in supernumerary cryopreserved euploid blastocysts available for frozen embryo transfer (FET). Often faced with a selection of chromosomally normal embryos, embryologists and clinicians turn to embryo morphology, morphokinetics, and timing of blastulation and cavitation to develop prognostic criteria. A recent study showed that re-expansion of vitrified/rewarmed blastocysts strongly correlated with implantation compared to blastocysts that did not re-expand. Yet, that study did not incorporate PGT-A and was limited by small sample size. Thus, our objective was to evaluate the association between degree of re-expansion prior to FET and clinical outcomes among euploid blastocysts.

DESIGN: Retrospective, cohort study.

MATERIALS AND METHODS: The study included patients at an academic center who underwent single euploid PGT-A cycle(s) from 2012-2019. Embryo vitrification/rewarming were performed with the Cryotop method (Kitazato). Embryos were classified into 3 groups: (1) fully re-expanded, (2) partially re-expanded, and (3) not re-expanded. Images of embryos recorded as not re-expanded after 3-4 hours post-warming were manually compared to the image taken immediately post-warming to determine whether partial re-expansion had occurred during the culture period. Primary outcome was ongoing pregnancy/live birth (OP/LB) rate. Secondary outcomes were rates of clinical pregnancy (CP) and early pregnancy loss (EPL). Data were evaluated with T-tests, chi-square tests, and generalized estimating equations.

RESULTS: The study included 4440 single euploid FET cycles from 2968 patients. There were 118 cycles (2.7%) where embryos were not fully re-expanded 3-4 hours post-warming. Of these, 58 had partially re-expanded and 59 did not re-expand prior to FET. There was a higher proportion of day 7 embryos (27.1%) in the not re-expanded compared to the fully re-expanded cohort (2.6%). After controlling for confounders, blastocysts that did not re-expand after 3-4 hours were associated with a significant decrease in OP/LB (OR 0.19 [95% CI 0.09-0.40], p<0.0001) and CP (OR 0.19 [95% CI 0.10-0.35], p<0.0001), compared to fully re-expanded blastocysts. There was no significant difference in OP/LB or CP rates between partially and fully re-expanded groups. There was no difference in EPL rate between the 3 groups.

CONCLUSIONS: In this study assessing the contribution of embryo re-expansion after vitrification/rewarming in a single euploid FET model, we showed reduced CP and OP/LB rates in embryos that did not re-expand. Our findings are consistent with Coello et al. who found a lower implantation rate for embryos that did not fully re-expand at FET compared to those that did. Though transfer of blastocysts that did not re-expand resulted in a 76% decrease in OP/LB rate, our study also found no difference in EPL. Patients can therefore be reassured that once implantation has been achieved, there is no demonstrable increase in EPL.


SUPPORT: None.
to multiple embryo transfer, frozen embryo transfer, transfer of morula or cleavage stage, was missing charted data on morphologic grading criteria, or if transfer occurred on a culture day other than 5. On selected data, logistic regression models were used to test the association between the occurrence of pregnancy and i) each blastocyst grading criteria (ES, trophoectoderm [TD] and inner cell mass score [ICM]) and ii) the total embryo score stratified by blastocyst stage (early blastocyst, blastocyst, expanded blastocyst). All tests were performed at a 5% significance level. The area under the receiver operating characteristic (AUROC) curve was used to evaluate the performance of both TD and ICM in pregnancy prediction.

RESULTS: For each one point increase in score for ES, TD and ICM, there was a statistically significant increase in the odds of pregnancy of 1.78 (95% CI: 1.27 – 2.58), 1.38 (95% CI: 1.18 – 1.63), and 1.41 (95% CI: 1.19 – 1.69) respectively. The AUROC curve was nearly identical for both TD and ICM (0.62) and thus both discriminate similarly in predicting pregnancy. It does not appear that one offers greater predictive ability over the other.

CONCLUSIONS: This study suggests that ES, TD quality, and ICM quality may be useful for predicting clinical pregnancy rates amongst women undergoing transfer of an early blastocyst, blastocyst, or expanded blastocyst on culture day 5. Interestingly, it seems that TD and ICM are equivalent in terms of predictive ability. The importance of blastocyst expansion on the likelihood of pregnancy was demonstrated. When embryo score was stratified by stage, the transfer of an expanded blastocyst was associated with an increased likelihood of pregnancy. Transfer of an early blastocyst or blastocyst was not.


TABLE 1. Relationship between timing of transfer in different models

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Crude Model</th>
<th>Model I</th>
<th>Model II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timing of ET</td>
<td>β(95%CI)</td>
<td>P-value</td>
<td>β(95%CI)</td>
</tr>
<tr>
<td>Fresh ET</td>
<td>1.0</td>
<td>0.001</td>
<td>0.73 (0.58, 0.92)</td>
</tr>
<tr>
<td>Frozen ET</td>
<td>0.68 (0.55, 0.85)</td>
<td>1.0</td>
<td>0.73 (0.58, 0.92)</td>
</tr>
</tbody>
</table>

ET, embryo transfer ; CI, confidence interval
Crude model: we did not adjust other covariants
Model I: we adjusted female age
Model II: we adjusted female age, fertilization type, infertility type, infertility duration, no. of oocyte retrieved, no. of embryo transferred and D3/D5 embryo transfer.
CI confidence interval

OBJECTIVE: To compare the clinical outcome of frozen-thawed embryo transfer and frozen single embryo transfer in GnRH antagonist protocol.

DESIGN: A total of 1430 normo-responder women from a single ART center (from January 2015 to January 2019) were enrolled in this retrospective cohort study. Women aged <40 years, no. of oocyte retrieved between 3 and 10, good embryo quality, underwent fresh embryo transfer or frozen-all strategy and transferred in subsequent cycle were included. Endometriosis, PCOS/PFS cycles were excluded.

MATERIALS AND METHODS: The primary outcome was clinical pregnancy rate. A logistic regression analysis was performed to determine the variables that could be independently associated with clinical pregnancy rate. Models were adjusted for covariates including female age, fertilization type, infertility type, infertility duration, no. of oocyte retrieved, no. of embryo transferred and D3/D5 embryo transfer.

RESULTS: In total, 495 women were treated with fresh embryo transfer, whereas 935 patients were treated with frozen-thawed embryo transfer.

P-119 Tuesday, October 15, 2019 6:30 AM

IS THERE A RELATIONSHIP BETWEEN MITOCHONDRIAL DNA CONTENT AND ABORTION RATE IN PATIENTS UNDERGOING SINGLE EUPLOID FROZEN EMBRYO TRANSFER? Ahmed El-Damen, MSc, Ibrahim Elkhatab, Msc, Asina Bayram, MSc, Ana Aranz, Msc, Suzan Samir, BVM, Neelke De Munk, PhD, Barbara Lawrenz, MD, PhD, Human M. Fatemi, MD, PhD. IVIRMA Middle East Fertility Clinic, Abu Dhabi, United Arab Emirates.

OBJECTIVE: The mitochondrial DNA (mtDNA) content of trophoectoderm cells is related to the energy supply of the blastocyst, which could affect its ability either to implant in the uterine cavity or not. While it has been demonstrated that euploid blastocysts present a lower mtDNA content as compared to aneuploid blastocysts, there are no data evaluating whether there is a difference in the mtDNA content between pregnant and non-pregnant groups, leading to an ongoing pregnancy or an abortion. Unpaired two-tailed t-Student test was used to compare means of numerical variables and chi-square test for testing independence between categorical variables. A logistic regression model was performed controlling for maternal age, BMI, transfer distance from the fundus, endometrial thickness, cycle regimen and embryo quality. A p-value < 0.05 was considered statistically significant.

RESULTS: 355 euploid blastocysts were selected for SEFET in 314 patients with an average age of (33.7±5.55); 255 of them were biopsied on day 5 (71.8%) and 100 on day 6 (28.2%). Embryo transfer (ET) was performed in an HRT cycle (n=255; 71.8%) or a NC (n=100; 28.2%). A pregnancy rate of 66.2% (235/255) was obtained with ongoing pregnancy and abortion rates of 52.4% and 5.6%, respectively. There was no significant difference in the mtDNA content between pregnant and non-pregnant groups (p=0.095) and between the abortion and ongoing pregnancy group (p=0.15). Multivariate analysis showed the same non-significant relationship except for abortion rate and BMI (p=0.011).

CONCLUSIONS: Mitochondrial DNA content of the human blastocyst is unable to predict the abortion rate of implanted euploid blastocysts.

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FROZEN-THAWED EMBRYO TRANSFER IS BETTER THAN FRESH EMBRYO TRANSFER IN GNRH ANTAGONIST CYCLE IN NORMO-RESPONDERS: A RETROSPECTIVE COHORT STUDY. Xitong Liu, Resident, Haiyan Bai. Physician, Northwest women’s and children’s hospital, Xi’an, China.

OBJECTIVE: To compare the clinical outcome of frozen-thawed embryo transfer and fresh embryo transfer in GnRH antagonist protocol.

DESIGN: A total of 1430 normo-responder women from a single ART center (from January 2015 to January 2019) were enrolled in this retrospective cohort study. Women aged <40 years, no. of oocyte retrieved between 3 and 10, good embryo quality, underwent fresh embryo transfer or frozen-all strategy and transferred in subsequent cycle were included. Endometriosis, PCOS/PFS cycles were excluded.

MATERIALS AND METHODS: The primary outcome was clinical pregnancy rate. A logistic regression analysis was performed to determine the variables that could be independently associated with clinical pregnancy rate. Models were adjusted for covariates including female age, fertilization type, infertility type, infertility duration, no. of oocyte retrieved, no. of embryo transferred and D3/D5 embryo transfer.

RESULTS: In total, 495 women were treated with fresh embryo transfer, whereas 935 patients were treated with frozen-thawed embryo transfer.
Clinical pregnancy rate (54.50% vs 63.70%, p < 0.001) were significantly higher with frozen embryo transfer compared to fresh embryo transfer. Variables that were found to be independently associated with clinical pregnancy rate were fresh/frozen embryo transfer, female age and no. of embryo transferred. After adjusting for variables, frozen embryo transfer (0.75 (0.59, 0.95), p = 0.016) was protective factor of clinical pregnancy rate.

CONCLUSIONS: Frozen embryo transfer is better than fresh embryo transfer in GnRH antagonist cycle in normo-responders.

P-121 Tuesday, October 15, 2019 6:30 AM
REGAINING OF FULL EXPANDED STAGE AT 3 HOURS POST-WARMING IS A SUPERIOR MORPHOLOGICAL MARKER FOR LIVE BIRTH RATES IN VITRIFIED-WARMED SINGLE BLASTOCYST TRANSFER CYCLES. Natchandra Manohar Rao Chimote, M.Sc., Ph.D.a Bindu N. Chimote, M.Sc., M.Phil, Ph.D.(Biochemistry); M.Sc. Clinical Embryology (Leeds-UK).b 3Scientific Director, Vannshdhara Fertility Centre, Nagpur, India. 4Consultant Clinical Embryologist, Nagpur, India.

OBJECTIVE: No study has yet unequivocally established significance of ICM gradation, TE gradation and degree of blastocoelexpansion/re-expansion in enhancing live-births. Also, most studies have clubbed results from fresh/frozen and single/double transfer cycles. We aimed to individually assess the relevance of grades of inner cell mass, trophoectoderm and degree of post-warm blastocoelexpansion on live-birth rates exclusively in vitrified-warmed single blastocyst transfer cycles.

DESIGN: Retrospective study of vitrified-warmed cycles involving women (n = 380) undergoing elective single blastocyst transfer. Oocyte donation, Embryo donation, assisted hatching and preimplantation genetic diagnosis cycles were excluded. Ethics Committee of the centre approved this study. All blastocysts were graded as per Gardner and Schoolcraft method of classification as 1-6 for degree of expansion and grades A/B/C for ICM and TE.

MATERIALS AND METHODS: Natural-cycle endometrial preparation was done with hormone supplementation followed by luteal-phase support with micronized progesterone. Endometrial response (thickness and homogeneity) was noted by ultrasound. Single blastocyst was transferred 3 hours after warming. Pre-vitrification grade of blastocyst was compared with the live birth rate of DBT-GP, double embryo transfer of good quality blastocyst (SBT-G), single embryo transfer of poor quality blastocyst (SBT-P), double embryo transfer of good quality blastocysts (SBT-GG), double embryo transfer of good and poor quality blastocysts (SBT-GP) and double embryo transfers of poor quality blastocysts (SBT-PP).

RESULTS: 1379 cycles were included in the study. The mean age (SD) of the whole study population was 37.8 years (±4.0 years). 1020 cycles in women who received SBT-G, 167 cycles in women who received SBT-P, 56 cycles in women who received DBT-G, 74 cycles in women who received DBT-GP and 62 cycles in women who received DBT-PP. There was no significant difference in the age of each group. The live birth rate (SBT-G: 21.4%, SBT-P: 12.6%, DBT-GG: 32.1%, DBT-GP: 23.0%, DBT-PP: 19.4%) was significantly higher in the SBT-G group and the DBT-GG group than in the SBT-P group. The miscarriage rate (SBT-G: 28.3%, SBT-P: 42.2%, DBT-GG: 17.4%, DBT-GP: 35.7%, DBT-PP: 36.4%) tended to be lower in the DBT-GG, but with no significant difference between each group.

P-122 Tuesday, October 15, 2019 6:30 AM
THE IMPACT OF TEMPERATURE AND RELATIVE HUMIDITY ON OUTCOMES OF OVARIAN STIMULATION AND IN VITRO FERTILIZATION USING AN OOCYTE DONATION COHORT. Avery J. Gaskin, B.S.a,b 1Samantha C. Quinones, ScD.a,b 2Zsolt Peter Nagy, MD, PhD.a, c 3Sarah M. Capelouto, MD, c Daniel B. Shapiro, MD, b Jessica B. Spencer, MD, MSc,a Heather S. Hipp, MD.a 1Emory University, Atlanta, GA; 2Reproductive Biology Associates, Atlanta, GA; 3The University of Texas, Southwestern Medical Center, Dallas, TX.

OBJECTIVE: To determine the effect of temperature, humidity, and precipitation prior to oocyte retrieval on ovarian stimulation outcomes among oocyte donors and early in vitro fertilization (IVF) outcomes among recipients.

DESIGN: Retrospective cohort study of data from a frozen donor oocyte bank from 2008 to 2015.

MATERIALS AND METHODS: A total of 350 oocyte donors residing in the metro-Atlanta area underwent 553 ovarian stimulation cycles with an antagonist protocol. Mature oocytes were vitrified and later thawed in individual cohorts among 989 unique recipients. Mean temperature, relative humidity, and precipitation levels were calculated for the 90 days prior to oocyte retrieval using information from the Parameter-elevation Regressions on Independent Slopes Model. The associations between these climate variables and outcomes of ovarian stimulation (e.g. estradiol level at trigger and number of total and mature oocytes retrieved) and early IVF outcomes (e.g. % fertilized oocytes and % usable embryos) were modeled using generalized estimating equations adjusted for donor age, body mass index (BMI), race, and retrieval year.

RESULTS: The mean (standard deviation) age and BMI among oocyte donors was 25.4 (2.8) years and 22.6 (2.5) kg/m². Approximately 25% were racial/ethnic minorities and all were non-smokers. Donors exposed to warmer temperatures prior to oocyte retrieval had significantly higher...
estradiol levels at trigger (p-trend=0.04) despite no differences in the total dose of gonadotropins. Specifically, women in the highest quartile of temperature (76.0-81.4°F) had an average estradiol level of 3761 pg/ml (95% CI 3403, 4119) compared to 3341 pg/ml (95% CI 3034, 3647) among women in the lowest quartile (38.6-49.6°F). There was no impact of temperature on oocyte counts. Lower temperatures and higher humidity prior to oocyte retrieval were associated with a slightly higher percentage of usable embryos after oocyte warming and fertilization (p-trend=0.03 and 0.04). Greater mean precipitation prior to oocyte retrieval was associated with a slightly higher percentage of mature oocytes retrieved (p-trend=0.06) but was not associated with any of the IVF outcomes.

CONCLUSIONS: While warmer temperatures prior to oocyte retrieval were associated with higher estradiol levels at trigger, the resulting oocytes resulted in a lower percentage of useable embryos once thawed and fertilized among recipients. Vitrified oocyte donation represents an excellent model to determine the impact of environmental exposure such as climate variables on IVF outcomes given that exposures experienced by the donor and recipient are uncorrelated in time and space.

SUPPORT: Supported in part by R00ES026648 from the NIEHS.

P-125 Tuesday, October 15, 2019 6:30 AM

AUTOMATED HALO IDENTIFICATION: A NOVEL PREDICTIVE FEATURE FOR IVF SUCCESS IDENTIFIED THROUGH AN ARTIFICIAL INTELLIGENCE (AI) ALGORITHM. Marcos Meseguer, PhD,a Ron Uriel Maor, BSc,a Lucia Alegre, PhD,a Raquel Del Gallego, PhD,a Antonio Pellicer, MD, PhD,b Daniel S. Seidman, M.D, MMSc,c Daniella Gilboa, MSc,a d VIVRM Global, Valencia, Spain; a 2IVF, Tel Aviv, Israel; a The Foundation For Embryonic Competence, Basking Ridge, NJ; b Department of Obstetrics and Gynecology Sheba Medical Center affiliated to The Sackler Faculty of Medicine, Tel Aviv, Israel.

OBJECTIVE: To identify in fertilized oocytes previously unrecognized predictive features for live birth following IVF treatment that can apparently be revealed only by an advanced novel AI algorithm.

DESIGN: The study used AI to analyse TL videos of embryos in their pronuclear stage.

MATERIALS AND METHODS: We analyzed video images of 123 fertilized embryos obtained from a time-lapse system Embryoscope. Of the 123 videos, 111 were clear enough for analysis. All embryos analyzed were graded as Top-Graded embryos and were transferred back to the uterus. Of these embryos 88 (71.5%) successfully implanted and 45 (36.6%) resulted in a live birth.

Using a machine learning algorithm, we were able for the first time to characterize a previously unrecognized feature, the pale cytoplasm creating a “halo” surrounding the nucleus of the fertilized oocyte. The measurable amount of this halo over a range of images was compared to a set threshold. The resulting yes/no decision was assessed in relation to the likelihood of the embryo to implant successfully.

We calculated a relative brightness/smoothness measure, comparing each image to a reference image of the same embryo 7 hours earlier. These measurements were compared to an internal threshold obtained experimentally, with the result reported as above threshold (significant halo identified) or below threshold (no significant halo identified).

RESULTS: The halo was identified in 42% of 49 videos of embryos that successfully implanted versus in only 17% of embryos that failed to implant. There was no difference in the proportion of embryos that implanted, where a halo was identified, according to whether they carried out to a live birth or miscarried.

Using the halo to predict successful implantation of a Top-Graded transferred embryo had a sensitivity of 42% and a specificity of 83%, with a positive predictive value of 85% and a negative predictive value of 46%.

CONCLUSIONS: An AI algorithm identified in video images of fertilized oocytes a previously unrecognized feature that is associated with a high predictive value for successful subsequent implantation. The Automated Halo Identification may help improve embryo selection and result in higher live birth rates.

P-126 Tuesday, October 15, 2019 6:30 AM

HIGHER CUMULATIVE LIVE BIRTH RATES (CLBR) ARE EXPECTED WITH A FREEZE-ALL POLICY AS COMPARED TO A FRESH EMBRYOTRANSFER POLICY: WHEN MORE THAN TWO BLASTOCYSTS ARE AVAILABLE. Petroula Tatsi, MSc,a Tatiana Chantamitsidou, MSc,a Christina Vlachou, MSc,a George Michos, MD, PhD,a Robert Najdecki, MD, PhD,a Evangelos Papanikolaou, MD, PhD,a Eros Nikitos, MSc,a Evangelia Timotheou, MSc,a a Assisting Nature, Center of Assisted Reproduction and Genetics, Thessaloniki, Greece; b 3rd Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki, Thessaloniki, Greece; c Institute of Life, Athens, Greece.

OBJECTIVE: The purpose of the study is to evaluate if there is any advantage in terms of pregnancy expressed as CLBR between patients having at least 2 blastocysts, who follow Freeze-all strategy and patients who have first a fresh ET and then subsequent frozen-thawed ETs (FET).

DESIGN: This is a prospective observational study, which includes two groups of patients; Group FRALL: couples which followed freeze-all policy (no fresh ET) and up to 3 FET and Group FRESH: couples which completed one fresh ET and two subsequent FET. All couples had at least two blastocysts available for ET.

MATERIALS AND METHODS: Women included in the study were younger than 40 and had at least 4 blastocysts available. Exclusion criteria were: Preimplantation Genetic Testing (PGT), Testicular Sperm Extraction (TESE) cycles or poor responders (oocytes <4). Study was performed...
between 2017 and 2018 in Assisting Nature, Centre of Assisted Reproduction and Genetics, Thessaloníki, Greece. FRALL-Group included 87 couples with a mean female age of 32.8 years, while FRESH-Group included 86 women with an average age of 33.1. The Controlled Ovarian Stimulation (COS) was based in an antagonist protocol.

RESULTS: The total CLBR was estimated for each group of patients, as well as for each ET separately. X² test was used to compare live birth rates between the two groups. In FRALL-Group the Live Birth Rate after the first FET was 57.5% and in FRESH-Group was 39.5%. The LBR was significantly higher in FRALL-group compared to FRESH-Group after the first ET (frozen versus fresh, p<0.05). The total CLBR for all the completed ETs was 81.6% in FRALL-Group and 71.3% in group B. Cumulatively, the live birth rates were again higher for the Freeze-all group though not statistically significant (p>0.05).

CONCLUSIONS: The CLBR is higher in patients who follow freeze-all strategy compared to those who undergo fresh and then FET. Our results indicate that in case of blastocyst ETs an artificially prepared endometrium (in a frozen cycle) might be superior than that after a stimulation cycle. This indicates that women considered normal or high responders have better chances of achieving live birth, if they follow Freeze-all policy. With appropriate consultation women do not argue about fresh and frozen ET, and once some criteria met, they are happy to follow our instructions. A cut-off of 2 blastocysts may look favorable into freezing all, however, higher number of cases is required in order to confirm the obtained results.

P-127 Tuesday, October 15, 2019 6:30 AM
IMACT OF MEIOTIC SPINDLE IMAGING ON FERTILIZATION, EMBRYO DEVELOPMENT, CLINICAL OUTCOME AND MORPHOKINETIC PARAMETERS: AN ANALYSIS OF 415 IN-VIVO MATURED AND 317 IN-VITRO MATURED HUMAN OOCYTE SIBLINGS, Yukiko Nakajo, AS,a Nobuya Aono, Ph.D.,b Hiromitsu Hattori, M.Sc.,c Yusuke Nakamura, BS,c Chiyuri Kumaos,BS,c Noriyuki Okuyama, M.Sc.,c Tomoko Hashimoto, M.D.,c,b Mayumi Toya, M.D.,Ph.D,c Hideki Igarashi, M.D.,Ph.D.,c Koichi Kyono, M.D.,Ph.D,c Kyono ART Clinic, Sendai, Miyagi, Japan;b3-13-1, takanawa, Minato-ku, Tokyo, Japan; c Kyono ART Clinic Takanawa, Tokyo, Japan.

OBJECTIVE: To evaluate the relationship between meiotic spindle imaging of in-vivo and in-vitro matured human oocytes and intracytoplasmic sperm injection (ICS) outcomes.

DESIGN: This study was a retrospective observational study conducted at Kyono ART Clinic in Japan from September 2012 to January 2019.

MATERIALS AND METHODS: This study included a total of 259 ICSI cycles in which were retrieved six or fewer mature oocytes and at least one immature oocyte. ICSI was performed on matured oocytes immediately after denudation. After denudation, MI oocytes were cultured for 4 hours to allow oocyte maturation. We categorized each sibling MI oocyte into an in-vivo matured group (n=415 oocytes) and an in-vitro matured oocyte group (n=317 oocytes). Both groups, the oocytes’ meiotic spindles were visualized with a Polscope before ICSI. We compared fertilization rate, embryo development and clinical pregnancy rate between the two groups with or without a spindle. Furthermore, 196 embryos (96 in-vivo matured oocytes with spindle, and 7 without spindle; 39 in-vitro matured oocytes with spindle, and 44 without spindle) were analyzed for morphokinetic parameters and incidence of direct unequal cleavage (DUC) by time-lapse imaging (TLS: Embryoscope+®). Statistical comparisons between the experimental groups were performed through Fisher’s exact test. Statistical difference was considered to be significant at P<0.05.

RESULTS: The mean patient age was 39.0±4.1 years (range: 25-45yrs). The spindle was detected in 85.3% (325/381) and 22.1% (70/317) of the in-vivo and in-vitro matured oocytes, respectively. In both groups, fertilization, blastocyst formation, and good-quality blastocyst rates were significantly higher when spindles were detected (Table). When the spindle was detected, there were no significant differences in fertilization rate or embryo development competence between in-vivo matured and in-vitro matured oocytes. Also, there was no significant difference in clinical pregnancy rate in each group (Table). In the morphokinetic parameters analysis, there were no significant differences in time points of cell division (tPNf to t8), interval of cell cleavage (C2 and S2), or incidence of DUC.

CONCLUSIONS: Meiotic spindle imaging may be useful for prediction in both in vitro and in-vitro-matured oocyte development. When meiotic spindle is detected in matured oocytes, developmental competence may not be influenced by whether maturation occurs in vivo or in vitro.

P-128 Tuesday, October 15, 2019 6:30 AM
CORRELATION BETWEEN BLASTOCYST STAGE OF EXPANSION AND CLINICAL OUTCOME: A RETROSPECTIVE ANALYSIS OF 810 SINGLE EUPOID BLASTOCYST TRANSFER CYCLES AT A SINGLE IVF CENTER, Vikrant V. Reddy, M.Sc,b Qianning Zhao, M.Sc,b Odgerel Badamjav, M.Sc,a Jennifer Dasig, M.Sc,c Jeong Hee Moon, Ph.D.,c Yimin Qin, Ph.D.,c Ali Masoudi, BS,c Kenney Tuyen, BS,c Barry R. Behr, Ph.D.c Sanford University Medical Center (LPCH), Sunnyvale, CA; Sanford Fertility and Reproductive Medicine Center (LPCH), Sunnyvale, CA; Sanford Fertility and Reproductive Medicine Center, Sunnyvale, CA.

OBJECTIVE: To determine whether a correlation exists between the stage of expansion of a euploid blastocyst and clinical outcome.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: A total of 810 PGT-A euploid single blastocyst transfer cycles between 2014 and 2018, graded using the Gardner criteria (Gardner et al., 1999), were retrospectively analyzed at a single IVF center. We assessed the correlation between the stage of euploid blastocyst expansion and clinical outcome irrespective of ICM and TE grade. These 810 cycles included a total of 119 fresh blastocyst transfers and 691 frozen-thawed blastocyst transfers. Clinical pregnancy was defined as a visible sac by ultrasound. All embryos were partially hatched at the pre-blastocyst stage.

RESULTS: Blastocyst expansion stages of 4 and 5 had a significantly higher (p < 0.001) clinical pregnancy rate (67.1% and 59.2%, respectively) compared to the expansion stages of 6 (46.4%). The expansion stages of 2 and 3 do not have a statistical significance/difference compared to the expansion stage 6. The expansion score did not have a correlation with spontaneous abortion (table). Our results contradict previously published work that found no correlation between fully hatched (grade 6) and non-hatching or partially hatched blastocysts (Rodriguez-Purata et al., 2016).

CONCLUSIONS: Fully hatched (grade 6) euploid blastocysts had a significantly higher (p = 0.001) clinical pregnancy rate (67.1% and 59.2%, respectively) compared to the expansion stages of 6 (46.4%). The expansion stages of 2 and 3 do not have a statistical significance/difference compared to the expansion stage 6. The expansion score did not have a correlation with spontaneous abortion. However, our results did indicate that blastocyst stage of expansion is an important factor for clinical success, which should be taken into consideration at the time of transfer. Our study contradicts a previously published study that found no correlation between fully hatched and non-hatched blastocysts. Artificial hatching could impact expansion grades at biopsy. Future research could focus on determining whether the implantation potential is compromised due to the biopsy procedure itself.

TABLE. Fertilization rate, embryo development and clinical outcomes

<table>
<thead>
<tr>
<th>Meiotic spindle in in-vivo matured oocytes</th>
<th>Meiotic spindle in in-vitro matured oocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detected</td>
<td>Not detected</td>
</tr>
<tr>
<td>No. of oocytes</td>
<td>325</td>
</tr>
<tr>
<td>Fertilization rate</td>
<td>73.2% * (273/373)</td>
</tr>
<tr>
<td>Blastocyst rate</td>
<td>45.6% * (93/204)</td>
</tr>
<tr>
<td>Good quality blastocyst</td>
<td>20.1% * (41/204)</td>
</tr>
<tr>
<td>No. of vitrified oocytes</td>
<td>83</td>
</tr>
<tr>
<td>No. of transferred oocytes</td>
<td>63</td>
</tr>
<tr>
<td>Clinical pregnancy rate (fresh and vitrified)</td>
<td>28.2% (29/103)</td>
</tr>
</tbody>
</table>

*P<0.05
**Expansion Stage** | **Euploid** | **Average Age** | **Clinical IU** | **p-value**
--- | --- | --- | --- | ---
Morula | 1 | 42.2 | 0.00% | 
1 | 3 | 36.4 | 0.00% | 
2 | 3 | 35.4 | 66.70% | 0.6
3 | 32 | 37.3 | 50.00% | 0.712
4 | 85 | 37 | 67.10% | 0.001
5 | 434 | 36.7 | 59.20% | 0.001
6 | 252 | 37.5 | 46.40% | 

**Expansion Stage** | **Clinical IU** | **Average Age** | **SAB** | **p-value**
--- | --- | --- | --- | ---
1 | 2 | 35.4 | 0.00% | 
2 | 16 | 37.3 | 12.50% | 0.655
3 | 57 | 37 | 15.80% | 0.215
4 | 257 | 36.7 | 10.56% | 0.854
5 | 118 | 37.5 | 9.30% | 

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**P-129** Tuesday, October 15, 2019 6:30 AM

**PREGNANCY OUTCOMES OF FROZEN THAWED CLEAVAGE STAGE EMBRYOS WITH OR WITHOUT EXTENDED CULTURE TO BLASTOCYST STAGE.** Cindy Chan, MD, Huang Yung Ling, MS, Chi-Huang Chen, MD, PhD, Chii-Ruey Tzeng, MD, MPH. Taipei Medical University Hospital, Taipei, Taiwan.

**OBJECTIVE:** Evaluate pregnancy outcomes of frozen thawed cleavage stage embryos with or without extended culture to blastocyst stage.

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** Frozen embryo transfer (FET) cycles from January 2017 to April 2018 that included cleavage stage embryo transfer (D3 FET) were compared to cleavage stage embryos that underwent extended culture after thawing to blastocyst stage before transfer (EC D5 FET) and thawed blastocyst stage embryo transfer (D5 FET). Pregnancy outcomes such as pregnancy rate, implantation rate, abortion rate and live birth rate were compared. Patients with any of the following were excluded: endometrial thickness less than 0.7 cm, undergoing simultaneous controlled ovarian stimulation or fresh embryo transfer, only day 2/4/7 embryos available for transfer, or thawing or culture failure.

**RESULTS:** Total of 1182 cycles were reviewed, and, after exclusion, 843 cases were included in this study. Overall pregnancy rate for D3 FET, D5 FET and EC D5 FET were 34.84%, 50.01% and 47.87%, respectively. The percentage implantation rate for D3 FET, D5 FET and EC D5 FET were 19.30%, 29.63% and 25.36%, respectively. The abortion rate for D3 FET, D5 FET and EC D5 FET were 27.06%, 14.23% and 17.78%, respectively. Significant statistical differences were found when comparing D3 FET pregnancy rates with D5 FET and EC D5 FET pregnancy rates. However, D5 FET and EC D5 FET pregnancy rates were comparable.

**CONCLUSIONS:** From our results, we have found comparable pregnancy outcomes among transfer of thawed blastocyst embryos and cleavage stage embryos with extended culture to blastocyst stage. The outcomes are also superior to thawed cleavage stage embryo transfer. This offers a new approach for patients who have many cryopreserved embryos from the past years when laboratory techniques were not yet readily available for blastocyst culturing. In addition, extended culture allows self-selection which enables identification of embryos with potential for better pregnancy outcomes.

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**P-130** Tuesday, October 15, 2019 6:30 AM

**FACTORS PREDICTIVE OF HAVING SUPERNUMERARY EMBRYOS IN FREEZE-ALL CYCLES; AN ANALYSIS OF SART CORS DATA.** Yetunde O. Ibrahim, MD, Greg Stoddard, MS, Erica Johnstone, MD *Utah Center for Reproductive Medicine, Salt Lake City, UT; Affiliation not provided; *University of Utah, Salt Lake City, UT.

**OBJECTIVE:** The field of IVF has focused on embryo selection and PGT-A was touted as the optimal method. However, publications demonstrating euploid live births from embryos found to be abnormal have demonstrated the limitations of PGT-A [1-3]. A selection technique only enhances the chances of success if there is a cohort of embryos from which to select. Freeze-all cycles are gaining wide acceptance due to evidence of equal or increased live birth compared to fresh transfers especially in hyper-responders [4, 5]. Therefore, we sought to identify factors predictive of having supernumerary embryos in freeze-all cycles.

**DESIGN:** Retrospective cohort study of women who underwent freeze-all cycles in 2014.

**MATERIALS AND METHODS:** Data were obtained from the Society for Assisted Reproductive Technology Registry. We defined supernumerary as having two or more embryos cryopreserved and computed the proportion of cycles resulting in this outcome. To identify predictive factors for supernumerary embryos, we first fitted a univariable Poisson regression model with a robust variance estimate. We then combined all variables with a p-value < 20 into a multivariable model.

**RESULTS:** Of 31,537 freeze-all cycles in 2014, 18,250 (57.9%, 95% CI: 57.3 – 58.4%) produced supernumerary embryos. On average, there were six embryos cryopreserved in cycles producing supernumerary embryos. Women with AMH > 3 or < 35 years each had on average 7 embryos cryopreserved. We included 12,173 subjects in the Poisson regression after excluding cycles missing important covariates. Factors predictive of having supernumerary embryos are presented in table 1.

**CONCLUSIONS:** Several factors are predictive of having supernumerary embryos. Women with AMH > 3 or younger than 35 had more opportunities for fresh embryo transfers such that a selection technique could be applicable.


**TABLE 1.**

<table>
<thead>
<tr>
<th>Variable (Referent)</th>
<th>Adjusted Risk Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (&lt; 35)</td>
<td>35 - 37</td>
<td>1.02 (0.99 - 1.05)</td>
</tr>
<tr>
<td></td>
<td>38 - 40</td>
<td>0.96 (0.93 - 0.99)</td>
</tr>
<tr>
<td></td>
<td>41 - 42</td>
<td>0.87 (0.82 - 0.91)</td>
</tr>
<tr>
<td></td>
<td>&gt; 42</td>
<td>0.70 (0.64 - 0.76)</td>
</tr>
<tr>
<td>BMI (18.5 – 24.9)</td>
<td>&lt; 18.5</td>
<td>1.03 (0.97 - 1.09)</td>
</tr>
<tr>
<td></td>
<td>25.0 - 29.9</td>
<td>0.96 (0.93 - 0.99)</td>
</tr>
<tr>
<td></td>
<td>&gt; 30</td>
<td>0.97 (0.94 - 1.00)</td>
</tr>
<tr>
<td>AMH (1.0 – 3.0)</td>
<td>&lt; 1.0</td>
<td>0.90 (0.86 - 0.95)</td>
</tr>
<tr>
<td></td>
<td>&gt; 3.0</td>
<td>1.02 (0.99 - 1.05)</td>
</tr>
<tr>
<td>Nulligravida</td>
<td>Gravida 1+</td>
<td>1.06 (1.04 - 1.09)</td>
</tr>
<tr>
<td>Prior fresh transfer (0)</td>
<td>1</td>
<td>0.94 (0.91 - 0.98)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>0.93 (0.88 - 0.97)</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>0.93 (0.86 - 0.99)</td>
</tr>
<tr>
<td></td>
<td>4+</td>
<td>0.97 (0.90 - 1.04)</td>
</tr>
<tr>
<td>Prior frozen transfer (0)</td>
<td>1</td>
<td>1.07 (1.02 - 1.13)</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>1.07 (1.01 - 1.15)</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>1.13 (1.04 - 1.23)</td>
</tr>
<tr>
<td></td>
<td>4+</td>
<td>1.09 (0.99 - 1.21)</td>
</tr>
<tr>
<td># eggs retrieved (0 – 3)</td>
<td>4 - 8</td>
<td>5.46 (4.56 - 6.54)</td>
</tr>
<tr>
<td></td>
<td>9 - 13</td>
<td>8.42 (7.05 - 10.1)</td>
</tr>
<tr>
<td></td>
<td>14 - 20</td>
<td>10.3 (8.59 - 12.3)</td>
</tr>
<tr>
<td></td>
<td>21 - 45+</td>
<td>11.0 (9.18 - 13.1)</td>
</tr>
<tr>
<td>Sperm source (partner)</td>
<td>Donor</td>
<td>1.05 (1.00 - 1.11)</td>
</tr>
<tr>
<td>ICSI (no ICSI)</td>
<td>All mature</td>
<td>1.22 (1.18 - 1.27)</td>
</tr>
<tr>
<td></td>
<td>Some mature</td>
<td>1.18 (1.11 - 1.26)</td>
</tr>
</tbody>
</table>
LIVE BIRTH DATA FROM 498 ELECTIVE AND NON-ELECTIVE AUTOLOGOUS OOCYTE THAW CYCLES (2009-2018). Anne Martini, DO,1 Rachel Horowitz, MD,2 Kate Devine, MD,3 Jui-He Tsai, PhD,4 Micah J. Hill, DO,4 Alan H. DeCherney, MD,5 Joseph Doyle, MD,6 Caleb Kallen, MD, PhD,3 National Institute of Child Health and Human Development, NIH, Bethesda, MD;4 Shady Grove Fertility and Lankenau Medical Center, Philadelphia, PA;5 Shady Grove Fertility, Rockville, MD.

OBJECTIVE: We present live birth data from 498 autologous treatment cycles using frozen/thawed oocytes. We hypothesized that elective oocyte cryopreservation results in higher live birth rates (LBR) than non-elective (onco-fertility, unanticipated lack of sperm, or limited insemination).

DESIGN: Retrospective Cohort.

MATERIALS AND METHODS: We identified all autologous In Vitro Fertilization (IVF) cycles using frozen oocytes (2009-2018). Ovarian stimulation, oocyte freeze/thaw, IVF, intracytoplasmic sperm injection (ICSI), embryo culture/transfer/vitrification were performed using published protocols. Primary outcome was live birth per thaw cycle. Secondary outcomes were stratified by indication for oocyte freezing, age at oocyte retrieval and by utilization of preimplantation genetic testing (PGT). Cumulative LBRs were compared using age-adjusted logistic regression.

RESULTS: In 498 thaw cycles involving 4,554 MII oocytes (average 9.1 oocytes/thaw), oocyte survival and fertilization rates were similar across all ages and indications for freezing (85.7% and 69.5% in aggregate). More than half of patients had a fresh embryo transfer (ET) and 48% had at least one embryo for vitrification (average 1.7 blastocysts frozen/thaw). Ten percent of thaw cycles had zero embryos for transfer or vitrification. On average, elective egg freezing patients thawed more MIIIs (11.4 vs 7.4) and generated more vitrified blastocysts than non-elective (2.4 vs 1.1). Average LBR per fresh ET was 36.7% (n=300) and per frozen ET was 51.5% (n=163). Elective patients were more likely to utilize PGT compared to non-elective patients (43.6% vs 14.3%). LBR was higher when using PGT-confirmed euploid embryos. For all thaw, cumulative LBR from electrolytically frozen oocytes was higher than from those frozen for non-elective indications (P<0.001). Across all age groups, cumulative LBR ranged from 30%-40% per oocyte thaw cycle.

CONCLUSIONS: We observed 30%-40% cumulative LBR after oocyte cryopreservation in all age groups and significantly higher rates when electively frozen oocytes were utilized. This underscores the overall probability for live birth per oocyte thaw as 27% of our cohort still has unused embryos. LBR in the >40 group should be cautiously interpreted given the small cohort and higher mean numbers of MIIs thawed.

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SUITABLE TIMING TO TRANSFER BLASTOCYSTS VITRIFIED ON DAY 6 IN FROZEN-TAUGHTED CYCLES MAY BE DAY 5, NOT DAY 6. Huiying Xu, master,* Shumin Qiu, bachelor,† Beihong Zheng, bachelor,‡ Fujian Provincial Maternity and Children’s Hospital, Fuzhou, China; †Affiliation not provided.

OBJECTIVE: To investigate the suitable timing to transfer blastocysts vitrified on day 6 in frozen-thawed cycles.

DESIGN: Retrospective analysis.

MATERIALS AND METHODS: This is a retrospective cohort study of 1788 frozen-thawed cycles of blastocysts vitrified either on day 5 or 6 and transferred between June 2017 and November 2018. There were 518 cycles included blastocysts vitrified on day 6 (Group A) and 1270 cycles included blastocysts vitrified on day 5 (Group B). According to the timing for blastocyst transfer which was 5 or 6 days after ovulation or progesterone use in hormone replacement therapy (HRT) cycle, the cycles in Group A were divided into two groups: cycles with blastocysts transferred on day 5 (Group C, 103 cycles) and cycles with blastocysts transferred on day 6 (Group D, 415 cycles).

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WHAT ARE THE CHANCES OF SUCCESS FOR COUPLES PERFORMING AN IVF CYCLE WITH ONLY POOR QUALITY DAY-3 EMBRYOS CULTURED TO THE BLASTOCYST STAGE? Camille Grysole, MD, Simon Phillips, PhD, Lise Preaubert, MD, PhD, Louise Lapensée, MD Ovo Clinic, Montréal, QC, Canada.

OBJECTIVE: In recent years, more and more IVF centers have chosen to culture all embryos until the blastocyst stage, in order to increase implantation rates. Therefore, it is important to inform couples of the strategy and to estimate their chances of getting a good quality blastocyst; especially if the entire embryo cohort is of poor quality. The objective of this study was to evaluate the rate of usable blastocysts and the live birth rate, in couples undergoing an IVF/ICSI who obtained only poor quality day-3 (D3) embryos.

RESULTS: This retrospective cohort study carried out between 2012 and 2016, analyzed 59 cycles of IVF/ICSI that resulted in at least one D3 embryo without any high quality embryos. A comparison to a control group comprising 122 cycles with D3 embryos of both good and poor quality was performed.

MATERIALS AND METHODS: Cycles in which all D3 embryos were of poor quality were included. All embryos were cultured until day 5 or 6 and were either transferred, cryopreserved or discarded. Exclusion criteria were egg donors, patients performing fertility preservation or modified natural cycle IVF. The embryo quality was scored according to the classification of the Istanbul consensus (Alpha / EHSRE 2011). Thus, D3 embryos were considered of poor quality if the blastomeres had a fragmentation rate > 25% (= grade 3 embryos) or if the number of cells was less than 6 (= slow-developement embryos). The usable blastocysts rate was defined as the ratio of the number of transferred or cryopreserved blastocysts (if Gardner score ≥ 2BB) to the total number of D3 embryos. Blastulation and live birth rates were expressed as a percentage and compared between the groups by the Chi² test.

RESULTS: In a total of 136 poor quality D3 embryos (from 59 patients), the blastulation rate was 23.5% (compared to a mean blastulation rate of 62% in our laboratory), the rate of usable blastocysts was 11.0% and the live birth rate was 26.7% per embryo transfer. The rate of usable blastocysts was significantly lower if they originated from grade 3 embryos compared to slow-developement embryos (6.8% vs 24.2%, p = 0.0054). The live birth rates were comparable by origin of blastocysts. Patients were statistically older and had lower anti-Mullerian hormone (AMH) levels than the control group, composed of 270 poor quality D3 embryos. Blastulation rates were statistically lower than in the control group (23.5% vs 37.4%, p = 0.005). However, the rates of usable blastocysts and rates of live birth did not differ between the two groups. In the control group, the rate of usable blastocysts was also higher for slow-developement embryos compared to grade 3 embryos (16.1% vs 7.7%, p = 0.048).

CONCLUSIONS: Despite the absence of good quality D3 embryos, a cohort composed entirely of “rejected” embryos can result in a transferable blastocyst and live birth. It appears that the high fragmentation rate of blastomeres is associated with a poorer prognosis than the decreased number of cells on D3. This study could improve the counseling of couples facing this situation.
RESULTS: Compared with Group A, the female patients in Group B was younger(31.37 ±4.42 VS 31.95 ±4.63, P < 0.05). There was no significant difference in male age, thickness of endometrium, endometrial preparation methods and the proportion of primary infertility patients between Group A and Group B. The rate of single blastocyst transfer (SBT), clinical pregnancy rate(cPR) and implantation rate in Group B were significantly higher than those in Group A (84.2% VS 65.8%, 66.0% VS 40.9%, 62.1% VS 35.1%, P < 0.001), and the early miscarriage rate and multiple pregnancy rate in Group B were significantly lower than those of Group A (11.2% VS 17.9%, 8.9% VS 15.1%, P < 0.001). The cPR and implantation rate in Group C were significantly higher than those in Group D (55.3% VS 37.3%,44.8% VS 32.6%, P < 0.01). No significant differences were found between Group C and Group D in terms of early miscarriage rate and multiple pregnancy rate. The rate of SBT, cPR and implantation rate in Group B were significantly higher than those in Group C (84.2% VS 61.2%, 66.0% VS 55.3%, 62.1% VS 44.8%, P < 0.05), and the early miscarriage rate in Group B was significantly lower than that of Group C (11.2% VS 21.1%, P < 0.05).

CONCLUSIONS: Transfer the blastocysts on 5 days, instead of 6 days after ovulation or progesterone use in HERT cycle, could improve the cPR and implantation rate of the blastocysts vitrified on day 6 in frozen-thawed cycles. The cPR and implantation rate of blastocysts vitrified on day 5 are significantly higher compared with blastocysts vitrified on day 6, and the early miscarriage rate is lower, no matter the timing to transfer blastocysts vitrified on day 6. Hospital Project of Fujian Provincial Maternity and Children Hospital(grant no.YXQ-25).

SUPPORT: National Key R&D Program of China(grant no.2018YFC10002105).

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DOES THE DAY OF FINAL OOCYTE MATURATION INJECTION PREDICT OUTCOMES IN COUPLES UNDERGOING IN VITRO FERTILIZATION/INTRACYTOPLASMIC SPERM INJECTION — AN ANALYSIS BASED ON AGE AND INDIVIDUAL CONTROLLED OVARIAN STIMULATION PROTOCOL. Abey Eapen, MBBS DRCOG PhD, Amy E. Sparks, PhD, Yunshu Zhou, MS, Karen M. Summers, MPH CHES, Patrick Ten Eycz, MS PhD, Eypu Hakan Duran, MD University of Iowa, City, IA.

OBJECTIVE: Optimizing outcomes for assisted conception treatment remains a clinical challenge. Previous studies have evaluated the role of oocyte number, stage and number of embryos transferred, and the endometrium. The goal of this study was to evaluate the impact of treatment cycle duration and the influence of maternal age in individual controlled ovarian stimulation (COS) protocols on predicting live birth outcomes in in-vitro fertilization (IVF) treatment.

DESIGN: Retrospective study using data from a single academic center.

MATERIALS AND METHODS: Demographic and outcome data for 1831 IVF cycles performed between Jan 2014 and Jun 2018 were analyzed. Cycle duration was defined as the number of days of gonadotrophin treatment until the day of final oocyte maturation injection. Live birth rate (LBR) was the primary outcome and logistic regression was used for all models. The main predictor was treatment cycle duration. Cycles were analyzed in total, and in categories of COS protocol used and maternal age (<38 and ≥38 years). Secondary outcomes included biochemical and clinical pregnancy. Cycle duration was analyzed as a continuous variable. Analyses were performed using SAS version 9.4 (SAS Institute, Cary, USA).

RESULTS: We included 1314 treatment cycles using autologous oocytes which resulted in fresh embryo transfers, without the use of pre-implantation genetic testing. There were 617 live births with an overall LBR of 47%. A total of 475 (36.1%) utilized a long agonist (LA) protocol, 346 (26.3%) utilized an agonist protocol with human chorionic gonadotropin (hCG) trigger, 335 (26%) utilized an antagonist protocol with gonadotropin releasing hormone (GnRH) agonist, 286 (21.8%) utilized a GnRH agonist flare protocols. On analysis of individual protocols, increasing cycle duration was a strong negative predictor for LBR in women <38 using a LA protocol (OR 0.80; 95% CI[0.69-0.92], P =0.001) and also in women ≥38 using an antagonist protocol with hCG trigger (OR 0.72; 95% CI[0.54-0.96], P =0.022). A combined analysis of all treatment protocols and ages also suggested a significant association between increasing cycle duration and IVF outcomes (OR 0.83; 95% CI[0.78-0.89], P<0.001). For other types of COS treatment protocols, increasing cycle duration was not a statistically significant predictor of LBR.

CONCLUSIONS: Our large retrospective study suggests a relationship between IVF cycle duration, individual COS protocol and LBR. Our study while adding evidence to the existing body of evidence on detrimental effects of prolonged ovarian stimulation, can also aid in clinical decision making on an ‘optimal day’ for final oocyte trigger injection based on maternal age and the individual type of COS protocol.

Statistical analysis for other age/treatment combinations: (Protocol, Age, OR, 95%CI, P value)
1. LA ≥38 - 1.02; [0.74-1.40], 0.91
2. antagonist – hCG <38 - 0.90; [0.78-1.05], 0.17
3. Antagonist - agonist <38 - 0.87 [0.75-1.02], 0.08
4. Antagonist - agonist ≥38 - 0.88 [0.51-2.49], 0.80
5. Flare <38 - 0.98 [0.79-1.22], 0.85
6. Flare ≥38 - 0.98 [0.76-1.26], 0.88


SUPPORT: Funding support:Á Statistical analysis for this project was supported by the Clinical and Translational Science Award (CTSA) from the National Center for Advancing Translational Sciences at the National Institutes of Health (NIH).

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ASSISTED HATCHING: IS IT ALL IT S CRACKED UP TO BE?. Charis E. Ng, BHSc, Marta Waïs, MD, Crystal Chan, MD, MSc. 1. University of Toronto, Toronto, ON, Canada; 2. Lunenfeld-Tanenbaum Research Institute, Mount Sinai Hospital, Toronto, ON, Canada.

OBJECTIVE: Observational studies show that blastocyst embryos must spontaneously hatch from their surrounding zona pellucida in order to implant. In IVF, assisted hatching (AH) is a laboratory procedure that intentionally breaches the embryo’s zona pellucida prior to transfer. The putative benefit is to augment an embryo’s ability to implant; however, there is still clinical equipoise regarding whether AH improves IVF outcomes, particularly for frozen-thawed embryos at the blastocyst stage. AH has also been associated with an increased risk of monozygotic twinning (MZT), although this is also controversial due to the small sizes of previous studies and the rare nature of this outcome.

This study aims to determine the effect of AH on pregnancy outcomes in IVF patients undergoing frozen-thawed blastocyst stage embryo transfers.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All frozen-thawed embryo transfers that occurred at Mount Sinai Fertility between Jan 2013 and Dec 2017 were included. Exclusion criteria included: cancellation of cycle prior to transfer, use of preimplantation genetics testing of the embryo, and ≥2 embryos transferred with discordant use of AH. The primary outcome was clinical pregnancy rate. Secondary outcomes included biochemical pregnancy, early pregnancy loss, live birth, and MZT rates. RR ratios, 95% CI, and p-values were calculated.

RESULTS: A total of 2165 transfer cycles were carried out. The AH group (n=1986) had similar biochemical pregnancy (38.7% vs 42.1%, aRR 0.92, CI 0.77-1.10), clinical pregnancy (29.1% vs 30.3%, aRR 0.96, CI 0.76-1.21), early pregnancy loss (43.5% vs 40.9%, aRR 1.06, CI 0.79-1.44), and live birth (19.9% vs 20.5%, aRR 0.97, CI 0.71-1.32) rates when compared to the control. MZT rates were comparable between groups (1.39% vs 1.85%, RR 0.76, CI 0.1-5.95) although the low numbers of events in this outcome limits interpretation. Interestingly, six pairs of dichorionic/diamniotic (di/di) twins resulted from single blastocyst embryo transfers. Subgroup analyses of single embryo transfers (n=1599) demonstrated that AH in embryos with expansion grades ≤3 was associated with a statistically significant increase in biochemical pregnancy (32.5% vs 44.3%, aRR 0.45, CI 0.23-0.84), and clinical pregnancy (40% vs 32.6%, aRR 0.61, CI 0.17-1.87). There were no statistically significant differences in early pregnancy loss and live birth rates in this population, nor any pregnancy outcomes for embryos with expansion grades of 4.

CONCLUSIONS: This study demonstrates that AH of frozen-thawed blastocyst stage embryos resulted in similar outcomes to transfers that did not use this technique. AH was not associated with any improvement in pregnancy.
outcomes including implantation, clinical pregnancy, early pregnancy loss, and live birth. The identification of d/di twins from single blastocyst embryo transfers challenges previously held notions that di/di MZT only occurs from division prior to the blastocyst stage. This study also demonstrates that AH of embryos with expansion grades ≤3 may be associated with poorer rates of beta pregnancy and clinical pregnancy.

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RELATIONSHIP BETWEEN THE PREGNANCY AND THE SIZE OF ARRESTED BLASTOMERE DERIVED FROM ABNORMAL CYTOKINESIS IN BLASTOCYST TRANSFER CYCLES. Hiroki Izumi, M.S., a Manabu Satoh, Ph.D., b Shu Hashimoto, Ph.D., b Yoshiharu Nakaoka, MD, Ph.D., b Yoshiharu Morimoto, MD, Ph.D. b

1N VAMBA CLINIC, Osaka, Japan; 2 Reproductive Science, Osaka City University Graduate School of Medicine, Osaka, Japan; 3 HORAC Grand Front Osaka clinic, Osaka, Japan.

OBJECTIVE: From observation continual morphological changes, about 25% of normally-fertilized ova shows abnormal cytokinesis at 1st mitosis (AC). The abnormal cytokinesis is a marker to be eliminated from transfer due to chromosomal abnormal and low developmental competence. However, it has been shown that a few AC embryos develop to morphologically-good blastocysts, showing implantation potential comparable to blastocysts derived from normally-cleaved embryos. Chromosome abnormality of blastocysts derived from AC-embryos is equivalent to that of blastocysts derived from normally-cleaved embryo. Some of infertility couples have only morphologically-good blastocysts developed from AC embryos. There is an urgent task to distinguish embryo with implantation potential from morphologically-good blastocysts which showed abnormal cytokinesis at 1st mitosis.

DESIGN: Clinical research

MATERIALS AND METHODS: Retrospective study of single blastocyst transfer (vitrified-warmed 415 blastocysts) between February 2018 and January 2019 were conducted. Blastocysts were separated into three groups: embryos which underwent normal cytokinesis at both 1st and 2nd mitoses (control group), embryos which showed normal cytokinesis at 1st mitosis but abnormal cytokinesis at 2nd mitosis (1A, n = 108). Blastocysts developed from AC embryos were classified according to the diameter of arrested blastomere (30 and greater than 30 mm: SAB and over 30 mm: LAB). Morphological changes of embryos has been recorded using a commercial time-lapse incubator (CCM-IBIS, ASTEC). Cleavage patterns and the diameter of arrested blastomeres were determined by time-lapse data analyzing. Blastocyst quality were scored by blastocyst quality score (BQs) according to the Gardner grading system. Clinical pregnancy and miscarriage rates were compared. Tukey-Kramer, t- and chi-squared tests were used for statistical analysis.

RESULTS: There was no significant difference in pregnancy rates (control: 50.4%, 1N: 57.8%, 1A: 44.4%) after single blastocyst transfer and miscarriage rates (control: 22.7%, 1N: 11.5%, 1A: 22.9%) among 3 groups. The BQs (26) of control blastocysts was significantly higher than 1N (18) and 1A (19, P < 0.05). Pregnancy rates of SAB in 1N was significantly higher than that of LAB (64.9% vs. 25%, P < 0.05). Pregnancy rates of SAB in 1A was significantly higher than that of LAB (50.0% vs. 12.5%, P < 0.05). Miscarriage rates of SAB in 1N was significantly lower than that of LAB (4.2% vs. 10.0%, P < 0.05). Miscarriage rates of SAB in 1A was significantly lower than that of LAB (19.6% vs. 100%, P < 0.05).

CONCLUSIONS: In some of embryos which undergo abnormal cytokinesis at 1st mitosis, abnormal cytokinesis might be occurred by fragmentation and their chromosomal normally separated. In this case, if embryos lost large volume of cytoplasm as fragmentation, their pregnancy potential would be decreased. Observing the size of arrested blastomere can predict pregnancy non-invasively in the case of morphologically-good blastocyst transfer developed from AC embryos.

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EMBRYO SELECT ASSAY: A NON-INVASIVE, DIPSTICK ELISA STRIP ASSAY TO IDENTIFY THE MOST COMPETENT EMBRYO FROM THE COHORT. Elizabeth E. Puscheck, MD, MS, MBA, a Michael J. Kirk, E.L.D., a Antony Anderson, D.H.Sc., a Milica Ivanovic, B.S., B.A., a Seth Levant, M.D., a Aleksandra Lazarevic, B.A., a Rajasangam Jeyendran, Ph.D, HCLD, a Wayne State University, Detroit, MI; a Michigan Center for Fertility and Women’s Health, Warren, MI; a Aspire Fertility San Antonio, San Antonio, TX; a Andrology Laboratory Services, Chicago, IL; a Partners in Reproductive Health, Tinley Park, IL; a Androlab Inc, Chicago, IL.

OBJECTIVE: Identifying the single best embryo for transfer in vitro fertilization (IVF) frozen embryo transfer (FET) is critical to improve pregnancy rates and decrease multiple gestations. To date, embryo selection has relied on embryo morphology (quality) and sometimes genetic data from pre-implantation genetic testing (PGT). Early in pregnancy, the trophoderm of the developing embryo secretes hCG which enters the maternal blood stream to signal implantation and is detectable in maternal serum about 8-12 days after embryo transfer. Previous work by Dr. Edwards and others have shown hCG levels can be identified in spent culture media (approximately 0.2 mIU/mL on day 2, 0.5 mIU/mL on day 3, and 1.4 mIU/mL on day 5). We developed a dipstick, enzyme linked immunosorbent assay (ELISA) to measure hCG in the spent embryo culture media as a novel model fluid after the embryo is biopsied. The objective is to identify the most competent embryo with the highest reproductive potential from its cohort—rapidly, non-invasively, and cost effectively.

DESIGN: Experimental.

MATERIALS AND METHODS: The embryo select assay is a dip stick strip assay which is able to quantitatively measure small amounts of hCG using a chemiluminescent substrate and Spectramax L. We performed 2 studies to evaluate this method. The first study evaluated embryo biopsy fluid output from the same couples to determine if this method can determine the most competent (metabolically functional) embryo with the highest reproductive potential from its cohort. Non-parametric Kruskal-Wallis Test was used to examine differences in hCG levels by embryo grade and PGT outcome. Analyses were performed using SAS (v9.4) and p-values < 0.05 are statistically significant.

RESULTS: For Study 1, we collected fluid from 101 embryo biopsies and measured the hCG levels. Quantitative hCG levels were detected in 60.4% of 101 samples; no hCG in 39.6%. In study 2, individual embryo biopsy fluid media from 51 embryos obtained from 15 couples were assessed to compare with current embryo selection methods (embryo quality and PGT results). 5 embryos had no detectable hCG level, which may indicate the embryos did not make hCG and would not implant. Alternatively, it may indicate that there was dropout in the assay. The other 46 samples had measurable hCG levels. There was no association between hCG levels and embryo grade (p = 0.19) or PGT outcome (p = 0.14).

CONCLUSIONS: Embryos need to make hCG in order to survive as an implanting embryo. This rapid, quantitative, novel “dipstick” assay of individual embryos provides new information regarding the embryo’s metabolic function, independent of current methods (embryo morphology and PGT). Future studies of live birth outcomes using these embryos in FETs will corroborate whether this method helps to identify the best, reproductively competent embryo for transfer.

SUPPORT: None.

E.M. P-138 Tuesday, October 15, 2019 6:30 AM

SINGLE VITRIFIED-WARMED BLASTOCYST TRANSFER: WHAT ARE THE BEST PREDICTIVE FACTORS FOR SUCCESS? Evelyne Boulet, BSc, Jason Ka Man Au, MSc, Jill Anne Mellon, MSc, Jon Havelock, MD. Pacific Centre for Reproductive Medicine, Burnaby, BC, Canada.

OBJECTIVE: To determine if the endometrial thickness, the blastocyst expansion, the inner cell mass (ICM) quality and trophoderm (TE) quality, or day of embryo freezing (5 vs 6), while controlling for the patient age at freezing, is a good indicator in predicting the clinical pregnancy outcome for single vitrified-warmed embryo transfers.

DESIGN: A retrospective observational study.

MATERIALS AND METHODS: From Jan 2016 to Dec 2018, a total of 771 frozen embryo transfers (FETs), where only a single autologous blastocyst was transferred, were analyzed. Exclusion criteria include patients over 42 years of age and cycles with preimplantation genetic testing and gestational carriers. All embryos were vitrified and warmed with the Vitrolife RapidFreeze RAPidWarm™ on Rapid-i™ devices. All embryos were graded with the Gardner’s scoring system immediately prior to transfers. We excluded 38 cycles (4.9%) from the analysis due to their small numbers – blastocyst expansion, the inner cell mass (ICM) quality and trophoderm (TE) quality, or day of embryo freezing (5 vs 6), while controlling for the patient age at freezing, is a good indicator in predicting the clinical pregnancy outcome for single vitrified-warmed embryo transfers.

RESULTS: 733 FETs were analyzed and divided into two groups: positive and negative implantation. The comparison results and the regression analysis were performed using SAS (v9.4) and p-values < 0.05 are statistically significant.

RESULTS: 733 FETs were analyzed and divided into two groups: positive and negative implantation. The comparison results and the regression analysis were performed using SAS (v9.4) and p-values < 0.05 are statistically significant.
Maturity of COC can be used as an indicator to predict outcome of ART. Dysmature COC resulted in poor fertilization rate, implantation rate, and pregnancy rate. In this study, we present that the maturity of COC affects the results of ART, such as fertilization rate, implantation rate, and pregnancy rate. Statistical analysis was performed using Chi-square test. P < 0.05 were considered significant.

### OBJECTIVE:
Cumulus oocyte complex (COC) at oocyte retrieval with assisted reproductive technology (ART) can be easily classified in a visual manner by its maturity. We have classified them into three categories, mature, immature, and dysmature, for more than ten years. Dysmature COC is thought to be taken from atretic follicles. Although the classification has been generally used for over three decades, there is little study to identify whether the maturity of COC affects the results of ART, such as fertilization rate, implantation rate, and pregnancy rate. In this study, we present that the maturity of COC can be used as an indicator to predict outcome of ART.

### DESIGN:
We demonstrate that dysmature COC results in poor outcome of ART. The infertile patients who underwent in vitro fertilization can be easily classified in a visual manner by its maturity. We have classified them into three categories, mature, immature, and dysmature, for more than ten years. Dysmature COC is thought to be taken from atretic follicles. Although the classification has been generally used for over three decades, there is little study to identify whether the maturity of COC affects the results of ART, such as fertilization rate, implantation rate, and pregnancy rate. In this study, we present that the maturity of COC can be used as an indicator to predict outcome of ART.

### MATERIALS AND METHODS:
All slow-developing embryos that became blastocysts on day 6 that were transferred in single FET cycles from January 2015 through December 2017 at an academic medical center were included. Cycles involving transfers of multiple embryos or those cycles that involved PGT were excluded. Slow-developing embryos were categorized in 3 different groups based on day-5 morphology: compacted morula, cavitating morula, early blastocyst. Live birth rate (LBR) and miscarriage rate (MR; defined as miscarriages per viable pregnancy) were calculated. Data were analyzed using Chi square and Fisher’s exact t-test.

### RESULTS:
Results are summarized in Table 1. Of the 474 FET cycles that reached embryo transfer criteria, 124 were classified as compacted morulae, 235 as cavitating morulae, and 115 as early blastocysts. A significantly lower LBR was achieved in the compacted morula group as compared to the cavitating morula and early blastocyst groups. This difference persisted even when limiting analysis to good-quality embryos, i.e., those of grade BB or above.

### CONCLUSIONS:
Decreased pregnancy rates have been demonstrated when transferring blastocysts on day 6 as compared to day 5 in both fresh and frozen cycles. However, previous data have been limited on the potential of slow-developing blastocysts based on embryo development and morphology prior to blastocyst formation and vitrification. Recent data have suggested increased pregnancy rates involving transfer of slow-developing embryos that have begun to cavitate on day 5; however, sample sizes have been small. Our analysis reveals significantly lower LBRs and a trend toward higher MRs with the transfer of compacted embryos versus cavitating morulae or early blastocysts in day-6 single blastocyst FET cycles. These differences persisted when controlling for embryo quality. These results suggest that the developmental curve of slow-developing embryos prior to vitrification may provide helpful insight into the reproductive potential of these embryos, informing the selection of the best embryo for transfer.

### REFERENCES:

### SUPPORT:
None.

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**TABLE 1. Embryos with Positive and Negative Implantation and Odds Ratio:**

<table>
<thead>
<tr>
<th>Sample Size</th>
<th>Positive Implantation</th>
<th>Negative Implantation</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>346</td>
<td>326 ± 3.3</td>
<td>33.9 ± 3.8</td>
<td>0.92 (0.88-0.96)</td>
</tr>
<tr>
<td>387</td>
<td>9.2 ± 2.0</td>
<td>8.8 ± 1.7</td>
<td>1.17 (1.08-1.28)</td>
</tr>
</tbody>
</table>

Day of Freezing

| 5         | 70.2% 62.0% | 0.90 (0.63-1.28) |
| 6         | 29.8% 38.0% |              |

Blastocyst Expansion

| 2         | 7.8% 14.5% | 2 to 3: 1.46 (0.84-2.53) |
| 3         | 28.0% 31.5% | 3 to 4: 1.24 (0.88-1.75) |
| 4         | 64.2% 54.0% | 4 to 2: 1.13 (1.07-3.05) |

ICM + TE

| AA        | 56.1% 38.8% | BB to AA/BA: 1.71 (1.10-2.64) |
| AB or BA  | 23.1% 23.3% | BB to AA: 2.27 (1.52-3.38) |
| BB        | 20.8% 38.0% | AB/BA to AA: 1.33 (0.90-1.19) |

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**TABLE 1. D6 FET outcomes by D5 morphology (all embryos)**

<table>
<thead>
<tr>
<th>Transfers (n)</th>
<th>Compact</th>
<th>Cavitating</th>
<th>Early Blastocyst</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>124</td>
<td>23.39%</td>
<td>34.04%</td>
<td>32.17%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>235</td>
<td>34.09%</td>
<td>26.61%</td>
<td>30.19%</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Good Quality Embryos**

<table>
<thead>
<tr>
<th>Transfers (n)</th>
<th>Compact</th>
<th>Cavitating</th>
<th>Early Blastocyst</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>110</td>
<td>25.45%</td>
<td>38.38%</td>
<td>35.92%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>198</td>
<td>33.30%</td>
<td>24.80%</td>
<td>27.50%</td>
<td>NS</td>
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**P-140 Tuesday, October 15, 2019 6:30 AM**

**THE PREDICTIVE VALUE OF DAY 5 MORPHOLOGY FOR SLOW DEVELOPING EMBRYOS.** Joseph Chernych, M.D.,a Joshua Stewart, M.D.,b Nikica Zaninovic, Ph.D.,b Steven Spandorfer, M.D.,b Zev Rosenwaks, M.D.,b Department of Ob/Gyn, New York Presbyterian-Weill Cornell Medicine, New York, NY; The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

**OBJECTIVE:** To compare pregnancy outcomes of slow-developing embryos (elective single embryo transfer of day-6 blastocysts) in frozen embryo transfer (FET) cycles based on day-5 embryo morphology.

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** All slow-developing embryos that became blastocysts on day 6 that were transferred in single FET cycles from January 2015 through December 2017 at an academic medical center were included. Cycles involving transfers of multiple embryos or those cycles that involved PGT were excluded. Slow-developing embryos were categorized in 3 different groups based on day-5 morphology: compacted morula, cavitating morula, early blastocyst. Live birth rate (LBR) and miscarriage rate (MR; defined as miscarriages per viable pregnancy) were calculated. Data were analyzed using Chi square and Fisher’s exact t-test.

**RESULTS:** Results are summarized in Table 1. Of the 474 FET cycles that reached embryo transfer criteria, 124 were classified as compacted morulae, 235 as cavitating morulae, and 115 as early blastocysts. A significantly lower LBR was achieved in the compacted morula group as compared to the cavitating morula and early blastocyst groups. This difference persisted even when limiting analysis to good-quality embryos, i.e., those of grade BB or above.

**CONCLUSIONS:** Decreased pregnancy rates have been demonstrated when transferring blastocysts on day 6 as compared to day 5 in both fresh and frozen cycles. However, previous data have been limited on the potential of slow-developing blastocysts based on embryo development and morphology prior to blastocyst formation and vitrification. Recent data have suggested increased pregnancy rates involving transfer of slow-developing embryos that have begun to cavitate on day 5; however, sample sizes have been small. Our analysis reveals significantly lower LBRs and a trend toward higher MRs with the transfer of compacted embryos versus cavitating morulae or early blastocysts in day-6 single blastocyst FET cycles. These differences persisted when controlling for embryo quality. These results suggest that the developmental curve of slow-developing embryos prior to vitrification may provide helpful insight into the reproductive potential of these embryos, informing the selection of the best embryo for transfer.
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ENDOMETRIAL THICKNESS IN PREDICTION OF PREGNANCY OUTCOME IN FRESH EGG DONATION CYCLES: A RETROSPECTIVE COHORT ANALYSIS. Jakob Doblinger, MD.1 Elena Labarta, MD PhD.1 Ernesto Bosch, MD, PhD.1 2IVIRMA Valencia, Valencia, Spain;3IVI-RMA, Valencia, Spain.

OBJECTIVE: To analyse the relationship between endometrial thickness and pregnancy outcome in fresh oocyte donation cycles.

DESIGN: Retrospective cohort analysis.

MATERIALS AND METHODS: Single centre retrospective cohort analysis of 1928 fresh single embryo transfer oocyte donation cycles. Treatment took place at a private infertility clinic (IVIRMA Valencia, Spain) between January 1st, 2016 and December 31st, 2017. We included women under 50 years old undergoing fresh oocyte-donation treatment in the context of a hormone replacement therapy (HRT) cycle for endometrial preparation. Only women with a normal uterus on the 2D ultrasound and accepting a single transfer of a day 5 blastocyst were included. Only one good quality blastocyst according to the Spanish ASEBIR classification was transferred after 5 days of progesterone administration (Micronized Progesterone, 400 mg/12h. vaginally). We excluded cases in which an endometrial preparation under a natural cycle was performed, when more than one embryo was transferred, or any good quality blastocyst was available.

RESULTS: Mean age was 42.5 ± 4.8 and BMI was 23.0 ± 3.6. The overall live birth rate was 45.6%. The mean endometrial thickness was 8.7±1.7 mm, ranging from 3.0 to 17.0 mm. The distribution by percentiles is as follows: p10=6.9mm; p25=7.75mm; p50=8.5mm; p75=9.5mm; p90=11.0mm. For the purpose of the analysis, patients were categorized in to 6 groups defined by percentiles. LBR in women with endometrium ≤ p10, (≤ 6.9 mm), was significantly reduced compared to the rest of the population (36.7% vs 46.2%; p=0.015). When submitted to a multivariate logistic regression analysis in which all variables related to live birth were included (i.e. age, BMI, number of oocytes, number of fertilized oocytes and number of good quality blastocysts available), endometrial thickness remained as an independent factor related to live birth. An endometrial thickness ≤ 6.9 mm was associated with a significantly reduced probability of live birth compared with patients with an endometrial thickness of 7 mm or more (OR: 0.70; 95% CI: 0.50-0.97).

CONCLUSIONS: Our results indicate a reduction of live birth rate for more than 9 % with an endometrial thickness lower than 7 mm. This finding even remains as an independent factor after multivariate logistic regression analysis controlling for all potentially relevant confounders. To our best knowledge this study seems to represent the largest cohort investigating live birth rate in fresh oocyte donation cycles and including only single embryo transfers.


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WHAT IS THE CLINICAL IMPACT OF THE ENDOMETRIAL RECEPTIVITY ARRAY IN PG-T AND OOCYTE DONATION CYCLES? Francisca Martinez, PhD.1 Ana Raquel Neves, MD, PhD.2 Marta Devesa, PhD.2 Sandra García-Martínez, ScB.3 Ignacio Rodriguez, MSc.3 Buenaventura Coroleu, PhD, MD.4 *Hospital Universitario Dexeus, Barcelona, Spain; 5Coimbra Hospital and University Centre, Coimbra, Portugal; 6Hospital universitario Dexeus, Barcelona, Spain.

OBJECTIVE: Despite the extensive investigation in the field of assisted reproduction, implantation still remains a challenge. The endometrial receptivity array (ERA) has been studied in both implantation failure (IF) and non-IF populations yielding conflicting results. We hypothesized that controlling for the embryonic factor might allow for a more accurate interpretation of the endometrial assessment.

Our aim was to evaluate the influence of the ERA test on the implantation rate (IR) and pregnancy rate (PR) in patients with previous failed euploid embryo transfers (EET) and previous failed oocyte donation embryo transfers (RET).

DESIGN: Single centre retrospective study, case-control study.

MATERIALS AND METHODS: There were 333 patients with previous failed EET or RET. Selected cases were patients with at least 1 previous failed EET (n=24) or 2 failed RET (n=32) who underwent an ERA test and a post-ERA euploid embryo transfer (EET) or oocyte donation embryo transfer (RET) between 2012-2018. Controls were patients with at least 1 previously failed EET (n=119) or 2 failed RET (n=158) who underwent EET or RET during the same period without undergoing an ERA test. Only blastocyst stage embryos were included. IR and PR were compared between the post-ERA ET and the last ET in the control arms.

RESULTS: There were 98 clinical pregnancies(CP) among 143 EET (14CP among 24 EET in ERA group, and 84 CP among control group); and 114 CP among 190 RET ( 11CP among 32 ERA group, and 103 CP among control group).

There was no statistically significant difference regarding IR (55.6% [34.6%-76.5%] vs.65.0% [56.9%-73.1%]) and PR (38.3% vs 70.6%, p=0.238) in the ERA vs. control group in the EET arm, while in the RET arm (26.8% [12.3%-41.4%] vs. 57.2% [50.1%-64.3%]) and PR (34.4% vs. 65.2%, p=0.001) were significantly lower in the ERA group. Multivariate logistic regression confirmed that the performance of an ERA test did not significantly influence the PR in the EET arm and was associated with a diminished PR in the RET arm. In the ERA group, 41.1% patients were non-receptive (NR). No significant difference was found regarding IR or PR in NR vs. receptive patients in both EET and RET arms.

CONCLUSIONS: In our sample, the performance of an ERA test did not improve pregnancy outcomes. Future prospective studies in larger samples are needed to confirm the role of the ERA test in EET and RET.

SUPPORT: None to declare.

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INTENTIONAL ENDOMETRIAL INJURY TRYING TO IMPROVE CLINICAL OUTCOMES OF AN OOCYTE DONATION PROGRAM IN PATIENTS WITHOUT RIF. INTERIM ANALYSIS OF A RANDOMIZED CONTROLLED TRIAL. Carmen Vidal, M.D., Ph.D.1 Juan Giles, M.D., Ph.D.1 Elena Labarta, MD PhD.1 Gemma Castillon, M.D., Ph.D.1 Javier Martinez-Salazar, MD.2 Laura Fernandez, MD.3 Yanira Aylton, Sr, MD.2 Manuel Muñoz, MD,2 Jose Bellver, MD Ph.D.3 Antonia Tocino, Sr, MD.2 Elkin Muñoz, M.D., Ph.D.2 Antonio Pelllicer, MD Ph.D.2 Nicolás Garrido, PhD1 IVIRMA Valencia, Valencia, Spain; 3IVI-MA Valencia, Valencia, Spain; 4IVI-MA, Valencia, Spain; 5IVI-MA Barcelona, Barcelona, Spain; 6IVI- Madrid, Madrid, Spain; 7IVI Murcia, Murcia, Spain; 8IVIRMA, Las Palmas de GC, Spain; 9IVIRMA ALICANTE, Alicante, Spain; 1Affiliation not provided; 1IVI-MA, Sevilla, SEVILLA, Spain; 1IVI-MA Vigo, Vigo, Spain; 1IVF Foundation, IIS La Fe, Valencia, IIS, Spain.

OBJECTIVE: Oocyte donation program (OD) provides the ideal setting for investigate if endometrial scratching improves 10 % the ongoing implantation rate, as the recipient’s endometrial priming guarantees the homogeneity of the endometrium and also the equality of quality of the transferred embryos and limiting the confounding factors.

DESIGN: A multicentric,open-label, randomized, controlled trial has been conducted in a private setting since Oct 2013. Eligible recipients were
DO PATIENTS WITH A HISTORY OF CHRONIC ENDOMETRITIS BENEFIT FROM CORTICOSTEROIDS AND ANTIBIOTICS BEFORE FROZEN EMBRYO TRANSFER?

Nicole D. Yoder, MD,a David H. McCulloh, Ph.D., b James A. Grifo, MD, PhD, c

FROZEN EMBRYO TRANSFER?

Nicole D. Yoder,

CORTICOSTEROIDS AND ANTIBIOTICS BEFORE ENDOMETRITIS BENEFIT FROM

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the cycle preceding the OD embryo transfer in recipients without RIF would yield Z = 0.75-2.16. The endometrial biopsy procedure was well tolerated in most women. The final decision of continuing or not the study was taken by means of applying the stochastic curtailment approach, to test the null hypothesis rejection probability given the current data available. P value of 0.7633 yielded Z = 0.72, leading to keep the trial continuing.

CONCLUSIONS: The interim analysis shows that ES in the luteal phase of the cycle preceding the OD embryo transfer in recipients without RIF would not pose a significant benefit thus its application to all OD recipients cannot be advised at this point, although the study continues. There is not enough evidence supporting scratching to increase endometrial receptivity. SUPPORT: None.

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IS THERE AN ASSOCIATION BETWEEN ENDOMETRIAL THICKNESS AT TIME OF FROZEN EMBRYO TRANSFER AND THE INCIDENCE OF SUBCHORIONIC HEMATOMA OR VAGINAL BLEEDING? Sydney Chang, MD,a Lily Ottensooser, BA,b Sass Wodowslaski, BA,b Tananeh Gharib Nazem, MD,a Dmitry Gouanko, MA,a Joseph A. Lee, BA,b Alan B. Copperman, MD,a Beth Mcavey, MD,a Ichon School of Medicine at Mount Sinai, New York, NY;b Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Subchorionic hematoma (SCH) is observed in 4-48% of early pregnancies. The etiology is unknown, SCH is believed to result from partial detachment of the chorion from the uterine wall, and frequently present with vaginal bleeding (VB). Some studies have suggested that the incidence of SCH is higher in pregnancies that result from in vitro fertilization (IVF), but the mechanism and clinical significance are unclear. The endometrial lining proliferates under the influence of estradiol (E2) during synthetic preparation for a frozen embryo transfer (FET) cycle. Whether there is an endometrial thickness (EnT) beyond which the endometrium begins to outgrow its blood supply has yet to be discovered. Given that E2 levels are often supraphysiologic and EnT maximized during synthetic preparation, we asked whether there is an association between EnT and the incidence of SCH/VB in pregnancies achieved following single euploid FETs. DESIGN: Retrospective, cohort study. MATERIALS AND METHODS: The study included patients at a single, academic ART center who achieved a pregnancy following a synthetically prepared single euploid FET cycle from 2012 to 2019. Natural endometrial preparation cycles were excluded. Natural endometrial thickness at the time of interim analysis, 234 out of 600 patients were recruited (40%). OBJECTIVE: Current data suggests that use of oral antibiotics and corticosteroids (AC) prior to embryo transfer (ET) does not improve ET outcomes. We hypothesized that patients with a history of chronic endometritis (CE) may be an exception to this finding. The objective was to investigate the utility of AC prior to single thawed euploid embryo transfer (STEET) in patients with CE.

DESIGN: Retrospective cohort study. MATERIALS AND METHODS: Patients who underwent STEET at an academic medical center from 1/2000 to 4/2019 were identified. Cycles prior to the time of interim analysis, 234 out of 600 patients were recruited (40%). All Pre N=1870 n % All Post N=904 n % X2

NP+E 439 23% NP+E 197 22% 2.23

IUP 1247 67% IUP 628 69% DF = 2

BP 184 10% BP 79 9% NS

Pre +CE n % Post +CE n % X2

NP+E 80 40% NP+E 38 34% 9.31

IUP 46 37% IUP 61 54% DF = 2

BP 29 23% BP 13 12% SIG

Pre -CE n % Post -CE n % X2

NP+E 44 35% NP+E 36 37% 1.02

IUP 59 47% IUP 49 50% DF = 2

BP 23 18% BP 13 13% NS

Pre Untested n % Post Untested n % X2

NP+E 344 21% NP+E 123 17% 4.23

IUP 1142 71% IUP 518 75% DF = 2

BP 132 8% BP 53 8% NS

SUPPORT: None.

TABLE 1. Pregnancy outcomes after STEET by treatment with AC (Pre) vs without AC (Post). Results were divided into 3 groups: Untested, CE positive (+CE) vs CE negative (CE-). X2 = Chi Squared, DF = Degrees of Freedom, SIG = Significant difference, NS = Non-significant difference.

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DO PATIENTS WITH A HISTORY OF CHRONIC ENDOMETRITIS BENEFIT FROM CORTICOSTEROIDS AND ANTIBIOTICS BEFORE FROZEN EMBRYO TRANSFER? Nicole D. Yoder, MD,a David H. McCulloh, Ph.D., b James A. Grifo, MD, PhD, c Frederick L. Lisciariati, M.D. aNYU School of Medicine, New York, NY; bNYU Langone Health, New York, NY; cNYU Langone Prelude Fertility Center, New York, NY.

OBJECTIVE: Current data suggests that use of oral antibiotics and corticosteroids (AC) prior to embryo transfer (ET) does not improve ET outcomes. We hypothesized that patients with a history of chronic endometritis (CE) may be an exception to this finding. The objective was to investigate the utility of AC prior to single thawed euploid embryo transfer (STEET) in patients with CE.

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Pre Untested n % Post Untested n % X2

NP+E 344 21% NP+E 123 17% 4.23

IUP 1142 71% IUP 518 75% DF = 2

BP 132 8% BP 53 8% NS

SUPPORT: None.
RESULTS: The study included 2515 patients who underwent 2927 single euploid FET cycles that progressed to a clinical pregnancy. The overall incidence of SCH was 7.99% (n = 228). Multivariate analysis demonstrated a significant difference in oocyte age, body mass index (BMI), and endometrial pattern (EnP) at FET between patients with and without SCH. There was not a statistically significant association between EnT at time of FET and incidence of SCH (OR 0.97 [95% CI 0.91-1.03], p = 0.32) or VB (OR 0.97 [95% CI 0.93-1.06]) when controlling for oocyte age, BMI, and EnP. There was no difference between rates of OP/LB (89.04% vs 86.62% p = 0.30) or clinical pregnancy loss (10.96% vs 13.38% p = 0.63) amongst patients with and without SCH.

CONCLUSIONS: In the largest study to evaluate the association between EnT and SCH using a single euploid FET model, we demonstrated no increase in the incidence of SCH or VB with increasing EnT in synthetically prepared FET cycles. Clinicians can be reassured that patients undergoing synthetic preparation for FET are not being placed at a higher risk for SCH or VB as a result of having a thicker endometrium. While EnT does not appear to be correlated with SCH, future studies that identify risk factors at the molecular level—such as markers of placental invasion—would offer a deeper look at the pathophysiology of SCH and help elucidate interactions at the maternal fetal interface.


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ENDOMETRIAL PREPARATION WITH ETANERCEPT INCREASES EMBRYO IMPLANTATION AND LIVE BIRTH IN WOMEN SUFFERING FROM IMPLANTATION FAILURE DURING IN VITRO FERTILIZATION, Karla Y. Santiago, MD,a Esther López-Bayghen, PhD, b Ingenes México, Mexico City, DF, Mexico; Centro de Investigación y Estudios Avanzados IPN, México, EM, Mexico.

OBJECTIVE: Repeated implantation failure (RIF) plague many women undergo in vitro fertilization (IVF). The exact cause and definition are currently under debate. Carrying out >3 failed IVF cycles with the accumulated transfer of at least 8 embryos is considered an initial definition of RIF. Typical RIF patients under 40 years with good ovarian reserve, normal endometrial morphology, normal karyotypes, antiangiopipin, and normal lupus anticoagulant as well as common thrombophilias. During implantation, Tumor Necrosis Factor-a (TNFα) stimulates MMP9 for endometrial invasion by the embryo, stimulates the expression of MUC1, gives embryo protection effects on teratogenic stress, and induces COX-2 response. Etanercept, a TNFα antagonist, has been shown to improve pregnancy rates in women with recurrent reproductive failure and with endometriomas. The aim of this study was to determine the effectiveness of etanercept treatment in IVF outcomes in women with RIF.

DESIGN: Single-arm, prospective study.

MATERIALS AND METHODS: Sixty-seven women suffering from RIF were recruited from the Ingenes Institute in Mexico City. All patient underwent a similar IVF protocol. Each woman received Etanercept (4 x 25 mg every 3 days) during endometrial preparation and at embryo transfer (25 mg). IVF outcomes that were assessed were embryo implantation (hCG >10 mIU/mL at Day 14), the presence of gestational sacs at week 8 by ultrasound, and live birth.

RESULTS: All women reported no side-effects associated with the treatment. 70.1% of the cohort achieved embryo implantation, 67.2% developed gestational sacs; however, the live birth rate was at 44.8%. Frozen cycles (n = 26) did perform better than fresh cycles (n = 41) for implantation (75.6% vs 61.5%), gestational sac (73.2% vs 57.7%), and live birth rate (48.8% vs 38.5%, respectively); however, these results were not significant.

CONCLUSIONS: Here, we showed that using Etanercept during endometrial preparation improves IVF outcomes in women suffering from RIF.

SUPPORT: Conacyt A 231793.
MATERIALS AND METHODS: In an academic center for reproductive medicine, a series endometrial echo pattern monitoring were carried out in 146 patients after hCG trigger: hCG day, from 1 through 3 days after ovum pick-up (OPU+1, OPU+2, OPU+3). The endometrial echogenicity value was obtained by ImageI software. Patients were compared according to their pregnancy status. For further analysis, endometrial echogenicity value was sorted into five groups: ≤60%, 61%-70%, 71%-80%, 81%-90%, and >90%. And Clinical pregnancy rate and embryo implantation rate were compared among the five echogenicity groups.

RESULTS: The endometrial echogenicity value was calculated as the ratio of the hyperechogenic endometrial area over the whole endometrial area. The endometrial echogenicity value on OPU+1,2,3 were differed markedly between clinical pregnant group and non-pregnant group (P <0.001). Clinical pregnancy rate and embryo implantation rate had positive relationship with echogenicity value. The ROC curve analysis of endometrial echogenicity for pregnancy showed the area under curve was greatest on OPU+2 (0.738, 0.765, 0.714 respectively). Endometrial echogenicity value on the OPU+2 had the most predictive value, and the cutoff value was 76.5%. The sensitivity was 61.3% and specificity was 82.0%.

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CLINICAL UTILITY OF THE ENDOMETRIAL RECEP TIVITY ARRAY IN WOMEN WITH PRIOR FAILED TRANSFERS. Laura E. Eisman, MD, a Margaretta D. Pisarska, MD, a Sahar Wertheimer, MD, a Jessica L. Chan, MD, MSCE, a Alin Lima Akopians, MD, PhD, a Mark W. Surrey, MD, a Hal C. Danzer, MD, a Shahin Ghadir, MD, a Wendy Y. Chang, MD, a Carolyn J. Alexander, MD, a Erica T. Wang, MD, a MAS, a Cedars-Sinai Medical Center, Los Angeles, CA; bSouthern California Reproductive Center, Beverly Hills, CA.

OBJECTIVE: To determine the clinical utility of the Endometrial Receptivity Array (ERA) in women with ≥1 prior failed embryo transfer (ET).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: This study included 214 women who underwent an ERA biopsy with a subsequent frozen ET between January 2016 and February 2019. Those with a nonreceptive endometrium were exposed to an ongoing pregnancy/live birth. Descriptive statistics were performed to compare outcomes in women with receptive versus non-receptive ERA results.

RESULTS: The endometrial echogenicity value on OPU+2 was recommended to evaluate endometrial receptivity. While it seemed appropriate to freeze the embryos from the present cycle and transfer them in a subsequent thaw cycle when echogenicity value ≤76.5% on OPU+2. More data are needed to avoid the useless and costly embryo cryopreservation in the high percentage of false positive. Further investigations are required to elaborate the key mechanism behind the regulation of endometrial secretory transformation and to adopt treatment to accelerate the appearance of ultrasonic hyperchoic endometrium after oocyte retrieval.

CONCLUSIONS: The endometrial echogenicity value on OPU+2 had the most predictive value, and the cutoff value was 76.5%. The sensitivity was 61.3% and specificity was 82.0%.

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PROGNOSTIC VALUE OF UTERINE NATURAL KILLER (uNK) CELLS DENSITY IN PERI-IMPLANTATION ENDOMETRIUM FROM WOMEN WITH RECURRENT IMPLANTATION FAILURE. Xiaoyan Chen, PhD. The Chinese University of Hong Kong, Hong Kong, Hong Kong.

OBJECTIVE: CD56+ uterine natural killer (uNK) cells constitute major components in human endometrium and play an important role around the time of implantation. The aim of this study is to investigate the prognostic value of uNK cells density for subsequent pregnancy outcome in women with recurrent implantation failure (RIF) after IVF-ET treatment.

DESIGN: It is a prospective cohort study carried out in a university-affiliated IVF center.

MATERIALS AND METHODS: A total of 59 women with RIF participated in the study. Endometrial biopsies were obtained precisely 7 days after luteinization hormone surge in the natural cycle preceding frozen embryo transfer. Endometrial sections were immunostained for CD56 and cell count was performed using a standardised protocol. Results were expressed as percentage of positive uNK cell/total stromal cells.

RESULTS: No significance difference in uNK cell density was observed between women who did not get pregnant (n=31; median 2.2% range 0.3-7.2%) and women who get pregnant (n=28; median 1.9% range 0.2-8.5%). There was also no significant difference in uNK cell density between women who miscarried (n=9; median 2.2% range 1.0-8.5%) and women who had a live birth (n=19; mean 2.0% range 0.2-7.9%) in a subsequent pregnancy.

CONCLUSIONS: Uterine NK cells density in the peri-implantation endometrium is of no predictive value for subsequent pregnancy outcome in women with RIF.

SUPPORT: This study was supported by Hong Kong Health and Medical Research Fund.

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IMPACT OF ENDOMETRIAL PREPARATION IN CRYOPRESERVED-WARMED EMBRYO TRANSFER (FET) CYCLES ON PERINATAL OUTCOME. Anna Sokalska, MD, PhD, Nathanael C. Koepler, MPH, Chariklea Kalliara, MD, Monica Mainigi, MD, Christos Coutifaris, MD, PhD, Suneeeta Senapati, MD, MSCE. University of Pennsylvania, Philadelphia, PA.

OBJECTIVE: There is clinical equipoise regarding the safety and superiority of the cryopreserved-warmed (FET) over fresh embryo transfer cycles with respect to perinatal outcomes. Prior studies suggest, that elevated estradiol (E2) level leads to abnormal placentation and preeclampsia (PEC). Recent data demonstrate a potential increased risk of PEC in FET (physiologic E2 level) compared to fresh embryo transfer cycles (supraphysiologic E2 level).

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Specifically, the absence of a corpus luteum may play a role in disorders of placentaion, however the mechanism is not well understood. The aim of this study was to evaluate the factors influencing pregnancy and perinatal outcomes in natural FET cycles (nFET) and programmed FET cycles (pFET).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All autologous FET cycles from a single academic center (N=584; Jan 2013 - Jan 2017) resulting in a positive pregnancy test were reviewed. Cycles were analyzed based on the endometrial preparation protocol: pFET (N=529) vs. nFET (N=55). Data regarding potential confounders including: maternal age, diagnosis, embryo stage at transfer, number of embryos transferred, endometrial thickness, number of delivered infants, neonates, and singletons; E2 and progesterone were collected and analyzed using t-test. Fisher’s exact test or χ² as appropriate. Random effects mixed linear regression models were used to assess the impact of endometrial preparation protocol on Human Chorionic Gonadotropin (HCG) rise.

RESULTS: Baseline characteristics including age, ethnicity, history of chronic hypertension, parity, history of prior preterm and full term birth, embroyo stage at transfer, number of embryos transferred, endometrial thickness and preimplantation genetic testing were comparable for both groups. Patients in nFET group had lower BMI comparing to patients in the pFET group (22.9 vs. 25.2 kg/m², p<0.002).PEC and composite of hypertensive disorders of pregnancy (PEC and gestational hypertension) rates were significantly higher in the pFET group compared to nFET group (p=0.022 and p=0.026, respectively). Notably, PEC occurred only in the pFET group (50/383 live births; 13.1%) and these pregnancies had a slower HCG rise compared to the pFET group without PEC (p=0.015) and nFET (p=0.05). Interestingly, in 83% of PEC cases, E₂ prior to progesterone initiation was above 300 pg/mL. There was no difference in the rate of clinical pregnancy, miscarriage, biochemical pregnancy, ectopic pregnancy, live birth, fetal sex and birth weight between the groups. No differences were observed in the HCG rise by the endometrial preparation protocol (p=0.8). In singleton pregnancies, there was no difference in the rate of preterm birth, placental abruption, placenta previa, small for gestational age (SGA) and cesarean section for gestational age or birth defects. If the JZ was measured in 3 locations (fundus and right/left uterus’s sides).

CONCLUSIONS: Programmed FET cycles are associated with an increased risk of PEC in singleton pregnancies compared to natural FET cycles. These findings suggest that hormonal milieu of the uterine environment in the absence of corpus luteum especially in the settings of elevated E₂ level may affect placentaation leading to PEC.

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SUBENDOMETRIAL JUNCTION ZONE THICKNESS: IMPACT ON IVF OUTCOMES IN AN OOCYTE RECEPTOR PROGRAM

Federico Galera Fernandez, OBGYN, Enriqueta Garjio Lopez, OBGYN, Carmen Galera, Biologist, Laura Garcia Bernardo, OBGYN, Instituto Madrileno de Fertilidad, Madrid, Spain; IMF, Madrid, Spain; Instituto Madrileno de fertilidad, Madrid, Spain.

OBJECTIVE: Endometrial-myometrial interface constitutes a distinct, hormone-dependent uterine compartment, denominated junction zone (JZ). Growing evidence suggests that a normal and functional JZ plays a key role in different reproductive disorders, as well as, for embryo implantation. Coronal section in three-dimensional transvaginal ultrasound (3D-TVS) of the uterus, offers accurate evaluation and measurement of JZ.

The aim of our study was to analyze the role of JZ subendometrial thickness assessment by 3D-TVS on IVF outcome in an ovocyte receptor’s program.

DESIGN: This was an observational prospective study. From January 2016 to May 2018, 58 women who met the inclusion criteria were enrolled.

MATERIALS AND METHODS: A total of 188 fresh or frozen embryo transfer were done. In all cases, only 1-2 good quality embryos (grade A and B) were used to be transferred.

Inclusion criteria were: nulliparous women with age range 30-50 years old, body mass index (BMI) between 18.5-25 kg/m², regular 28-day cycle; absent (grades III, IV of R), O), respectively. 3D-TVS, subendometrial JZ was measured from basal endometrium to the internal layer of outer myometrium on coronal sections. JZ was measured in 3 locations (fundus and right/left uterus’s sides).

Estrogen and progesterone were administrated consecutively for endometrium preparation in a mock cycle. Estradiol valerate 2mg/8h was started on the second cycle. When endometrium reached ≥8 mm, estradiol was maintained and vaginal micronized progesterone 200 mg/8h was started to initiate the secretory changes.

RESULTS: Eighty women were assessed. Mean age was 41.3 years old (range 30-48). Mean JZ thickness was 4.1 mm (range 3.2-5.3). Mean endometrial thickness was 8.44 mm (range 6.5-9.6). Subendometrial color Doppler evaluation of flow was rich in 80.1% (7694) of cases, medium in 6.4%,(6/94) and poor in 12.8% (12/94).

A total of 94 (fresh or frozen embryos) were transferred. Pregnancy rate was 39.36% (37/94), clinical pregnancy rate 28.76% (27/94), chemical pregnancy rate 27.07% (10/37), abortion rate 40.74% (11/27) and live birth rate17.02% (16/94).

CONCLUSIONS: Our results showed that JZ thickness may have prognostic implications for poorer IVF outcomes. We found no differences between fresh or frozen embryo transfer, both indicating low clinical pregnancy rate, high chemical and abortion rate and, as a consequence, a very low live-birth rate. Future, well designed studies are needed to evaluate the role of the JZ in IVF.

IVF OUTCOME PREDICTORS - GESTATIONAL CARRIERS

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CAN BIRTH WEIGHT AND GESTATIONAL AGE AT DELIVERY OF SINGLETON GESTATIONAL CARRIER PREGNANCIES BE PREDICTED BY THE GESTATIONAL CARRIER’S OWN PREVIOUS SINGLETON PREGNANCIES?

Rachel S. Mandelbaum, MD, Meghan B. Smith, MD, Jacqueline Ho, MD MS, Kristin Bendikson, M.D., Richard J. Paulson, MD, MS, University of Southern California, Los Angeles, CA.

OBJECTIVE: Gestational carriers (GC) represent a unique population in which to study the effect of assisted reproductive technology on obstetric outcomes, as they are not infertile and have usually had favorable obstetric outcomes in the past. In GC pregnancies, important questions remain regarding how perinatal outcomes are differentially impacted by the genetic parents versus the GC. This study sought to compare birth weight and gestational age at delivery between a GC’s prior own pregnancies versus the current GC pregnancy.

DESIGN: A retrospective analysis of all GC singleton deliveries from a single agency between 2008-2019.

MATERIALS AND METHODS: Data from a large surrogate agency that consisted of matched GCs and intended parent couples for an index GC pregnancy were reviewed. GCs with a history of or current multiple gestation as well as a history of or current preterm delivery were excluded. All available birth weights of the GC’s own children as well as the gestational age at delivery for the GC’s last own birth were collected. Both average birth weight and last singleton birth weight of the GC’s prior own deliveries were correlated to the birth weight of the index GC pregnancy. Gestational age at delivery of the GC’s last own delivery was compared to the gestational age at delivery for the index GC pregnancy.

RESULTS: Of 856 GCs, 101 were eligible for inclusion in this study. Average age of GCs at time of delivery was 34.9 years (SD 4.4) and their average BMI was 24.3 (SD 3.13). 93 GCs (76.9%) had a prior parity of ≥3, and 27 (22.3%) had grand multiparity (≥5). The average birth weight of all GC’s prior spontaneously conceived singletons was 7.83 lbs (SD 3.01) and 7.68 lbs (SD 1.01) for the GC’s most recent own singleton delivery. Average BW of index GC pregnancies was 7.62 pounds (SD 1.05). While average birth weight of all the GC’s prior singleton children was not correlated with the birth weight of the index GC pregnancy (r=0.051, P = 0.623), the birth weight of the GC’s most recent own singleton birth was significantly correlated with the birth weight of the index GC pregnancy (r=0.298, P = 0.003). Birth weight of the index GC pregnancy was not correlated with GC BMI (r = 0.083, P = 0.423). Mean gestational age at delivery was similar between the GC’s last own singleton delivery and the index GC pregnancies (mean 39.1 (SD 0.993) vs. 39.1 (SD =0.983), P<0.001). Gestational age at delivery of the GC’s last own singleton pregnancy was also significantly associated with the gestational age at delivery for the index GC pregnancy (P<0.001).

CONCLUSIONS: While birth weight and gestational age at delivery are likely multifactorial and impacted by both genetic and environmental factors, we found that in singleton GC pregnancies birth weight and gestational age are correlated with birth weight and gestational age of a GC’s last own delivery. This data is of value when counseling both intended parents and evaluating candidacy for potential surrogacy.

P-155 WITHDRAWN
OBJECTIVE: Published data suggest that clinical pregnancy and live birth rates are higher in cycles using gestational carriers (GC) compared to non-GC IVF cycles. This data includes fresh and frozen, Day 3 and Day 5 transfers of both tested and untested embryos, preventing effective isolation and evaluation of the uterine factor. Studies to date have not evaluated clinical outcomes between GC and non-GC GC euploid elective single embryo transfers (eSETs) in programmed frozen embryo transfer (FET) cycles. Our objective was to compare clinical outcomes of euploid eSETs in programmed FET cycles in GCs with non-GC cycles.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: Our study included all patients who underwent embryo transfer of a single Day 5 or Day 6 euploid embryo in a programmed FET cycle at a single IVF center in 2018. Preimplantation genetic testing for aneuploidy was performed following trophectoderm biopsy and next generation sequencing. FET cycle outcomes were compared between the GC and non-GC FET groups. Statistical analysis was performed using the student t-test and chi-square, where applicable.

RESULTS: A total of 115 GC and 428 non-GC FET cycles met inclusion criteria. There was no statistically significant difference in embryo day (63% Day 5 for GC vs 69% Day 5 for non-GC, p=0.22), or embryo grade (72.2% Good for GC vs 66.2% for non-GC, p=0.39) between the GC and non-GC cycles. Oocyte age was significantly younger in the GC compared to the non-GC group (31.2±6.6 vs 34.5±4.9, p<0.001), however in the setting of euploid single embryo transfer, oocyte age has been shown not to impact clinical pregnancy outcomes. Positive pregnancy test, biochemical pregnancy, clinical pregnancy, miscarriage and ongoing pregnancy rates did not differ between GC and non-GC cycles (Table 1).

<table>
<thead>
<tr>
<th>TABLE 1. Pregnancy outcomes in GC vs non-GC cycles</th>
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<tbody>
<tr>
<td>GC cycles (n=115)</td>
</tr>
<tr>
<td>Positive hCG</td>
</tr>
<tr>
<td>Biochemical pregnancya</td>
</tr>
<tr>
<td>Clinical pregnancyb</td>
</tr>
<tr>
<td>Miscarriagec</td>
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<tr>
<td>Ongoing pregnancyd</td>
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</table>

a Transient serum b-hCG rise.

b Visualization of a gestational sac on ultrasound.

c Spontaneous loss of a clinical pregnancy at <20 weeks of gestation.

d Ongoing viable pregnancy at 10 weeks of gestation.

CONCLUSIONS: Our study indicates that use of a gestational carrier does not improve pregnancy rates after single euploid frozen embryo transfer when compared with an unselected infertility population undergoing autologous IVF. As equivalent pregnancy rates are seen in GC vs non-GC cycles, this may indicate an underlying benefit of euploid single FET in autologous cycles.

(PRG) frozen embryo transfer (FET) cycles; compared to natural (NAT) FETs where estradiol (E2) levels were lower. We analyzed whether E2 levels were associated with an increased incidence of SCH formation.

DESIGN: Retrospective cohort study of all single thawed euploid embryo transfer cycles resulting in clinical pregnancy from 1/2016 to 12/2018 at our center.

MATERIALS AND METHODS: All single euploid (by Next Generation Sequencing) FETs resulting in clinical pregnancy (presence of a gestational sac) were included. FET cycles with ploidy determined by aCGH, or cycles in which untested, mosaic, or multiple embryos were transferred were excluded. PRG cycles were defined by treatment of oral E2 daily followed by progesterone (P4); either 50-75mg intramuscular in oil or vaginal suppository. A NAT cycle, with and without with letrozole, was defined by monitoring until a dominant follicle reached >18mm and ovulation was confirmed, followed by supplementation with vaginal P4 suppository. SCH was defined as a measurable clot behind the gestational sac at time of luteal ultrasound. The primary outcome was E2 levels in patients with SCH. Statistical analysis included Shapiro-Wilk test for normality for continuous variable, Mann-Whitney U and Fisher’s Exact tests where appropriate. Median values are presented, as continuous variables were not parametric. A p-value <0.05 was considered significant.

RESULTS: 1,273 cycles were identified and included; 213 NAT and 1,060 PRG. Age (p=0.73), endometrial thickness (p=0.65), P4 level on cycle day (CD) 28 (p=0.82) and CD of SCH diagnosis (p=0.78) were similar between groups, though first hCG levels were lower in PRG cycles (196 vs 164 mIU/mL, p<0.001). The formation of SCH was significantly lower in NAT cycles compared to PRG cycles (-0.24 vs -0.78, p<0.001). There was no association with SCH incidence by P4 type (IM vs vaginal, p=0.40) in PRG cycles. Additionally, E2 levels were significantly higher in PRG cycles on day of P4 start (351.5 vs 268.5, p<0.001) and CD 28 (356.5 vs 249, p<0.001). However, there was no relationship between SCH formation and continuous E2 levels on day of P4 start (NAT p=0.76, PRG p=0.44) or on CD 28 (NAT p=0.71, PRG p=0.11) in either protocol. Within PRG cycles, SCH incidence was not associated with the change in E2 from day of P4 initiation to CD 28 (p=0.25). E2 levels were then reclassified as high (>299pg/mL) or low based on the median E2 at day of P4 initiation (249 pg/mL). There was no association between rate of SCH formation in PRG cycles with high E2 (RR 0.75 (0.51-1.10), p=0.09) or with high E2 on CD 28 (RR 1.10 (0.72-1.65), p=0.38). Interestingly, in NAT FET cycles, patients with high E2 levels were more likely to have SCH formation (RR 3.23 (1.10-9.11), p=0.03). In PRG cycles, patients with high E2 levels were more likely to have SCH formation (RR 3.23 (1.0-9.11), p=0.03).

CONCLUSIONS: Both SCH formation and serum E2 levels are higher in PRG FETs. However, high E2 levels was not associated with SCH formation. Further analysis is needed to determine the physiologic cause for an increased rate of SCH formation in PRG cycles and an estimation of obstetric risk.


SUPPORT: None.

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CLINICAL MASS DATA ANALYSIS(CMDA) OF DIFFERENCE IN PREGNANCY RATE BETWEEN FROZEN-THAWED AND FRESH EMBRYO TRANSFER AT VARIOUS E2 LEVELS. The Seop Shin, MS, Eun Ah Kim, MS, aGyu Hee Choi, MS, bChun Kyu Lim, Ph.D., aHwang Kwon, M.D, Ph.D., cSoo Yeon Kim, MD, cJee Hyun Kim, MD, cEun Kyung Kim, Ph. D. aFertility Center, CHA Bundang Medical Center, CHA University, Seongnam-si, Gyeonggi-do, Korea, Republic of (South); aFertility Center, Seongnam-si, Gyeonggi-do, Korea, Republic of (South); bFertility Center, CHA Bundang Medical Center, CHA University, Seongnam-si, Gyeonggi-do, Korea, Republic of (South); aCHA Bundang Medical Center, CHA University, Seongnam-si, Gyeonggi-do, Korea, Republic of (South).

OBJECTIVE: The purpose of this study was to compare the quantity and quality of oocytes according to estradiol levels in fresh embryo transfer and frozen-thawed embryo transfer, and the pregnancy rates were analyzed.

DESIGN: Retrospective cohort study in a reproductive center.

MATERIALS AND METHODS: This study included 17,601 cycles of 6,004 patients who underwent fresh embryo transfer or frozen-thawed embryo transfer between February 2014 and October 2018. All cycles were divided into 8 groups at 1,000pg/mL intervals according to serum E2 level. The quality of oocytes was analyzed by evaluating the maturity of oocytes immediately after oocyte retrieval. Fresh embryos were transferred in 10,237 cycles and frozen embryos were transferred in 6,824 cycles. Statistical analyses were performed using t-test or Chi-square test. P-values < 0.05 were considered statistically significant.

RESULTS: As the E2 level increased, the number of follicles increased. However, oocyte maturation rate was highest in group 1 in which the lowest number of follicles were observed under ultrasonic guidance (47.8% in fresh embryo transfer, 48.2% in FET) and lowest in group 6 in which the highest number of oocytes were observed (39.2% in fresh embryo transfer, 38.0% in FET). The pregnancy rates of respective group are shown in the table below. In fresh embryo transfer cycles, pregnancy rates were lower in group in which the lowest number of follicles were observed (group 1) or the group in which the largest number of follicles were observed (group 8) than other groups. In FET cycles, pregnancy rates of the groups in which large number of follicles were observed (group 7, 8) were higher than other groups.

CONCLUSIONS: The number of follicles gradually increases as the E2 level increases in both fresh ET and FET group. However, the proportion of mature oocyte has decreased. The pregnancy rate of the FET was higher than that of fresh ET in each group. This mass data analysis may be an indicator of choice for selecting fresh embryo transfer or frozen-thawed embryo transfer depending on the E2 level.

| TABLE 1. Results of Follicles, Mature oocyte and Pregnancy rates in Fresh,Frozen Embryo Transfer |
| Groups | Follicles | Mature oocyte (%) | PR* | Follicles | Mature oocyte (%) | PR* |
| Fresh-ET | | | | Frozen-Thawed ET | | |
| 0~1000 | 6.3 ± 4.2 | 47.9 ± 29.5 | 4.9 ± 4.4 | 48.2 ± 41.0 | 2000~3000 | 14.5 ± 40.0 | 43.9 ± 16.6 | 23.7 ± 5.2 | 39.0 ± 47.4 | 5000~7000 | 18.9 ± 46.0 | 44.0 ± 21.3 | 40.1 ± 38.2 | 37.7 ± 43.9 | 7000~ | 21.3 ± 46.0 | 40.1 ± 23.7 | 49.6 ± 39.1 | 44.6 ± 53.6 |
| P<0.05; Pregnancy rates column analyzed by T-test, P<0.05; Pregnancy rates in Fresh ET and Frozen-thawed ET analyzed by χ2-test, Pregnancy rates in Fresh ET and Frozen-thawed ET analyzed by χ2-test |

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"PREDICTIVE VALUE OF SERUM PROGESTERONE LEVEL ON DAY 4, DAY 7 AND DAY 11 AFTER BLASTOCYST TRANSFER IN A HORMONAL REPLACEMENT THERAPY CYCLE." Elena Labarta, MD PhD, Giulia Mariani, MD, Ernesto Bosch, MD PhD, aIVI-RMA, Valencia, Spain; bTVI-RMA, Valencia, Spain.

OBJECTIVE: Recent studies have suggested that low serum progesterone (P) levels on day of embryo transfer (ET) are associated with poorer pregnancy outcome. Determination of serum P in hormonal replacement therapy (HRT) cycles reflects the absorption of exogenous P because no endogenous production exists until pregnancy week 5-6. It is of interest to know if serum P levels during mid and late luteal phase are related with the risk of miscarriage or of ongoing pregnancy. In this study, we wanted to evaluate the predictive value of P levels from mid luteal phase (4 and 7 days after ET) to the day of the β-hCG check (11 days after ET) for ongoing pregnancy in HRT cycles.

DESIGN: Prospective cohort study performed between June 2017 and August 2018 in IVI-RMA Valencia,Spain.

MATERIALS AND METHODS: Eligible patients were aged between 18-42 years, with a normal uterus, and being transferred 1-2 good quality blastocysts from own or donated eggs after an HRT cycle with estradiol valerate and vaginal micronized P (400mg/12h).

Serum P levels were measured three times during the mid and late luteal phase on the 4th, 7th and 11th day after ET.

Correlation between pregnancy results and hormonal time 2-degree polynomial fitted data was analyzed by linear model. A logistic linear model and ROC analysis were performed to assess P polynomial coefficients as a predictive test for ongoing pregnancy.

RESULTS: A total of 150 patients were included. Mean age was 38.1±3.9y, with a BMI of 23.4±3.6kg/m2 and endometrial thickness before introducing exogenous P of 9.1±1.1mm. The overall ongoing pregnancy rate was 47.3% (95%CI=39.3-55.3). The AUC for P exposure during the luteal phase was significantly higher in ongoing pregnancies (101.2ng/ml (95%IC=90.8-111.6)) when compared with negative β-hCG cases (79.4ng/ml (95%IC=66.5-92.4)), p=0.027.
On ET+11, ongoing pregnancies showed a significantly higher serum P levels when compared with negative β-hCG (mean difference 5.5 ng/mL (95%CI = 2.6-8.3), p = 0.001). The ROC curve showed that there is a significant predictive value of serum P levels for ongoing pregnancy rate, being the AUC (95% CI) = 0.63 (0.54-0.72) on ET+4; 0.65 (0.56-0.74) on ET+7; and 0.73 (0.65-0.81) on ET+11 with best cutoff values of 9.9, 21.3 and 11.6 ng/mL, respectively.

CONCLUSIONS: In HRT cycles in which vaginal progesterone is used, P levels across luteal phase days are associated with pregnancy outcome. Ongoing pregnancies showed a higher exposure to P. These results suggest that absorption to vaginal P can vary among patients and this can influence on the results.

SUPPORT: None.

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THE PREDICTIVE VALUE OF FSH BASAL LEVELS FOR ART OUTCOMES IS AGE DEPENDENT. Jose Buratini, DVM, PHD, Claudia M. M. Brigante, MD, Silvana Gippone, MD, Mara Zanirato, MD, Maria Cristina Guglielmo, BSci, PHD, Mariabeatrice Dal Canto, BSci, PHD, Mario Mignini Renzini, MD, Rubens Fadini, MD. Biogenesi Reproductive Medicine Center, Monza, Italy.

OBJECTIVE: Studies with robust numbers of patients to clarify the predictive value of FSH levels for ART outcomes are still needed. In this study, we examined a large cohort of ICSI patients aiming to assess across different maternal age groups the association of FSH basal levels with implantation, clinical pregnancy and abortion rates.

DESIGN: We performed a retrospective analysis of data collected since 2016 including 2503 autologous ICSI cycles. Each ICSI cycle represents a distinct patient. Patients were grouped according to FSH plasma concentrations measured on the second or third day of the ICSI cycle (FSH groups: <7.5; >7.5/10; >10 IU/L), and age (Age groups: <34; 34/37; >38; >40).

MATERIALS AND METHODS: Patients ageing 20 to 45 years with unexplained, male-related or tubal sub-fertility were subjected to controlled ovarian stimulation utilising a GnRH antagonist protocol, with FSH dose individually adjusted and oocyte maturation triggered with HCG 36 hours before oocyte collection. Matured oocytes were subjected to ICSI and one to three embryos were transferred fresh three days later. The effects of FSH levels on implantation, clinical pregnancy and abortion rates were assessed in different age groups by the Fisher’s exact test.

RESULTS: Overall, FSH levels were negatively correlated with implantation and clinical pregnancy rates, but not with abortion rate. For patients with basal FSH <7.5, >7.5/10 and >10 IU/L, clinical pregnancy rates were 19.9% (230/1156), 19.9% (150/753) and 13.5% (80/594); P = 0.001, respectively. Implantation rates were 18.3% (338/1844), 19.9% (232/1168) and 15.2% (130/853); P = 0.026, respectively. For 19.0% (55/289), 23.6% (47/199) and 25.0% (27/108); P = 0.29, respectively. Interestingly, when patients were stratified by age, FSH levels only significantly affected implantation and pregnancy rates in patients under 34 years. For patients under 34 years with basal FSH <7.5, >7.5/10 and >10 IU/L, clinical pregnancy rates were 29.5% (131/447), 28.2% (35/124) and 20.3% (14/69); P = 0.032, respectively. Implantation rates were 35.3% (110/312), 32.1% (54/173) and 19.4% (18/93); P = 0.013, respectively. As expected, implantation and clinical pregnancy rates decreased progressively with age, but did not consistently vary with FSH levels in patients older than 34. For patients older than 40 years with basal FSH <7.5, >7.5/10 and >10 IU/L, clinical pregnancy rates were 9.9% (41/416), 9.2% (20/284) and 6.7% (19/283); P = 0.345, and implantation rates were 9.9% (73/741), 10.1% (48/476) and 9.5% (42/443); P = 0.96, respectively.

CONCLUSIONS: Higher FSH basal levels are associated with poorer ART outcomes in patients under 34 years and thus represent a useful ART prognostic tool for this age group. Interestingly, the predictive value of FSH basal levels for ART outcomes seems to fade as maternal age advances. New studies are needed to clarify the mechanisms linking higher FSH levels with impaired fertility in younger patients, and whether these mechanisms are absent, not reflected by a single FSH measurement or clinically not perceived due to their interaction with other age-related modifications in older patients.

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THE RELATIONSHIP BETWEEN ANTI-MÜLLERIAN HORMONE AND ANEUPLOIDY IN REPRODUCTIVE-AGE WOMEN UNDERGOING PREIMPLANTATION GENETIC TESTING: IS THERE A CORRELATION? Monica Pasternak, MD,a Micha Thompson, BA,a Steven Spandorfer, M.D.b aRonald O. Perlman and Claudia Cohen Center for Reproductive Medicine, New York, NY; bThe Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: The primary objective of this study was to investigate whether there is a correlation between serum anti-Müllerian hormone (AMH) levels and embryo chromosomal abnormality as determined by pre-implantation genetic testing for aneuploidy (PGT-A), and whether this differs by patient age.

DESIGN: This is a retrospective single-institution study. Demographics of patients undergoing in vitro fertilization (IVF) with PGT-A during a 4-year period were recorded, as well as characteristics of their resultant embryos.

MATERIALS AND METHODS: There were 1653 IVF/PGT-A cycles performed by patients who also had a serum AMH assay measured at our FERTILITY & STERILITY® e171
institution; patients who had AMH drawn elsewhere were not included in this study. The percent of euploid embryos per number of embryos biopsied and cryopreserved at day 5/6 of embryogenesis was calculated for each IVF cycle. Patients were separated into two age groups: less than 39 yo and greater than or equal to 39 yo. AMH values were classified as low if <1.0 and normal if ≥1.0. Statistical analysis was performed by using the Kruskal-Wallis and Chi-square tests as appropriate.

RESULTS: Of the 1653 IVF/PGT-A cycles analyzed, 1266 cycles included patients who had an AMH ≥1.0, and 387 had an AMH <1.0. We further stratified the patients by age (<39 and 39yo). A total of 735 cycles included patients who were <39yo, and 531 were ≥39yo. For women who were <39yo, there was an average of 48.2% euploid embryos per IVF/PGT-A cycle for those with an AMH ≥1.0, compared to women <39yo with an AMH <1.0 for whom there was an average of 40.1% euploid embryos per cycle (p=0.01). For women ≥39yo with an AMH ≥1.0, there was an average of 16.9% euploid embryos per IVF/PGT-A cycle, compared to those with an AMH <1.0 for whom there was an average of 15.4% euploid embryos per cycle (p=0.062).

CONCLUSIONS: The relationship between serum AMH levels and embryo chromosomal abnormality in patients undergoing IVF with PGT-A has yet to be determined. Previous studies have limited data pertaining to the relationship between AMH and aneuploidy prior to embryo transfer (ET) and conception in patients utilizing IVF. Most research on this subject has been disparate in terms of how and when these serum assays were obtained, and without controlling for the use of IVF. Additionally, most studies measured AMH during a clinical pregnancy, at which time AMH levels will be suppressed physiologically. The results from our study found that in women less than 39yo, AMH is significantly correlated with percent euploid embryos per the number of embryos biopsied in a given IVF/PGT-A cycle. No significant difference was found in women greater than or equal to 39yo. Therefore, it is reasonable to expect that women of younger reproductive age who have a disparity in terms of yield of euploid embryos after IVF/PGT-A depending on ovarian reserve as determined by AMH level, and to discuss it with our patients as part of IVF/PGT-A counseling.

SUPPORT: NONE.

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COMPARING FROZEN EMBRYO TRANSFER OUTCOMES WITH BASELINE LH LEVELS. Ariel Z. Benor, M.D., Richard Grazi, M.D., Maimonides Medical Center, Brooklyn, NY.

OBJECTIVE: To see if, during a programmed frozen-embryo transfer (FET) cycle, an endogenous rise in the LH level prior to initiation of progesterone supplementation may influence live birth rate (LBR). In the absence of concomitant pituitary suppression, high estradiol (E2) levels will often stimulate luteinizing hormone (LH) to rise to levels commonly associated with the periovulatory LH surge. In our study, we sought to correlate the live birth rates following FET when LH rose beyond a threshold level prior to supplementation with progesterone (P).

DESIGN: This was a single-center, retrospective cohort study from 2016-2018.

MATERIALS AND METHODS: The programmed preparation of endometrium started with estradiol pretreatment for a minimum of 14 days followed by five days of P given by intramuscular or vaginal route, or both, with FET performed on day 6 of P replacement. Two groups were stratified by LH levels >15 mIU/mL and LH <15 mIU/mL. Patients who were found to have a periovulatory follicle were excluded from the analysis. The periovulatory LH surge. In our study, we sought to correlate the live birth rates following FET when LH rose beyond a threshold level prior to supplementation with progesterone (P).

RESULTS: One hundred fifty-five patients who underwent a frozen embryo transfer had LH levels drawn prior to the start of progesterone supplementation (pret-P). Seventy patients had a live birth and 111 patients did not. Of the 70 with a live birth, the mean LH level was 14.5 ± 1.5 mIU/mL and of the 111 without a live birth, the mean LH was 14.2 ± 1.3 mIU/mL. Whether pre-P LH levels were <15 or >15 mIU/mL made no difference to the LBR (p=0.7). There was no pre-P LH level beyond which a decrease in LBR was seen. Of those patients who live birth, 40% had an LH >15 (range of 15-15.0), while 60% had an LH <15 (range of 0-14.5); the mean LH level was 14.5 (95% CI 12.0-17.0). Of those without a live birth, 63% had an LH <15 (range of 0-14.8), while 37% had an LH >15 (range of 15.2-33.8); the mean LH level was 14.3 (95% CI 12.3-16.3). We found that regardless of what threshold level was set for LH, no level was predictive of an effect on LBR.

CONCLUSIONS: LH levels that exceed 15 mIU/mL prior to initiating P supplementation in a programmed FET cycle have no significant effect on LBR. In the absence of a maturing follicle, there appears to be no threshold beyond which LH levels affect LBR.

References: None.

SUPPORT: No financial support was received for this abstract.

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SERUM hCG LEVEL MEASURED 5 DAYS AFTER SINGLE THAWED BLASTOCYST TRANSFER AS A PREDICTOR OF OUTCOME. Angela H. Liu, M.D.; Ankita Raman, M.D.; Carrie E. Bedient, M.D.; Leah A. Kaye, M.D.; Forest C. Garner, M.S.; Bruce Shapiro, M.D., Ph.D., H.C.L.D.; University of Nevada, Las Vegas, Las Vegas, NV; Fertility Center of Las Vegas, Las Vegas, NV.

OBJECTIVE: Investigate serum hCG level measured 5 days after vitrified-warmed single-blastocyst transfer as a predictor of transfer outcomes...
DESIGN: Retrospective cohort study of vitrified-warmed single-blastocyst transfers performed from in a 5-year period at a private fertility center.

MATERIALS AND METHODS: Vitrified-warmed blastocysts were transferred after artificial endometrial preparation on the 6th day of eogenous progesterone exposure. Serum hCG levels were measured 5 and 10 days after transfer. Levels rising above 5 IU/L on any day defined pregnancy. Clinical pregnancy was defined by sonographic finding of an intrauterine gestational sac 5-7 weeks after transfer. Multiple pregnancies were those with motion of multiple fetal hearts observed at any point. Ongoing pregnancies were those with fetal cardiac activity at 10 weeks.

RESULTS: There were 932 single-blastocyst transfers in the 5-year study period. All 932 transfers, a day 5 hCG level 5 IU/L was predictive of each outcome except multiple pregnancy. Sensitivity, specificity, positive predictive value, negative predictive value, and P-values are shown in Table 1. The live birth rate among transfers with day 5 hCG level 5 IU/L was 77.0%; while failure to achieve that criterion was associated with a live birth rate of only 12.0%. The area under the ROC curve for day 5 hCG level as a predictor of live birth was 0.830.

CONCLUSIONS: Serum hCG level measured 5 days after blastocyst transfer is a useful early predictor of outcome following single thawed blastocyst transfers in artificially prepared cycles. However, the sensitivity for predicting ongoing pregnancy and live birth was only 94%, indicating that a later confirmatory test is still required. The correlation between day 5 hCG and outcome highlights the importance of early implantation and the putative peri-implantation period in multiple pregnancy outcomes in overweight patients. The tested metabolites were adipokines (resistin, leptin and adiponectin), pro-inflammatory cytokines (IL6, IL18, TNF, CRP, chemerin, prolactin and insulin (all p<0.01).

CONCLUSIONS: To our knowledge, this is the most comprehensive study to examine the effect multiple adipokines and cytokines have on metrics of oocyte and embryo quality in humans. While some cytokines that affect oocyte quality and embryology outcomes in fertility treatments correlate with BMI in overweight patients, others do not. Notably, IL6, IL18, TNF, CRP, chemerin, prolactin, insulin and leptin all affect different aspects of oocyte and embryo development. Therefore, they should be considered as potential biomarkers to predict success in fertility treatments of overweight patients. Such biomarkers could help delineate patients of similar BMI with differing fertility potential. Further research should focus on larger-scale studies exploring these relationships in non-obese patients and determining if patients’ serum can be utilized to predict fertility treatment success. SUPPORT: This study was funded through reinvestment of clinical earnings by CReAte Fertility Centre.

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<table>
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<th>Outcome</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>RR (95% CI)</th>
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<td>83.4</td>
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<td>88.2</td>
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<td>Live birth</td>
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<td>77.0</td>
<td>88.0</td>
<td>6.40 (4.42-9.28)</td>
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P-167 Tuesday, October 15, 2019 6:30 AM

A NOVEL CYTOKINE PANEL CAN BETTER PREDICT OOCYTE COMPETENCY IN OVERWEIGHT PATIENTS. Miranda K. Defer, BA, Brandon A. Wyse, MSc, Peter Sarraz, PhD, Sahar Jahangiri, MSc, Noga Fuchs Weizman, MD, Clifford Lawrence Librach, MD. CReAte Fertility Centre, Toronto, ON, Canada.

OBJECTIVE: Body composition affects outcomes in fertility treatments, however there is no clear correlation between measurement of body composition (BMI, lean/fat ratio and waist/hip ratio) and outcomes. The study aimed at creating a panel of metabolites to predict oocyte quality and competency in overweight patients.

DESIGN: A retrospective cohort of biobanked follicular fluid (FF) samples collected between April 2017-December 2018 at a university-affiliated fertility clinic.

MATERIALS AND METHODS: Consented patients were included if they were undergoing IVF, did not have a female factor related diagnosis, and had a BMI ≥ 25. Luminex Multiplex Bead Assays (R&D Systems) were performed on FF from 14 patients. The analytes were chosen based on an a priori literature review which highlighted metabolites previously correlated with fertility treatment outcomes in overweight patients. The tested metabolites were adipokines (resistin, leptin and adiponectin), pro-inflammatory cytokines (IL6, IL18 and TNF), the anti-inflammatory cytokine IL10, the acute inflammation marker CRP, and factors associated with fat and glucose homeostasis (insulin, prolactin and chemerin). All samples and standards were assayed in duplicate (MACS-Quant Analyser). Absolute quantification was performed by comparing fluorescence of the samples to standard curves using Flowjo (v10). Linear regression determined the impact changes in these metabolites have on embryo quality outcomes, while controlling for demographic factors (R v3.5.1).

RESULTS: Patients were similar in terms of age (35.6 ± 1.1 years), BMI (30.9 ± 1.0 kg/m²) and AMH (18.3 ± 1.7 pmol/L). The mean maturation rate was 70.6%, fertilization rate was 82.5%, cleavage rate was 99.2% and blastulation rate was 50.9%. Of all analysed factors, TNF and IL18 were negatively associated with BMI and positively affected fertilization rate. Notably, leptin and CRP were not associated with BMI. However, increased leptin concentration negatively affected maturation rate, and increased CRP levels showed a tendency towards decreasing blastulation rate. Interestingly, several factors were negatively associated with blastocyst quality, including: IL6, IL18, chemerin, prolactin and insulin (all p<0.01).

CONCLUSIONS: Serum hCG level measured 5 days after blastocyst transfer is a useful early predictor of outcome following single thawed blastocyst transfers in artificially prepared cycles. However, the sensitivity for predicting ongoing pregnancy and live birth was only 94%, indicating that a later confirmatory test is still required. The correlation between day 5 hCG and outcome highlights the importance of early implantation and the putative peri-implantation period in artificial cycles.

IVF OUTCOME PREDICTORS - LUTEAL SUPPORT

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IN PATIENTS WITH SUB-OPTIMAL ENDOMETRIAL LINING, DOES THE ROUTE OF ADMINISTRATION OF SUPPLEMENTAL ESTROGEN CORRELATE WITH FROZEN EMBRYO TRANSFER OUTCOMES? Devora Aharon, MD, a Sass Wodoslawsky, BA, b Ariel Megan Schunir, RN, BSN, b Jordyn Banks, RN, b Melissa Bell, RN, b Margaret Daneyko, RN, a Lawrence Grunfeld, MD, a Alan B. Copperman, MD, a, b Icahn School of Medicine at Mount Sinai, New York, NY; a Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Patients routinely receive supplemental oral estrogen in preparation of the endometrial lining prior to a frozen embryo transfer (FET). In patients with suboptimal growth, additional vaginal or transdermal estrogen supplementation may be prescribed in attempt to increase estrogen absorption and optimize uterine lining thickness. To date, there are limited data analyzing the clinical utility of either route. This study aims to evaluate the correlation of vaginal or transdermal estradiol supplementation with patient FET cycle outcomes.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The study included patients who underwent an autologous or donor egg FET cycle with an endometrial thickness of ≤ 7 mm on cycle day 10-15 from November 2005-April 2019. Patients were separated into groups by route of additional E2 supplementation (vaginal estradiol tablets (E2 PV group); transdermal estrogen patch (E2 TD group)). Baseline demographics and cycle characteristics were collected. Outcomes included endometrial stripe (EMS) at embryo transfer, chemical pregnancy rate, clinical pregnancy rate, and live birth rate. A sub-analysis of euploid FET was performed. A sub-analysis was performed in patients with a structural uterine factor (as identified by an initial hysterosalpingogram (HSG) or saline infusion sonohysterography (SIS)). Statistical significance was calculated using chi-square test and t-test. A p value of 0.05 was set for statistical significance.

RESULTS: A total of 414 patients underwent 461 FET cycles within the study, including 396 E2 T2 cycles and 65 E2 PV cycles. Baseline demographics were similar between the two groups. A statistically significant increase in EMS at transfer was seen in the E2 PV group compared to the E2 TD group, however, the absolute difference was 0.01 mm (E2 TD 8.34 (4.6-15.5), SD ± 1.57 vs E2 PV 8.35 (5.1-15.63), SD ± 2.23, p = 0.0002). No statistically significant differences in chemical pregnancy, clinical pregnancy, or live birth rates were seen. In the sub-analysis of euploid FETs, EMS at transfer was significantly greater in the E2 PV compared to E2 TD group (8.60 (5.1-15.6), SD 2.06) vs. 8.32 (5.3-13.7),
CONCLUSIONS: Supplemental vaginal and transdermal estradiol were equal in achieving endometrial thickness >7mm, and both methods resulted in similar pregnancy outcomes. Patients can be comforted in knowing that both routes of estrogen supplementation are effective in supporting the endometrial lining prior to FET, and choice of method may be based on patient and provider preference.

Reference: None.

SUPPORT: None.

Vol. 112, No. 3, Supplement, September 2019

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NATURAL FROZEN EMBRYO TRANSFER WITH HCG BOOSTER FOR OPTIMIZATION OF CYCLE OUTCOMES: A RETROSPECTIVE COHORT

STUDY: Claire Stewart, BA,a David Reichman, MD,b Zev Rosenwaks, M.D.a  Weill Cornell Medical College, New York, NY; bWeill Cornell Medicine, New York, NY; aThe Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To determine whether luteal support with intramuscular injection of human chorionic gonadotropin 1 day-post-luteinizing hormone (LH) surge in natural cycle frozen embryo transfers (FET) increases ongoing pregnancy rates.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All patients undergoing natural cycle FET with transfer of a single euploid blastocyst between January 2017 and December 2018 were included in the analysis. Patients were divided into two groups based on whether they received one bolus of hCG (typical dose, 3300 IU) 1 day after identification of the LH surge. All patients received vaginal progesterone support after transfer. Groups were further stratified by embryo quality. Patients with uterine factor infertility were excluded. The primary outcome of this study was ongoing pregnancy rate. Secondary outcomes included first trimester miscarriage and biochemical pregnancy rates. Outcomes were analyzed with Chi-squared test, Fisher exact test, and logistic regression where appropriate. Odds ratios (OR) with 95% confidence intervals (CI) were calculated and adjusted for patient age at time of transfer, embryo quality assessed by blastocyst grade, BMI, gravidity, parity, and peak endometrial thickness. P<0.05 was considered statistically significant.

RESULTS: A total of 529 FET cycles were included. Patients receiving hCG (n = 146) had a statistically significant higher ongoing pregnancy rate than those without treatment (n = 383) (69.9% vs. 57.4%; adjusted odds ratio 1.72, 95% CI, 1.13-2.65). There were no significant differences observed in the rates of first trimester miscarriage or biochemical pregnancy (Table). CONCLUSIONS: This study provides evidence that natural cycle FET in which the luteal phase is buttressed with both a single hCG injection after the endogenous LH surge, as well as vaginal progesterone after transfer, are associated with higher clinical success rates with minimal negative impact on the patient experience.

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LUTEAL PHASE SUPPORT USING GONADOTROPIN RELEASING HORMONE AGONIST (GNRHA) VERSUS ESTROGEN AND PROGESTERONE SUPPLEMENTATION IN HIGH RESPONDERS FOLLOWING GnRHA TRIGGERING – A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL.

Lilach Marom Haham, M.D.,a Yariv Shlomo Gidoni, M.D,b Ohad Baruchin, M.D.b, Jonathan Barkat, M.D.b, Michal Youngster, M.D.b, Ariel Revel, M.D.a, Ido Ben-Ami, M.D.PHDb, aShamir medical center, Tel Aviv university, Beer Yakov, Israel; bShamir Medical Center, Be’er Ya’akov, Israel; cTel Aviv university, Tel Aviv, Israel.

OBJECTIVE: GnrHAs triggering is used as an alternative to hCG in GnRH antagonist protocols to almost eliminate the risk of OHSS. However, its main disadvantage is a significant lower pregnancy rate which is thought to be caused due to luteolysis. In order to preserve high pregnancy rates, several luteal support regimens were investigated including an intensive estrogen and progestrone supplementation and daily GnRHa treatment. However, no study, so far, compared the efficacy of these two regimens. Our aim was to compare the efficacy of GnRHa versus intensive estrogen and progesterone supplementation for luteal phase support in high responders following GnrHa triggering.

DESIGN: A prospective randomized controlled trial

MATERIALS AND METHODS: High responder patients defined as either reaching a serum estradiol levels of ≥2500 pg/ml on the day of trigger or having ≥15 oocytes retrieved, were recruited between October 2017 until March 2019. The patients were randomly assigned to either daily intranasal GnRHa (nafarelin 200 mcg nasally twice daily) or a combination of estrogen and progesterone (Estraderm 4 mg twice daily, vaginal Endometrin 300 mg daily and intramuscular injection of progesterone retard 250 mg once every five days) for luteal support. The GnRH antagonist protocol using GnRHa triggering was initiated. Patients with a BMI>35 or <19, recurrent implantation failure, moderate to severe endometriosis or hydroalpinax were excluded. Study groups characteristics were compared using independent t-test. Implantation rates and clinical pregnancy rates were compared using chi square test.
RESULTS: A total of 47 women were allocated, 23 were assigned to the GnRHa arm and 24 were assigned to estrogen and progesterone treatment arm. Patients' characteristics including age, BMI, gravidity, parity as well as basal FSH levels didn’t differ significantly between the study groups. Treatment’s characteristics including the FSH dosage, duration of stimulation, peak estradiol levels, number of oocytes retrieved, fertilization rates and number of embryo transferred also didn’t differ significantly between the study groups. The implantation rate was 56.5% and 37.5% in the GnRHa arm and in the estrogen and progesterone arm, respectively (P=0.1). The clinical pregnancy rate was higher in the GnRHa treatment group compared to the estrogen and progesterone group although the difference was not statistically significant (60.8% vs. 50%, P=0.45). Of note, no cases of OHSS were observed in both study groups.

CONCLUSIONS: Luteal support using GnRHa alone is as effective and safe as using intensive estrogen and progesterone supplementation following GnRHa triggering in high responders. This new approach in fresh embryo transfer in high responders after GnRHa triggering offer a more convenient luteal support without compromising implantation and clinical pregnancy rates.

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PROSPECTIVE ANALYSIS OF PROGESTERONE DURATION IN PROGRAMMED SINGLE THAWED EUPLOID EMBRYO TRANSFER CYCLES. Carly I. Hirschberg, MD,* Jennifer K. Blakemore, MD,* Mary Elizabeth Fino, MD,* James A. Grifo, MD, PhD,* NYU Langone School of Medicine, New York, NY; NYU Langone Fertility Center, New York, NY; NYU Langone Prelude Fertility Center, New York, NY.

OBJECTIVE: In the era of personalized medicine and the simultaneously increasing use of frozen embryo transfer (FET), assays of the endometrium’s receptivity prior to transfer has gained popularity, especially among patients. However, the optimal timing for single thawed euploid embryo transfers (STEET) in a programmed FET has yet to be determined. We sought to examine the outcomes of euploid FETs by length of progesterone (P4) exposure at our clinic.

DESIGN: Prospective cohort study of all programmed FETs of single euploid embryos between 6/1/2018 and 12/18/2018 at our center.

MATERIALS AND METHODS: All patients undergoing FET in the inclusion time period were asked to write down the exact time of P4 initiation and then report the start time on the day of P4 serum level check (2 days later) prior to embryo transfer. All FETs were then reviewed. Programmed FET cycles were defined as treatment of oral estradiol daily followed by either 50-75mg intramuscular P4 in oil or vaginal P4 suppository with transfer of a euploid embryo (tested by either array comparative genomic hybridization or Next Generation Sequencing). Programmed FETs with untested, mosaic embryos between 6/1/2018 and 12/18/2018 at our center.

RESULTS: 253 programmed STEET cycles met criteria and were included in the analysis. The average patient age at time of ET was 38.0±4.5 years, 3 cycles utilized an assay for endometrial receptivity for adjusted timing. The mean duration of P4 exposure was 112.8±24.9 hours with a range from 98.25-124.5 hours for all unadjusted cycles. Overall, 166 women had an ongoing pregnancy (OP), 25 had a spontaneous loss (SAB), 12 a biochemical pregnancy (BP) and 50 a negative pregnancy (NP) test, for a 65.6% ongoing pregnancy rate. There was no significant difference in P4 duration between outcome groups (112.8±4.3 OP, 112.4±6.4 SAB, 111.6±1.7 BP, 113.9±5.7 NP; F 1.76, df 3, p = 0.156). A ROC curve assessing the ability of P4 duration to predict ongoing pregnancy (OP) had an area under the curve of 0.467 (p=0.38). Furthermore, there was no correlation in the day 28 serum hcg value based on the duration of P4 exposure (rs = 0.058, p = 0.399)

CONCLUSIONS: Duration of P4 is critical to the success of a programmed FET. At our center, duration of P4 was not associated with FET outcomes. 65.6% of cycles resulted in ongoing pregnancy with our center’s standard instructions, which may vary from other centers who have equivalent euploid embryo implantation rates. With growing popularity for individualized treatment, these results provide evidence for patient counseling of the high likelihood of desired outcome (ongoing pregnancy) without need for personalized testing. These results also support the need for further prospective or randomized controlled study of optimal FET cycle across clinics and protocols.


SUPPORT: None.

A NOVEL PROGESTERONE RELEASING INTRAVAGINAL RING FOR LUTEAL PHASE SUPPORT: PHARMACOKINETICS AND SAFETY IN A SHEEP MODEL. David R. Friend, PhD. Dare Bioscience, Inc., SAN DIEGO, CA.

OBJECTIVE: To evaluate the in vitro release and in vivo pharmacokinetics and local tolerability of a novel, segmented ethylene-vinyl acetate (EVA) intravaginal ring (IVR) (DARE-FRT1) delivering progesterone (P) in drug-naïve female Dorset crossbred sheep. These rings are being developed to provide luteal phase support and supplementation during ART cycles and early pregnancy.

DESIGN: IVRs capable of releasing P at 4 mg/d, 8 mg/d and 12 mg/day were administered to female sheep to assess the pharmacokinetics and safety compared to vaginal administration of Crinone 8% gel or Prometrium (200 mg) capsules.

MATERIALS AND METHODS: IVRs were prepared by hot-melt extrusion to create segments of varying length and drug content. The appropriate segments were used to create segmented IVRs capable of releasing P at rates of approximately 4, 8, and 12 mg/day. Release rates of P from the three IVR formulations were measured in vitro to determine whether the target release rates had been attained. Release rates were tested using 200 mL 0.5% sodium dodecyl sulfate as a release medium, in shakers at 37°C. Sampling (2 mL) was conducted on Days 1-4, 7-11, and 14. Animals were randomized into one of six treatment groups: Group 1) Crinone 8% gel (90 mg); group 2) Prometrium 200 mg capsules; group 3) placebo IVR; group 4) P IVR 4 mg/day; group 5) P IVR 8 mg/day; group 6) P IVR 12 mg/day. All IVRs were inserted on Day 1 and removed in place through Day 14; the rings were removed and a new ring inserted on Day 15. The second ring remained in place until Day 29. Blood samples were taken at scheduled times for pharmacokinetic (PK) analysis. Concentrations of P in plasma were measured using a validated LC/MS/MS method. Postmortem examinations performed on all IVG groups included vaginal irritation, macroscopic and microscopic evaluations, including irritation scoring and histopathology.

RESULTS: Following a relatively large amount of released P on Day 1, in vitro release rates confirmed that P was released at approximately 4, 8, or 12 mg/d over Days 2 - 14. IVRs were retained over 28 days in all animals with two exceptions. Clinical observations showed no significant abnormal findings in any group. PK analysis in animals showed sustained release of P from Days 0 through 14 of ring use. PK parameters from the three different IVRs were consistent with the in vitro release rates. Cmax increased in a dose-related manner, with mean values of 455, 682, and 1,040 pg/mL for the 4, 8, and 12 mg/day IVR groups, respectively. The lower dose Crinone gel (90 mg P) showed substantially greater relative bioavailability compared with the higher dose Prometrium capsules (200 mg P). Irritation scores and microscopic assessments were consistent with the IVRs being well tolerated following 28 days of exposure.

CONCLUSIONS: The data obtained from this study demonstrate that the segmented DARE-FRT1 EVA-based IVRs are capable of sustained release of P at different rates over a 14-day period. The rings were well tolerated with minimal to mild local irritation. These results suggest the rings are suitable for evaluation in a Phase 1 clinical study in women for PK and safety.

IVF OUTCOME PREDICTORS - OOCYTES

P-174 Tuesday, October 15, 2019 6:30 AM
INCREASED NUMBER OF OOCYTES RETRIEVED IN FROZEN DONOR OOCYTE CYCLES DOES NOT HAVE A NEGATIVE IMPACT ON OUTCOMES. Rita Ann Fields, MS,* Andrew Dorfmann, MS,* Laurence Udoff, MD,* Fairfax EggBank, Fairfax, VA; Genetics and IVF Institute, Fairfax, VA.

Does not have a negative impact on outcomes.
OBJECTIVE: There is mounting evidence that outcome parameters from retrievals that yield high numbers of oocytes are not negatively impacted compared to cycles where fewer oocytes are retrieved. However, the perception persists that when many oocytes are retrieved, the oocytes are of poorer quality and lead to inferior embryo development and pregnancy rates. This research aims to determine if the number of oocytes retrieved in frozen donor egg cycles is correlated with IVF outcomes as measured by the following parameters: oocyte survival after vitrification, fertilization, blastocyst development and clinical pregnancy rate.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Oocytes were retrieved from anonymous egg donors at 12 IVF clinics for use in a commercial egg bank between 2016-2018. Mature eggs were vitrified using a commercially available vitrification media from Repro Life. Retrieved, mature oocytes were divided into cohorts of 6-8 oocytes for use by multiple recipients. Egg warming was performed using Repro Life warming media at 195 different recipients’ clinics. All reported warmings from the retrieval period were included. Retrivals were sorted by total egg number retrieved and divided into 4 groups: <13, 13-24, 25-32 and >32 oocytes retrieved. Outcomes were evaluated t-test between percents. For pregnancy outcomes, only primary transfers were assessed.

RESULTS: A total of 714 retrievals and 1721 warmings were assessed. There was no statistically significant difference between groups 2-4 for oocyte survival, fertilization, blastocyst conversion or clinical pregnancy rate. There was a statistically significant difference between group 1 compared to groups 3 and 4 for oocyte survival, but this was not considered clinically meaningful.

CONCLUSIONS: Analysis of the data from this study supports the hypothesis that the number of oocytes retrieved from donors does not have a negative impact on embryo or cycle outcomes. Because blastocyst conversion rates and clinical pregnancy rates are similar between all groups, it stands to reason that the groups with larger numbers of oocytes retrieved will result in more quality embryos produced which in turn will lead to more pregnancies per retrieval. Very high oocyte yields should be avoided as it stands to reason that the groups with larger numbers of oocytes retrieved does not have a negative impact on embryo or cycle outcomes. Because blastocyst conversion rates and clinical pregnancy rates are similar between all groups, it stands to reason that the groups with larger numbers of oocytes retrieved will result in more quality embryos produced which in turn will lead to more pregnancies per retrieval. Very high oocyte yields should be avoided due to concerns about safety for oocyte donors, not outcomes for donor recipients.

SUPPORT: None.

P-175 Tuesday, October 15, 2019 6:30 AM

ARTIFICIAL OOCYTE ACTIVATION (AOA) TREATMENT OFFERS A NEW OPTION IN PREVIOUSLY UNSUCCESSFUL CASES DUE TO POOR FERTILIZATION HISTORY; A PAIRED COHORT STUDY. Alberto Tejera, Sr., PhD, Lucia Alegre, PhD, Arantzak Delgado, PhD, Jose Maria De los Santos, Sr., PhD, Jose Alejandro Remohi, MD, PhD, Marcos Meseguer, PhD Embryologist, Valencia, Spain; IVIRMA Global, Valencia, Spain; IVIRMA Valencia, Valen-cia, Spain; Affiliation not provided; IVIRMA Valencia, Valencia, Spain

OBJECTIVE: To improve of treatment outcome in terms of fertilization, implantation and pregnancy rates as well as cancelation rate after applying AOA in the following treatments for those patients with previous very low or failed fertilization attempts. Additionally were tested both delivery rate and obstetric outcomes in children born after AOA use.

DESIGN: Retrospective Cohort Study.

MATERIALS AND METHODS: A total of 311 patients (311 cycles; mean age: 35.1 ± 3.7 years) that underwent minimal-stimulation in vitro fertilization (mini-IVF) followed by freshly cleaved single-embryo transfer (SET) from August 2017 to September 2018 were retrospectively analyzed. Retrieved oocytes were inseminated by intracytoplasmic sperm injection (ICSI) after meiotic spindles were confirmed. Oocytes were cultured in a time-lapse incubator (EmbryoScope+® Vitrolife) after ICSI. The oocyte cytoplasmic volume at 5 morphokinetic events during fertilization (tICSI), time before 2nd polar body (PB) extrusion (tPB2b), time of 2nd PB extrusion (tPB2), time before 3rd PB extrusion (tPB3), and time of PN fading (tPNf) were recorded. Measurements were recorded at 5 morphokinetic events: after ICSI (tICSI), time before 2nd PB extrusion (tPB2b), time of 2nd PB extrusion (tPB2), time before PN fading (tPNf), and time of PN fading (tPNf). The mean areas of oocytes at the morphokinetic events were compared (Study 1). In addition, the rates of change of oocyte cytoplasmic volume from tPB2 to tPNf (area of tPNf / tPB2; group A), tPB2 to tPNf (area of tPNf / tPB2; group B), and tPNf to tPNf (area of tPNf / tPNf; group C) were calculated. A multivariable logistic regression analysis was performed, which includes the significant confounding factors and yields adjusted odds ratios (aORs) and 95% confidence intervals (CIs), to evaluate the correlation between oocyte cytoplasmic volume change and clinical pregnancy (gestational sac observation) after SET (Study 2).

RESULTS: Study 1: The mean area of oocytes at tICSI, tPB2, tPNf, and tPNf were 11.452, 10.826, 10.587, 10.237, and 10.308 μm², respectively.

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<th># Retrievals</th>
<th># Warming Cycles</th>
<th>Oocyte Survival</th>
<th>Fertilization</th>
<th>Blastocyst Conversion</th>
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</table>

CONCLUSIONS: The results of the study indicate that AOA in the following treatments for those patients with previous very low or failed fertilization attempts. Additionally, no adverse obstetric and perinatal outcomes were found after the use of AOA compared to conventional ICSI.

OBJECTIVE: After applying AOA, we observed a significant increase in the fertilization rate (51% vs 13.1%), ongoing pregnancy rate (47% vs. 21.7%) as well as implantation rate (31% vs 13.1%) and lower chances of cancellation (22.7% vs 69.3%). Additionally, no adverse obstetric and perinatal outcomes were found after the use of AOA compared to conventional ICSI.

RESULTS: After applying AOA, we observed a significant increase in the fertilization rate (51% vs 13.1%), ongoing pregnancy rate (47% vs. 21.7%) as well as implantation rate (31% vs 13.1%) and lower chances of cancellation (22.7% vs 69.3%). Additionally, no adverse obstetric and perinatal outcomes were found after the use of AOA compared to conventional ICSI.
respectively. The oocyte areas at tPNb and tPNf were significantly smaller than those at tICSI, tPB2b, and tPB2 (P < 0.05). Study 2: The multivariable logistic regression analysis showed that clinical pregnancy had significant associations with group A (area of tPNb / tPB2b, aOR: 4.8, 95% CI: 1.07–23.08) and group B (area of tPNf / tPB2b, aOR: 7.3, 95% CI: 1.22–47.58, p < 0.05), but not with group C (area of tPNf / tPNb, aOR: 2.08, 95% CI: 0.30–14.1, p=0.4549).

CONCLUSIONS: A significant decrease in oocyte cytoplasmic volume was observed from sperm penetration to PN fading. In addition, there were significant associations between clinical pregnancy and the degree of cytoplasmic volume change from 2nd PB fertilization to PN fading. These results suggest that the regulation of oocyte cytoplasmic volume during fertilization would influence oocyte competence, which may predict successful pregnancy after SET.

SUPPORT: None.

P-178 Tuesday, October 15, 2019 6:30 AM

**ASSOCIATION BETWEEN THE NUMBER OF OCYTES RETRIEVED, CANCELLATION RATES, AND CLINICAL OUTCOMES IN IVF PGT CYCLES WITH SINGLE EMBRYO TRANSFER (SET) - A 2273 CYCLES REVIEW.** Oleksei O. Barash, Ph.D., a Kristen Ivani, Ph.D., H.C.L.D., b Mary D. Hinckley, MD, d Louis N. Weckstein, MD. e Reproductive Science Center, San Ramon, CA; Reproductive Science Center of the San Francisco Bay Area, San Ramon, CA.

OBJECTIVE: The number of chromosomal aneuploidies in preimplantation embryos progressively increases with advancing maternal age. The combined effect of diminished ovarian response and increased aneuploidy rates in the older patient population is manifested in an increased proportion of IVF PGT cycles where no euploid embryos are detected. The objective of this study was to assess the correlation between the number of oocytes retrieved, cancellation rates, and clinical outcomes in IVF PGT cycles.

DESIGN: A retrospective study of IVF PGT cycles was conducted to identify differences in cancellation rates (no biopsy or no euploid embryos) and clinical outcomes based on the number of mature (M2) oocytes retrieved.

MATERIALS AND METHODS: 2273 IVF PGT cycles (26677 M2 oocytes, 11.6 ± 7.85 per cycle) between January 2013 and January 2019 were included in the study (1741 patients, average maternal age – 36.9 ± 4.9). In 242 cycles (1775 M2 oocyte, 7.3 ± 5.7 per cycle) no embryos that met criteria for biopsy were developed. In 487 cycles (4058 M2 oocytes, 8.3 ± 7.4 per cycle) all biopsied embryos were aneuploid. In 1544 PGT cycles at least one euploid embryo was available (20844 M2 oocytes 13.5 ± 8.1 per cycle), and 1601 SETs were performed. All embryos were vitrified after biopsy, and selected embryos were subsequently thawed for SET. Clinical pregnancy rate per cycle (PR) was defined by the presence of a fetal heartbeat at 6-7 weeks of pregnancy.

RESULTS: Analysis of the data had shown statistically significant differences in cancellation rates in the group of young patients (≤ 37 y.o.) versus older patients (≥ 41 y.o.) where only 1-5 eggs were retrieved (54.4 % vs 85.9 %, respectively, χ²=15.9, OR = 0.21, CI = 0.09 – 0.47, p<0.05). The difference in cancellation rates between young and older patients in the cycles where 6-10 eggs were retrieved was 29.2 % vs 62.1 %, respectively, χ²=50.5, OR = 0.22, CI = 0.15 – 0.34, p<0.05). The biggest statistically significant difference in cancellation rates between young and older patients was found in cycles where >10 eggs were retrieved (8.7% vs 51.9 %, respectively, χ²=22.72, OR = 0.09, CI = 0.06 – 0.13, p<0.05). At the same time, ongoing PR after SET was not statistically different between different age groups. Moreover, clinical PR was not statistically different between PGT cycles where 1-5 and over 10 eggs were retrieved (70.7 % (41/58) and 67.6 % (870/1288), respectively, χ²=0.25, OR = 1.16, CI = 0.65 – 2.06, p=0.62). Live birth rate (LBR) after SET in PGT cycles where 1-5 oocytes were retrieved was 66.7 % (26/39), in cycles where 6-10 oocytes were retrieved LBR was 65.1 % (71/109), and in cycles where 6-10 oocytes were retrieved LBR was 61.7 % (577/936), χ²=0.4, OR = 1.24, CI = 0.63 – 2.45, p=0.53.

CONCLUSIONS: The results of this study proved that the ongoing PR and LBR in PGT cycles after SET are independent of the number of eggs retrieved and maternal age. At the same time diminished ovarian response and high aneuploidy rates in the older patient population significantly increase the risk of cycle cancellation. Cycle cancellation rates should be taken into consideration for proper patient consultation and choosing a future treatment strategy.

SUPPORT: N/A.

**IVF OUTCOME IN WOMEN WITH ENTIRE COHORT OF OCYOTES WITH COARSE GRAINULATION IN PERIVITELLINE SPACE.** Raiza Ashraf, M.B.B.S. a Aswathy Shanavas, M.S, D.N.B., b Alex C. Varghese, Ph.D. c Sankalp Singh, M.D, D.N.B, MRCOG, d Mohamed Ashraf, M.D, D.G.O, DPS, e Noushin Abdul Majidy, M.D, MRCOG, MRCP. e 1Indian Medical Association, THRISSUR, India; 2INDIAN MEDICAL ASSOCIATION, KOLLAM, India; Astra Fertility Clinic, Mississauga, ON, Canada; craft hospital, kodungallur, India; 3chairman of CRAT hospital & Research center, Kodungallure, India; 4Rogc,RCPI TRAVENCORE MEDICAL COUNCIL, INDIAN MEDICAL ASSOCIATION, thrissur, India.

OBJECTIVE: The purpose of this study aims to compare embryo quality (clinical pregnancy rate (CPR) and implantation rate(IR) between the the patients having all oocytes with single abnormality i.e coarse granulation in PVS( study N=52) against patients with all oocytes having normal morphology (control N=49).

DESIGN: This is a retrospective case control study conducted during the period from June 2015 - February 2018 at CRAFT Hospital and Research centre, Kerala, India.

MATERIALS AND METHODS: The study protocol has been approved by the Institutional review board (IRB).

The inclusion criteria:maternal age ≤40yrs and male partners with normal semen parameters were selected. Exclusion criteria: Patient with history of recurrent implantation failure, chromosomal abnormalities or uterine abnormalities and those having oocytes with coarse granularity in pvs with other morphological abnormalities were excluded to avoid the bias factor.

Controlled ovarian stimulation was done with flexible antagonist protocol with individualised dose of gonadotrophin started from day 2.On the day of ICSI the oocytes were denuded and checked for their morphology based on ISTANBUL consensus 2011 such as intracytoplasmic and extracytoplasmic dysmorphisms . Patients with entire cohort of oocytes having coarse granulation in PVS with no other oocyte abnormalities were taken into the study. After ICSI oocytes were cultured in 6%co2 and 5%O2. On Day 3 embryo morphology was assessed based on the Istanbul consensus as Grade 1,2 and 3. Grade 1 embryos were vitrified on day 3 followed by endometrial preparation and frozen embryo transfer. The primary outcome was to compare CPR. Secondary outcome was to assess day 3 grade1 embryos, IR between the two groups.

Sample Size Calculation and Statistical Analysis: The IBM SPSS statistics version 21 was used for statistical calculations. Sample size based on the result of Clinical pregnancy rate among control and intervention group (32.3%)group occurred in an earlier publication (1)and with 80%power and 95%confidence, the minimum sample size comes to 80(40 in each group).

Statistical analysis: Chi-square test was used to compare Fertilisation rate(FR),CPR, IR between study and control group.

RESULTS: The baseline characteristics did not differ significantly between two groups. A total of 1240 oocytes retrieved 577 oocytes belonged to study and 663 oocytes in control group.When compared between two groups, FR (67.38% vs 82.53%), CPR( 18% vs 54.16%) IR (10.58% vs 33.66%), Live birth rate (14% vs 48%) showed statistically significant difference (p value<0.05). Though Day 3grade1 embryo quality was not statistically significant(33% vs 40.75%) control group showed better embryo quality. Limitation of this study is that sample size is small and that it was powered to detect CPR and not live birth rate.

CONCLUSIONS: Coarse granulation in PVS shows low fertilisation, clinical pregnancy and implantation rate.Study intends to show that coarse granulation in perivitelline space may predict poor ART outcome and patients can be counselled regarding the same.


SUPPORT: None.
IVF OUTCOME PREDICTORS - OTHER

P-179 Tuesday, October 15, 2019 6:30 AM

THE CAUSAL EFFECT OF DYNAMIC FERTILITY TREATMENT STRATEGIES ON THE PROBABILITY OF PREGNANCY: A NOVEL APPLICATION OF MARGINAL STRUCTURAL MODELS (MSMS).
Soudhe Ansari, PhD,1 Michael P. LaValley, PhD,2 Sara Lodi, PhD,2 Brooke Hayward, SM, MBA,3 Gilbert L. Mottla, MD,4 Mary Mahony, PhD,2 Judith J. Lok, PhD,5 Prometrika LLC, Cambridge, MA;6 EMD Serono, Inc., Rockland, MA;7 Boston University, Boston, MA;6 Shady Grove Fertility Center, Annapolis, MD;6 US Medical Affairs, KGaA, Darmstadt, Germany), Rockland, MA, USA.

OBJECTIVE: To estimate the probability of clinical pregnancy, had all patients or subgroups of patients (based on age) followed 1 specific treatment strategy: eg, 4 cycles of ovulation induction (OI, with/without intrauterine insemination) using clomiphene or letrozole (OI Oral), 3 cycles of OI + Gonadotropin (OI Gn), or 1 cycle of assisted reproductive technology (ART) with fresh or cryopreserved embryo transfer.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Electronic medical record data from 84,301 US patients who underwent multiple treatments (219,925 cycles) in 2009-2016 were examined. Female patients included were initially treatment-naive; patients with an initial diagnosis of male infertility were excluded. Inverse Probability (IP) of Censoring Weighting adjusted for stopping treatment before getting pregnant and IP of Treatment Weighting adjusted for patient characteristics (eg, diminished ovarian reserve) that made them more likely to choose a treatment strategy (eg, 1 ART over 4 OI Gn cycles).

RESULTS: In either age group, patients needed ≥4 OI Gn cycles, or to switch to 1 OI Gn cycle after 3 failed OI Oral cycles to have a similar chance of pregnancy as 1 ART cycle. Chance of pregnancy was below 50% for 4-cy-cle treatment strategies with <1 ART cycle.

CONCLUSIONS: Patients ≥35 y may be better served by starting with or switching to ART sooner rather than repeating multiple cycles of OI. For patients <35 y, the estimated chance of pregnancy with 4 OI Oral cycles is close to 1 ART cycle. Evaluation of real-world data using MSMS to account for patient dropout and changes in patient characteristics and prognosis over time can provide important insights into treatment-decision trends and evidence for improving personalized medicine.


SUPPORT: Study sponsored by EMD Serono, Inc. (a business of Merck KGaA, Darmstadt, Germany), Rockland, MA, USA.

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ECTOPIC/HETEROTOPIC PREGNANCY OUTCOMES AFTER BLASTOCYST-STAGE FROZEN-THAWED EMBRYO TRANSFERS COMPARED WITH CLEAVAGE STAGE: A SART-CORS STUDY.
Kavitha Krishnammooorthy, MD,1 Barry E. Perlman, DO,2 Sara S. Morelli, MD, PhD,3 Patricia Greenberg, MS,3 Sangita K. Jindal, Ph.D,3 Peter Megovern, MD,3 Rutgers New Jersey Medical School, Newark, NJ;4 Rutgers School of Public Health, New Brunswick, NJ;5 Einstein COM, Montefiore, Hartsdale, OR;6 University Reproductive Associates, NJ.

OBJECTIVE: It is well established that fresh embryo transfers at the blastocyst stage result in improved pregnancy outcomes compared with cleavage-stage embryo transfers. Using the Society for Assisted Reproductive Technologies Clinical Outcomes Reporting System (SART CORS) dataset, we have recently shown that blastocyst-stage frozen embryo transfer (FET) is also associated with higher live-birth rates compared with cleavage-stage FETs. However, other outcomes such as ectopic and heterotopic pregnancy rates between cleavage-stage and blastocyst-stage FETs have not been well studied. The objective of this study was to investigate whether there is a difference in ectopic/hetero-topic pregnancy rates in blastocyst-stage FETs compared with cleavage-stage FETs.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All in vitro fertilization (IVF) cycles reported to the Society for Assisted Reproductive Technology from 2004 to 2013 were evaluated. Patients included were those with recorded treatment and pregnancy outcomes undergoing FETs at either the blastocyst-stage (n=118,616) or the cleavage-stage (n=137,671). Main outcome measures were pregnancy outcomes, specifically ectopic pregnancy rates and hetero-topic pregnancy rates. Demographic criteria from each cycle was also collected. Statistical analysis was performed using SAS and Microsoft Excel. Chi-square analysis for bivariate associations and generalized estimating equations for adjusted associations were used with p<0.05 considered as statistically significant.

RESULTS: There was a statistically significant increase in pregnancy rates with blastocyst-stage FETs compared with cleavage-stage FETs (60.6% vs. 41.0%; p<0.001). Among those who became pregnant, there was a significantly lower incidence of ectopic/heterotopic pregnancy rates in blastocyst-stage FETs vs. cleavage-stage FETs (0.8% vs. 1.1%; p<0.001). Differences in ectopic/heterotopic pregnancy rates remained statistically significant after controlling for confounders such as tubal factor infertility and number of embryos transferred.

CONCLUSIONS: Blastocyst-stage frozen embryo transfer is associated with lower ectopic/heterotopic pregnancy rates compared with cleavage-stage frozen embryo transfer.

Estimated Cumulative Clinical Pregnancy Rate, % (95% Confidence Interval)

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ART: 1 43.1 (63.1, 65.1) 37.4 (42.8, 44.7) 3 77.6 (76.7, 78.6) 57.4 (56.3, 58.5)
LEVERAGING A COMPOSITE OVARIAN RESERVE SCORE IN A MACHINE LEARNING MODEL OF LIVE BIRTH OUTCOMES IN IVF.

OBJECTIVE: As the number of predictive measures for IVF prognosis proliferates, there is a growing need for machine-driven tools to aid patients and their healthcare providers in navigating the complex landscape of decision making. In previous work, we identified that multiple indirect measures of ovarian reserve (baseline FSH, LH, E2, BAFC, AMH) can be combined to measure a latent variable representing a patient’s overall ovarian reserve. Here, we aimed to develop a predictive model that utilizes a composite ovarian reserve score to predict cumulative live birth (LB) outcomes and risk of multiples based on the number of transferred embryos.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: 48,357 cycles were included from 34,734 patients age 25-45 undergoing autologous IVF treatment between 2010-2017 at 13 fertility centers in the US. We excluded cycles using pre-implantation genetic testing and transfer of 3 or more embryos. The dataset was divided into 2/3 for training (36,401 cycles), with the remaining 1/3 set aside as an independent validation set. We used a Bayesian approach because, in contrast to traditional regression models, this allowed us to incorporate the unobserved, but clinically relevant, composite variable of ovarian reserve as a feature of the model for cumulative LB rate and risk of multiples. Accordingly, the number of LBs per initiated cycle was modeled using a zero-inflated binomial distribution to account for patient cancellation prior to transfer, and ovarian reserve was included in the model as a latent variable dependent on baseline levels of FSH, LH, AMH, and BAFC. To compensate for nonrandom patient dropout across multiple cycles, inverse probability of censoring weighting (IPCW) was used to more accurately predict later cycles. Considered variables in the larger model included patient age, ovarian reserve, BMI, diagnosis, number of transferred embryos, and partner semen analysis.

RESULTS: When our model was tested with an independent validation set, we found that had an AUC of 0.73 for prediction of a LB and an AUC of 0.82 for prediction of multiples. The most important features of the model included patient age, number of transferred embryos, number of previous failed cycles, and BMI.

CONCLUSIONS: For machine-driven tools to truly augment traditionally expert-driven decisions, it is important for the underlying models to grow in sophistication with the growing list and varying importance of prognostic measures. The use of Bayesian models to better determine likely number of ovarian reserve (baseline FSH, LH, E2, BAFC, AMH) can be combined to measure a latent variable representing a patient's overall ovarian reserve.

OBJECTIVE: To evaluate the effect of the selective oxytocin antagonist barusiban, administered on the day of transfer, on ongoing implantation rate in IVF/ICSI patients.

DESIGN: Randomized, double-blind, placebo-controlled, phase 2 trial (BASIC) in 255 IVF/ICSI patients, 18-37 years, with a history of repeated implantation failures. Uterine pathology and thrombophilia disease were excluded. Patients had undergone controlled ovarian stimulation, hCG triggering, oocyte retrieval, and luteal phase progesterone supplementation.

MATERIALS AND METHODS: Women were randomized 1:1 on the day of transfer to barusiban (40 mg 45 min pre-transfer + 10 mg 15 min post-transfer) (n=130) or placebo (n=125), administered subcutaneously. Randomization was stratified by day of transfer (day 3 or 5) and number of embryos/blastocysts transferred (1 or 2). In total, 440 good-quality embryos/blastocysts were transferred (barusiban: 225; placebo: 215). Ongoing implantation (primary endpoint) and pregnancy were assessed 10-11 weeks after transfer. To adjust for imbalances in baseline characteristics between groups, the effect of barusiban was tested using a logistic regression model with treatment, embryo/blastocyst quality, reason for infertility, and center as factors. There were more transfers of excellent-quality blastocysts in the placebo group than in the barusiban group (51% vs 29%) as well as more couples in the placebo group with male factor infertility (51% vs 35%), supporting the value of the adjusted analyses. Both unadjusted and adjusted analyses were performed, and the latter are presented.

RESULTS: There was no significant difference in overall ongoing implantation rate between barusiban and placebo with rates of 27.9% and 23.1%, respectively [odds ratio 1.11 (95% CI: 0.69; 1.78), p=0.663]. However, the day of transfer had a significant interaction on the primary endpoint. A significantly higher ongoing implantation rate was observed for barusiban over placebo for day 5 transfers, with 41.3% for barusiban versus 23.2% for placebo [odds ratio 2.34 (95% CI: 1.13; 4.84), p=0.022], but not for day 3 transfers (11.8% versus 17.6% [odds ratio 0.63 (95% CI: 0.30; 1.34), p=0.227]). The overall ongoing pregnancy rates were 34.1% for barusiban and 35.1% for placebo, with 49.7% for barusiban and 33.4% for placebo for day 5 transfers, and 19.2% and 29.9% for day 3 transfers, respectively.

More mild/moderate injection site reactions were observed with barusiban than with placebo, but there was no difference in severe reactions. No serious drug reactions were reported, and neonatal outcome was comparable between groups.

CONCLUSIONS: The present trial was unable to demonstrate the efficacy of barusiban in patients with a history of repeated implantation failures, but it revealed a time window for a clinically relevant effect of barusiban. Barusiban increased the implantation of blastocysts when administered closer to the time of the actual implantation, but not when administered at the early luteal phase during transfer of cleavage-stage embryos. Subcutaneous administration of 50 mg barusiban was well-tolerated.

SUPPORT: Ferring Pharmaceuticals.
but not statistically different (17.4% vs 15.4%, \( P = 0.08 \)). There was no sign-
ificant difference in percentage of pre-term births between frozen and fresh
ovocytes (13.7% vs 13.5%, \( P > 0.05 \)). However, frozen donor oocytes were
associated with significantly increased percentage of very pre-term births
compared to fresh donor oocytes (3.7% vs 1.9%, \( P = 0.0003 \)).

CONCLUSIONS: The use of frozen donor oocytes in IVF treatment has
become increasingly commonplace, but knowledge of related pregnancy
outcome risks is currently sparse. This study using the largest SART data
available so far shows that IVF patients using frozen donor oocytes had a
lower live birth rate and have a significantly increased twin birth rate even
even with eSET when compared to fresh donor oocytes, which is likely a strong
contributing factor in the significantly increased occurrence of very pre-
term births and should be taken into account when counseling patients about
to undergo IVF treatment.

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factor and IVF outcomes was evaluated by dividing SDF-1 (<125, 125-200, 200-275, 275-350, and ≥ 350 pg/ml) and VEGF (<180, 180-270, 270-360, 360-450, and ≥ 450 pg/ml) concentrations into five intervals creating five approximately similar sized groups. The follicular concentration of SDF-1 and VEGF were not significantly associated with fertilization and cleavage outcome, and embryo morphology. The rates of full blastocysts and good-quality blastocysts were significantly higher in follicles with an SDF-1 concentration of 275–350 pg/ml than in the follicles with SDF-1 concentrations of <200 pg/ml and ≥ 350 pg/ml (P < 0.05). The follicular concentration of VEGF was not associated with the blastocyst morphology.

CONCLUSIONS: Our findings suggest that SDF-1 plays important modulatory roles in early luteinization and its follicular concentration may be a valuable biochemical marker of blastocyst development.

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PREDICTIVE FACTORS FOR OOCYTE RETRIEVAL FAILURE IN TREATMENT CYCLES WITH ASSISTED REPRODUCTIVE TECHNOLOGY: A RETROSPECTIVE COHORT STUDY USING THE NATION-WIDE ART REGISTRY OF JAPAN. Toshifumi Takahashi, M.D., Kuniaki Ota, M.D., Fukushima Medical University, Fukushima, Japan.

OBJECTIVE: The purpose of this study was to evaluate the prognostic factors for oocyte retrieval failure in patients undergoing assisted reproductive technology (ART) treatment cycles.

DESIGN: A retrospective cohort study.

MATERIALS AND METHODS: This present study was approved by the Ethical Committee on human subjects. The data analyzed in this study were part of the Japanese ART registry database, which was collected by the Japan Society of Obstetrics and Gynecology from 2010 to 2012. We analyzed the data of 464,480 fresh cycles with transvaginal oocyte aspiration. The cycles with oocyte retrieval failure and those with one or more oocytes retrieved were compared to determine predictive factors for oocyte retrieval failure using multivariate logistic regression analyses.

RESULTS: The number of cycles with oocyte retrieval failure was 36,600 (7.9%). According to the multivariate analysis, age, cause of infertility, and controlled ovarian hyperstimulation (COH) were the independent prognostic factors for oocyte retrieval failure. The percentages of oocyte retrieval failure in the age groups of 29 years old and under, 30-34 years old, 35-39 years old, 40-44 years old, and over 45 years old were 3.2%, 4.2%, 5.9%, 10.2%, and 18.6%, respectively. The odds ratios were 1.7 times those of the male factor group, respectively. The percentages of oocyte retrieval failure that corresponded to infertility caused by a male factor, tubal factor, endometriosis, and unknown factors were 5.6%, 7.3%, 8.0%, and 9.2%, respectively. The odds ratios for oocyte retrieval failure in the tubal factor, endometriosis, and unknown groups were 1.3, 1.4, and 1.7 times those in the male factor group, respectively. The percentages of oocyte retrieval failure in the COH cases using aromatase inhibitor or clomiphene (AI+CC) protocols were 2.4 and 5.3 times those for the GnRH-agonist pituitary suppression protocols, respectively. The percentages of oocyte retrieval failure in the age groups of 29 years old and under, 30-34 years old, 35-39 years old, 40-44 years old, and over 45 years old were 3.2%, 4.2%, 5.9%, 10.2%, and 18.6%, respectively. The odds ratios for oocyte retrieval failure in the male factor group, respectively. The percentages of oocyte retrieval failure that corresponded to infertility caused by a male factor, tubal factor, endometriosis, and unknown factors were 5.6%, 7.3%, 8.0%, and 9.2%, respectively. The odds ratios for oocyte retrieval failure in the tubal factor, endometriosis, and unknown groups were 1.3, 1.4, and 1.7 times those in the male factor group, respectively. The percentages of oocyte retrieval failure in the COH cases using aromatase inhibitor or clomiphene (AI+CC) protocols were 2.4 and 5.3 times those for the GnRH-agonist pituitary suppression protocols, respectively.

CONCLUSIONS: The predictive factors for oocyte retrieval failure might be related to a patient’s age, particular causes of infertility, and COH protocols. These results provide information that may be useful for counseling patients before ART treatments.

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PREDICTING CLINICAL PREGNANCY BY MACHINE LEARNING ALGORITHM USING NONINVASIVE EMBRYO MORPHOKINETICS AT AN ACADEMIC CENTER. Liubin Yang, MD, PhD,1 Mary Peavey, MD,2 Khadek Kaskar, MS,3 Neil Chappell, MD, MSCI4 Darius J. Devlin, BS,5 Terri Woodard, MD,6 Paul Zarutskie, MD,7 Richard Cochran, PhD,8 William Gibbons, MD9 1Baylor College of Medicine, Houston, TX; 2Mary Peavey, MD, MD; 3Khadek Kaskar, MS, Neil Chappell, MD, MSCI; 4Darius J. Devlin, BS, Terri Woodard, MD, Paul Zarutskie, MD, Richard Cochran, PhD, William Gibbons, MD.

OBJECTIVE: To develop and examine the feasibility of a time-lapse microscopy (TLM)-based assay to predict pregnancy outcomes in patient IVF cycles.

DESIGN: Retrospective and prospective cohort analyses of clinical pregnancy data with embryo TLM data that were transferred at an academic fertility center.

MATERIALS AND METHODS: Embryos that underwent EmbryoScope™ TLM and subsequent transfer with clinical pregnancy (defined by fetal heart beat after 6 weeks) or no clinical pregnancy were included from 2014 to 2018. Machine classifiers were used for morphokinetic parameters from fertilization to blastocyst formation that were annotated manually. Data were analyzed by multivariate analysis of covariance, Fisher’s exact, Chi-square tests, and binomial logistic regression using R and Scikit learn, and Python software.

RESULTS: Learning curves were applied to a training set of 180 embryos and a validation set of 80 embryos. Supervised algorithms tested included naïve bayes classifiers, support vector machines, logistic regression, and decision trees. Highest accuracy scores were achieved with logistic regression and decision tree models. Accuracy scores of 0.6 for the two sets converged for the logistic regression model at 100 training set numbers whereas Decision Tree algorithm reached a 0.7 accuracy score converging at 180 training set numbers. Furthermore, the logistic regression prediction model (Chi square =26.3, p=0.010), termed the Yang-Peavey Embryo Enhancement Algorithm, correctly predicted 70% of clinical pregnancies for patients under age 35. A receiver operating characteristic curve was developed and found to be significant with an area under the curve value of 0.757 (95% CI 0.667-0.848, p<0.0001). In a separate prospective cohort study, the algorithm was applied to 140 embryos that were transferred, which were manually annotated and blinded from the pregnancy outcome. The VPEEA algorithm yield 68% sensitivity and 53% positive predictive value (PPV) when applied to the full dataset.

CONCLUSIONS: This study demonstrates that novel Machine Learning algorithms can be used for embryo selection based on as few as 200 embryos, and be applicable to a prospective cohort of embryos. The predictive value of the algorithm is comparable or even superior in a subset of patients to that of preimplantation genetics screening and therefore is a valuable non-invasive technology to predict clinical pregnancy in IVF.

SUPPORT: Baylor College of Medicine Department of Obstetrics and Gynecology, the Division of Reproductive Endocrinology and Infertility, the 2016 Robert and Janice McNair Medical Scientist Training Program Scholarship.

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Recent years have seen a dramatic rise in the number of frozen-thawed embryo replacement (FER) cycles. Between 2012 and 2016, the annual number of FETs in the UK increased by 77%, while the number of fresh cycles declined by 2%. Despite FER accounting for 30% of UK IVF workload, the optimum method of endometrial preparation for FER is unknown.

OBJECTIVE: This study assesses current UK trends in endometrial preparation for FER and compares the outcomes of women undergoing medicated FER with GnRH-agonist and GnRH-antagonist pituitary suppression.

DESIGN: The first national UK survey of practice on endometrial preparation for FER and a retrospective cohort study comparing GnRH-agonist with GnRH-antagonist pituitary suppression.

MATERIALS AND METHODS: All 84 UK IVF clinics were asked to complete an online survey between September 2018 and January 2019.

RESULTS: Sixty-five clinics (77%) responded, together undertaking approximately 24,419 FERs annually. The preferred developmental stage of cryopreservation is blastocyst, favoured by 98% of clinics. In the UK 77% of FETS are medicated, 18% natural cycle, 5% modified natural cycle and <1% ovulation induction. In ovolutory women 69% of clinics favour medicated, 26% natural cycle and 5% modified natural cycle FER.

In natural cycle FET, 31% always, 44% sometimes and 25% never prescribed luteal support. Fifty-one percent of clinics transfer a thawed blastocyst on the fifth day after the predicted day of ovulation, 21% on the fourth, 14% on the third, 9% on the second and 5% on the seventh day.

In medicated FET, 2% of clinics undertake blastocyst transfer on the third day of progesterone, 3% on the fourth, 21% on the fifth, 61% on the sixth and 7% on the seventh day.
13% on the seventh. Luteal support is continued from six to beyond twelve weeks’ gestation, with the majority (69%) stopping at 12 weeks. The use of pituitary suppression in medicated FER varies widely. Fifty-five percent of clinics favour GnRH-agonist down-regulation, 11% GnRH-antagonist and 34% no supplementary pituitary suppression.

Consequently, we analysed all women undergoing medicated FER of one or two unbiopsied blastocysts at a UK IVF clinic between January 2014 and June 2016 comparing GnRH-antagonist with GnRH-agonist medicated FER. 578 patients (188 antagonist, 390 agonist) were included. Baseline characteristics were similar. Live birth (36.7% (antagonist) vs. 39.5% (agonist), p = 0.519), clinical pregnancy (59.5% vs. 60.5%, p = 0.482) and miscarriage rates (33.3% vs. 34.5%, p = 0.857) were similar. In the antagonist group there were less clinic visits (median (range): 2(5) vs 3(5), p = 0.01) and ultra-sound scans (1(3) vs 2(5), p < 0.01).

CONCLUSIONS: Wide variation exists in the preferred method of endometrial preparation for FER, emphasising the need for more research to determine the optimum protocols. The survey results highlight particular inconsistency in approach to pituitary suppression in medicated FER. Our cohort study historical control benefits to GnRH-antagonist as an alternative to GnRH-agonist for pituitary suppression in medicated FER. However, more research is needed to confirm similar clinical outcomes.

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IMPROMPTU IMPLANTATION RATE BY ADDING RECOMBINANT LH SUPPLEMENTATION TO RECOMBINANT FSH DURING CONTROLLED OVARIAN STIMULATION IN GNRH ANTAGONIST REGIMEN
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OBJECTIVE: Gonadotropin-releasing hormone (GnRH) antagonist profoundly suppresses pituitary gland, avoiding premature luteinizing hormone (LH) surge. Consequently, recruited follicles are radically deprived of LH sustenance. The aim of this study was to investigate the effect of LH supplementation in GnRH antagonist regimen on the outcomes of consecutive ICSI (intracytoplasmic sperm injection) cycles.

DESIGN: Historical control within-subject study.

MATERIALS AND METHODS: Data were obtained via chart review of 228 matched cycles performed in 114 patients undergoing ICSI between 2015 and 2018, in a private university-affiliated IVF center. For all patients, recombinant follicle stimulating hormone (rFSH, Gonal-f) was used for controlled ovarian stimulation (COS) in the first ICSI cycle (rFSH group), followed by ovarian stimulation with rFSH and rLH (Pergoveris) in the next cycle (rFSH + rLH group). Pituitary suppression was achieved with GnRH antagonist (cetrorelix acetate) in both groups. The sample size calculation suggested that 200 cycles would be enough to demonstrate a 20% effect with 80% power and 5% significance level considering as primary outcome implantation rate (IR). Data was analyzed by Generalized Linear Models followed by Bonferroni post hoc test.

RESULTS: Higher estradiol levels (1151.73 vs. 1139.04 pg/mL, p = 0.0006), oocyte yield (63.41% vs. 69.78%, p = 0.045), day-3 high-quality embryos rate (34.13% vs. 47.71%, p = 0.029) and IR (18.57% vs. 26.67%, p < 0.001), and lower miscarriage rate (33.0% vs. 50.0%, p = 0.031) were observed in rFSH + rLH group compared to rFSH group. In patients aged < 35 years, IR was higher in rFSH + rLH group compared to rFSH group (34.86 vs. 21.43, p < 0.001). In patients aged ≥ 35 years, higher estradiol levels (1161.80 ± 215.94 pg/mL vs. 1966.55 ± 220.13 pg/mL, p = 0.009), oocyte yield (61.28% vs. 68.52%, p = 0.038), day-3 high-quality embryos rate (32.01% vs. 48.81%, p = 0.013), and IR (17.75% vs. 23.64%, p < 0.001) were observed in rFSH + rLH group compared to rFSH group. In patients with low response to COS (< 5 retrieved oocytes), oocyte yield (56.82% vs. 63.29%, p = 0.001), mature oocyte rate (69.87% vs. 78.12%, p < 0.001), normal cleavage speed (62.5% vs. 75.83%, p < 0.001), IR (10.00% vs. 20.45%, p < 0.001) and miscarriage rate (100% vs. 0.00%, p < 0.001) were improved in rFSH + rLH group compared to rFSH group. In patients with normal response to COS (> 4 retrieved oocytes), higher estradiol levels (1725.74 ± 303.65 pg/mL vs. 2788.37 ± 281.12 pg/mL, p = 0.010), oocyte yield (75.37% vs. 82.69%, p = 0.006), and IR (23.3% vs. 29.35%, p < 0.001) were observed in rFSH + rLH group compared to rFSH group.

CONCLUSIONS: Ovarian stimulation with LH supplementation may prevent the decrease in estradiol levels after GnRH antagonist administration, resulting in higher IRs, independent of maternal age and response to COS, compared to cycles stimulated with rFSH only. Improvements were also observed for ICSI laboratory outcomes and miscarriage rate when patients were stratified by age and number of retrieved oocytes.

Reference: NA.

Support: None.

P-191 Tuesday, October 15, 2019 6:30 AM
FRESH VERSUS FREEZE-ALL STRATEGY IN ASSISTED REPRODUCTIVE TECHNOLOGY – A COCHRANE REVIEW
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OBJECTIVE: In vitro fertilisation (IVF) treatments imply a fresh embryo transfer, possibly followed by one or more frozen-thawed embryo transfers in subsequent cycles. Alternatively, one can opt to freeze all suitable embryos and transfer frozen-thawed embryos in subsequent cycles only, which is also known as the freeze-all strategy. We compared the effectiveness and safety of these treatment strategies.

DESIGN: We searched the Cochrane Gynaecology and Fertility Group Trials Register, the Cochrane Central Register of Studies (CRSO), MEDLINE, Embase, PsyCINFO, CINAHL, and two registers of ongoing trials in February 2019 for relevant studies, and checked references and contacted study authors in the field to obtain additional data.

MATERIALS AND METHODS: We used standard methodological procedures as recommended by Cochrane for our search, data extraction, and analyses. The primary outcome was cumulative live birth rate (cLBR). Secondary outcomes included ovarian hyper stimulation syndrome (OHSS), pregnancy complications, and time to pregnancy.

RESULTS: We included six RCTs in our meta-analyses, that together reported on 4324 women. The studies compared the freeze-all strategy to IVF with fresh transfer in women with a high risk of OHSS, in ‘good prognosis’ women based on the number of follicles, in women with PCOS, and in young women without PCOS. The evidence was of moderate to low quality due to serious risk of bias, serious imprecision for four studies, and serious unexplained heterogeneity for one study.

For cLBR we found an OR of 1.0 (95% CI 0.97 to 1.24; 6 RCTs; 4324 women; I² = 0%, moderate quality of evidence) for the freeze-all strategy versus IVF with fresh transfer of embryos. These data suggest that for a cLBR of 63% following IVF with fresh transfer of embryos, the cLBR following the freeze-all strategy would be between 62% and 67%.

Women developed less OHSS after the freeze-all strategy compared to IVF with fresh transfer of embryos (OR 0.29, 95% CI 0.19 to 0.44; 4 RCTs; 4065 women; I² = 5%, low quality evidence). These data suggest that for an OHSS rate of 10%, following the freeze-all strategy, the rate following the freeze-all strategy would be between 1% and 2%.

The risk of maternal hypertensive disorders and having a large for gestational age baby was increased following the freeze-all strategy (OR 2.15, 95% CI 1.42 to 3.25; 3 trials; 3940 women; I² = 29% and OR 1.87, 95% CI 1.43 to 2.44; 3 trials; 3119 women; I² = 0%, respectively, both low-quality evidence). The risk of having a small for gestational age baby was lowered following the freeze-all strategy (OR 0.68, 95% CI 0.53 to 0.89; 3 trials; 3119 women; I² = 56%, low-quality evidence).

One trial reported on time to conception and one trial reported on time to live birth which were both longer in the freeze all strategy.

CONCLUSIONS: We did not find a clear difference in cLBR between the two strategies. The freeze-all strategy lowered the risk of OHSS, increased the risk of maternal hypertensive disorders of pregnancy, increased the risk of a large for gestational age baby, and lowered the risk of a small for gestational age baby. The time to pregnancy was longer in the freeze-all strategy. Reference: None.

Support: None.

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PREDICTING CUMULATIVE LIVE BIRTH RATE FOR THE FIRST CYCLE OF IN VITRO FERTILIZATION
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OBJECTIVE: To develop a prediction model to estimate the chances of cumulative live birth following the first cycle of in vitro fertilization (IVF) and cumulative embryo transfers based on female demographics and cycle stimulation characteristics.

DESIGN: Retrospective study.

MATERIALS AND METHODS: All women at the age of 20-50 years old who underwent their first IVF treatment in the reproductive center of Ren Ji hospital from Jan 2014 to Dec 2015 were screened. Cumulative live birth was defined as first live birth from all fresh and frozen thawed embryo transferred within 2 years after oocyte retrieval. A multiple fraction polynomial (MFP) regression model was used to predict the probability of live birth for an individual woman. Two clinical prediction models were developed: pre-treatment model using information available before starting ovarian stimulation and the post-treatment model based on additional information collected after oocyte retrieval.

RESULTS: After excluding cycles with PGT and oocyte freezing, 7796 women with 7796 cycles were included. In total 5146 (66.0%) cumulatively had a live birth following their first IVF retrieval. Key pre-treatment predictors of live birth were the woman's age (≥ 35 vs. <35 years; adjusted odds ratio 0.34, 95% confidence interval, 0.29 to 0.38), BMI (≥ 24 vs. ˂24; 0.82, 0.72 to 0.92), and a basal FSH (≥ 10 vs. <10 IU/L: 0.54, 0.46 to 0.64). Post-treatment predictors included number of fertilization (1.03, 0.99 to 1.08), basal FSH (≥ 10 vs. <10 IU/L: 0.89, 0.83 to 0.99), woman's age (≥ 35 vs. <35 years: 0.69, 0.55 to 0.84), endometrial thickness on the day of trigger (≥7.5 vs. <7.5 mm: 1.19, 1.01 to 1.49) and cumulative number of embryos transferred (≥ 2 vs. <2: 1.83, 1.40 to 2.40). A pre-treatment model for the same women with 6 fertilized oocytes and an endometrial thickness of 9 mm, has an estimated 77.6% of having a live birth.

CONCLUSIONS: This study provides an individualized estimate of a couple’s cumulative chance of having a live birth after the first IVF cycle both before treatment and after oocyte retrieval. This may help physicians better counsel couples in preparation for their IVF journey both emotionally and financially.

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PRO CASPASE-3 AND CLEAVED CASPASE-3 GENE AND PROTEIN EXPRESSION AND PROPORTION OF MATURE OCYTES RETRIEVED. Camila P. Almeida, Ms, Camila O. Silveira, MD, MS, Enio F. Ferreira, Sr., PhD, Marcia C. Ferreira, MD, PhD, Gabriella Graças Oliveira, BS, Emerson S. Veloso, Ms, Felipe H. S. Silva, Sr., Ms, Santuza S. Ceduho, Ms, Leonardo M. Moraes, MD, MS, Fernando M. Reis, MD, PhD, Helen L. Del Puerto, PhD. "UFMG, Belo Horizonte, Brazil; "Fertibaby, Belo Horizonte, Brazil.

OBJECTIVE: To evaluate the clinical correlates of pro-caspase-3, cleaved caspase-3 and other apoptosis related genes expressed in human granulosa cells (GCs) of patients undergoing controlled ovarian stimulation (COS).

DESIGN: Luteinized GCs obtained from in vitro fertilization (IVF) and fertility preservation patients were evaluated for their expression of pro-caspase-3, cleaved caspase-3 and gene expression of BAX, BCL2, CASPASE3 and CASPASE8, that later were correlated with patient’s clinical data, such as length of infertility, length of COS and proportion of mature oocytes collected.

MATERIALS AND METHODS: Follicular fluid (FF) samples were collected from 35 patients referred to a private clinic for couple infertility treatment and cumulative embryo transfers based on female demographics and cycle stimulation characteristics. FF samples were collected from 35 patients referred to a private clinic for couple infertility treatment and cumulative embryo transfers based on female demographics and cycle stimulation characteristics.

RESULTS: Cleaved caspase-3 correlated positively with the length of COS (r = 0.445, p < 0.05) and the length of infertility (r = 0.476, p < 0.05). However, only pro-caspase-3 expression presented a positive correlation with the proportion of mature oocytes collected (r = 0.427, p < 0.05). Gene expression of CASPASE 3 and CASPASE 8 also correlated directly with the length of COS (r = 0.462, p < 0.05; r = 0.420, p < 0.05, respectively).

CONCLUSIONS: These findings suggest that pro-caspase-3 is constitutively expressed in human granulosa cells and correlates with the proportion of mature oocytes retrieved, therefore it better indicates granulosa cell integrity than imminent cell death by apoptosis. Conversely, the activation of caspase-3 in granulosa cells is associated with a longer time of infertility and longer duration of COS in IVF patients.

SUPPORT: PRPq UFMG. Fapemig. CNpq.
APOTOPSIS OF CUMULUS GRANULOSA CELLS IS HIGHER IN NON-PREGNANT GROUP IN PATIENTS UNDERGOING IVF/ICSI. Yuting Fan, M.D., a Xiaoyan Liang, M.D., Ph.D., b Sherman Silber, M.D. a The Sixth Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; bIn Fertility Center of St. Louis, Chesterfield, MO.

OBJECTIVE: To evaluate apoptosis of granulosa cells in clinical pregnant group versus non-pregnant group in women undergoing in-vitro fertilization(IVF)/intracytoplasmic sperm injection(ICSI).

DESIGN: A prospective cohort study.

MATERIALS AND METHODS: A prospective cohort study was initiated at a single IVF center involving a total of 164 women undergoing IVF/ICSI cycles. Mural and cumulus granulosa cells, and follicular fluid were collected during oocyte retrieval. Annexin V-FITC/PI apoptosis staining and flow cytometry analysis were performed to evaluate apoptosis rate of mural granulosa cells and cumulus cells. Serum and follicular fluid hormones including estradiol (E2), progesterone (P), testosterone (T), anti-Mullerian hormone (AMH) were measured by ECLIA. Laboratory and clinical outcomes were analyzed.

CONCLUSIONS: Apoptosis of cumulus cells was significantly higher in the non-pregnant group. Follicular estradiol level was lower in clinical pregnant group. The apoptosis rate of mural cells was negatively correlated with worse ovarian response, with fewer egg and embryo numbers in IVF/ICSI as well as with age. Early apoptosis rate of cumulus cells might also have influence on clinical pregnancy.


DOES MASSAGE THERAPY IMMEDIATELY PRIOR TO EMBRYO TRANSFER IMPROVE CLINICAL PREGNANCY RATE IN IVF-PGT-A (IN-VITRO FERTILIZATION-PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY) CYCLES? Sarah Z. Gavriizi, M.D., a Amanda Skillem, MD. FACOG. b UT Dell Medical School, Austin, TX; bAspire Austin, Austin, TX.

OBJECTIVE: Prior retrospective research (1) has suggested improved implantation rate in FET (frozen embryo transfer) cycles with untested blastocysts. This purpose of this study is to evaluate whether massage therapy immediately prior to SET (single embryo transfer) of PGT-A euploid embryos improves clinical pregnancy rate.

DESIGN: Prospective, Double-blind, Randomized Controlled Trial.

MATERIALS AND METHODS: Patients undergoing SET of autologous PGT-A euploid embryo in controlled FET cycles (exogenous estrogen, intramuscular progesterone) beginning in May 2017 were considered for participation in this study. Exclusion criteria: 2 or more prior failed FETs, uterine anomaly, prior uterine surgery, and patients already undergoing massage or acupuncture therapy. A total of 65 embryo transfers were included and were randomly assigned to group by computer randomization software. Patients in the treatment group (n=31) received a standardized 20-minute massage by one therapist (GK) beginning 45 minutes prior to SET. Patients in the control group (n=34) arrived at the same time prior to SET and received standard care without massage. Patients were blinded to group allocation until arrival for SET. One physician (AS) performed all SETs and is blinded to group allocation.

RESULTS: There was no significant difference in age, body mass index, underlying fertility diagnosis, number of prior embryo transfers (0 vs 1), or endometrial thickness between the two groups. All patients had trilaminar endometrium of at least 7 mm thickness by ultrasound prior to progesterone start. Implantation rate (positive quantitative beta human chorionic gonadotropin 14 days post SET) was 80.6% (n=25) in the treatment group and 64.3% (n=21) in the control group, p=0.09. The live birth rate was 64.5% (n=20) in the treatment group and 47.1% (n=16) in the control group, p=0.16.

CONCLUSIONS: Despite advances in modern fertility treatment, clinical pregnancy rates remain well below 100%, even in good prognosis patients. Therefore, a low-cost, low-risk intervention which may benefit this population is of great interest. The standardized massage in the study includes elements of both lower abdominal massage, which can theoretically increase blood flow to the pelvis, and head and neck massage, which may improve relaxation. Prior retrospective research (1) has suggested improved implantation rate in FET cycles with untested blastocysts. Our randomized controlled double-blind trial appears to demonstrate a clinical benefit of
WOMEN WITH PREVIOUS FAILED IVF BENEFIT FROM INTRACUTERINE INSTILLATION OF PLATELET RICH PLASMA.

Mamtta Sudhir Katidakond, DNB, a,b Sangeeta Dheerendra Deshmukh, MD, c Shubhada Sanjiv Khandeparkar, MD, d Nandkishor Jagannath Naik, B.Sc, a Pratiksha Khandare, MSc, a Firuza Rajesh Parikh, MD DNB PhD, e FertilTree-Jaslok International Fertility Centre, MUMBAI, India; eJaslok Hospital and Research Centre, Mumbai, India; Dr.Khandeparkar IVF centre, MUMBAI, India.

OBJECTIVE: To record the improvement in the endometrial lining and pregnancy rates in Frozen Embryo Transfer (FET) cycles of women following intrauterine Platelet Rich Plasma (PRP) instillation.

DESIGN: A prospective case control study was carried out during the period of August 2018 to March 2019 at our centre. Women in the age group of 25 to 45 years with a history of previous cancelled cycles due to poor endometrial lining undergoing FET were included.

MATERIALS AND METHODS: 101 women undergoing FET at our centre were included in the study, following their consent. Intrauterine instillation of approximately 1 ml of autologous PRP was carried out on day 5, day 12 of endometrial priming and 48 hours prior to embryo transfer. The endometrial thickness was evaluated by Transvaginal Ultrasound on the days of metrial priming and 48 hours prior to embryo transfer. Serum BHC levels were checked 14 days after the embryo transfer.

RESULTS: 96 out of 101 women showed improvement in the endometrial lining. Of 101 women in the study, 29 women conceived (28.7%). Also, there were 10 biochemical pregnancies (9.9%). Of these 39 women, 14 of endometrial thinning and clinical pregnancy rates particularly in women with multiple failed attempts and also holds promise for women with past history of Genital TB where implantation rates are low.

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THE ROLE OF VITAMIN D ON PREGNANCY OUT- COMES OF IVF/ICSI. Cai Safen, master, a Zeng Suiming, Graduate, student, b Li Jian, doctor, c Fei Gong, PhD, a Hocher Berthold, doctor, d Ge Lin, M.D., Ph.D. d Basic Medicine College, Central South University, changsha, China; Department of Basic Medicine, Hunan Normal University School of Medicine, changsha, China; eHunan Normal University, changsha, China; fCentral South University, Changsha, China.

OBJECTIVE: To study the relationship between maternal vitamin D(vitD) status and pregnancy outcome of IVF/ICSI.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: A total of 2577 female patients were collected who were received IVF/ICSI treatment in our hospital from 2017.1-2018.11. Peripheral blood was collected one day before transplantation to test the total and free vitD . All patients were divided into three groups according to the level of total vitD : adequacy group(total vitD≥30pg/ml), insufficiency group(total vitD≥20pg/ml and < 30pg/ml) and deficiency group(total vitD<20pg/ml).

RESULTS: There were 1384 patients in deficiency group (53.7%), 1113 patients in insufficiency group (43.2%) and 80 patients in adequacy group (3.1%). There was no significant difference in age, weight, BMI, basic FSH, LH, E2, T and AMH among the three groups. There was also no significant difference in the number of ovocytes received, transplantable embryos, high quality embryos and fertilization eggs of 2PN, pregnancy rate and abortion rate among the three groups ( Tab. 1 ). The total vitD level between pregnant group (19.62(16.59,22.83)) and non-pregnant group (19.14(16.35,22.79)) had no significant difference( p>0.45). The free vitD level between pregnant group (4.71(4.1,5.34)) and non-pregnant group (4.71(4.1,5.27)) had no significant difference ( p=0.76).

CONCLUSIONS: Although the pregnancy rate tended to increase with vitD level, neither total vitD nor free vitD seems was associated with IVF pregnancy rate and abortion rate.


2. Chi-Square test among groups.

SUPPORT: The company of DIAsource ImmunoAssays S.A.Â provided vitamin D kits.

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NON-INVASIVE OCYTE SELECTION BASED ON CUMULUS GENE EXPRESSIONS OF CAMKID, EFNB2 AND SASH1 PREDICTS PREGNANCY: A RETROSPECTIVE STUDY IN AN ASIAN POPULATION. Tom Adriaenssens, MSc, a,b Inge Van Vaerenbergh, PhD, c Nazli Akin, MSc, a Wim Coucke, PhD, b Cong Fang, MD, c Chuanchuan Zhou, MD, d Zeng Haitao, MD, PhD, e Kazuhisa Tomita, MS, f Yoshiharu Morimoto, MD, PhD, d Yi-An Chen, MS, e Chii-Ruey Tzeng, MD, MPH, e Elien Van Hecke, Msc, f AndrÃ© Rosenthal, Prof., f Johan Smitz, MD, PhD Prof. a,b,Follicle Biology Laboratory, Vrije
OBJECTIVE: Non-invasive testing for embryo selection is not yet well estabished. Recently a three-gene expression model in cumulus cells was evaluated for embryo selection in a Caucasian population (JARG 2019) and showed a significant increase of clinical pregnancy rate in day 3 single embryo transfer (SET). This study investigates if the same genes, CAMK1D, SASH1 and EFNB2, are also predictive in an independent Asian ART population.

DESIGN: International retrospective multicentre study with individual oocyte denudation.

MATERIALS AND METHODS: Oocytes from 39 Asian women in three centres (China, Taiwan, Japan) scheduled for ICSI and SET underwent individual oocyte denudation after pick-up. The women were stimulated with HP-hMG (n=9) or combo HP-hMG & rFSH (n=30) and received a day 3 or day 5 fresh or frozen SET. mRNA expression analysis for three predictive genes CAMK1D, EFNB2 and SASH1 (Corona Test) and 2 endogenous control genes (UBC, B2M) was performed by QRT-PCR using the cumulus cells of the oocytes. The CC of all oocytes developing into an embryo, that was selected for transfer based on the embryo morphology, were analysed. The expression of the three predictive genes was used for multivariate stepwise regression analysis.

RESULTS: Of the 58 transferred embryos from the 39 Asian women 22 implanted and resulted in a clinical pregnancy. Thirty six embryos did not implant. The three-gene expression model separated CC samples from pregnant and non-pregnant women with an accuracy of 93%. The sensitivity was 100%, specificity 89% and the area under the curve (AUC) was 0.9848.

CONCLUSIONS: There is debate in literature about the ideal number of oocytes retrieved from egg donors during COS, and if there are any deleterious effects on blastocyst number or quality. This preliminary study demonstrated a trend towards a significant decrease in the percentage of good quality, usable blastocysts per oocyte retrieval in cycles where 30 or more oocytes were retrieved. In conclusion, additional work is needed to further elucidate the impact of high oocyte retrieval numbers on embryo quality.

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CAN WE PREDICT WHO WILL DEVELOP A BLASTOCYST FROM AN IVF/ICSI CYCLE? Rakia Aljasser, MD,a Sara Ilinitsky, MD,a Lynda Hughes, BSc,a Angelos Vilos, MD,b George Vilos, MDb, Basim Abu-Rafea, MD,c Clinical Fellow, London, ON, Canada; bFertility Clinic London Health Sciences Centre, London, ON, Canada; cWestern university, London, ON, Canada; dWestern University, London, ON, Canada.

OBJECTIVE: As IVF laboratory techniques have advanced, extended culture and blastocysts transfer has become a mainstream of treatment. More and more clinics are employing blastocyst only transfer policies. Unfortunately, not all patients will have embryos that attain blastocyst stage meaning that a proportion of patients will not have an embryo transfer. The objective of this study is to identify patient or cycle characteristics predictive of blastocyst development.

DESIGN: We performed a retrospective database review of clinic and embryology data from all patients who had an IVF/ICSI cycle at our academic hospital-based fertility clinic.

MATERIALS AND METHODS: From February 1, 2012 to February 28, 2019 we looked at all cycles that had extended culture and compared patient and cycle characteristics from cycles with blastocyst development to cycles without (ie. no embryo development past cleavage stage or morula). Donor oocyte, onco-fertility, and social oocyte cryopreservation cycles were excluded. Bivariate statistical analysis was used to identify characteristics associated with blastocyst development and multivariate analysis used to create a prediction model for blastocyst development.

RESULTS: Of the 2474 IVF/ICSI cycles performed, 803 met inclusion criteria and had extended culture. Seventy-nine percent of patients developed blastocysts by day 5 or 6 with an average number of 2.8 blasts per cycle. Conventional IVF reduced the chance of no blastocyst development by 46% compared to ICSI (OR 0.54, 95% CI 0.33-0.89, p=0.01). The number of good quality day 3 embryos (more than 6 cells) was also associated with a better outcome; each good quality day 3 embryo reduced the chance of no blastocyst development by 14.5% (p<0.001). No other characteristics, including female age, BMI, parity, infertility diagnosis, gonadotropin dose, protocol, estradiol level, number of oocytes retrieved, and fertilization were associated with blastocyst development. The prediction model using


Support: None.

The effect of interleukin 6 on controlled ovarian stimulation results and IVF outcome in infertile women with adenomyosis undergoing IVF. Chung-Hoon Kim, M.D., Ph.D., Jei-Won Moon, M.D., Shin Yong Moon, M.D., Ph.D., Fertility Center, Seoul, Korea, Republic of (South).

Objective: To investigate the effect of serum interleukin 6 (IL-6) on controlled ovarian stimulation (COS) results and IVF outcome in infertile women with adenomyosis undergoing IVF.

Design: Retrospective cohort study.

Materials and methods: A total of 59 infertile women with adenomyosis who had their blood taken for analysis of serum IL-6 during the same period (P<0.05). Clinical pregnancy rate was significantly higher in infertile women with adenomyosis than in patients without adenomyosis who underwent IVF during the same period (P=0.1). The demographic characteristics of patients with adenomyosis were comparable among the three groups according to the serum IL-6 levels. There were also no differences in the three groups with respect to the number of oocytes retrieved, mature oocytes retrieved and fertilized oocytes. However, the number of grade I or 2 embryos was significantly lower in group 3 (P<0.05). Clinical pregnancy rate was significantly lower in group 3, compared with group 1 or 2 (P<0.001, P<0.023, respectively). None of the patients with serum IL-6 levels more than 8.0 achieve pregnancy following the corresponding IVF cycle.

Conclusions: High serum IL-6 levels in infertile women with adenomyosis can have an adverse effect on the IVF outcome including embryo quality and clinical pregnancy rate.

Support: None.

The effect of body mass index on the implantation potential of euploid embryos. Mohamad Irani, MD, Vinay Gunnala, MD, Steven Spandorfer, M.D., Zev Rosenwaks, M.D., The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

Objective: Obesity has been associated with higher miscarriage rates following natural conception and IVF. However, the underlying mechanism, whether obesity affects egg quality or endometrial receptivity, is not well understood. Here we aim to determine the impact of body mass index (BMI) on the outcomes of frozen-thawed euploid embryo transfer cycles.

Design: Retrospective cohort study.

Materials and methods: Frozen-thawed embryo transfer (FET) cycles of euploid embryos between 2013 and 2017 were included. Embryos were cultured in time-lapse incubators. Preimplantation genetic testing for aneuploidy was performed using array comparative genomic hybridization or next-generation sequencing. Cycles were divided into three groups according to the female patients’ BMI: < 25 kg/m², 25-29.9 kg/m² (overweight), and ≥ 30 kg/m² (obese). The miscarriage rate and live birth rate (LBR) were compared between the three groups. χ² and Fisher’s exact tests were used for categorical variables. Student’s t test and ANOVA were used for parametric data. Values were expressed as mean ± standard deviation.

Results: A total of 1011 FET of euploid embryos (s) were included: 758 with a BMI <25 kg/m², 174 with a BMI 25-29.9 kg/m², and 79 with a BMI ≥ 30 kg/m². The women were of comparable age between the three groups (P =0.93) (Table 1). There was a trend toward a lower LBR in women with a BMI ≥25 kg/m² compared to women with a BMI <25 kg/m² (48.1% vs. 57.5%, respectively; P =0.1), but it did not reach statistical significance. The LBR for women with a BMI 25-29.9 kg/m² (54%) was comparable with the other two groups (P =0.93). There was no significant difference in miscarriage rates between the three groups (8.8% for BMI <25 kg/m², 9.6% for BMI 25-29.9 kg/m², and 11.6% for BMI ≥ 30 kg/m²; P =0.2).

Conclusions: Overweight and obesity do not significantly affect the implantation potential of euploid embryos.

BMI (kg/m²) <25 25-29.9 ≥ 30 P value

Age (years) 36.3 ± 4.1 37.0 ± 4.3 36.7 ± 4.0 0.09

Live birth rate (%) 57.5 54.0 48.1 0.1

Miscarriage rate (%) 8.8 9.6 11.6 0.8

Support: None.

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The effect of interleukin 6 on controlled ovarian stimulation results and IVF outcome in infertile women with adenomyosis undergoing IVF.

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The effect of interleukin 6 on controlled ovarian stimulation results and IVF outcome in infertile women with adenomyosis undergoing IVF.

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CELL FREE DNA IS AN IDEAL OVARIAN RESERVE MARKER FOR LOW OVARIAN RESPONSE FOR STIMULATION. Siddhartha Nagireddy, MCh/Reproductive medicine and Surgery, a Lahari Katneni, MS (Ob & Gyn), b Assistant Professor, Sri Ramachandra Institute of Higher Education and Research, Chennai, India; c 25-19-10 N R Peta West Godavari District, Eluru, India.

OBJECTIVE: Primary: 
- To find the correlation of cfDNA to ovarian reserve in ICSI cycles. 
Secondary: 
- To correlate cfDNA with other markers of ovarian reserve.
- To establish a cut-off of cfDNA level for predicting poor ovarian response.

DESIGN: This prospective study.

MATERIALS AND METHODS: 65 serum samples collected at day 3 of menstrual cycle from patients undergoing ICSI procedure. FSH, Anti-Mullerian hormone (AMH) and cfDNA levels were measured in each serum sample in order to compare their predictive value for patient’s ovarian response to stimulation.

RESULTS: Cell-free DNA concentrations (mean ± SD: 23.88 ± 39.78 ng/ml) were significantly and positively correlated with patient's FSH (r = 0.175, p = 0.053), negative correlated with AFC (r = 0.339, p = 0.055) and AMH (r = -0.178, p = 0.001). Cell-free DNA level was significantly correlated to the number of oocyte retrieved (p = 0.0001). cfDNA level in peer were predicted in low responder (Number of oocytes retrieved < 6). ROC curve were plotted for no of oocyte retrieved and cf DNA levels in serum (AUC = 0.87), which predicted cfDNA response in low ovarian reserve patient with sensitivity of 80.8% and specificity of 98.6%.

CONCLUSIONS: cfDNA level on 3 day of cycle in serum can predict the ovarian reserve to stimulation. It can independently identify ovarian reserve cut off more the 37.5 is used by identifying high amount of cfDNA in serum.

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IS THE ‘OESTRO-ANDROGENIC’ HORMONE DEHYDROEPIANDROSTERONE SULPHATE (DHEAS) THE INTRACRINE REGULATOR OF IMPLANTATION AND EARLY PREGNANCY?: A PROSPECTIVE STUDY IN WOMEN UNDERGOING IVF. Bindu N. Chimote, M.Sc., M.Phil, Ph.D.(Biochemistry); M.Sc. Clinical Endymology (Leeds-UK), a Natchandra Manoharrao Chimote, M.Sc., Ph.D.,b Consultant Clinical Embryologist, Nagpur, India; c Scientific Director, Vaunshdhara Fertility Centre, Nagpur, India.

OBJECTIVE: Decidualization of endometrial-stroma is necessary for successful implantation. Very high levels of dehydroepiandrosterone (DHEA), which inhibit endometrial-stromal cell differentiation via prevention of glucose-flux through pentose-phosphate-pathway, could be a probable cause for higher incidence of implantation failure among PCOS women. Contrarily, low DHEA women with diminished ovarian-reserve, when supplemented with DHEA show significant reduction in early miscarriage rates. Sulphonated-DHEA (DHEAS) is more stable than DHEA and is the most abundant circulating ‘oestro-androgenic’ steroid precursor for estrogen production in humans. Objective of this study was to evaluate significance of innate, endogenously circulating DHEAS during implantation in predicting implantation failure/early miscarriage in eumenorrheic women undergoing IVF.

DESIGN: Prospective pilot study of n = 145 non-PCOS eumenorrheic normo-responder women undergoing conventional antagonist stimulation protocol IVF. All cycles involved day 5 fresh, elective single-blastocyst transfer (eSTB). Luteal phase support was provided to all women.

MATERIALS AND METHODS: Serum DHEAS levels in baseline as well as day 7, day 14 post-eSTB were measured by radio-immuno-assay using diagnostic kits. Serum estradiol, β-hCG and progesterone levels were also measured on day 7/day14 post-eSTB. β-hCG measurement on d7 of eSTB was considered early indicator of pregnancy. Implantation rate, live-birth rate were main outcome measures. Cycles were classified based on the outcome of live birth (LB, n = 52), biochemical pregnancy (BEP, n = 5), early miscarriage (EM, n = 6), no implantation (NI, n = 77). Statistical analysis was done using Graph-pad Prism VI software. Sample size was devised to give >80% power to the study.

RESULTS: Overall rates of LB, BCP, EM and NI were found to be 37.14%, 3.57%, 4.28%, and 55% respectively. DHEAS levels depicted a steady rise from baseline to d7 to d14 post-eSTB in women with LB (174±12.23 vs. 355±37.15 vs. 741±54.38 respectively). Although a rising trend was also observed in women with EM, the rise from baseline to d7 post-eSTB was rather steep (73.25±3.4 vs. 255.5±7.5 vs. 280.71±11.4). However, the rising pattern was disrupted in BCP cycles where the levels dropped from baseline to d7 and then increased on d14 post-eSTB (227±28.9 vs. 121±5.2 vs. 270±10.98); and in NI cycles where a sharp rise on d7 was followed by a decrease in levels on d14 post-eSTB (218.4±11.62 vs. 1380±131 vs. 801.7±98.8). A significant difference in the ratio of d7/baseline DHEAS levels was observed in LB vs. BCP vs. EM vs. NI cycles (2.3 vs. 0.53 vs. 3.5 vs. 6.3; p = 0.0005). Similarly, the ratio of d14/d7 DHEAS levels differed significantly in LB vs. BCP vs. EM vs. NI cycles (2.1 vs. 2.23 vs. 1.1 vs. 0.58; p < 0.0001). Thus, a twofold rise in DHEAS levels from baseline to d7 and d7 to d14 is critical for successful implantation leading to a live-birth.

CONCLUSIONS: Maintenance of a steady/balanced rise in serum DHEAS levels is an early indicator of successful implantation and predicts implantation-failure/early miscarriage in eumenorrheic women undergoing IVF.

SUPPORT: None.

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HIGH PINK1 EXPRESSION RELATED TO AGEING IN CUMULUS CELLS IS ASSOCIATED WITH ASSISTED REPRODUCTIVE TECHNOLOGY OUTCOME. Chia-Jung Li, Ph.D. Department of Obstetrics and Gynecology, Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan.

OBJECTIVE: Is high PINK1 expression associated with ageing in granulosa cells as well as assisted reproductive technology (ART) outcome, and what is the underlying mechanism of action of PINK1?.

DESIGN: Experimental laboratory study.

MATERIALS AND METHODS: In a prospective study, fresh granulosa cells were obtained from 48 women aged 20–40 years who underwent IVF with embryo transfer and who were divided into two groups: the diminished ovarian reserve (DOR) group (n = 20) and the control group (n = 28). Patient characteristics including age, infertility duration, body mass index, FSH, anti-Mullerian hormone (AMH) and cumulus cell PINK1 expression levels, autophagy, mitochondrial mass were analysed.

RESULTS: The DNM1L in the DOR group is activated and the PINK1 is translocated to the outer membrane of the mitochondria, and the formation of lysosomes is increased, thereby increasing the mitophagy. We also observed a significant reduction in the mass of the mitochondria in the DOR group and a severe imbalance in mitochondrial dynamics.

CONCLUSIONS: High PINK1 expression levels in cumulus cells were related to ageing, which may be involved in the clinical outcome of ART by promoting cell death and affecting mitochondrial function.

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PREGNANCY OUTCOMES OF PATIENTS WITH A CONGENITAL DIDEPHYS UTERUS: AN ANALYSIS OF 76 WOMEN FOLLOWING IN VITRO FERTILIZATION EMBRYO TRANSFER. Jingzi Xiao, Master, Xihong Li, MD./Ph.D, Yan Ouyang, MD./Ph.D, Yuyao Mao, Master Reproductive and Genetic hospital of Citech-Xiangya, Changsha, China.

OBJECTIVE: To evaluate the pregnancy outcomes in women with a didephys uterus after in vitro fertilization-embryo transfer (IVF-ET).

DESIGN: A retrospective analysis.

MATERIALS AND METHODS: Seventy six women with a didephys uterus who obtained clinical pregnancies via IVF-ET from September 2005 to December 2017 were retrospectively analyzed. The pregnancies included 56 cases of singleton pregnancies and 20 cases of twin pregnancies. In addition, there was 1 case of monochorionic twins among the twin pregnancies. Pregnancy outcomes including the rates of preterm delivery, cesarean section, live birth and perinatal mortality, birth weight, etc were analyzed.

RESULTS: In the patients with a didephys uterus, the total miscarriage rate was 18.4% (14/76); the early pregnancy loss rate was 15.8% (12/76), and the late miscarriage rate was 2.6% (2/76). The rates of preterm delivery and term delivery were 27.6% (21/76) and 53.9% (41/76), respectively.
The number of babies born was 75, including 67 cases of live births and the live birth rate was 76.3% (58/76) (80.4% in singleton (45/56) and 65% in twin (13/20) pregnancies). The overall perinatal mortality was 10.7% (8/75), including 2 cases of still birth and 6 cases of neonatal death. There was a high cesarean section rate with 75.8% (47/62), and the rate of low live birth weight was 34.3% (23/67). Furthermore, the rate of very preterm birth was 11.3% (7/62) and the average gestational age at delivery was 31.5 ± 7.5 weeks of gestation.

Among the twin pregnancies, there was 1 case received selective reduction, unfortunately, the women suffered a miscarriage in the 2nd month of gestation.

CONCLUSIONS: The pregnancy outcomes of a didelphys uterus in women who underwent IVF-ET were associated with an increased incidence of premature delivery, perinatal mortality, low live birth weight and low gestational weeks at delivery, but the live birth rate was relatively satisfactory.

**TABLE. Pregnancy outcomes of didelphys uterus**

<table>
<thead>
<tr>
<th>Number</th>
<th>76</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miscarriage rate</td>
<td>18.4% (14/76)</td>
</tr>
<tr>
<td>early pregnancy loss</td>
<td>15.8% (12/76)</td>
</tr>
<tr>
<td>late miscarriage</td>
<td>2.6% (2/76)</td>
</tr>
<tr>
<td>Preterm delivery</td>
<td>27.6% (21/76)</td>
</tr>
<tr>
<td>Term delivery</td>
<td>53.9% (41/76)</td>
</tr>
<tr>
<td>Babies born</td>
<td>75</td>
</tr>
<tr>
<td>Live births</td>
<td>67</td>
</tr>
<tr>
<td>Perinatal mortality</td>
<td>10.7% (8/75)</td>
</tr>
<tr>
<td>Caesarean section rate</td>
<td>75.8% (47/62)</td>
</tr>
<tr>
<td>Live birth rate</td>
<td>76.3% (58/76)</td>
</tr>
<tr>
<td>Gestational age at delivery</td>
<td>31.5±7.5</td>
</tr>
<tr>
<td>&lt;37week</td>
<td>33.9% (21/62)</td>
</tr>
<tr>
<td>20-32week</td>
<td>11.3% (7/62)</td>
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<tr>
<td>Live birth weight&gt;2500g</td>
<td>65.7% (44/67)</td>
</tr>
<tr>
<td>&lt;2500g</td>
<td>34.3% (23/67)</td>
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</tbody>
</table>

**P-209** Tuesday, October 15, 2019 6:30 AM

**IS FIRST TRIMESTER SUBCHORIONIC HEMORRHAGE ASSOCIATED WITH ADVERSE PREGNANCY OUTCOMES AFTER IN VITRO FERTILIZATION?** Kelsey Anderson, MD, Emily S. Junghem, MD, MSCI, Patricia T. Jimenez, MD, Kenan Omurtag, MD, Washington University School of Medicine, St. Louis, MO.

**OBJECTIVE:** To determine the association between incidental SCH on ultrasound and pregnancy outcomes in IVF pregnancies.

**DESIGN:** Prospective cohort study.

**MATERIALS AND METHODS:** His was a retrospective cohort study of women identified from a first-trimester ultrasound database kept for IVF pregnancies from 2009 to 2017. Women with a viable first trimester pregnancy after fresh or frozen embryo transfer were included. Exclusion criteria were absence of heartbeat on ultrasound, gestational carriers, women who used donor eggs or who had a multiple gestation pregnancy. The primary outcome was live birth and secondary outcomes included spontaneous abortion, preterm delivery and infant weight at delivery. Appropriate bivariate analyses were performed followed by a multivariate regression model to further investigate associations between significant covariates and outcomes. All analyses were performed in SPSS.

**RESULTS:** 1004 women met criteria and 18.6% had a SCH. In bivariate analysis, SCH was not risk factor for decreased live birth (87.5% vs 90.2%, OR 0.7, 95% CI 0.2-1.1) or increased preterm birth (90.1% vs 85.9%, OR 0.7, 95% CI 0.4-1.2) or SAB (12.5% vs 9.3%, OR 1.4, 95% CI 0.9-2.3) There was also no difference in fetal weight with those with SCH (3334g vs 3269g, p=0.224) and only increasing maternal age was negatively associated with live birth (32.8 vs 34.7 p<0.001). In multivariate regression analysis, all outcomes were still not statistically significant although those with SCH tended to have fewer live births (aOR 0.4, 95% CI 0.2-1.1) and higher rates of SAB (aOR 2.6, 95% CI 1.0-6.9).

**CONCLUSIONS:** Incidentally detected subchorionic hemorrhage on first trimester ultrasound is not associated with infant birth weight or probability of live birth or preterm birth after IVF. This information may be reassuring to IVF patients with SCH and otherwise viable pregnancy noted on first trimester ultrasound.

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**PEROXIREDOXIN 4, A NEW OXIDATIVE STRESS MARKER IN FOLLICULAR FLUID MAY PREDICT IVF OUTCOMES.** Yi Qian, PhD, Yan Meng, MD, Jiayin Liu, MD, State Key Laboratory of Reproductive Medicine, Clinical Center of Reproductive Medicine, Nanjing, China.

**OBJECTIVE:** For better predicting in vitro fertilization (IVF) outcomes, it is necessary to identify some non-invasive and sensitive markers. Studies indicated that oxidative stress status in patients was closely associated with IVF outcomes, while the results are still controversial. Prdx4 as one member in Prdx family, can catalyze the reduction of reactive oxygen species. While little data on the relationship of Prdx4 and female reproduction were demonstrated.

**DESIGN:** Our study is a prospective clinical study.

**MATERIALS AND METHODS:** All participants were recruited in the center of clinical reproductive medicine from September 2017 to December 2018. Infertile women with either tubal factor or male factor (n = 138) undergoing controlled ovarian hyperstimulation and IVF were recruited in our study. FF samples from patients were collected on the day of oocyte collection and then centrifuged and frozen up for analysis. Prdx4 concentration in FF were measured in each participant. Furthermore, the correlation between Prdx4 level and IVF outcomes, such as clinical pregnancy rate and oocyte quality was analyzed. And subsequently, we divided all participants into three groups according to their levels of Prdx4 in FF (low, moderate and high group), then the clinical pregnancy rate and oocyte quality outcomes were all analyzed.

**RESULTS:** The pregnant women had higher levels of Prdx4 in FF than non-pregnant women. Prdx4 was positively correlated with oocyte fertilization rates (r = 0.326; p = 0.013) and good quality embryo rates (r = 0.334; p = 0.011). Furthermore, we found the pregnancy rate was positive correlated to Prdx4 level with a concentration dependent manner in three groups (pregnancy rate were 28.1%, 46.8% and 70.3% in low, moderate and high group, respectively). In the oocyte quality outcomes, the fertilization rates were significantly higher in the high group than the low group (p < 0.01), and the good quality embryo rates of moderate (p < 0.01) and high (p < 0.01) groups were significantly higher than the low group.

**CONCLUSIONS:** Our results provide evidence that the upregulated expression of antioxidants in IVF patients follicular fluid (FF), such as Prdx4, tend to increase the potential pregnancy via oocyte quality mechanism.

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**FOLLICULAR FLUID (FF) CONCENTRATION OF ANTI-MULLERIAN HORMONE (AMH) IN WOMEN PURSUING IN VITRO FERTILIZATION (IVF): VARIABILITY AND PREDICTORS.** Caitlin R. Sacha, MD, Lida Minguéz-Alarcón, PhD, Jorge E. Chavarro, PhD, Jennifer B. Ford, RN, Patricia K. Donahoe, MD, Irene Souther, MD, Russ Hauser, MD, MPH, Sc.D., David Pepin, PhD, MGH Fertility Center and Harvard Medical School, Boston, MA; Harvard T.H. Chan School of Public Health, Boston, MA; Harvard School of Public Health, Boston, MA; MGH Pediatric Surgical Research Laboratories, Boston, MA.

**OBJECTIVE:** To investigate the correlation of follicular fluid (FF) AMH concentrations between pre-ovulatory follicles within and between IVF cycles, and the association of FF AMH with demographics and reproductive characteristics.

**DESIGN:** Prospective cohort study.

**MATERIALS AND METHODS:** FF was analyzed from 2 or 3 pre-ovulatory follicles in 162 women (1 to 3 IVF cycles, 2-13 months apart) enrolled in the Environment and Reproductive Health (EARTH) Study at Massachusetts General Hospital Fertility Center (2010-2016). AMH concentration was quantified from a total of 217 cycles using a sandwich enzyme-linked immunosorbent assay (ELISA) method and corrected for sample volume. Spearman correlation was used to assess the correlation of FF AMH concentrations between follicles, and intra-class correlation (ICC) was calculated to
assess variability of mean cycle FF AMH concentrations between IVF cycles for each woman and between participants. Mean cycle FF AMH concentrations were then divided into tertiles (T1-T3), and Kruskal-Wallis and x²-tests were applied as appropriate to explore associations of demographic and reproductive characteristics across tertiles.

RESULTS: The mean FF AMH concentration was 1.20 ng/ml (range = 0 to 24.0 ng/ml). There was high correlation between follicles within each IVF cycle (Spearman r = 0.78 to 0.86), and ICC indicated low within-woman variability of mean cycle FF AMH concentrations [0.87 (95% CI 0.81 to 0.92)]. Compared to women in T1 of FF AMH concentrations (0.2 ng/mL), on average women in T3 (2.3 ng/mL) were younger (mean age in T3 = 33.5 vs. T1 = 36.0 years, p = 0.04), leaner (mean body mass index (BMI) in T3 = 22.4 vs. T1 = 24.5 kg/m², p = 0.04), had higher serum AMH concentrations (mean in T3 = 0.6 vs. T1 = 0.1 ng/mL, p = 0.0001), and lower day-3 follicular stimulating hormone (FSH) levels (mean T3 = 6.4 vs. T1 = 7.0 IU/L, p = 0.03). Although most diagnoses were similar across tertiles of FF AMH concentrations, as expected, women in T3 were more often diagnosed with ovulatory disorders compared to women in T1 (T3: 17% vs. T1: 4%, p = 0.30). Smoking, education, and peak estradiol levels were not significantly associated with pre-ovulatory FF AMH concentrations.

CONCLUSIONS: We observed that pre-ovulatory FF AMH concentrations are highly correlated within an IVF cycle and that within-woman variability is low across cycles, suggesting that a dominant follicle’s AMH concentration may reflect a woman’s overall FF AMH concentration. Furthermore, mean cycle FF AMH concentrations were associated with other markers of ovarian reserve, suggesting a possible role in predicting future reproductive outcomes.

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IMPACT OF ACUPUNCTURE ON OUTCOMES FOLLOWING FROZEN EUPLOID BLASTOCYST ESET. Nancy L. Bossert, PhD, a Hannah Van Der Geest, BS, a April Batcheller, MD, a William B. Schoolcraft, MD, a Jason E. Swain, PhD. 1. CCRM Minneapolis, Edina, MN; 2. Colorado Center for Reproductive Medicine, Lone Tree, CO; 3. CCRM Fertility Network, Lone Tree, CO.

OBJECTIVE: The use of acupuncture in IVF has gained widespread acceptance, with numerous clinics offering this technique during embryo transfer. A clear consensus as to whether acupuncture improves outcomes does not exist and analysis is complicated due to confounding variables. The objective of this study was to determine if acupuncture provided at the time of frozen embryo transfers using single euploid blastocysts demonstrated any benefit compared to no acupuncture treatment.

DESIGN: Retrospective data analysis.

MATERIALS AND METHODS: Data were collected over a 4 year time period from 2015-2019. All lab conditions were the same for the duration of the study period and monthly quality control analysis confirmed no significant variations. Controversy exists over whether the largest follicle(s) or the complete cohort of follicles best predicts outcome for IVF. Past efforts have concentrated on predictors of pregnancy and live birth following IVF with fresh transfer. Now there is increasing interest in retrieving oocytes for cryopreservation or for embryo production with preimplantation genetic testing for aneuploidy (PGT-A). It remains unclear whether there is a preferred size of follicles to obtain euploid oocytes or oocytes that will become euploid blastocysts.

MATERIALS AND METHODS: Consented oocyte donors (N = 22) underwent retrieval of oocytes, one-by-one, from follicles with diameters measured during the retrieval. Oocytes were cultured individually, fertilized by intracytoplasmic sperm injection (ICSI) and monitored for development. Quality blastocysts, achieving Gardner grades of AA, AB, BA, BB or BC, underwent trophectoderm biopsy on days 5 or 6 and biopsies were sent to a commercial PGT-A lab in the US. Results of maturity, fertilization, development and ploidy were considered with reference to the size of the follicle from which the oocyte was retrieved. Analysis of data involved Student’s T tests, and receiver operating characteristic (ROC) curves with significance determined using Mann-Whitney U test.

RESULTS: Oocytes were retrieved from follicles with measured diameters averaging 17.4 +/- 2.9 mm (N = 315). Of the oocytes, 80.4% had 1 polar body (MII), 9.8% had a germinal vesicle (GV) and 9.1% had neither a polar body nor a GV (MI). The sizes of the follicles from which these oocytes came were significantly different: MII, 18.3 +/- 2.2 mm; GV, 12.5 +/- 1.6 mm; and MI, 15.3 +/- 3.2 mm. ROC curves indicated that follicle diameter was a “grade A” predictor of GV oocytes (AUC = 0.96; P < 0.0001, Mann-Whitney U test) and a “grade B” predictor of MII oocytes (AUC = 0.87; P<0.0001, Mann-Whitney U test). Among MII oocytes, follicle size did not predict fertilization by ICSI (ROC AUC = 0.54, not significant), formation of quality blastocysts (ROC AUC = 0.53, not significant), or blastocyst ploidy ROC AUC = 0.53, not significant.

CONCLUSIONS: Significant AUCs for ROC curves indicate that follicle diameter is an excellent predictor of oocyte maturity. However the diameter of the follicle from which an MII oocyte was retrieved did not predict its quality as assessed by its fertilizability with ICSI, its ability to develop into a quality blastocyst or its ploidy. Whereas follicle diameter can predict maturity of the oocytes retrieved from them quite well, follicle diameter is a poor predictor of oocyte quality including blastocyst ploidy. Since oocyte ploidy was not directly assessed, it remains unclear whether oocyte ploidy is associated with follicle diameter. However, with most embryo aneuploidy arising from errors in meiosis, we believe that follicle size is unlikely to be a good predictor of oocyte ploidy.

SUPPORT: None.
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THE PREVIOUS CESAREAN DELIVERY DOESN'T AFFECT THE PROGNOSIS OF IVF-ET: A LARGE SAMPLE RETROSPECTIVE CASE CONTROL STUDY. Shao Yang, MD, Peking University Third Hospital, Beijing, China.

OBJECTIVE: To investigate whether the previous cesarean delivery would affect the treatment outcomes of multiparities accepted IVF/ICSI-ET.

DESIGN: Retrospective case control study of one reproductive medical center, from 1 Jan. 2009 to 31st Dec. 2015. The main outcome measures were Clinical pregnancy rate (CPR) and Live birth rate (LBR).

The study group (Group 1) were patients with previous cesarean section history, the control group (Group 2) were patients with history of vaginal delivery.

MATERIALS AND METHODS: This is a retrospective case control study, and data collection protocol was approved by the hospital ethics. All patients were multiparities, the study patients with previous cesarean section history, the control group (Group 2) were patients with history of vaginal delivery. MatchIt package of R software was used for propensity score matching. The matching factors were age, number of oocytes retrieved and treatment time. According to 1:2 matching, the nearest neighbor matching method was used.

RESULTS: There were 461 cycles were included in the Group 1, and matched with 922 multiparities for the Group 2. The basic characteristics of patients refers to age, BMI, basal FSH and AFC were with no significantly difference. The initial dose of Gn was comparable between two groups, but the day of Gn injection was longer in control group and the total dose of Gn was higher too (11.3±2.4 vs. 11.9±2.7 P<0.001, 3328.5±1422.8 vs. 3595.9±1503.5, P<0.05, respectively).

The number of oocytes peek-up, the rate of ICSI, MII oocyte and 2PN embryo plantation rate on oocyte recipient pregnancy achievement in recipient cycles, allowing continuous improvement in outcomes.

CONCLUSIONS: The multiparities with history of Cesarean section accepted IVF/ICSI treatment, got similar outcomes compared with those with history of vaginal delivery.

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OOCYTE DONOR IMPLANTATION AND PREGNANCY RATES PREDICT OOCYTE RECIPIENT PREGNANCY CHANCE IN AN EGG-SHARING DONATION PROGRAM. Daniela Paes de Almeida Ferreira Braga, PhD,a Amanda Souza Setti, MSc,b Mathes de Castro Azevedo, BSc,b Assampto Iaconelli, Jr., MD,c Edison Borges, Jr., PhD,d Fertility Medical Group / Sapientiae Institute, Sao Paulo, Brazil;e Fertility Medical Group, Sao Paulo, Brazil.

OBJECTIVE: Studying oocytes from the same cohort submitted to different situations may provide greater insight into possible predictors of pregnancy in recipient cycles, allowing continuous improvement in outcomes.

The objective of this study was to investigate which are the predictive factors of successful pregnancy in oocyte recipient intracytoplasmic sperm injection (ICSI) cycles in an egg-sharing donation program.

DESIGN: Historical cohort study.

MATERIALS AND METHODS: This study was performed in a private university-affiliated IVF center. Analyzed data were obtained via chart review of 1505 vitrified oocytes donated to 225 oocyte recipients undergoing 307 ICSI cycles, participating in an egg-sharing donation program, between January/2015 and May/2017. For that sample size, computed achieved post-hoc power was 100%, considering pregnancy achievement as the main outcome measure. Donors were between the age of 19 and 34 years, and recipients were between the age of 26 and 50 years. Adjusted generalised linear models were used to investigate the impact of oocyte donors and recipients characteristics on recipients’ pregnancy achievement. The results are expressed as exponentiation of regression coefficient (ExpB), 95% confidence interval (CI), and p-value. A receiver operating characteristic (ROC) curve was constructed to investigate the predictive value of oocyte donor implantation rate on oocyte recipient pregnancy chance.

RESULTS: Implantation rate in oocyte donor was highly correlated with pregnancy achievement in oocyte recipient cycles (ExpB: 1.181, CI: 1.138 – 1.226, p < 0.001). The ROC curve analysis demonstrated that the implantation rate in oocyte donor has a strong predictive value on the achievement of pregnancy in oocyte recipient area (under the curve: 0.98, CI: 0.95 - 0.99, p < 0.001).

The achievement of pregnancy in oocyte donors and recipients were highly associated (ExpB: 3.46, CI: 28.7 – 105.8, p < 0.001), irrespective of oocyte recipient age. Oocyte donor age, body mass index, number of follicles, retrieved oocytes, total dose of FSH administered and estradiol peak were not associated with oocyte recipient pregnancy achievement. In oocyte recipients, no association was found between the fertilization rate and the achievement of pregnancy, but the high-quality embryos rates on days 2 (ExpB: 3.397, CI: 1.635 – 7.054, p= 0.001) and 3 (ExpB: 6.629, CI: 1.185 – 37.092, p= 0.031), and blastocyst development rates (ExpB: 2.331, CI: 1.086 – 5.001, p= 0.030) were positively associated with pregnancy achievement.

CONCLUSIONS: Oocyte donor implantation rate and successful pregnancy, high-quality embryos rate, and blastocyst development rate predict pregnancy achievement in the oocyte recipient cycle. The strong association in pregnancy success between donors and recipients, and the lack of correlation between donor characteristics and cycles’ outcomes, demonstrates the power of oocyte quality on the success of ICSI treatment.

Reference: NA.

SUPPORT: None.

P-216 Tuesday, October 15, 2019 6:30 AM

NATURAL VERSUS MANAGED NATURAL CYCLE PRIOR TO FET: A RANDOMIZED CONTROLLED TRIAL. Shari Mackens, MD,a Alexandre Marie Stubbe, MD,b Samuel Santos-Ribeiro, MD, PhD,c Arne van de Vijver, MD, PhD,d Herman Tournaye, MD, PhD,e Christophe Blockeel, MD, PhD,f Universitair Ziekenhuis Brussel, Jette, Belgium;gIVI-RMA Lisbon, Lisbon, Portugal;hAZ Sint-Jan, Brugge, Belgium.

OBJECTIVE: To determine whether a NC-FET is superior to a managed NC-FET.

DESIGN: This randomized controlled trial (RCT) included patients transferring a cleavage stage vitrified/warmed embryo in a natural cycle between January 2014 and December 2018. Women were randomized to receive spontaneous luteinizing hormone (LH) surge (NC) or to trigger ovulation by a single injection of human chorionic gonadotropin (hCG) (managed NC). None of the patients received additional luteal phase support. The primary outcome was ongoing pregnancy rate (OPR). Secondary outcomes included biochemical pregnancy rate, early pregnancy loss and the number of visits, blood samples and ultrasonographic exams prior to embryo transfer.

MATERIALS AND METHODS: A total of 260 subjects were randomized (130 per study arm), with 229 actually starting monitoring for the study-FET (117 allocated to spontaneous LH surge and 112 to hCG injection). Seven patients needed to be switched to a hormonal replacement treatment protocol due to the absence of follicular development, 12 had no embryo available for transfer after warming and 37 had a spontaneous LH surge before hCG injection although they were allocated to the induced ovulation group following the study protocol stating hCG injection could be performed once endometrial thickness reached 7mm and the dominant follicle 17 mm.

RESULTS: The study groups did not significantly differ in baseline patient characteristics, nor in relevant variables of the fresh cycle generating the vitrified/clear stage embryo(s). Regarding the study-FET, circulating serum estradiol and progesterone values were comparable in both groups, as was the last measured endometrial thickness before embryo transfer and the rate of single versus double embryo transfer. Intention-to-treat (ITT), nor per protocol (PP) analysis revealed any statistically significant difference in OPR, biochemical pregnancy rate or early pregnancy loss of NC-FET in terms of whether ovulation was spontaneous or triggered. Respectively, the primary outcome parameter OPR was 27.4% vs 25.9% (p=0.80) for ITT and 29.1% vs 20.2% (p=0.38) for PP analysis. However, patients in the managed NC-FET group had significantly fewer visits to the clinic and blood samples performed than the NC-FET group (3.03 ±1.16 vs 4.05±1.40, p<0.001).

CONCLUSIONS: This RCT adds new high quality evidence to the existing controversial literature concerning the performance of NC-FET versus managed NC-FET. Based on our results showing equal clinical outcomes for both protocols, we propose to by default plan patients for managed NC-FET, as this is associated to one visit less for blood sampling and is thus more patient-friendly.

Reference: NA.

SUPPORT: NA.
P-218 Tuesday, October 15, 2019 6:30 AM

IVF PREGNANCY RATES IN WOMEN UNDERGOING ACUPUNCTURE VS. CONTROLS. Phyllis L. Jennifer, DO,1 Yan Zhang, PhD,2 Idit Blais, MSce,2 Sergei Shnizer, MD, PhD,2 Mara Koifman, MSc,2 David Ishitai, MD,2 Ido Feferkorn, MD,2 Sivan Skvisky, MD,2 Martha Diminfeld, MD2 Head of Fertility and IVF Unit, Haifa, Israel; Affiliation not provided; 2Head of IVF Lab, Haifa, Israel; 2Carmel Medical Center IVF Lab, Haifa, Israel; 2Senior consultant, Haifa, Israel; 2Carmel medical center, Haifa, Israel; 2Faculty of Medicine Technion, Haifa, Israel.

OBJECTIVE: To evaluate a possible association between oxidative parameters in COC medium as measured by Thermochromiluminescence (TCL) assay and outcome parameters in IVF.

DESIGN: A prospective cohort study.

MATERIALS AND METHODS: Sixty four women undergoing a fresh IVF cycle using conventional oocyte insemination during 2017-2019 participated in the study. COCs were incubated in a well containing 680 μl of culture media for approximately 4-6 hours. Immediately prior to addition of semen, 20 μl of COC culture media were removed from each dish, examining for each sample 4 parameters: TCL amplitudes, after 50 seconds (TCLH1), 150 seconds (TCLH2), 250 seconds (TCLH3) and TCL ratio ((TCLH3-TCLH1)/100). TCL amplitudes were measured as counts per second (CPS).

RESULTS: We examined 97 COC fertilization media. Mean patients’ age was 38 ±4.7 years. Mean number of aspirated oocytes, COCs per well and number of wells per patient were 6.2±3.7, 4.6±2.0 and 1.48±0.5 respectively. Of 64 IVF cycles, 32.4% were not fertilized, 13 cycles (12.7%) no embryos developed and 8 (12.7%) cycles, all embryos were frozen. Altogether fresh embryos were transferred in 46 cycles. Twenty one pregnancies were achieved (33.3% per started cycles, or 45.9% per embryo transfer cycle). In order to find an optimal cutoff that would distinguish between TCL values that were associated with higher chances of pregnancy, Youden index used. A discriminatory TCLH2 value of >62.9 CPS was associated with higher chances for pregnancy (46.5% vs. 8.3%, OR=0.72, p<0.05). This value had a 95.2% sensitivity (95% CI=76.2-99.9), 32.4% specificity (95% CI=17.4-50.5), a positive predictive value of 46.5% (95% CI=31.2-62.3) and a negative predictive value of 91.7% (95% CI=61.5-99.8). No association was found between TCL parameters, regrading patient’s age and number of aspirated oocytes. Multivariate analysis, correcting for age and number of aspirated oocytes, revealed that TCLH2 >62.9 was the only significant variable associated with the occurrence of pregnancy (p<0.03).

CONCLUSIONS: Oxidative parameters of COC medium may affect the likelihood of pregnancy. Measurement of oxidative parameters may serve as a potential aid in prediction of treatment outcome.

P-220 Tuesday, October 15, 2019 6:30 AM

RISK OF PREGNANCY FAILURE IN AN OPTIMIZED UTERINE ENVIRONMENT: LIVE BIRTH RATE FROM PGT-A EUPLOID EMBRYOS IN A PROVEN UTERUS. Renee N. Rivas, MD, PhD,f Michael K. Simoni, MD,a Alan S. Penzias, M.D.,b Denny Sakkas, PhD,bs Pasquale Patrizio, M.D. A Yale New Haven Hospital, New Haven, CT; bBoston IVF, Waltham, MA; aYale Fertility Center, New Haven, CT.

OBJECTIVE: Assess the magnitude of the pregnancy failure rate from the transfer of euploid embryos after Pre-implantation Genetic Testing for Aneuploidy (PGT-A) into a proven uterine environment. An optimal uterine environment, or...
proven uterus, is defined as a live birth ensuing from a multiple embryo transfer (MET) where at least one embryo results in a successful birth. While PGT-A has been shown to increase the success rate of live birth, the remaining failure rate can still be due to a multitude of factors. This study seeks to control for the uterine environment to minimize the remaining chance of failure for the cycle.

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** Using all completed MET cycles at our academic fertility center at Yale and from Boston IVF from 2012-2017, we identified 3,680 embryos transferred in 1,726 cycles to a proven uterus. Percentage of embryos not implanted in a proven receptive uterus utilizing PGT-A was compared to those transferred without using PGT-A. Difference of proportions analysis using a one-tailed Z-test compared the percentage lost among proven-uterus that utilized PGT-A to cycles that did not.

**RESULTS:** Based on the data from these two centers, forty-six of 1,726 cycles (2.7%) transferred multiple embryos after PGT-A to a proven uterus. These cycles resulted in 30/87 embryos (34.5%) failing to result in a live birth. For non-PGT-A embryos transferred to a proven receptive uterus (MET-only cycles), 1,973/593 embryos (54.9%) did not result in a live birth. The difference of proportion of embryos failing to result in a live birth between proven uterus cycles that utilized PGT-A was statistically significant when compared to controls without PGT-A (p = 0.000008).

**CONCLUSIONS:** The false negative rate of PGT-A testing, whereby euploid embryos transferred into a receptive uterus (since in the same cycle sibling embryos had implanted and produced a live birth), is 34.5%. This study eliminated the endometrium as a cause for the failed implantation of euploid embryos and adds support to the inability of PGT-A to completely correctly identify suitable embryos for transfer. Ongoing research may help establish the false-negative rate of PGT-A and understand whether genetic mutations, non-chromosomal or developmental errors could be responsible for the lack of implantation and live birth.

**SUPPORT:** None.

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**P-221 Tuesday, October 15, 2019 6:30 AM**

**MITOCHONDRIAL REPLACEMENT THERAPY GIVE NO BENEFITS TO PATIENTS OF ADVANCED MATERNAL AGE.**

**AGE:** Pavlo Mazur, MSc, Lada Dyachenko, MSc, Yuliya Masliy, PhD, Maksym Borysov, PhD, Dmytro O. Mykytenko, MD, DSc, Valery Zukin, MD, Darwin Life Nadiya, Kyiv, Ukraine; Na-diya Clinic, Kyiv, Ukraine; LLi Darwin Life-Nadiya, Kyiv, Ukraine.

**OBJECTIVE:** To determine if mitochondrial replacement therapy (MRT) could increase blastulation rates, euploidy rates and pregnancy rate in patients of advanced maternal age (AMA).

**DESIGN:** The study period was from December 2015 to November 2018. Patients were informed and consent to possible risks and the experimental protocol was approved by ethics committee of local association of reproductive medicine. Inclusion criteria were: (1) no less than two failed previous IVF attempts, (2) low blastulation rates of less than 50% of embryo arrest, (3) low number or absence of euploid embryos; (4) age ≥ 37 years.

**MATERIALS AND METHODS:** 30 patients (37-47 years old, Mean age was 42±2 years) participated in this study. Five types of MRT (germinal vesicle transfer (GVT), MI spindle transfer (MIST), MI spindle transfer (MIIST), polar body 1 genome transfer (PB1GT) and pronuclear transfer (PNT)) were assisted by HVJ-E cell fusion kit. Intracytoplasmic sperm injection (ICSI) had been performed for all cases. If possible, reverse reconstitutions were done. Embryos obtained after reconstitution were cultured until blastocyst stage in time-lapse incubator, were biopsied for array comparative genomic hybridization (aCGH) or next generation sequencing (NGS) analysis and then were vitrified.

**RESULTS:** After performing various types of MRT, 109 zygotes were obtained, that resulted in 33 blastocysts (30%); 3 of which (one per patient) were euploid (2.7%). One try of elective single embryo transfer (cET) of thawed zygote resulted in 21 embryos, 3 of which (one per patient) were euploid (11%). After spontaneous pregnancy were confirmed only for one patient (42 y.o., PNT group).

The healthy baby boy was born on 15th of March 2018 by Cesarean section. After unsuccessful attempt of MRT, one of 30 patients (41 y.o.) had an euploid embryo from conventional aCGH cycle using donor sperm and the other patient (45 y.o.) became spontaneously pregnant and gave birth to a healthy baby at full term. Zygotic cytoplasmas of woman of AMA were competent enough to support normal embryonic development when patient had AME. In patients without AME, there were 41% blastulation rates and 70% euploidy rates for reversely reconstituted zygotes.

**CONCLUSIONS:** Pregnancy rate after applying MRT was lower than 1%, thereby patients of AMA should be advised not to undergone such procedures in order to increase the number of euploid embryos or pregnancy rate.

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**P-222 Tuesday, October 15, 2019 6:30 AM**

**EFFECT OF THE VAGINAL MICROBIOME ON THE PREGNANCY RATE IN PATIENTS UNDERGOING ASSISTED REPRODUCTION TECHNIQUES.**

Belen Lledo, PhD, Andrea Bernabue, PhD, Mayka Diaz, MSc, Vicente Ruiz, MSc, Francisca M. Lozano, MSc, Jorge Ten, PhD, Joaquin Llacer, PhD, Rafael Bernabue, Ph D M D, Instituto Bernabue, Alicante, Spain.

**OBJECTIVE:** Recent evidence seems to indicate that there is a relationship between the vaginal microbiome and fertility, however, it is unknown whether this effect occurs when couples undergo ART. The aim of this study is to investigate if the vaginal microbiome of the day of the transfer in couples undergo ART could affect the pregnancy rate.

**DESIGN:** A prospective study was performed. Patients attended to our clinic were recruited from May 2017 to April 2018. We included 31 patients performing PGT-A at blastocyst stage, elective embryo vitrification and single chromosomally normal embryo transfere. Vaginal samples were collected at the moment of the transfer from the posterior sac of the vagina (patients with positive pregnancy test n=17, patients not pregnant n=14).

**MATERIALS AND METHODS:** DNA was extracted using the PureLink Microbiome DNA Purification kit. Sequencing and bioinformatics analysis were performed according to Illumina Metagenomics protocol using the NexteraXT library on the MiSeq instrument. The analysis of the rRNA16S V3/V4 region and the bioinformatic tools qiime2, MicrobiomeAnalyst and Phyloseq have been used to determine the microbiome.

**RESULTS:** We obtained the vaginal microbiome from the 31 patients which 17 achieved a positive pregnancy test and 14 not achieved. A total of 7,089,699 sequences were analyzed and 116 OTUS (97% similarity) were identified. Regarding diversity analysis, the alpha diversity index Chao1 is higher in patients who did not achieve pregnancy (p<0.05). As for, the beta index a lower diversity was obtained in vaginal samples from patients that achieve a pregnancy, although without reaching statistical significance (p=0.08). Moreover, we analysed the taxonomic composition of the samples. We showed a dominance of Lactobacillus with predominance of L. crispatus (47.35%), L. helveticus (22.85%), L. iners (21.55%) and L. leucograpta (3.97%). The patients who achieved pregnancy, have higher average percentage of the genus Lactobacillus compared to those who do not. There is a correlation between the vaginal microbiomes dominated by Lactobacillus and greater reproductive success against another profile not dominated by Lactobacillus and with the presence of Gardnerella.

**CONCLUSIONS:** The patients who achieve pregnancy have a lower diversi ty than who do not achieve it. These results suggest that the presence of a low diverse vaginal microbiome predisposes to the pregnancy. Also, Lactobacillus in the vaginal microbiome seems to be key to embryo implantation and the genus Gardnerella has a negative influence on pregnancy.

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**P-223 Tuesday, October 15, 2019 6:30 AM**

**TRIGGER DAY FOLLICLE-STIMULATING HORMONE (FSH) “BOOST” INCREASES COSTS BUT DOES NOT IMPROVE OUTCOMES IN PATIENTS UNDERGOING IVF WITH PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A).**

Isaac J. Chamani, B.A., David H. McCallum, Ph.D., Frederick L. Lippiard, M.D., New York University School of Medicine, New York, NY; NYU Langone Health, New York, NY.

**OBJECTIVE:** An FSH boost on trigger-day may improve outcomes in fresh transfers by enhancing folliculogenesis and endometrial receptivity. As more patients are freezing all of their embryos, the endometrial effect is less of a concern, but folliculogenesis remains relevant. Recent reports conflict over the clinical effects of an FSH boost. We therefore examined the effect of an FSH boost on oocyte retrieval, quality, and development, specifically in patients undergoing PGT-A.

**DESIGN:** Retrospective cohort.

**MATERIALS AND METHODS:** Patients undergoing GnRH-antagonist IVF cycles from 1/2015 through 12/2018, were separated into two groups for comparison: those receiving only trigger injections on trigger day (NB), and those also receiving an FSH boost (B). Demographics, days of gonadotropin, #oocytes retrieved, #mature, #blastocysts, and #euploid embryos, were compared (Student’s t-test or X²).

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RESULTS: Both groups were stratified into SART registry age groups. Initial comparisons between the groups, without matching for trigger day estradiol levels (E2Trig), revealed a selection bias. B patients had weaker responses, with lower estradiol levels and fewer eggs. In order to examine the effect of B in each age group, we created NB comparison groups with E2Trig values indistinguishable from the B’s. This was done by randomly selecting NB patients from the same age group and E2Trig stratum as B.

1,394 patients were included in this matched comparison, 697 received B, and 697 did not. B patients had significantly more days of gonadotropin administration (~1 day) than NB patients. There were no consistent differences for #oocytes retrieved, #mature, fertilization rate, #blastocysts, or # euploid embryos (see table). Overall, costs associated with B amounted to $276,923, or close to $400 per patient.

CONCLUSIONS: No benefit of B was found for #oocytes retrieved, #mature, fertilization rates, #blastocysts, or # euploid embryos. There are significant cost savings associated with NB.


P-224 Tuesday, October 15, 2019 6:30 AM

EFFECTIVENESS OF RECOMBINANT HUMAN FOLLICLE-STIMULATING HORMONE (r-hFSH) VERSUS HUMAN MENOPAUSAL GONADOTROPIN (u-hMG) IN ASSISTED REPRODUCTIVE TECHNOLOGY (ART): A STUDY BASED ON GERMAN REAL-WORLD DATA. Klaus F. Bühler, MD,a Sandra Gaeddes, PharmD, MSc,b Arthur Allignol, PhD, Dr.c Thomas D’Hooghe, MD, PhD,b Wilma Bilger, PhD,c Emilia Richter, MD, MSc,b Klaus F. Büchler, MD, Germany; aCentre for Gynaecological, Endocrinology, and Reproductive Medicine, Ulm and Stuttgart, Germany; bKoch University School of Medicine, Istanbul, Turkey; cMerck Serono GmbH, Darmstadt, Germany.

OBJECTIVE: To compare clinical outcomes with r-hFSH (GONAL-f, Merck KGaA, Darmstadt, Germany) vs u-hMG (Menogen HP®, Ferring GmbH, Kiel, Germany).

MATERIALS AND METHODS: Oocyte donors were started 225IU/day rFSH on cycle day 2-3, 0.25mg/day GnRH antagonist and 10mg/day medroxyprogesterone acetate (MPA) was started on stimulation day 7 when the leading follicle reached 14mm, whichever came first. One mg leuprolide acetate was given when there were >3 follicles >17 mm. Oocytes were fertilized with the recipients’ partners’ sperm. Recipients were prepared in an artificial cycle, i.e. estradiol valerate 6 mg/day orally for 10 days, vaginal micronized progesterone was added 4 or 6 days before cleavage and blastocyst stage embryo transfer, respectively. Medications were continued until a negative pregnancy test or 10th gestational week. Data are defined with percentages or median (25th – 75th percentile), depending on variables. Non parametric tests and chi square test were used for comparisons.

RESULTS: 150 oocyte donors were included. 75 in each group. Donors in both groups were similar for age. None of them had premature ovulation and yielded similar oocyte and metaphase two oocytes with similar gonadotropin consumption. 86 women received oocytes from IPPOS and 105 women from ART treatment type, drugs used for ovulation triggering and luteal phase support) in the Cox proportional hazards models. In the FC analysis, log-binomial regression was adjusted for confounding factors by inverse probability of treatment weighting. Results for PP are presented as adjusted hazard ratios (HR) with 95% confidence intervals (CI) and for FC as relative risk (RR) with 95% CI.

P-225 Tuesday, October 15, 2019 6:30 AM

A NOVEL FLEXIBLE PROGESTIN PRIMED OVARIAN STIMULATION PROTOCOL: COMPARISON OF PREGNANCY OUTCOMES WITH THE FLEXIBLE GnRH ANTAGONIST PROTOCOL IN AN OOCYTE DONATION PROGRAM. Sule Yildiz, MD,a Engin Turkgeldi, MD,a Alper Eraslan, MD,a Berk Angun, MD,b Mustafa Baris Ata, M.D.c aKoc University Hospital, Istanbul, Turkey; bDunya IVF Center, Kyrenia, Cyprus; cKoc University School of Medicine, Istanbul, Turkey.

OBJECTIVE: To compare a novel flexible progestin primed ovarian stimulation (IPPOS) protocol with the flexible GnRH antagonist protocol in an oocyte donation program.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Oocyte donors were started 225IU/day rFSH on cycle day 2-3, 0.25mg/day GnRH antagonist and 10mg/day medroxyprogesterone acetate (MPA) was started on stimulation day 7 when the leading follicle reached 14mm, whichever came first. One mg leuprolide acetate was given when there were >3 follicles >17 mm. Oocytes were fertilized with the recipients’ partners’ sperm. Recipients were prepared in an artificial cycle, i.e. estradiol valerate 6 mg/day orally for >10 days, vaginal micronized progesterone was added 4 or 6 days before cleavage and blastocyst stage embryo transfer, respectively. Medications were continued until a negative pregnancy test or 10th gestational week. Data are defined with percentages or median (25th – 75th percentile), depending on variables. Non parametric tests and chi square test were used for comparisons.

RESULTS: 150 oocyte donors were included. 75 in each group. Donors in both groups were similar for age. None of them had premature ovulation and yielded similar oocyte and metaphase two oocytes with similar gonadotropin consumption. 86 women received oocytes from IPPOS and 105 women from
CONCLUSIONS: This novel IPPOS protocol seem to yield oocytes that has similar reproductive potential as oocytes from GnRH antagonist cycles. This new IPPOS protocol, is novel as progestin is not started simultaneously with gonadotropins as in prior studies of PPOS. IPPOS involves even less medication and can represent an inexpensive and patient friendly alternative when a fresh embryo transfer is not intended, e.g. oocyte cryopreservation, oocyte donation or PGT cycles, as well as anticipated over responders in whom a frozen embryo transfer would be safer and more effective.

SUPPORT: None.

P-228 Tuesday, October 15, 2019 6:30 AM

THE IMPACT OF OVARIAN RESPONSE ON CLINICAL PREGNANCY AND DELIVERY RATES IN AN OOCYTE DONOR POPULATION. Brent M. Hanson, MD,a Julia G. Kim, MD, MPH, Emily K. Osman, MD,a Ashley W. Tieg, MD,a Ashley A. Neal, MD,a Marie D. Werner, MD,b Richard Thomas Scott, Jr., MD,a† IVI-RMA New Jersey, Basking Ridge, NJ; bIVI-RMA.

OBJECTIVE: In the general IVF population, it has been reported that an optimal window of ovarian response may exist, with live birth rates declining if fewer than 15 or greater than 20 oocytes are retrieved. The relationship between pregnancy outcomes and ovarian response has not been thoroughly investigated in oocyte donors. This study seeks to characterize the relationship between ovarian response, clinical pregnancy rates, and delivery rates in oocyte donors.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: This study was performed at a large IVF practice. Oocyte donors who underwent their first oocyte retrieval followed by an embryo transfer in a recipient between January 1, 2012 and December 31, 2017 were included. All donors were under the age of 40. All donors had their first retrieval and transfer cycle prior to January 1, 2012. The relationship between ovarian response, clinical pregnancy rate and delivery rates were assessed. Ovarian response was defined as the 2PN oocytes retrieved and defined as follows: 8-10, 11-14, 15-19, ≥20. All donors were treated with a GnRH antagonist protocol. Only the first FET cycle was included in the final analysis. Mean age (SD) was 31.7 (4.1) and BMI was 21.3 (3.0). Computerized randomization was conducted to assign participants to one of four treatment groups: (1) Low responders (≤8 oocytes), (2) Intermediate responders (8-10 oocytes), (3) High responders (11-14 oocytes), and (4) Very high responders (≥15 oocytes). Findings were compared with a control group of volunteers who underwent their first retrieval and transfer cycle prior to January 1, 2012 and December 31, 2017.

RESULTS: A total of 569 donors who underwent their first retrieval and transfer cycle prior to January 1, 2012 and December 31, 2017 were included in this analysis. The mean age of the total population was 31.7 (4.1) and BMI was 21.3 (3.0). The mean (SD) number of transferred embryos was 1.9 (0.4). Clinical pregnancy rate/cycle was 40.4% (231/572) in the overall population and 41.4% (165/399) in women with embryo transfer. Baby take-home rate was 40.4% (231/572). Clinical pregnancy rate was highest in the control group (41.4%) compared to the Low responders (35.6%), Intermediate responders (36.5%) and High responders (33.7%). Delivery rates were highest in the control group (34.6%) compared to Low responders (27.5%), Intermediate responders (28.0%) and High responders (26.1%). The relationship between response and delivery rates was statistically significant (P<0.05).

CONCLUSIONS: Ovarian response and delivery rates were not statistically significant (P>0.05) but showed a trend suggesting that the optimal window of ovarian response may exist. The optimal window of ovarian response is likely different than that in the general IVF population. This finding has important clinical implications and should be further investigated in a larger, prospective cohort study.
Table 1. Clinical pregnancy rate and delivery rate based on ovarian response

<table>
<thead>
<tr>
<th>Oocytes retrieved</th>
<th>Clinical Pregnancy Rate</th>
<th>Delivery Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;15 oocytes</td>
<td>68.3%</td>
<td>60.3%</td>
</tr>
<tr>
<td>15-20 oocytes</td>
<td>67.8%</td>
<td>60.6%</td>
</tr>
<tr>
<td>&gt;20 oocytes</td>
<td>72.1%</td>
<td>64.1%</td>
</tr>
</tbody>
</table>

*P = 0.6126* (Not significant)

*P = 0.7204* (Not significant)

RESULTS: In normal responders, there were no significant differences between the mild and the long agonist stimulation protocols in clinical pregnancy (OR = 1.11 (95% CI = 0.82-1.49)) and ongoing pregnancy rates (OR = 1.18 (95% CI = 0.75-1.88)). Similarly, in poor responders, there were no significant differences between the mild and the long agonist stimulation protocols in clinical pregnancy (OR = 0.97 (95% CI = 0.37-2.57)) and ongoing pregnancy rates (OR = 0.82 (95% CI = 0.57-1.18)). However, the mean number of oocytes retrieved was lower in the mild protocol compared to long agonist protocol both in normal responders (MWD = -0.159, 95% CI = -0.807-0.500) and poor responders (MWD = -0.968; 95% CI = -1.650 to -0.486). The mean amount of gonadotropins used was also significantly lower in the mild compared to the long stimulation protocol both in normal responders (MWD = -1.650, 95% CI = -2.500 to -1.750) and in poor responders (MWD = -0.807; 95% CI = -1.555 to -0.054). The mean delivery rate of the two groups was not significantly different in normal responders (OR = 0.82 (95% CI = 0.57-1.18)) and ongoing pregnancy rates (OR = 0.82 (95% CI = 0.57-1.18)).

**P-229 Tuesday, October 15, 2019 6:30 AM**

MILD VERSUS LONG LUTEAL AGONIST STIMULATION PROTOCOL IN NORMAL AND POOR RESPONDERS IN ASSISTED REPRODUCTION. A META-ANALYSIS OF RANDOMIZED STUDIES.


**SUPPORT:** None.

P-230 Tuesday, October 15, 2019 6:30 AM

EFFECTS OF Estradiol Pretreatment DURING FOLLICULAR PERIOD ON OUTCOME OF IN VITRO FERTILIZATION AND EMBRYO TRANSFER TREATMENT FOR POOR OVARIAN RESPONDER WITH HIGH FSH LEVEL. Yi Tang, PhD, Central South University, Changsha, China.

OBJECTIVE: To observe the effects of estradiol pretreatment during follicular period on outcomes of in vitro fertilization and embryo transfer (IVF-ET) treatment for poor ovarian responder (POR) with high FSH level.

DESIGN: A prospective randomized controlled study.

MATERIALS AND METHODS: A total of 323 POR with high level who have undergoing IVF-ET treatment were randomly divided into the pretreatment group (n = 163) and non-pretreatment group (n = 160) according to whether the estradiol pretreatment (oral administration with 1.5-2.0mg/d at the second day to the fourth day of menstrual cycle) were conducted before super ovulation induction. General information and indices relevant to the outcome of IVF-ET treatment of two groups were compared.

RESULTS: In the pretreatment group, serum follicle-stimulating hormone (FSH) (13.77±14.17IU/ml, P = 0.53) and serum estradiol (E2) (161.5±231.10pmol/l, P = 0.00) were significantly lower than the values in the non-pretreatment group. The differences of age (31.13±5.69years, P = 0.5), BMI (22.13±1.34kg/m², P = 0.16), AMH (0.89/0.91ng/ml, P = 0.57), basal antral follicle count ( AFC ) (3.57/3.59, P = 0.23), the number of eggs retrieved (40.70/38.70, P = 0.70), unbalanced rate (15.34/13.13, P = 0.56), endometrial thickness (10.49/10.49mm, P = 0.41), the number of embryos transferred (1.60/1.63, P = 0.12), transplant cancellation rate (12.98/12.90, P = 0.47) and clinical pregnancy rate (13.30/11.70, P = 0.10) were not statistically significant between the two groups.

CONCLUSIONS: Estradiol pretreatment in follicular phase at POR patients with high FSH level did not increase the number of MI eggs rate and clinic pregnancy rate. On the contrary, an increased Gn dosage and extended treatment period can impose unnecessary burden on a patient, both financially and mentally. To some extent, the level of FSH only reflects the function of the ovary. Therefore, reducing the blood FSH level cannot increase the number of eggs or improve the clinical pregnancy outcome.
IVF OUTCOME PREDICTORS - PROGESTERONE LEVELS

P-231 Tuesday, October 15, 2019 6:30 AM
LONGER DURATION OF PROGESTERONE ELEVATION ADVERSELY IMPACTS PREGNANCY OUTCOMES DURING IVF IN WOMEN ≤ 40 YEARS. Chantal Bartels, MD, Jeffrey Thorne, MD, Reeva B. Malkhijani, MD, Grow R. Daniel, MD, John Nulsen, MD, Claudio Benadiva, MD, Lawrence Engmann, MD Center for Advanced Reproductive Services, University of Connecticut, Farmington, CT.

OBJECTIVE: The purpose of this study is to evaluate the impact the number of days of progesterone (P) elevation during an IVF cycle on the fresh embryo transfer live birth rate (LBR) at different ages. We hypothesize that the longer the duration of P exposure, the greater the likelihood for asynchronous endometrium manifested as a lower LBR for ages <35 years and 35-40 years.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We included all patients ≤40 years who underwent fresh IVF embryo transfer between 1/2011 and 12/2017 at a large IVF clinic. Morning serum P levels were collected every 1 to 2 days during the IVF cycle starting day 4, with frequency of collection determined by the follicle size through ultrasound monitoring. We evaluated the effect of prolonged elevation of P ≥ 1.0ng/mL on live birth rates by age group. ANOVA was used for continuous variables, and Chi-square was used for categorical data. Logistic regression was performed controlling for age, BMI, embryo stage at transfer and number of embryos transferred.

RESULTS: 3339 IVF cycles were included for analysis, with 1850 blastocyst transfers and 1489 day 3 embryo transfers. The LBR was lower if the day of trigger serum P was elevated (1.0-1.4ng/mL: 49.5% [330/666] and ≥ 1.5ng/mL: 43.3% [58/132]) compared to P < 1.0ng/mL: 57% [585/1027] (p < 0.001). Moreover, a longer duration of P elevation was associated with lower LBR (Table 1). After controlling for the potential confounding variables, prolonged duration of P elevation ≥ 1.0ng/mL (OR: 0.61; 95% CI: 0.47-0.86, p < 0.001) and day of trigger P ≥ 1.0ng/mL (OR: 0.73; 95% CI: 0.63-0.84, p < 0.001) were still associated with lower LBR.

Table 1. Live birth rate by age and number of days of P elevation ≥ 1.0 ng/mL

<table>
<thead>
<tr>
<th>Age</th>
<th>0 days</th>
<th>1 day</th>
<th>2 days</th>
<th>≥3 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>49.9%</td>
<td>44.0%</td>
<td>41.9%</td>
<td>39.1%</td>
</tr>
<tr>
<td>&lt;35 years</td>
<td>55.9%</td>
<td>47.0%</td>
<td>44.8%</td>
<td>42.8%</td>
</tr>
<tr>
<td>35-40 years</td>
<td>42.3%</td>
<td>40.1%</td>
<td>38.0%</td>
<td>34.5%</td>
</tr>
<tr>
<td>Blast transfer</td>
<td>Overall</td>
<td>57.7%</td>
<td>49.4%</td>
<td>46.5%</td>
</tr>
<tr>
<td>n=1850</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;35 years</td>
<td>60.2%</td>
<td>50.2%</td>
<td>47.7%</td>
<td>47.3%</td>
</tr>
<tr>
<td>35-40 years</td>
<td>53.5%</td>
<td>48.1%</td>
<td>44.6%</td>
<td>42.9%</td>
</tr>
</tbody>
</table>

CONCLUSIONS: The greater the number of days of P elevation during a fresh IVF cycle, the less likely the transfer is to result in a live birth. The trend is apparent for all ages, though it was only statistically significant for those <35 years. An early rise in P warrants a timely conversation about the benefits of a freeze-all approach.

SUPPORT: None.

P-232 Tuesday, October 15, 2019 6:30 AM
INCREASING LUTEAL PROGESTERONE LEVELS ARE ASSOCIATED WITH HIGHER ONGOING PREGNANCY RATES AND LOWER EARLY PREGNANCY LOSSES FOLLOWING SINGLE EUPLOID FROZEN EMBRYO TRANSFER. Sydney Chang, MD,a Dmitry Gounko, MA,b Joseph A. Lee, BA,b Eric Flisser, MD,b Lucky Sekhon, MD,b Alan B. Copperman, MD,a Ichsan School of Medicine at Mount Sinai, New York, NY;b Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Endometrial programming with exogenous estradiol (E2) and progesterone (P4) during a frozen embryo transfer (FET) cycle mimics the hormonal environment of a natural cycle, while allowing for synchroni-

zation of embryo and endometrial development. While studies have investigated the ideal timing of P4 initiation and the association of supraphysiologic E2 levels with FET and perinatal outcomes,1 less is known about how the level of P4 exposure impacts implantation and placentation. Prior research has suggested that elevated P4 levels during FETs are associated with a lower ongoing pregnancy/live birth (OP/LB) rate and higher early pregnancy loss (EPL) rate.2 Other studies have suggested an association between FETs and large for gestational age (LGA) and postdates infants.3 Yet, there is no known mechanism for these findings.4 The objective of this study is to determine whether the level of P4 exposure at time of FET and throughout the first trimester impacts FET or perinatal outcomes.

DESIGN: Retrospective, cohort study.

MATERIALS AND METHODS: The study included patients undergoing a single euploid FET at an academic center from 2012-2019. Luteal support methods other than intramuscular P4 were excluded. Serum P4 level was treated as a continuous variable. Peri-implantation P4 was defined as P4 level on the day prior to FET, and first trimester P4 was defined as average P4 from the day prior to FET until ~10 weeks of gestational age (GA). Primary outcomes were rates of OP/LB and EPL. Secondary outcomes were clinical pregnancy (CP) rate, GA at delivery, and neonatal birth weight. Small for GA (SGA)/LGA were defined using sex-specific data for the 10th/90th percentile.5 Data were evaluated using univariate linear regressions with generalized estimating equations.

RESULTS: A total of 3773 single euploid FET cycles from 2699 patients were included. After controlling for age, BMI, gestational age, and days required for blastulation, there was a significant association between average P4 and OP/LB (OR 1.15 [95% CI 1.13-1.17], p < 0.001), as well as EPL (OR 0.83, [95% CI 0.81-0.85], p < 0.001). There was no association between peri-implantation P4 and CP rate. There was a significant decrease in GA at delivery with increasing P4 (β = -1.0 week, p < 0.001). Mean first trimester P4 levels were not associated with birth weight after controlling for GA, fetal sex and BMI. There was no association between P4 and incidence of SGA/LGA infants.

CONCLUSIONS: In a large cohort of single euploid FETs, we showed that luteal P4 in early pregnancy is positively correlated with OP/LB rate, and inversely correlated with EPL rate. While the level of exposure to P4 is crucial for pregnancy maintenance, increasing P4 levels in the first trimester do not appear to have downstream effects on placentation. Increasing luteal P4 level is associated with a shorter duration of pregnancy, but is not associated with differences in birth weight, or incidence of SGA or LGA infants. Future studies might focus on the pharmacogenomic profiles of women undergoing synthetic endometrial preparation with the aim of individualizing FET protocols.

References: 1. Sekhon L, Feuerstein J, Pan S, et al. Endometrial prepara-
tion prior to the transfer of single, vitrified-warmed, euploid blastocysts: does the duration of estradiol treatment influence clinical outcome? Fertil Steril 2019; in press.
3. Maheshwari A, Pandey S, Raja EA, Shetty A, Hamilton M, Bhat-

SUPPORT: None.
SERUM PROGESTERONE ELEVATION MAY ADVERSELY AFFECT EMBRYOLOGICAL PARAMETERS. Fazilet Kubra Boyunakalin, M.D., MSc,a Meral Gultomrak, BSc,b Emre Turgut, M.D.,c Necati Findikli, Ph.D.,c Onder Coban, MSc,d Munevver Serdarogullari, Ph.D.d Mustafa Bahceci, M.D., Ph.D.d Bahceci Health Group-Fulya IVF Centre, ISTANBUL, Turkey; Bahceci Fulya IVF Center, ISTANBUL, Turkey; Bahceci Health Group-Fulya IVF Centre, Istanbul, Turkey; Bahceci Health Group, Lefkosa, Turkey; Bahceci Health Group, Nicosia, Turkey.

OBJECTIVE: To evaluate the association of progesterone (P) levels on the trigger day with the embryo quality in freeze all cycles.

DESIGN: A retrospective analysis of ICSI cycles followed by elective freezing between 2014 and 2018. The exclusion criteria were female age >37, BMI >30 kg/m², sperm concentration<2x10⁹/ml, more than two failed ICSI attempts and frozen cleavage stage embryos. The primary outcomes were fertilization, blastulation, embryo quality at blastocyst stage.

RESULTS: Baseline characteristics of the women and embryo development stratified according to P levels on the day of ovulation triggering were explored, to guide the selection of the hCG triggering time in the modified natural cycle of frozen-thawed embryo transfer.

MATERIALS AND METHODS: Five-hundred-and-ninety-two cycles of frozen-thawed transplantation of modified natural cycles from 2017 to 2018 were analyzed. According to the level of progesterone on human chorionic gonadotropin (hCG) days, patients were divided into two groups: group A (progesterone greater than or equal to 1 pg/ml) and group B (progesterone less than 1 pg/ml). According to LH levels, patients were divided into two groups: group C (LH greater than or equal to 20 IU/L) and group D (LH less than 20 IU/L). Pregnancy outcomes were compared and the influence of serum progesterone and LH levels on clinical outcomes on the hCG triggering day were explored, to guide the selection of the hCG triggering time in the modified natural cycle of frozen-thawed embryo transfer.

RESULTS: Compared with group B, group A baseline data and pregnancy rates showed no noticeable difference, but the embryo implantation rate was statistically lower in group A. There was no difference in baseline information and clinical pregnancy rates between group C and group D. The embryo implantation rate of group D was significantly higher than that of group C. Moreover, the implantation rate was significantly reduced in patients with simultaneous elevation of progesterone and LH levels (table1).

CONCLUSIONS: During the modified natural cycle of frozen-thawed embryo transfer, serum progesterone and LH levels on the trigger day have an impact on clinical outcomes. We suggest that hCG induction should be selected when the LH level is less than 20 IU/L and the progesterone level is less than 1 pg/ml.


TABLE 1. Comparison of modified natural cycle with progesterone and LH increased simultaneously and overall population.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>LH &gt;20 IU/L and P &gt;1 pg/ml (n = 127)</th>
<th>Total population (n = 592)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female age (year)</td>
<td>31.47 ± 5.01</td>
<td>31.65 ± 4.97</td>
<td>0.703</td>
</tr>
<tr>
<td>Male age (year)</td>
<td>32.47 ± 5.60</td>
<td>33.08 ± 5.71</td>
<td>0.271</td>
</tr>
<tr>
<td>HCG daily E2 (ng/ml)</td>
<td>319.53 ± 111.82</td>
<td>343.55 ± 226.74</td>
<td>0.245</td>
</tr>
<tr>
<td>HCG daily oocyte number</td>
<td>1.00 ± 0.22</td>
<td>1.01 ± 0.18</td>
<td>0.467</td>
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<tr>
<td>Size of dominant follicle</td>
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<td>10.07 ± 1.65</td>
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</tr>
<tr>
<td>Number of transferred embryos</td>
<td>1.35 ± 0.50</td>
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<td>0.346</td>
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<tr>
<td>Proportion of transferted blastocysts</td>
<td>40.9% (52)</td>
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<td>0.320</td>
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<tr>
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<td>Embryo implantation rate</td>
<td>44.16%</td>
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EFFECTS OF SERUM PROGESTERONE AND LH LEVELS BEFORE HCG TRIGGERING ON CLINICAL PREGNANCY OUTCOMES OF MODIFIED NATURAL FROZEN-TAUGHT EMBRYO TRANSFER CYCLES. Na Kong, M.M., Tianran Song, M.D., Jingyu Liu, M.M. Reproductive Medicine Center, The Affiliated Drum Tower Hospital of Nanjing University, nanjing, China.

OBJECTIVE: To investigate the effects of serum progesterone and luteinizing hormone (LH) levels on the clinical outcomes of the modified natural cycle of frozen-thawed embryo transfer.

MATERIALS AND METHODS: Five-hundred-and-ninety-two cycles of frozen-thawed transplantation of modified natural cycles from 2017 to 2018 were analyzed. According to the level of progesterone on human chorionic gonadotropin (hCG) days, patients were divided into two groups: group A (progesterone greater than or equal to 1 pg/ml) and group B (progesterone less than 1 pg/ml). According to LH levels, patients were divided into two groups: group C (LH greater than or equal to 20 IU/L) and group D (LH less than 20 IU/L). Pregnancy outcomes were compared and the influence of serum progesterone and LH levels on clinical outcomes on the hCG triggering day were explored, to guide the selection of the hCG triggering time in the modified natural cycle of frozen-thawed embryo transfer.

RESULTS: Compared with group B, group A baseline data and pregnancy rates showed no noticeable difference, but the embryo implantation rate was statistically lower in group A. There was no difference in baseline information and clinical pregnancy rates between group C and group D. The embryo implantation rate of group D was significantly higher than that of group C. Moreover, the implantation rate was significantly reduced in patients with simultaneous elevation of progesterone and LH levels (table1).

CONCLUSIONS: During the modified natural cycle of frozen-thawed embryo transfer, serum progesterone and LH levels on the trigger day have an impact on clinical outcomes. We suggest that hCG induction should be selected when the LH level is less than 20 IU/L and the progesterone level is less than 1 pg/ml.


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14. SUPPORT: The study was supported by National Natural Science Foundation of China(81601246.N.K).

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EFFECT OF PREMATURE SERUM LH AND PLASMA PROGESTERONE RISE ON THE CLINICAL OUTCOME OF ANOVULATORY PATIENTS TREATED WITH GONADOTROPINS. Hassan Sallam, MD, PhD (London), FRCOG, Olma Mustafa, MD, MCh, Abdel-Fattah Agameya, MD, PhD, Oona Sallam, MD, MCh, Alexandria University, Alexandria, Egypt; Alexandria Fertility Centre, Alexandria, Egypt.

OBJECTIVE: To study the effect of serum LH and plasma progesterone rise on the day of HCG administration on the clinical outcome of anovulatory patients treated with gonadotropins.

MATERIALS AND METHODS: Sixty consecutive anovulatory patients attending our infertility clinic and treated for ovarian stimulation with gonadotropins were studied during their first cycle of treatment. All patients had normogonadotropic hypogonadism (WHO group I) and had failed to become pregnant on clomiphene citrate therapy (up to 150 mg/day for 5 days). All patients were aged 20 to 38 years with a mean (±SD) of 26.7 (±9.2) years. All male partners had normal semen parameters according to the WHO standards. Patients with hyperprolactinaemia and those with congenital adrenal hyperplasia were excluded, as well as those with other causes of infertility. The mean (±SD) basal (day 3) serum FSH and LH levels were 7.27 (±1.82) mIU/mL and 7.57 (±0.78) mIU/mL, respectively. The mean (±SD) basal (day 3) LH/FSH ratio was 1.09 (±0.14) mIU/mL. Human menopausal gonadotropins (150 IU) were administered by daily IM injections starting day 5 of the menstrual cycle. Monitoring was effected by transvaginal ultrasound scanning of the follicles and the dose of gonadotropins adjusted accordingly. HCG (5000 IU) was administered by IM injection when 2 follicles reached 18 mm in diameter and venous blood was withdrawn on the same day and the serum/plasma kept at -20°C until the time of the LH and progesterone assay. Eighteen patients became pregnant, of whom 17 reached clinical viability (beating heart on ultrasound) and one had a miscarriage. Power calculation regarding the premature rise or otherwise of serum LH revealed that a minimum of 17 treatment cycles was necessary to study in each group to achieve an 80% study power at a 5% level significance. 

RESULTS: The mean (±SD) of serum LH and plasma progesterone levels on the day of HCG administration were 11.10 (±9.08) mIU/mL and 2.68 (±0.14) ng/mL, respectively. Twenty nine patients (48.3%) had an LH rise

body(PB) morphology. For each oocyte, each parameter was scored as +1, 0 and -1 to determine the oocyte quality score.

RESULTS: There was no significant difference between the groups in terms of patient age (p=0.11), BMI (p=0.12), duration of infertility (p=0.29), FSH (p=0.91), AMH (p=0.20) and AFC (p=0.60). There was a positive correlation between dose of gonadotropin and progesterone concentration on trigger day (p=0.001). There was a negative correlation between oocyte quality score and progesterone level on hCG day (p=0.001). In terms of oocyte quality score, a statistically significant difference was found between 3 groups (5.48, 4.97, 4.14, p=0.001, respectively). The quality score of the Group-3 oocytes was found to be significantly lower than both Group-1 and Group-2 oocytes (p=0.001). Also Group-2 oocyte quality score was significantly lower than Group-1 oocytes (p=0.001). There was a positive correlation between progesterone level and abnormal oocyte percentage (p=0.001). The highest abnormal oocyte ratio was found in Group-3 (%78.9) and lowest in Group-1 (%28.2). Ovoplasm (p=0.007), PVS (p=0.001) and ZP (p=0.04) abnormalities were statistically increased with higher progesterone concentration. Degeneration (p=0.55) and immature oocyte percentage (p=0.82) had no significant correlation between groups. Estradiol concentration on trigger day (p=0.001), total oocyte count (p=0.001) and mature oocyte count (p=0.001) had a positive correlation with progesterone concentration on trigger day.

CONCLUSIONS: This study comprehensively assessed the relationship between oocyte quality and progesterone. The data demonstrate that elevated progesterone levels (>1ng/ml) before oocyte maturation were consistently detrimental to the oocyte. Individualization of stimulation protocols and consideration of gonadotropin dose in late follicular phase will lead to positive results in terms of oocyte quality.
OBJECTIVE: While an elevated serum progesterone level (P) prior to trigger has been associated with embryo-endometrial asynchrony and decreased pregnancy rates during in vitro fertilization (IVF) with fresh embryo transfer, few data exist in the context of a planned frozen embryo transfer. E/P ratio (E/P) at time of ovulatory trigger on clinical pregnancy rate during subsequent frozen euploid embryo transfer.

DESIGN: Retrospective cohort analysis

MATERIALS AND METHODS: All frozen embryo transfers from January-December 2018 from a high-volume private practice fertility center were included. Serum E and P levels were measured on the day of ovulatory trigger by Immulite (Siemens). E/P was calculated in an effort to control for degree of response. Embryos were cultured to the blastocyst stage for trophectoderm biopsy and vitrified. Preimplantation genetic testing for aneuploidy (PGT-A) was performed using next generation sequencing (NGS). Euploid frozen embryo transfers were performed in a subsequent natural or controlled cycle. Oocyte maturity (MII/total oocytes retrieved) and euploidy rates (euploid/total embryos biopsied) were calculated. Clinical pregnancy and ongoing pregnancy (>10 weeks) following a first embryo transfer were examined in relation to E/P. Regression analyses were performed to analyze the impact of E/P as a continuous and categorical value (defined by quartile) on cycle outcomes.

RESULTS: A total of 134 women underwent a euploid frozen embryo transfer over the study period and had steroid levels at time of trigger available. Mean E at trigger was 3704±2234 pg/ml while mean P was 1.13±0.56 ng/ml for a mean E/P of 3.61±2.59. Cycle and pregnancy outcomes by quartile of E/P are listed in Table 1. There were no differences between quartiles of E/P with respect to cycle or pregnancy outcomes.

CONCLUSIONS: E/P ratio at the time of trigger does not appear to impact clinical outcomes in a subsequent euploid frozen embryo transfer cycle.

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EFFECT OF ESTROGEN TO PROGESTERONE RATIO AT TIME OF OVULATION TRIGGER ON SUBSEQUENT EUPLOID FROZEN EMBRYO TRANSFER PREGNANCY RATE. Hency Patel, MD,a Temeka Zore, MD,b Richard Buyalos, MD,b Gary Hubert, MD,b Chunmin Wang, PhD,b Meredith Brower, MD,b Moussa Shamonki, MD,b Molly M. Quinn, MD,b aUniversity of California, Los Angeles, Los Angeles, CA; bFertility and Surgical Associates of California, Thousand Oaks, CA.

OBJECTIVE: Determine the impact of E/P with respect to cycle or pregnancy outcomes.

MATERIALS AND METHODS: All frozen embryo transfers from January-December 2018 from a high-volume private practice fertility center (defined by quartile) on cycle outcomes. Regression analyses were performed to analyze the impact of E/P as a continuous and categorical value (defined by quartile) on cycle outcomes.

RESULTS: A total of 134 women underwent a euploid frozen embryo transfer over the study period and had steroid levels at time of trigger available. Mean E at trigger was 3704±2234 pg/ml while mean P was 1.13±0.56 ng/ml for a mean E/P of 3.61±2.59. Cycle and pregnancy outcomes by quartile of E/P are listed in Table 1. There were no differences between quartiles of E/P with respect to cycle or pregnancy outcomes.

CONCLUSIONS: E/P ratio at the time of trigger does not appear to impact clinical outcomes in a subsequent euploid frozen embryo transfer cycle.
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PROTOCOL MATTERS: PROGESTERONE RISE ON DAY OF TRIGGER IMPACTS ANTAGONIST BUT NOT AGONIST LIVE BIRTH RATES FOR FRESH IVF CYCLES. Janelle M. Jackman, M.B.B.S. 1 Chantal Bartels, M.D. 1 John Nulsen, M.D. 2 Grow R. Daniel, M.D. 2 The Brooklyn Hospital Center, Brooklyn, NY; 3University of Connecticut Health Center, Center for Assisted Reproductive Services, Farmington, CT.

OBJECTIVE: The purpose of this study is to determine if age and stimulation protocol influences the negative pregnancy outcome impact of progesterone rise on day of trigger during stimulated IVF-ET.

DESIGN: A retrospective cohort study using a large IVF database.

MATERIALS AND METHODS: IVF is a multicenter database for IVF that has collected over 122,548 patient IVF cycles between 2004 and 2018. We included all women who underwent elective fresh single blastocyst transfer and had excess embryos to freeze. Women were excluded for positive smoking status and day three follicle stimulating hormone level >12 IU/L. Progesterone (P4) levels were categorized into low (<1 ng/mL), medium (1-1.5 ng/mL), and high (>1.5 ng/mL). Age groups were divided by <35 years versus ≥35 years. Gonadotropin-releasing hormone (GnRH) Antagonist and GnRH-agonist protocols were compared separately in each age group. Statistics was analyzed using Chi-square, ANOVA, Student’s t-test and logistic regression. P < 0.05 was considered statistically significant.

RESULTS: 3936 cycles were included. Women in the two age groups did not differ significantly by cycle variables including BMI, AMH, FSH values. In all patients, live birth rates were lower when progesterone levels on day of trigger rose above 1 ng/mL using an antagonist suppression protocol (p = 0.006). This was particularly true and significant for women ≥35 years old (p = 0.007), but not statistically significant for women <35 years old. No significant difference was seen with progesterone level and live birth rate when an agonist suppression protocol was used for ovulation induction, regardless of the patients’ ages. Live birth rates were higher using GnRH-agonist suppression in every progesterone group and age category (p < 0.0001).

CONCLUSIONS: Elevated serum progesterone levels >1 ng/mL on the day of trigger is associated with reduced live birth rates following IVF/ICSI cycles in women ≥35 years when an antagonist protocol is used. Ovarian stimulation using GnRH-agonist suppression seems to protect from the adverse effect of rising progesterone and allows high pregnancy rates with fresh embryo transfer. Protocol should be considered when recommending a freeze-all cycle in the setting of elevated progesterone.


SUPPORT: N/A.

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SPERM INTRACELLULAR PH AS A PREDICTOR OF FERTILIZATION RATE IN NORMOSPERMIC INFERTILE MEN UNDERGOING IN VITRO FERTILIZATION. Stephanie Gunderson, M.D. 2 Lis C. Puga Molina, Ph.D. 1 Joan Riley, Ph.D, HCLD. 1 Emily S. Jungheim, M.D. 1 Stephanie Gunderson, M.D. 2 Washington University School of Medicine, St Louis, MO; 1Washington University In Saint Louis, Saint Louis, MO; 3Washington University School of Medicine, St Louis, MO.

OBJECTIVE: To know the effect of serum progesterone (P4) level on pregnancy rate in Vitriﬁed-Warmed Blastocyst Transfer (VBT).

METHODS: We conducted a prospective observational study of a large IVF database for 12 years. We included women who underwent elective fresh single blastocyst transfer and had excess embryos to freeze. Women were excluded for positive smoking status and day three follicle stimulating hormone level >12 IU/L. Progesterone (P4) levels were categorized into low (<1 ng/mL), medium (1-1.5 ng/mL), and high (>1.5 ng/mL). Age groups were divided by <35 years versus ≥35 years. Gonadotropin-releasing hormone (GnRH) Antagonist and GnRH-agonist protocols were compared separately in each age group. Statistics was analyzed using Chi-square, ANOVA, Student’s t-test and logistic regression. P < 0.05 was considered statistically significant.

RESULTS: 3936 cycles were included. Women in the two age groups did not differ significantly by cycle variables including BMI, AMH, FSH values. In all patients, live birth rates were lower when progesterone levels on day of trigger rose above 1 ng/mL using an antagonist suppression protocol (p = 0.006). This was particularly true and significant for women ≥35 years old (p = 0.007), but not statistically significant for women <35 years old. No significant difference was seen with progesterone level and live birth rate when an agonist suppression protocol was used for ovulation induction, regardless of the patients’ ages. Live birth rates were higher using GnRH-agonist suppression in every progesterone group and age category (p < 0.0001).

CONCLUSIONS: Elevated serum progesterone levels >1 ng/mL on the day of trigger is associated with reduced live birth rates following IVF/ICSI cycles in women ≥35 years when an antagonist protocol is used. Ovarian stimulation using GnRH-agonist suppression seems to protect from the adverse effect of rising progesterone and allows high pregnancy rates with fresh embryo transfer. Protocol should be considered when recommending a freeze-all cycle in the setting of elevated progesterone.


SUPPORT: N/A.

TABLE 2. Live birth rate by age and protocol for progesterone level

<table>
<thead>
<tr>
<th>P-value</th>
<th>Agonist ( % )</th>
<th>Antagonist ( % )</th>
<th>Agonist ( % )</th>
<th>Antagonist ( % )</th>
<th>All ( % )</th>
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</thead>
<tbody>
<tr>
<td>Low</td>
<td>50.5</td>
<td>37.4</td>
<td>42.5</td>
<td>30.68</td>
<td>48.1</td>
</tr>
<tr>
<td>P &lt; 1</td>
<td>187/380</td>
<td>306/818</td>
<td>68/160</td>
<td>154/502</td>
<td>255/530</td>
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<tr>
<td>Medium</td>
<td>54.5</td>
<td>34.6</td>
<td>41.6</td>
<td>21.3</td>
<td>50.9</td>
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<tr>
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<td>158/290</td>
<td>191/552</td>
<td>47/113</td>
<td>82/384</td>
<td>205/403</td>
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<tr>
<td>High</td>
<td>54.6</td>
<td>31.4</td>
<td>39.0</td>
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<td>50.42</td>
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<td>0.15</td>
<td>0.89</td>
<td>0.007</td>
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</table>
OBJECTIVE: To determine whether intracellular pH (pHi) of human spermatozoa can predict unsuccessful conventional fertilization outcomes in normospermic infertile men undergoing in vitro fertilization (IVF).

DESIGN: IRB approved, laboratory study of normospermic men undergoing IVF from September 2018 to present at a single institution. Couples were excluded if they used frozen sperm, had a known female factor or utilized intracytoplasmic sperm injection (ICSI) only. De-identified, normospermic fresh semen samples were also analyzed.

MATERIALS AND METHODS: Fresh semen was collected on the day of ovocyte retrieval from normospermic (≥32% progressive motility; ≥40% total motility; ≥15 × 10⁶ cells/ml) infertile men undergoing IVF. Sperm were subjected to standard swim up, then analyzed immediately or incubated in capacitating media (Quinn’s Advantage Fertilization, CooperSurgical) at 37°C and 5% CO₂ for 24 hours. pHi of spermatozoa was measured in all samples using flow cytometry (FACSCanto II TM cytometer) after incubation with pH sensitive fluorescent probe, BCECF-AM. Data were analyzed using FACS Diva and FlowJo software and included only single live sperm cells. The final sperm pHi was obtained by linearly interpolating the median fluorescence of the unknown sample in the calibration curve of known pH buffer solutions for each condition. Hyperactivated motility was measured by computer-assisted semen analysis. Standard univariate and bivariate analyses were performed, if data were not normally distributed a non-parametric test was performed.

RESULTS: A total of 28 fresh de-identified samples and 24 IVF samples were included in the analysis. The IVF couples included in the analysis were demographically similar. Previously, we measured pHi in capacitated fresh spermatozoa from deidentified samples and found that pHi positively correlated with the percentage of sperm that had intact acrosomes (r = 0.072, n = 17, P = 0.1214). Next, we measured pHi in sperm from IVF patients before and after capacitation and found that pHi did not change (6.97 ± 0.195 vs. 6.93 ± 0.257). Sperm pHi positively correlated with conventional fertilization rates (number of fertilized eggs/fetal number of mature oocytes, n = 24, P = 0.0197) but not with ICSI fertilization rates (n = 10, P = 0.655). Sperm samples that had a conventional fertilization rate greater than 70% had a significantly higher pHi than those with a fertilization rate lower than 50% (n = 10, P = 0.0175). The lower 99% confidence interval of pHi in sperm from the IVF cohort was 6.77. Fertilization rates were significantly higher with sperm with pHi >6.77 than with sperm with pHi <6.77 (n = 24, P = 0.0027).

CONCLUSIONS: Sperm pHi was a stable marker within patients before and after capacitation and positively correlated with conventional fertilization rates. This measurement may be used to predict poor conventional fertilization outcomes in normospermic men undergoing IVF.

Reference: None.

SUPPORT: None.

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NEUROTENSIN STIMULATES THE SPERM ACROSOME REACTION AND ALTERS PERCENTAGES OF FERTILIZATION IN VITRO. Genevieve E. Campbell, BS; Estella L. Jones, PhD; Pierre Comizzoli, DVM, PhD; Diane M. Duffy, PhD; Eastern Virginia Medical School, Norfolk, VA; Smithsoninan Institution, Washington, DC.

OBJECTIVE: Neurtensin (NTS) is a naturally-occurring, 13-amino acid peptide which was previously reported to stimulate the acrosome reaction in mouse and bull sperm. This study determined the impact of NTS on the function of human and non-human primate sperm.

DESIGN: Experimental, laboratory-based research study of semen from consenting, normozooospermic human donors and cynomolgus macaques.

MATERIALS AND METHODS: Human semen samples from CONRAD, Norfolk, VA were filtered to obtain motile sperm. Sperm acrosome status was assessed by staining with a fluorescencr lectin which binds the outer acrosomal membrane and permits microscopic visualization of the sperm acrosome (intact or reacted). Eosin-negrosin stained determining sperm viability. Computer assisted semen analysis (NIH) assessed sperm motility, progression, and velocity. For in vitro fertilization (IVF) studies, monkey oocytes were obtained after ovarian stimulation and follicle aspiration. Monkey sperm samples

were obtained from the Oregon National Primate Research Center. Fertilization was determined by the presence of a second polar body and 2 pronuclei.

RESULTS: NTS treatment of human sperm stimulated the acrosome reaction in both a dose-dependent (0.1-10 μM) and time-dependent (5-30 min) manner in vitro. After a 30 min incubation, intact acrosomes decreased from 81 ± 5% in untreated sperm to 46 ± 5% in sperm treated with 10 μM NTS (P < 0.05, n = 4 donors). NTS treatment (0.1-10 μM for 30 min) did not alter sperm motility or progression (n = 4 donors); however, there was a slight increase in proportion of viable sperm with NTS treatment (P < 0.05, n = 4 donors). Both a general NTS receptor antagonist (SR142948) and a NTSR1 selective antagonist (SR-48692) reduced the ability of NTS to stimulate the acrosome reaction. While 92 ± 2% of untreated sperm had intact acrosomes after 30 min, NTS treatment resulted in only 54 ± 7% of sperm with intact acrosomes (P < 0.05, n = 3 donors). Incubation with NTS plus SR142948 resulted in 88 ± 1% of sperm with intact acrosomes, and incubation with NTS plus SR48692 resulted in 87 ± 1% of sperm with intact acrosomes (P < 0.05, n = 3 donors). To determine if NTS treatment compromises the ability of sperm to fertilize an oocyte, monkey sperm were treated with NTS (10 μM for 30 min). Untreated monkey sperm had 87 ± 2% intact acrosomes, while sperm treated with NTS had 50 ± 1% intact acrosomes (P < 0.05, n = 3 separate experiments). Percentage of fertilization with untreated monkey sperm and monkey oocytes was 72%. Sperm pre-treated with NTS and then used for IVF yielded a significantly lower fertilization rate of 18% (different by Chi-squared test).

CONCLUSIONS: NTS effectively stimulates the acrosome reaction in human and monkey sperm. Pre-treatment of sperm with NTS significantly reduces fertilization. Therefore, the NTS pathway has potential for contraceptive development. Identification of NTSR1 as the mediator of NTS action provides a specific target for future studies. This work was supported by Eastern Virginia Medical School and NICHD (HD071875 to DMD). Gonadotropins and Ganirelix were generously provided by Merck and Co., Inc., Kenilworth, NJ.

SUPPORT: This work was supported by Eastern Virginia Medical School and NICHD (HD071875 to DMD).

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SPERM DNA FRAGMENTATION INDICES ARE NOT CORRELATED WITH BLASTULATION OR EUPLOIDY RATES IN PATIENTS UNDERGOING IVF WITH PGT-A. Carlos Hernandez-Nieto, MD; Joseph A. Lee, BA; Christine Briton-Jones, PhD, HCLD; Natan Bar-Chama, MD; Benjamin Sandler, M.D.; Alan B. Copperman, MD; Reproductive Medicine Associates of New York, New York, NY; Jacobi School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: It has been postulated that the sperm DNA integrity correlates with embryo development and implantation potential (1), also that men who suffer from high sperm DNA fragmentation experience a higher probability of sperm aneuploidy and meiotic anomalies. Theoretically, embryos from men whose ejaculates display elevated DNA fragmentation could be at a greater risk of aneuploidy following fertilization. Still, published data regarding the impact of sperm with high DNA fragmentation is highly heterogeneous and limited by small sample size, use of dated genetic testing platforms, and/or analysis of patients with recurrent pregnancy losses. The objective of this study is to examine the correlation between indices measuring sperm DNA damage and embryo quality and euploidy rate in a diverse population of infertile couples undergoing IVF/ICSI with preimplantation genetic testing for aneuploidy (PGT-A).

DESIGN: Retrospective and pooled patient analysis.

MATERIALS AND METHODS: All patients undergoing ICSI/PGT-A from 2012-2019 were included in the analysis. Cases in which Sperm DNA fragmentation Index (DFI) were analyzed were included. DFI was calculated using sperm chromatin dispersion, TUNEL, acridine Orange or Sperm chromatin structure assays. Patients were segregated into 2 groups: Normal DFI rate (≤50%) and Elevated DFI rate (≥50%). Some patients were segregated into 2 subgroups: Group 1: Elevated DFI rate (≥50%) treated with (P-243 2) Surgical extractions. Group 2: Surgical extractions were excluded of the analysis. Demographic characteristics of populations, clinical embryology parameters, and embryonic euploidy rates were compared between cohorts. T-test, Chi2, and multivariate regression with a GEE model were used for data analysis.
RESULTS: 1108 blastocysts derived from 259 IVF/PGT-A cases were included in the study. The groups consisted of 126 cases (n= 543 embryos) with elevated DFI and 133 cases (n= 565 embryos) with normal DFI. Significant differences were found in mean male age (39.8 ± 6, 37.8 ± 5, p = 0.004), female age (35.9 ± 6, 37.0 ± 5, p = 0.003) and oocyte morphology (p < 0.001) between cohorts. No differences were found in fertilization rate, zygotes achieving cleavage stage, and blastulation rates between study groups. Embryo euploidy rates were comparable (50.2% (n = 273/543), 46.7% (n= 264/565), p = 0.24).

After adjusting for female and male patient’s age, BMI, AMH, normal semen analysis and number of biopsied embryos, there were no association with elevated DFI incidence or lower odds of embryo euploidy (OR 1.39, C95% 0.97-2.0, p = 0.07).

CONCLUSIONS: Although multiple studies have reported poor outcomes in patients with elevated DFI, the exact mechanism of action is unclear. Our study analysis showed no correlation between high sperm DNA fragmentation and fertilization, blastulation, or embryo euploidy rates. Our study adds to the expanding body of evidence that shows no significant relationship between elevated DNA fragmentation, embryo development, or chromosomal composition. Future studies assessing the oocyte DNA-repair mechanism following fertilization should be performed to better understand the immediate impact of sperm chromatin damage during ART intervention.


SUPPORT: None.

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CYTOGENETIC ANALYSIS BY NEXT GENERATION SEQUENCING DISCLOSED THAT EXTREMELY HIGH EUPLOIDY RATE OF BLASTOCYSTS DERIVED FROM MONOPLEOCYCLIC EMBRYOS WITH TESTICULAR SPERM. Shimepi Mizuta, M.HS., Hidehiko Matsubayashi, MD., Takumi Takeuchi, MD, Ph.D., Yuki Tamura, Ph.D., Mitsuo Santo, B.H.S., Kotaro Kiiaya, MD., Yasuhisa Araki, Ph.D., Tomomoto Ishikawa, MD., Reproduction Clinic Osaka, Osaka, Japan; Reproduction Clinic Tokyo, Tokyo, Japan; Nippon Reprogenetics Inc., Maebashi, Japan.

OBJECTIVE: It has been reported that the blastocyst formation rate of monoprecordial (1PN) embryos was significantly lower than that of two nuclear (2PN) embryos (especially in ICSI). However, a recent study revealed that 1PN embryos contained normal chromosome copy numbers similar to those of 2PN embryos by preimplantation genetic testing for aneuploidy (PGT-A). We assessed euploidy rate of 1PN embryos derived from ICSI with testicular sperm (TESE-ICSI) comparing to ejaculated sperm-ICSI or IVF by chromosomal analysis with next generation sequencing (NGS).

MATERIALS AND METHODS: All Cryptozoospermia patients undergoing autologous IVF/ICSI with fresh blastocyst transfers from 2005 to 2019 were included. Cohorts were separated based on the source of sperm utilized (Ejaculated vs. Testicular). Demographic, clinical embryology parameters and pregnancy rates were compared among cohorts. T-test, X2, and multivariate regression with GEE models were used for data analysis.

RESULTS: A total of 188 patients were included in the analysis (Ejaculated sperm (n=147), Testicular sperm (n=41). Demographic characteristics were similar among cohorts. No differences were found among the ejaculated and testicular cohorts for in the number of cancelled cycles due to embryos unavailable for transfer (22.8%; 7.6%, p = 0.03), number of embryos transferred per cycle (1.35 ± 1.62; 1.10 ± 1.39, p = 0.15) respectively. A significant difference was found among the ejaculated and testicular cohorts for fertilization (61.7%; 64.9%, p = 0.17) blastulation rates (55.8%; 55.3%, p=0.86) and count of cryopreserved blastocysts (1.58 ± 2.61; 1.10 ± 1.9, p=0.15) respectively. A significant difference was found among the ejaculated and testicular cohorts for fertilization (61.7%; 64.9%, p = 0.17) blastulation rates (55.8%; 55.3%, p = 0.86) and count of cryopreserved blastocysts (1.58 ± 2.61; 1.10 ± 1.9, p = 0.15) respectively. A significant difference was found among the ejaculated and testicular cohorts for fertilization (61.7%; 64.9%, p = 0.17) blastulation rates (55.8%; 55.3%, p = 0.86) and count of cryopreserved blastocysts (1.58 ± 2.61; 1.10 ± 1.9, p = 0.15) respectively. A significant difference was found among the ejaculated and testicular cohorts for fertilization (61.7%; 64.9%, p = 0.17) blastulation rates (55.8%; 55.3%, p = 0.86) and count of cryopreserved blastocysts (1.58 ± 2.61; 1.10 ± 1.9, p = 0.15) respectively. A significant difference was found among the ejaculated and testicular cohorts for fertilization (61.7%; 64.9%, p = 0.17) blastulation rates (55.8%; 55.3%, p = 0.86) and count of cryopreserved blastocysts (1.58 ± 2.61; 1.10 ± 1.9, p = 0.15) respectively.}

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SEDIMENTATION VERSUS SURGERY: TESTICULAR AND EJACULATED SPERM RESULT IN SIMILAR IVF OUTCOMES IN PATIENTS WITH CRYPTOZOOSPERMIA. Carlos Hernandez-Nieto, MD., Joseph A. Lee, BA., Tamar Alkon, MD., Martha Luna-Rojas, MD., Christine Briton-Jones, PhD, HCLD., Natan Bar-Chama, MD., Alan B. Copperman, MD., Benjamin Sandler, M.D. Reproductive Medicine Associates of New York, New York, NY; Icahn School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: There are opposing views about whether to source sperm through surgical intervention or fresh ejaculation in men with cryptozoospermia. O’Connell et al. observed ejaculated sperm to be better than testicular sperms in cryptozoospermia patients, and suggested that fertilization rate is related to sperm maturation. (1) Conversely, Cui et al. demonstrated that the use of testicular sperm achieved better embryonic quality and IVF outcomes than ejaculated sperm. (2) That study concluded that sourcing spermatocytes via testicular extraction reduced exposure to oxygen free radicals and prevented DNA damage therefore improving IVF clinical outcomes.

MATERIALS AND METHODS: All Cryptozoospermia patients undergoing autologous IVF/ICSI with fresh blastocyst transfers from 2005 to 2019 were included. Cohorts were separated based on the source of sperm utilized (Ejaculated vs. Testicular). Demographic, clinical embryology parameters and pregnancy rates were compared among cohorts. T-test, X2, and multivariate regression with GEE models were used for data analysis.

RESULTS: A total of 188 patients were included in the analysis (Ejaculated sperm (n=147), Testicular sperm (n=41). Demographic characteristics were similar among cohorts. No differences were found among the ejaculated and testicular cohorts for in the number of cancelled cycles due to embryos unavailable for transfer (22.8%; 7.6%, p = 0.03), number of embryos transferred per cycle (1.35 ± 1.62; 1.10 ± 1.9, p = 0.15) respectively. A significant difference was found among the ejaculated and testicular cohorts for fertilization (61.7%; 64.9%, p = 0.17) blastulation rates (55.8%; 55.3%, p = 0.86) and count of cryopreserved blastocysts (1.58 ± 2.61; 1.10 ± 1.9, p = 0.15) respectively. A significant difference was found among the ejaculated and testicular cohorts for fertilization (61.7%; 64.9%, p = 0.17) blastulation rates (55.8%; 55.3%, p = 0.86) and count of cryopreserved blastocysts (1.58 ± 2.61; 1.10 ± 1.9, p = 0.15) respectively. A significant difference was found among the ejaculated and testicular cohorts for fertilization (61.7%; 64.9%, p = 0.17) blastulation rates (55.8%; 55.3%, p = 0.86) and count of cryopreserved blastocysts (1.58 ± 2.61; 1.10 ± 1.9, p = 0.15) respectively. A significant difference was found among the ejaculated and testicular cohorts for fertilization (61.7%; 64.9%, p = 0.17) blastulation rates (55.8%; 55.3%, p = 0.86) and count of cryopreserved blastocysts (1.58 ± 2.61; 1.10 ± 1.9, p = 0.15) respectively. A significant difference was found among the ejaculated and testicular cohorts for fertilization (61.7%; 64.9%, p = 0.17) blastulation rates (55.8%; 55.3%, p = 0.86) and count of cryopreserved blastocysts (1.58 ± 2.61; 1.10 ± 1.9, p = 0.15) respectively. A significant difference was found among the ejaculated and testicular cohorts for fertilization (61.7%; 64.9%, p = 0.17) blastulation rates (55.8%; 55.3%, p = 0.86) and count of cryopreserved blastocysts (1.58 ± 2.61; 1.10 ± 1.9, p = 0.15) respectively. A significant difference was found among the ejaculated and testicular cohorts for fertilization (61.7%; 64.9%, p = 0.17) blastulation rates (55.8%; 55.3%, p = 0.86) and count of cryopreserved blastocysts (1.58 ± 2.61; 1.10 ± 1.9, p = 0.15) respectively.

CONCLUSIONS: Our study demonstrated cryptozoospermia patients who source sperm through testicular extraction or ejaculation prior to ICSI had similar ART treatment outcomes. There does not appear to be a deleterious effect with regard to fertilization, blastulation, and embryonic quality in cryptozoospermia patients who utilize ejaculated sperm found after thorough research and sedimentation. Further prospective studies including patients undergoing single euploid embryo transfers should be performed, in order to...
generate personalized and evidence based recommendations for couples facing cryptozoospermia.


SUPPORT: None.

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DOES MALE AGE AFFECT THE SPERM PARAMETERS AND IVF OUTCOMES? Marta Belles, MSc, Mireia Florensa, MSc, Marga Esbert, PhD, Ivi RMA Barcelona, Spain.

OBJECTIVE: Compared with the effect of the aging oocyte, the effect of male age on reproductive success has been studied in much less detail. Some studies have reported that male age declines sperm parameters but also the outcomes of IVF (In Vitro Fertilization) cycles. The mechanisms responsible for the decline in sperm fitness are not fully understood but damage by oxidative stress could be an important contributor, being responsible for the majority of sperm DNA fragmentation. Advancing paternal age has also been associated with increased risk of genetic diseases in the offspring. The main objective of this study is to assess if male age has an effect on IVF outcomes and sperm parameters.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A total of 1898 IVF cycles performed by women younger than 35 years between 2014 and 2018 in the same clinic was analyzed. Inclusion criteria were the use of ejaculated autologous sperm, ICSI performance and single embryo transfer at D+5 without preimplantation genetic diagnosis.

We assessed if male age had an effect over sperm parameters. We also studied if male age was correlated with fertilization rate, embryo quality (measured as total blastocyst and usable blastocyst rates), pregnancy, implantation, miscarriage and live birth rates. Student’s t-test and Person’s product-moment correlation analysis were used for statistical analysis and level of significance was set at P<0.05.

RESULTS: Age was statistically correlated with semen volume (P<0.001), motility percentage (P<0.001), the total number of progressively motile sperm (P=0.001), total sperm count (P<0.001) and progressive motility percentage (P<0.001) but it was not related to sperm concentration (P=0.96). Global fertilization rate was 70% and it was negatively related to male age (P=0.04). Global blastocyst rate was 56.06% while good quality embryos rate was 46.12%. No significant differences were found on both parameters (P=0.93 and P=0.94, respectively). Overall, clinical pregnancy, implantation, miscarriage and live birth rates were 57.48%, 50.58%, 11.91%, and 38.51%, respectively. Combined pregnancy genetic diagnosis.

OBJECTIVE: To our knowledge, this is the largest study relating male age with IVF outcomes after a single blastocyst transfer. The fact that neither embryo quality nor clinical outcomes are affected by male age may suggest that other factors such as female age can be positively influencing the cycle results. On the other hand, the analysis of these retrospective data confirm an age-related decrease in volume, sperm motility and total sperm count as well as a lower fertilization rate by ICSI in older males.

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HIGH RATES OF ANEUPLOIDY, MOSAICISM AND ABNORMAL MORPHOKINETIC DEVELOPMENT IN CASES OF VERY SEVERE MALE FACTOR WITH FEMALE PARTNERS ≤35 YEARS. Semra Kahraman, Prof., Murat Celekaykaya, M.D., PhD, Yucel Sahin, MD, Hakan Kadir Yelke, MSc, Yesim Kuntepe Colakoglu, MSc, Mehmet Ali Tufekci, PhD, Mesut Yesil, MSc, Cigdem Cinar Yapan, MSc. Istanbul Memorial Hospital, Istanbul, Turkey.

OBJECTIVE: Male infertility is a factor in approximately 50% of ART cases. Therefore, the relationship between severe male infertility and embryo aneuploidy has long been a subject of interest. However, most studies into this relationship were based on data obtained using FISH and there have been only a limited number of studies using comprehensive chromosomal analysis. Our study evaluates the blastocyst chromosomal status and embryo development in cases from the highest level of severe male factor infertility (≤35y) according to severe male infertility subgroups ranging from 5million/ml to non-obstructive azoospermia (NOA).

DESIGN: Couples applied for ART with female age ≤35 years and presented with Severe Male Factor (SMF) indication (study group) were divided into the following 3 subgroups according to sperm concentration: 1) between five million and one million, 2) less than one million, 3) Azoospermia: obstructive azoospermia (OA) and Non-obstructive Azoospermia (NOA).

MATERIALS AND METHODS: Outcomes of the study group were compared with the control group that was composed of males with normal sperm parameters (>39 million and >40% motile sperm in the ejaculate). 543 severe male infertility cases with partners ≤35y and 310 control cases with normal sperm parameters were studied. Initially aCGH and latterly NGS were used for PGTA-a and time lapse microscope for morphokinetic evaluation.

RESULTS: Significantly higher chromosomal aneuploidy rates (58%) were found in couples with NOA than the other SMF groups and control groups with normal sperm parameters (p<0.001). Mosaicism rates were higher in all SMF subgroups than the controls but significantly so only in NOA (p<0.05). Higher rates of abnormality in chromosomes 2,10,11,17, 21 and sex chromosomes were observed in the most severe forms of SMF groups, NOA and less than 1m/ml groups. However, they were significantly higher only in the testicular sperm groups (p<0.05).

Embryo morphokinetic evaluation showed that embryos in the NOA groups reached the first cleavage significantly faster than those in the control group 26.79h vs. 27.01h, respectively (p=0.048). Furthermore, significantly higher rates of direct uneven cleavage (27%) and arrested embryos (p<0.05) from PN stage to the blastocyst stage were observed in NOA and in the less than 1m/ml sperm groups.

CONCLUSIONS: Higher rates of chromosomal abnormality, mosaicism and morphokinetic abnormalities were associated in severe male factor cases particularly with testicular sperm obtained from azoospermic cases with female partners ≤35 years.

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DOES USE OF TESTICULAR SPERM IMPROVE OUTCOMES IN NONAZOOOSPERMIC COUPLES WITH PREVIOUS IVF FAILURE USING EJACULATED SPERM? M. Blake Evans, DO, Jessica A. Marinaro, MD, Kate Devine, MD, Micah J. Hill, DO, Alan H. DeCherney, MD, Russell P. Hayden, MD, Paul Shin, MD, Cigdem Tanrikut, MD, NIH-NICHD, Bethesda, MD, and MedStar Georgetown University Hospital, Washington, DC, Shady Grove Fertility, Washington, D.C., 2Weill Cornell Medicine, New York, NY.

OBJECTIVE: Due to controversial evidence that testicular sperm is associated with lower sperm DNA fragmentation (SDF) and improved outcomes compared to ejaculated sperm, this study evaluates intracytoplasmic sperm injection (ICSI) outcomes using testicular sperm in nonazoospermic couples with prior IVF failure using ES.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Jan 2015-Aug 2018, 64 nonazoospermic couples with ≥1 prior failed ART cycles using ES underwent testicular sperm extraction (TESE) for ICSI-ICSI. Failed cycles with ES: those not progressing to clinical pregnancy, Outcomes using TESE sperm were compared to the mean values of couples’ prior cycles using ES. Primary outcomes: clinical pregnancy and live birth rates (CPR & LBR). Secondary outcomes: fertilization and blastocyst conversion.

RESULTS: Average number of prior failed ART cycles using ES: 2.5 (range: 1-8). 71.8% of males had abnormal semen parameters. A subset of men (n=28) had SDF assessment (measured by sperm chromatin dispersion) of ES. Mean SDF was 39% (7-84%). 21 patients had SDF >25%. 88 total ICSI cycles were performed using TESE sperm (64 cycles: fresh TESE, 24 cycles: frozen-thawed). There were 52 fresh blastocyst transfers, 15 frozen blastocyst transfers, and 21 cycles without transfer (9 additional FETs using supernumerary embryos; 76 total transfers). A comparison of TESE-ICSI cycles in those couples with ≥2 prior failed ART cycles using ES yielded similar findings to the whole group.
CONCLUSIONS: In nonazoospermic couples with failed ART using ES, ICSI using TESE sperm may improve blastocyst development, number of embryos available for vitrification, CPRs, and LBRs. Testicular sperm may avoid the adverse effects of elevated SDF from ES and improve pregnancy outcomes in some patients. Randomized studies are needed to determine if such a benefit exists.

IVF OUTCOME PREDICTORS - TRIGGER

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DOES OVULATORY TRIGGER CHOICE INFLUENCE MATURITY AND DEVELOPMENTAL COMPETENCE OF FROZEN-THAWED OOCYTES? Sydney Chang, MD, a Carlos Hernandez-Nieto, MD, b Dmitry Gounko, MA, b Beth McAvey, MD, a. Lucky Sekhon, MD, b Alan B. Copperman, MD, a aIcahn School of Medicine at Mount Sinai, New York, NY; bReproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: The luteinizing hormone (LH) surge stimulates resumption and progression of meiosis in oocytes from prophase to metaphase in preparation for fertilization. Given that oocyte maturity is a developmental continuum, it is unclear whether changes in the duration or level of the LH surge can have downstream effects on the microenvironment of the cumulus-oocyte complex, leading to variations in the integrity of oogenesis and early chromosomal segregation. Studies have investigated the effects of different oocyte maturation triggers—human chorionic gonadotropin (hCG), GnRH agonist (Lupron), or a combination of the two (dual)—on IVF outcomes.1,2 Some evidence has suggested pregnancy rates are lower with Lupron triggers, possibly due to the shorter duration of the LH surge.3

Use of oocyte cryopreservation has increased, but most patients have yet to utilize these oocytes. Consequently, the effect of trigger type on developmental competence of frozen oocytes suspended in metaphase II is still unknown. The objective of this study was to determine whether rates of oocyte survival post-re-warming, maturation, fertilization, blastulation, and euploidy were affected by trigger type.

DESIGN: Retrospective, cohort study

MATERIALS AND METHODS: The study included patients at an academic ART center who underwent oocyte cryopreservation and subsequent re-warming for IVF/ICSI between 2010 and 2019. Patients were grouped by oocyte maturation trigger type used during their initial cycle: (1) hCG, (2) Lupron, (3) dual. Primary outcomes were thaw survival and oocyte metaphase II (MII) rates. Secondary outcomes were fertilization, blastulation, and euploidy rates. Statistical analysis was performed with the use of T-tests, chi-square tests, and multivariate linear regressions with generalized estimating equations.

RESULTS: A total of 182 cycles from 167 patients were included in this study. Controlling for oocyte age, AMH, and gravidity, there was no statistically significant difference in rates of thaw survival, MII fertilization, or euploidy between groups. There was, however, a statistically significant difference in blastulation rate (Dual vs. Lupron: β=31.6, p=0.006, hCG vs. dual: β=10.5, p=0.34; hCG vs. Lupron: β=21.2, p=0.14).

CONCLUSIONS: Studies of the effects of oocyte maturation trigger on pregnancy outcomes are conflicting, and have focused on implantation in fresh IVF cycles. In contrast, this study examines surrogate endpoints for the efficacy of hCG, Lupron, and dual trigger in a group of non-infertile young women. We showed that trigger type does not affect survival rates following oocyte warming, or MII rate. There appears to be an increase in blastulation rates between patients using dual trigger, compared to Lupron only. This finding is in agreement with a prior study that compared dual trigger vs. Lupron alone in high responder patients undergoing autologous IVF. Future studies might aim to analyze oocytes and granulosa cells from follicles triggered with dual trigger vs. Lupron alone, focusing on early molecular pathways and gene networks that are integral to embryonic genome activation.


P-249 Tuesday, October 15, 2019 6:30 AM

DUAL TRIGGER USING RECOMBINANT HCG AND GONADOTROPIN-RELEASING HORMONE AGONIST IMPROVE OOCYTE QUALITY AND EMBRYO GRADE FOR NORMAL RESPONDERS IN GnRH ANTAGONIST CYCLES: RANDOMIZED CONTROLLED TRIAL. Ahmed Ali Abdelmaleem, MD,a Shymaa Ali, MSc,b Ahmed M. Abbas, MD,a Tarek Farghaly, MD,a Elwany Elsenoby, MD,a Gamal Sayed, MD,a bDepartment of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; bDepartment of Obstetrics and Gynecology, Faculty of Medicine, Suez University, Suez, Egypt.

OBJECTIVE: To evaluate the effectiveness of dual trigger using gonadotropin-releasing hormone (GnRH) agonist and recombinant human chorionic gonadotropin (rHCG) versus rHCG alone for normal responders in GnRH antagonist intracytoplasmic sperm injection (ICSI) cycles

DESIGN: Randomized, open-labeled, controlled trial (clinical trial.gov: NCT02916173).

MATERIALS AND METHODS: All women attended for first planned fresh embryo transfer ICSI cycles were invited to participate in the study if
they met our inclusion criteria. We included women aged less than 40 years, body mass index (BMI) ranges from 18-30 kg/m², Anti-mullerian hormone (AMH) levels more than one ng/mL, normal, mild or moderate male factor infertility. The study participants were randomized to either group I (HCG group-triggered by 250µg of hCG and GnRH agonist; 1 mg leuprolide acetate. The primary outcome was the number of MII oocytes in both groups. The secondary outcome included the number of oocytes retrieved, number of Grade 1 embryos, fertilization rate, implantation rate, clinical pregnancy rate, miscarriage rate, live birth rate, the cumulative pregnancy rate per embryo transfer and cumulative live birth rate among both groups. Student’s t-test and Chi-square test were used for the analysis of the outcomes.

RESULTS: One hundred and sixty women consented to participate and randomized (80 women in each arm). Both groups were similar in baseline demographic and clinical characteristics as mean age, BMI, duration, cause of infertility and hormonal profile. In comparison to the HCG group, women who received dual trigger had a statistically significantly higher number of retrieved oocytes (14.20±7.868 vs. 10.53±4.79, p=0.001), number of MII oocytes (10.78±6.758 vs. 8.48±2.4, p=0.01) and number of grade 1 embryos (5.28±3.79 vs. 4.29±2.66, p=0.04). The fertilization rate was slightly higher in the HCG group, but this did not reach a statistical significance (77.6% vs. 73.7%, p=0.442). No difference between both groups regarding the chemical hCG (p=0.312), clinical pregnancy (p=0.731), miscarriage (p=0.523), multiple pregnancy (p=1.00) and live birth rates (p=0.725) between both groups. The dual trigger group showed significantly higher clinical pregnancy (p=0.04) and live birth rates (p=0.03) after frozen-thawed embryos transfer. No significant difference among both groups regarding the cumulative pregnancy and cumulative live birth rates (p=0.08).

CONCLUSIONS: Dual trigger by GnRH agonist and hCG could improve the oocyte quality and embryo grading for normal responders in GnRH antagonist ICSI cycles.

SUPPORT: None.

P-250
WITHDRAWN

P-251 Tuesday, October 15, 2019 6:30 AM
TO BOOST OR NOT TO BOOST: DOES ADMINISTRATION OF RESCUE HCG IMPROVE OUTCOMES IN POOR RESPONDERS WITH LOW POST-TRIGGER VALUES? Jenna Friedenthal, MD, Joseph A. Lee, BA
Daniel E. Stein, MD, Tanmoy Mukherjee, MD, Alan B. Copperman, MD, Icahn School of Medicine at Mount Sinai, New York, NY; Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: Ovarian hyperstimulation syndrome (OHSS) is a potential complication of ART that can be concerning to patients and a difficult therapeutic challenge to physicians. One preventative measure to minimize the risk of OHSS is to lower the dose of hCG prior to retrieval. However, there is a threshold under which final maturation of the cumulus cell-oocyte complex might not occur. Several surrogate markers may be used to determine appropriate response to trigger, including serum progesterone (P4) or hCG on day after trigger administration. When these markers suggest an inadequate response, some clinicians supplement patients with booster or “rescue” hCG. However, there is limited data on the effectiveness of rescue hCG in improving oocyte yield. Our goal was to compare outcomes between patients who did or did not receive rescue hCG in a population of patients with an inadequate response to trigger.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Our study included patients at a single academic center who underwent controlled ovarian hyperstimulation and met criteria for rescue hCG (P4 <1.0 ng/dl or hCG level <40mIU/mL on day after trigger) from 2004 to 2019. Patients were separated into 2 groups based on administration of supplemental hCG (Case Group: hCG trigger 36 hours and rescue hCG 12-24 hours prior to retrieval; Control Group: hCG trigger 36 hours prior to oocyte retrieval). Patients were excluded if leuprolide acetate was used for trigger, either as a dual trigger or as leuprolide alone. A sub-analysis of poor responders to COH (Bologna criteria: age >40, antral follicle count < 10 follicles total, or AMH ≤ 1ng/mL) was performed. Primary outcome was the number of oocytes retrieved. Data were analyzed using students t-tests, chi square tests, and a multivariable logistic regression analysis, with p<0.05 considered significant.

RESULTS: A total of 732 patients who underwent 833 cycles were assessed. The case group consisted of 397 cycles in which both 36 hour and subsequent rescue hCG prior to retrieval were used. The control group consisted of 436 cycles in which a single hCG trigger 36 hours prior to retrieval was used. There were significant differences in age, AMH, BMI, the number of follicles ≥ 14mm visualized on day of trigger, estradiol, and progesterone on day of trigger between groups. After adjusting for the confounding variables, use of rescue hCG did not predict number of eggs retrieved (β = 0.05, p = 0.83). In our sub-analysis of poor responders that controlled for the same confounders, we found that the use of rescue hCG was significantly correlated with the number of eggs retrieved (β = 0.53, p = 0.03).

CONCLUSIONS: In the largest study to date evaluating the use of rescue hCG to improve oocyte yield, our data suggest an improvement in number of eggs retrieved in a subset of patients. While we did not demonstrate clinical advantage to using rescue hCG in the general study group, we found that a subset of poor responder patients benefited from supplemental hCG. Future studies should benefit from validating a threshold level for peak progesterone or hCG that customizes the use of rescue hCG.

SUPPORT: None.

P-252 Tuesday, October 15, 2019 6:30 AM
GNRH-AGONIST TRIGGER IN ‘FREEZE-ALL’ CYCLES: IMPROVES PREGNANCY RATES AND PATIENT SAFETY. Marcus J. Davenport, MBBS (Hons), BMedSc (Hons), Martin Healey, MBBS, MD, FRANZCOG, FRCOG, Vivien B. MacLachlan, BSc, Alon J. Talmor, MBMS, BSc(Hons), PhD, MRCOG, FRANZCOG, Beverley J. Vollenhoven, MBBS(Hons), PhD, FRANZCOG, CREL. Monash Health, Melbourne, Victoria, VIC, Australia; Monash IVF, Clayton, VIC, Australia; Department of Obstetrics and Gynaecology, Monash University, Melbourne, VIC, Australia.

OBJECTIVE: To evaluate whether GnRH-agonist (GnRHa) triggering improves embryo quality and live birth rates in ‘freeze-all’ cycles compared to human chorionic gonadotrophin (hCG).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: This retrospective cohort study from January 2012 and December 2014 compared GnRHa and hCG-triggered ‘freeze-all’ cycles. Limiting for first cycle per patient, 396 GnRHa and 1,868 hCG-triggered cycles were included. Only cycles where embryos were available and thawed for transfer were included for live birth rates (LBR). 217 GnRHa and 509 hCG-triggered cycles were analysed for LBR. A multiple imputation approach was used to account for missing data. The primary outcome was LBR. Secondary outcomes included number of oocytes collected, embryo grade and quality, clinical pregnancy rates and the incidence of ovarian hyperstimulation syndrome (OHSS). Regression analysis was performed to adjust for confounders. P-values <0.05 were considered statistically significant.

RESULTS: The singleton LBR after one embryo transfer was higher in GnRHa triggered ‘freeze-all’ cycles compared to hCG (38.4% vs. 24.6%, p=0.001), as well as a non-significantly higher cumulative LBR (57.4% vs. 41.1%, p=0.18). There was no difference in the number of embryos thawed or transferred, and there was no difference in embryo grade or expansion. The incidence of OHSS was significantly lower in GnRHa triggered cycles (0.5% vs. 1.9%, p=0.008).

CONCLUSIONS: GnRHa triggering resulted in a superior LBR compared to hCG in ‘freeze-all’ cycles, even after adjusting for confounders. GnRHa triggering did not compromise embryo quality and significantly reduced the risk of OHSS compared to hCG. Given these findings, GnRHa triggering appears to be the way of the future for ‘freeze-all’ cycles.

Reference: None.

SUPPORT: None.

P-253 Tuesday, October 15, 2019 6:30 AM
HOW WE TRIGGER MATTERS: INTRANASAL GnRH-AGONIST TRIGGER MAY REDUCE OOCYTE MATURATION COMPARED TO SUBCUTANEOUS ADMINISTRATION IN ICSI CYCLES. Marcus J. Davenport, MBBS (Hons), BMedSc (Hons), Vivien B. MacLachlan, BSc, Beverley J. Vollenhoven, MBBS(Hons), PhD, FRANZCOG, CREL.

As a helpful assistant, I have converted the text into a plain text format. This conversion is designed to make the content easily readable and comprehensible. If you need any further assistance or have specific requirements, feel free to ask!
OBJECTIVE: To evaluate oocyte maturation and fertilisation rates of intracytoplasmic sperm injection (ICSI) cycles triggered with intranasal and subcutaneous GnRH agonists (GnRHa).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: This retrospective cohort study from May 2016 to August 2018 compared intranasal and subcutaneous GnRHa triggers in ICSI cycles. Data was extracted from 9588 ICSI cycles. A total of 781 cycles were included for analysis after excluding cycles triggered with hCG (n=8521), duplicate patient cycles (n=182), where a duel trigger was used (n=55) or where the trigger was not recorded (n=49). 214 cycles utilised the intranal Na-farelin trigger (Synarel; Pfizer Pty Ltd) and 567 cycles used a subcutaneous formulation, either Triptorelin (Decapeptyl; Ferring Pharmaceuticals Pty Ltd) or Leuprolrelin (Lucrin; AbVie Pty Ltd).

The primary outcome was oocyte maturation rate. Secondary outcomes included number of mature oocytes collected, number of fertilised oocytes, fertilisation rate and the incidence of ovarian hyperstimulation syndrome (OHSS). Categorical data was presented as a proportion (%) and p-values were obtained by performing a Mann-Whitney U test. Continuous and count data was presented as a mean with standard deviation and standard error of mean, and p-values were obtained by performing the student’s T-test. Univariate and adjusted analyses were performed using negative binomial regression for count measures and linear regression for continuous measures. Statistical significance was defined as a p-value <0.05.

RESULTS: There was a trend towards higher oocyte maturation rates in patients receiving a subcutaneous GnRHa trigger compared to intranasal formulations (78.1% vs. 77.6%, p=0.059). There was a statistically significant difference in fertilisation rate in favour of the subcutaneous trigger (68.0% vs. 67.9%, p=0.016). There was no difference in the age or BMI of patients, nor was there a difference in the crude number of mature or fertilised oocytes. The incidence of OHSS was significantly lower in patients receiving the subcutaneous GnRHa triggered cycles (0.0% vs. 1.4%, p=0.004).

CONCLUSIONS: Subcutaneous administration of the GnRHa trigger may improve oocyte maturation and fertilisation rates in ICSI cycles, and is associated with lower rates of OHSS. Given these findings, a prospective randomised controlled trial is needed to further elucidate whether a subcutaneous formulation outperforms an intranasal GnRHa trigger.

SUPPORT: None.

P-255 Tuesday, October 15, 2019 6:30 AM

THE EFFECT OF FOLLICLE STIMULATING HORMONE ADMINISTRATION AT THE TIME OF HUMAN GONADOTROPIN TRIGGERING, IS IT IMPROVE THE OOCYTE/EMBRYO PROFILE IN IN VITRO FERTILIZATION CYCLES? Young Sang Kim, M.D.1 Dong Soo Park, M.D.2 Mi Kyong Youn, M.D.3 You Shim Kim, M.D.4 Ph.D.4 Myung Joo Kim, M.D.2,5 Ran Kim, M.D.6 Hyeok Kim, MD.7 Tae Ki Yoon, M.D.8 Chanhong Park, M.D.9 Hannah Kim, M.D. A.1,2,3,4,5,6,7,8,9 CHA Fertility Center Seoul Station, Obstetrics and Gynecology, Seoul, Korea, Republic of (South); 2Department of OB/GY CHA Fertility Center Seoul Station, CHA University, Seoul, Korea, Republic of (South); 3CH A Fertility Center Seoul Station, CHA University, Seoul, Korea, Republic of (South); 4Department of OB/GY, CHA Fertility Center Seoul Station, CHA University, Seoul, Korea, Republic of (South); 5Department of OB/GY CHA Fertility Center Seoul Station, CHA University, Seoul, Korea, Republic of (South); 6Department of OB/GY CHA Fertility Center Seoul Station, Seoul, Korea, Republic of (South); 7Department of OB/GY CHA Fertility Center Seoul Station, Seoul, Korea, Republic of (South); 8Department of OB/GY CHA Fertility Center Seoul Station, Bundang, Korea, Republic of (South).; 9Department of OB/GY CHA Fertility Center Seoul Station, Bundang, Korea, Republic of (South).

OBJECTIVE: To evaluate whether an additional follicle stimulating hormone (FSH) administration at the day of human chorionic gonadotropin (hCG) triggering can improve the oocyte/embryo quality and pregnancy rates in vitro fertilization (IVF) cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: 585 patients in fresh IVF cycles with antagonist protocol divided into two groups. FSH injection at hCG triggering day (N=211) and did not (N=374). We estimate the maturation rates of retrieved oocytes, fertilization rates, top quality (Grade 1–2) embryo counts and pregnancy outcomes in two groups.

RESULTS: There was no significant difference between two groups in patient’s demographics (age, body mass index, anti-mullerian hormone level, infertility etiology), and characteristics of fresh IVF cycles (total FSH injection dose, estradiol/luteinizing hormone/progesterone level on hCG triggering day, endometrial thickness on hCG triggering day). For outcomes of fresh IVF cycles, matured oocyte count (6.9±3.7 vs 7.1±4.0; p=0.502), fertilization rate (69.0% vs 70.3%; p=0.452), top quality embryo count (2.5±2.0 vs 2.2±1.6; p=0.086) were not significantly different. For pregnancy outcomes of fresh IVF cycles, implantation rate (54.5% vs 48.1%; odds ratio [OR], 1.29; 95% confidential interval [CI], 0.92-1.81) and clinical pregnancy rate (42.2% vs 35.0%; OR, 1.38; 95% CI, 0.98-1.95) were not significantly different, but ongoing pregnancy rate (38.4% vs 29.1%; OR, 1.51; 95% CI, 1.06-2.16) was significantly higher in FSH injection group.

CONCLUSIONS: The effect of an additional FSH administration at the day of hCG triggering did not improve the oocyte/embryo profile. Implantation rates and clinical pregnancy rates were increased in FSH injection group, but there was no significant difference between two groups. Ongoing pregnancy rates was significantly higher in FSH injection group compared with no FSH injection group.

P-256 Tuesday, October 15, 2019 6:30 AM

DOES POST-TRIGGER SERUM B-HCG VALUE MAT-TER IN PATIENTS WITH SUBOPTIMAL LH RESPONSE AFTER DUAL TRIGGER CYCLES? Kolbe Hancock, MD.1 Chelsea Canon, MD.1

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OBJECTIVE: The use of dual trigger during ovarian stimulation to initiate the final maturation of oocytes has become an increasingly popular technique, as it decreases the risk of ovarian hyperstimulation syndrome. In GnRH agonist trigger cycles, there is a subset of individuals who have a suboptimal response to GnRH agonist, and in turn decreased oocyte yield and oocyte maturity. Post trigger serum luteinizing hormone (LH) levels >15 mIU/mL and ideally ≥30 mIU/mL have been associated with improved cycle outcomes. In patients who received a dual trigger but had a suboptimal response to GnRH agonist trigger, we sought to investigate whether the post hCG value was correlated with oocyte maturity rate.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All patients 23-49 years old undergoing IVF stimulation cycles between 2010 and 2019 who received dual trigger with 4mg Lupron and variable doses of hCG ranging from 1,000-10,000 were analyzed for inclusion. Those whose LH post trigger was <30 mIU/mL were included. The primary outcome was oocyte maturity rate. STATA Statistical Software Version 11 (StataCorp LP) was used for data analysis. A multivariate linear regression was used to assess whether the summed value of post-trigger LH and b-hCG was associated with the oocyte maturity rate in all patients with LH <30. The same regression was performed for subgroups of LH <3 in increments of 5 mIU/mL. For patients with an LH <30, a multivariate linear regression was performed to assess whether the summed value of the post hCG and LH was associated with a difference in the oocyte maturity rate.

RESULTS: A total of 204 cycles meeting the inclusion criteria were analyzed. The average age was 36.7 ± 5.5 years, and the average BMI was 27.2 ± 6.9 kg/m². The post hCG values ranged from 15 to 425 mIU/mL. Comparing all patients with an LH <30 and controlling for BMI and age, there was no significant correlation between post hCG and percent mature oocytes (p=0.456). Similarly, when controlling for BMI and age, there was no significant correlation between the sum of post-trigger LH and b-hCG and the oocyte maturity rate (p=0.38). When the post-trigger LH value was stratified by increments of five mIU/mL from 0 to 30, there was still no significant correlation between the post hCG and the oocyte maturity rate (p values range from 0.46 to 0.88). Amongst those with a post trigger LH<15 mIU/mL, there was no significant difference in the oocyte maturity rate when the post hCG was above or below 50 mIU/mL. Similarly, amongst those with a post trigger LH between 15 mIU/mL and 30 mIU/mL, there was no significant difference in the oocyte maturity rate when the post hCG was above or below 50 mIU/mL.

CONCLUSIONS: In patients receiving dual trigger who fail to mount an optimal response to the GnRH agonist component, post hCG level does not correlate with oocyte maturity rate. When stratified by the post trigger LH level, we have shown that there is not a specific LH value at which post trigger hCG level has an impact on the primary outcome. There also does not appear to be an optimal summed value of post-trigger LH and b-hCG that is correlated with the oocyte maturity rate.
University of Texas Health Science Center at Houston, Houston, TX; 
1C2RM Fertility Houston, Houston, TX.

OBJECTIVE: To assess the content and accuracy of fertility counseling received via asynchronous peer and professional input through a digital women’s health clinic.

DESIGN: Quantitative and qualitative assessment of publicly available online content

MATERIALS AND METHODS: The fertility treatment forum of an established digital women’s health clinic, consisting of posts answered asynchronously by peers and professionals, were queried for available posts. All questions and answers were transcribed and then categorized by question topic and theme, quantity and quality of responses, and credentials of respondents. Answers were reviewed for accuracy by a board-certified reproductive endocrinologist.

RESULTS: 87 questions were available for review, posted over a 6-month timeframe in 2018-19. Of these, 47 (54.0%) related to in vitro fertilization (IVF), 20 (23.0%) to oocyte cryopreservation (OC), and 20 (23.0%) to intrauterine insemination (IUI). A minority of posts (17, 19.5%) primarily sought emotional support. Responders were as follows: 10 (17.2%) fellow patients, 9 (15.5%) allied health providers, 25 (43.1%) nurses or midwives, and 11 (19.0%) physicians, including 3 (5.2%) reproductive endocrinologists.

Of all 87 posts, 38 (43.7%) received no answer, 40 (46.0%) received 1 answer, and 9 (10.3%) received 2 answers. The unanswered questions (30) were mostly (78.9%) medical in nature, with 5 (13.2%) requests for emotional support and 3 (7.9%) seeking logistical clarifications. Of the 58 answers, 18 (31.0%) recommended a synchronous video follow-up appointment without offering any medical advice. Substantive answers offered a mix of the following attributes: 22 (37.9%) emotional encouragement or support, 11 (19.0%) narration of personal experiences, and 27 (46.6%) medical advice. Of those offering medical advice, 20 (34.5%) were deemed medically accurate.

CONCLUSIONS: Online forums and digital clinics are increasingly available and utilized for patients struggling with infertility. As access to high-quality infertility care remains limited due to cost and geography, asynchronous forums hold the potential to fill gaps in care and provide emotional support. However, in our analysis of the leading digital women’s health clinic, those patients seeking answers in the infertility treatment forum received asynchronous medical advice nearly half of the time, and only a third of responses were deemed medically accurate. Most responses (94.8%) were not from an individual specifically trained in reproductive endocrinology. Though further evaluation of similar sites and resources is indicated, we conclude that asynchronous digital medicine is currently a highly inaccurate and unreliable source of information for fertility patients. Further efforts are needed to ensure that women and couples can access appropriately-trained and specialized physicians and nurses to answer their detailed questions and guide treatment in a compassionate and evidence-based manner.

SUPPORT: None.

P-261 Tuesday, October 15, 2019 6:30 AM

A NEW ERA IN MEDICINE: SOCIAL MEDIA AND PATIENT CARE. Anisa Hussain, MA,* Jacqueline Sehring, MA,* Elisabeth Rosen, BS, MA,* Lauren Grimm, MA,* Jody M. Esquerra, MA,* Karine Matevosian, DO,* Poochi Kaushik Amin, MD,* Rooshi Ieliani, MD,* Angeline Beltsos, MD* Vios Fertility Institute, Chicago, IL;*Advocate Lutheran General Hospital, Park Ridge, IL;*Wayne State University, Detroit, MI.

OBJECTIVE: We compared physician social media goals to patient social media wants in order to optimize the physician-patient relationship in the digital world.

DESIGN: Anonymous survey completed by patients and physicians.

MATERIALS AND METHODS: An anonymous survey distributed over social media to patient and physician users investigated physician content goals and patient motivations and habits. Responses collected within a range of 0-10 were scaled as follows: 0-1 strongly disagree, 2-4 disagree, 5 neither agree nor disagree, 6-8 agree, 9-10 strongly agree.

RESULTS: 219 patients and 22 physicians participated in the study. 70% of the patients were 26-45 years old, 76% of the physicians were 31-50 years old. 81% of patients looked to physicians for emotional support on social media and 63% of physicians identified emotional support as a goal of their social media activity. However, mean patient response was 4.46 (disagree) and mean physician response was 7.18 (agree), p = .004. Of those offering any medical advice, 20 (34.5% of all answers) were deemed medically accurate.

CONCLUSIONS: There were no significant differences in barriers to treatment for women who screened positive for anxiety/depression compared to those who did not. Also, women endorsed emotional distress associated with infertility, regardless of a positive or negative screen for anxiety or depression. Despite this, few established with embedded psychological support in the clinic, reporting social/emotional reasons over logistical barriers. Although 1/2 of women reported desiring counseling, they questioned if their distress level warranted treatment. This demonstrates that women may benefit from education and normalization of psychological support regardless of severity of mood symptoms. Universal referral or integration of emotional support into medical care may be beneficial to target all women and optimize overall outcomes.

SUPPORT: None.

P-259 WITHDRAWN

P-260 Tuesday, October 15, 2019 6:30 AM

OPTIMIZING UTILIZATION OF EMOTIONAL SUPPORT DURING INFERTILITY TREATMENT. Sarah A. Hirsch, DO,* Pippa Simpson, PhD,* Kathryn E. Flynn, PhD,* Melodie Nugent, MA,* Abbey Kruter, PsyD* Medical College of Wisconsin, Milwaukee, WI;* Affiliation not provided.

OBJECTIVE: The psychological distress of infertility influences decision-making and treatment discontinuation. Yet, only 10-34% of patients with infertility pursue counseling. Historically, barriers included logistics of scheduling appointments and sufficient coping resources. The objective of this study was to identify barriers to counseling for women with infertility in a clinic with embedded psychological support; and determine if those barriers were dependent upon screening scores for anxiety or depression.

DESIGN: Cross sectional retrospective chart review.

MATERIALS AND METHODS: Female patients presenting for initial infertility consultation were screened for anxiety and depression with the Generalized Anxiety Disorder-7 Item Scale (GAD-7) and Patient Health Questionnaire-9 (PHQ-9) as standard of care. Subjects were recruited at follow up appointments at least 3 months after initial consultation. An 11-item survey designed to assess barriers, needs, and desires for psychological treatment was administered. Demographic data and medical history were obtained via chart review. The survey results were analyzed as a population and divided into 2 groups: those with a positive screen for anxiety or depression (score ≥ 5 on either scale) and those with a negative screen. Non-parametric Mann-Whitney test was used for continuous variables (reported as median and inter-quartile range) and the Fisher’s Exact test was used for categorical variables. A p-value of < 0.05 was considered significant.

RESULTS: The sample consisted of 68 participants. On a 1-5 Likert scale, emotional stress (3 (2-4) had a higher median than physical stress (2 (1-3); there was a positive correlation between emotional and physical stress (r = 0.616; p < 0.001). There were no differences in the survey items for barriers, needs, or desires between those that screened positive for anxiety/depression compared to those who did not. The primary barrier to treatment was social/emotional (65%); second was logistical (45%). The most cited barriers included alternative sources of support, scheduling conflicts, and patient perception that her stress level did not warrant treatment. Despite 50% identifying counseling as the primary preference for support, it was only utilized by 7%

CONCLUSIONS: There were no significant differences in barriers to treatment for women who screened positive for anxiety/depression compared to those who did not. Also, women endorsed emotional distress associated with infertility, regardless of a positive or negative screen for anxiety or depression. Despite this, few established with embedded psychological support in the clinic, reporting social/emotional reasons over logistical barriers. Although 1/2 of women reported desiring counseling, they questioned if their distress level warranted treatment. This demonstrates that women may benefit from education and normalization of psychological support regardless of severity of mood symptoms. Universal referral or integration of emotional support into medical care may be beneficial to target all women and optimize overall outcomes.

SUPPORT: None.
CONCLUSIONS: Both patients and physicians agreed that social media can be a patient education tool and that the role of a physician should extend beyond the physical practice. However, patient and physician responses on using social media accounts as a tool for emotional support did not align. This may be due to the prevalence of social support groups on social media that offer extensive emotional support. Additionally, while physicians reported higher satisfaction in patients that follow them on social media, patients who did so did not report higher satisfaction. Although both patients and physicians agreed that social media is a tool for patients to see a side to their doctors beyond medicine, there was a significant difference between their responses—physicians agreed with this statement more strongly than patients. Trust is a critical component of the physician-patient relationship, and appropriate physician social media use allows to optimize this relationship in the digital age, especially when working with a younger patient population.

P-263 Tuesday, October 15, 2019 6:30 AM

EFFECT OF MUSIC IN REDUCING PATIENT ANXIETY DURING COLOPSCOPY: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS. Ahmed M. Abdelhakim, MB BCH, b Ahmed Samy, MD, c Ahmed M. Abbas, MD, b, c Kasr Al-Ainy Faculty of Medicine, Cairo University, Cairo, Egypt; d Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt.

OBJECTIVE: Music therapy has been used greatly in various medical procedures to reduce associated anxiety and pain. This review aims to evaluate the evidence from published randomized clinical trials (RCTs) about the effect of music intervention in reducing patient’s anxiety during the colposcopy.

DESIGN: Systematic review and meta-analysis.

MATERIALS AND METHODS: We performed a comprehensive literature search using four electronic databases (PubMed, Cochrane library, Scopus and ISI Web of science) using the following search terms: (Music OR Symphony OR Rhythm OR Orchestra OR Song) AND (Colposcopy OR cervicoscope OR colposcope). All RCTs assessing the effect of music therapy versus no music in reducing anxiety during colposcopy were considered. Eighty-five studies were identified of which five studies deemed eligible for this review. The extracted outcomes were: anxiety, pain during and after the procedure, and satisfaction levels. Continuous outcomes were pooled as weighted mean difference (WMD) and standardized mean difference (SMD) using the Mantel-Hansel method with 95% confidence intervals (CI). All statistical analyses in this study were completed by the RevMan software package.

RESULTS: We included five studies with a total number of 836 patients in our final analysis. We found no effect of music therapy in reducing the anxiety levels when compared with the control group (SMD = -0.11, 95% CI [-0.36, 0.14], p = 0.4). No difference between music and control groups regarding pain during and after the procedure respectively (SMD = -0.20, 95% CI [-0.58, -0.18], p = 0.31) and (SMD = -0.10, 95% CI [-0.30, -0.10], p = 0.33). The pooled SMD showed a similarity between the music group in comparison with no music intervention group (SMD = 0.16, 95% CI [-0.02, 0.34], p = 0.08).

CONCLUSIONS: This systematic review suggests that music therapy has no great positive effect in reducing anxiety and pain levels and no effect in increasing satisfaction levels when compared with control groups during the colposcopy procedure.

SUPPORT: None.

P-264 Tuesday, October 15, 2019 6:30 AM

DIETARY PATTERNS ARE ASSOCIATED WITH OVARIAN RESERVE IN OVERWEIGHT AND OBESE WOMEN IN A REPRODUCTIVE AGE COHORT. Ashley Eskew, MD, MSCL, a Bronwyn Bedrick, BA,b Joan Riley, PhD, HCLD,c Jorge E. Chavarro, MD, Sc.D.d Emily S. Junghem, MD, MSCL. a Washington University School of Medicine, St. Louis, MO; b Washington University in St. Louis, Saint Louis, MO; c Washington University School of Medicine, St. Louis, MO; d Harvard School of Public Health, Boston, MA.

OBJECTIVE: The objective of this study was to examine the relationship between dietary patterns and markers of ovarian reserve as measured by serum antimullerian hormone (AMH) levels and antral follicle count (AFC) in a reproductive age cohort of women.

DESIGN: Cross-sectional cohort study.

MATERIALS AND METHODS: Women aged 18 to 44 years with regular menstrual cycles were recruited for this study. Women who were pregnant, had a history of infertility, ovarian surgery or major chronic illness were excluded. AFC was determined by transvaginal ultrasound. AMH was measured with a Roche cobas e411 analyzer. A validated food frequency questionnaire (FFQ) and the Kaiser Physical Activity Survey were used to

TABLE 1. pre- and post-class stress, sadness and hopefulness

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pretest Mean</th>
<th>Pretest SD</th>
<th>Posttest Mean</th>
<th>Posttest SD</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stress</td>
<td>6.96</td>
<td>2.14</td>
<td>4.00</td>
<td>2.15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sadness</td>
<td>5.67</td>
<td>2.99</td>
<td>3.11</td>
<td>2.37</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hopefulness</td>
<td>6.78</td>
<td>2.25</td>
<td>7.78</td>
<td>1.90</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Fertile Yoga class decreased student stress and sadness and increased hope. Students reported that they were likely to continue to use the mantra and spine movements during their infertility journey. Given that many infertility patients stop treatment prematurely due to stress and feelings of discouragement, the techniques used in Fertile Yoga class could ultimately provide our patients the emotional energy and skills necessary to continue with fertility treatment and succeed. Data is being collected to better elucidate the role of Fertile Yoga on our patients’ fertility journey.

Reference: None.

SUPPORT: None.

P-265 Tuesday, October 15, 2019 6:30 AM

OBESITY

Vol. 112, No. 3, Supplement, September 2019
assess diet and exercise patterns over the prior year. After assessment of physical activity and BMI, women with a caloric intake < 500 or > 5000 kcal/day were excluded. We assessed adherence to one of two dietary patterns: 1) the fertility diet (FD), characterized by a higher intake of vegetables and antioxidants, low ratio of monounsaturated to trans-fat, high-fat dairy, iron supplementation and a daily multivitamin, and 2) the pro-fertility diet (PFD), characterized by higher intakes of B12,olic acid, vitamin-D, dairy, and whole grains, low pesticide residue produce and soy or seafood as preferential protein sources. Adherence to a dietary pattern was defined by a factor score with higher values indicating greater adherence.

Linear regression was used to control for potential confounders.

RESULTS: Two-hundred women were recruited and 175 were included in the analysis. Subjects were a mean age of 31.0 (±6.6) years and had a mean BMI of 27.7 (±7.0) kg/m². After stratifying by BMI and adjusting for age, smoking and physical activity level, adherence to the PFD in overweight and obese women (BMI ≥ 25 kg/m²) was linearly associated with higher AMH concentrations. Women in the third and fourth quartiles of the PFD had mean AMH levels 1.45 ng/mL (95%CI 0.33-2.56, p=0.01) and 1.67 ng/mL (95%CI 0.60-2.74, p=0.003) higher than women in the lowest quartile respectively. The highest adherence to the PFD was also associated with a higher AFC in overweight and obese women (B=7.8, 95%CI 0.003-15.34, p=0.049). The FD was not significantly associated with AMH or AFC in overweight or obese women. Dietary patterns were not associated with markers of ovarian reserve in normal weight women.

CONCLUSIONS: Consumption of low pesticide residue produce and adherence to a PFD has been associated with improved reproductive outcomes in women undergoing IVF. Our study is the first to demonstrate that increased adherence to a PFD is linearly associated with AMH in an overweight and obese reproductive aged cohort of women. It is critical that further studies examine dietary patterns in at-risk populations to determine the potential impact on ovarian reserve in reproductive age women.


SUPPORT: Research reported in this publication was supported by the National Center For Advancing Translational Sciences of the National Institutes of Health under Award Numbers and KL2 TR000450 and TL1TR002344. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.
CONCLUSIONS: Obesity does not appear to impact post-warming cryo-
survival after oocyte vitrification. In humans, the intra-oocyte lipid stores that
could result as a consequence of obesity may not meaningfully impact toler-
ance to cryopreservation unlike other mammalian species. Additional
adequately powered studies are required to determine the impact of class
III obesity on post-warming cryosurvival after oocyte vitrification.

References:
1. Seidell JC, Jr. Modifying oocytes and embryos to improve their cryopreservation.
2. Gu L, Liu H, Gu X, Boots C, Moley KH, Wang Q. Metabolic control of
oocyte development: linking maternal nutrition and reproductive outcomes.
3. Pereira RM, Marques CC. Animal oocyte and embryo cryopreservation.
4. Prates EG, Nunes JT, Pereira RM. A role of lipid metabolism during
cumulus-oocyte complex maturation: impact of lipid modulators to improve
5. Robker RL, Akison LK, Bennett BD, Thrupp PN, Chura LR, Russell DL,
et al. Obese women exhibit differences in ovarian metabolites, metabo-
lites, and gene expression compared with moderate-weight women. J
to lipid-rich follicular fluid is associated with endoplasmic reticulum
stress and impaired oocyte maturation in cumulus-oocyte complexes. Fertil

SUPPORT: None.

P-268 Tuesday, October 15, 2019 6:30 AM

ABC TRIAL: BODY MASS INDEX AND PERCENTAGE BODY FAT ARE NOT DIFFERENT IN POSITIVE PREDECTIVE VAUE OF MISCARRIAGE OR PRETERM DELIVERY IN PATIENTS UNDERGOING IVF. Julia G. Kim, MD, MPH,* George Patounakis, MD, PhD,†
Caroline R. Juneau, MD,‡ Jason M. Franasiak, MD,a Scott J. Morin,
Julia G. Kim, MD, MPH, a George Patounakis, MD, PhD, b Scott J. Morin,
MD,‡ Shelby A. Neal, MD,§ Ashley W. Tieg, MD,¶ Emily K. Osman,
MD,¶ Brett M. Hanson, MD,¶ Emre Selii, M.D.,* Richard Thomas Scott,
Jr., MD,¶ IVI-RMA New Jersey, Basking Ridge, NJ; ¶IVI-RMA Florida,
Lake Mary, FL; §Audubon Fertility, New Orleans, LA; ¶IVI-RMA Northern
California, San Francisco, CA.

OBJECTIVE: Prior literature has suggested that maternal obesity in the
infertile population increases risk of miscarriage and large-for-gestational-
age (LGA) infants, and has unclear effects on gestational age. As previous
studies have only investigated these outcomes in the context of body mass
index (BMI), which may be an inaccurate metric for detailing body compo-
sition, this analysis also explores use of bioelectric impedance analysis (BIA)
and its estimation of adiposity as a more precise method of defining obesity in
patients undergoing IVF.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Patients at a single center undergoing
IVF from June 2016 – March 2019 were offered utilization of the InBody
770 BIA scale at time of vaginal oocyte retrieval to determine their body
composition. Participant demographics, BMI, percentage body fat (%
BF), IVF outcome, pregnancy, and delivery data were recorded prospect-
ively.

RESULTS: Pregnancy outcome data for 1037 females who underwent
 frozen embryo transfers were collected during this study period. Delivery
data was obtained for 873 cycles. The positive predictive values (PPV) of
BMI versus %BF were not different in investigating preterm delivery or

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OBESITY IS ASSOCIATED WITH INCREASED QUAN-
TITY BUT NO DIFFERENCE IN QUALITY OF OOCYTE
AND EMBRYOS IN WOMEN WITH LOW ANTI-MULLERIAN HORMONE LEVEL. Gufeng Xu,
M.D., Ph.D.,* Catherine Racowsky, PhDb aBrigham and Women’s Hospital,
Boston, MA; bBrigham and Women’s Hospital, Boston, MA.

OBJECTIVE: Both obesity and low AMH levels are associated with
reduced oocyte, embryo and clinical outcomes. Whether obesity further di-
minishes outcomes in women with low AMH is unclear. In this study, we
aimed to fill the knowledge gap by testing the hypothesis that obese women
with low AMH have lower oocyte and embryo yields with reduced quality
compared with women of normal weight.

DESIGN: Retrospective cohort of 1,542 cycles from 876 patients who
underwent autologous IVF/ICSI cycles from March 2013 to October 2018.

MATERIALS AND METHODS: Women without PCOS and with AMH
<1ng/ml were stratified by BMI: normal weight (18.5-24.9), overweight
(25.0-29.9) and obese (class I: 30.0-34.9). Total, mature (MII) and two pro-
nuclei (2PN) zygotes acted as surrogates for quantity. The % MII, %2PN/MI,
embryo scores on D5 (1=best, 6=worst), % usable (frozen-transferred)
D5 embryos and No. good quality (GQ) D5 embryos acted as surrogates for
quality. Implantation rate (IR) and live birth (LB) rate were assessed. We used
multivariable GEE modelling with Poisson, logistic or linear regression
adjusted for female age, stimulation protocol and FSH dose.

RESULTS: The results are shown in the table. All “quantity” parameters
were increased for obese compared with normal weight women, but none of
the “quality” parameters were different. Comparison of overweight vs.
normal weight women revealed no differences for any quantity or quality vari-
able except the No. of total oocytes. Decreased (not significant) trends were
found for IR and LB rates among the groups (normal weight, overweight and
obese, IR: 26.2, 23.9 and 25.0; LB: 27.1, 22.0 and 19.9).

CONCLUSIONS: Contrary to our hypothesis, obesity in low AMH women
is associated with increased, rather than decreased numbers of oocytes and em-
bloys compared with women of normal weight, with no compromise in overall
quality. Underlying mechanisms remain to be uncovered but the elevated
follicular androgen levels in obese women may be involved. Our findings
help to reassure obese women with low AMH regarding IVF outcomes.

SUPPORT: None.

Adjusted oocytes and embryos outcomes of low AMH women stratified by BMI

<table>
<thead>
<tr>
<th>Quantity</th>
<th>Normal weight (N=827)</th>
<th>Overweight (N=388)</th>
<th>Class I obese (N=160)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds Ratio (95% CI)</td>
<td>Odds Ratio (95% CI)</td>
<td></td>
</tr>
<tr>
<td>No. oocytes</td>
<td>6.7</td>
<td>7.3 (1.08, 1.03 — 1.13) *</td>
<td>8.2 (1.22, 1.15 — 1.29) *</td>
</tr>
<tr>
<td>No. MII</td>
<td>5.0</td>
<td>5.4 (1.07, 0.98 — 1.16)</td>
<td>6.5 (1.29, 1.14 — 1.44)</td>
</tr>
<tr>
<td>No. 2PN</td>
<td>3.4</td>
<td>3.6 (1.05, 0.93 — 1.17)</td>
<td>4.4 (1.28, 1.09 — 1.47)</td>
</tr>
<tr>
<td>% MII/Total</td>
<td>77.3</td>
<td>75.6 (0.91, 0.78 — 1.04)</td>
<td>81.4 (1.29, 0.96 — 1.61)</td>
</tr>
<tr>
<td>% 2PN/MII</td>
<td>68.1</td>
<td>66.9 (0.95, 0.78 — 1.12)</td>
<td>69.7 (1.08, 0.81 — 1.35)</td>
</tr>
<tr>
<td>D5 embryo grading</td>
<td>5.1</td>
<td>5.1 (-0.02, -0.22 — 0.18) #</td>
<td>4.9 (-0.21, -0.5 — 0.08) #</td>
</tr>
<tr>
<td>% D5 usable embryo / 2PN</td>
<td>59.5</td>
<td>56.0 (0.87, 0.70 — 1.04)</td>
<td>61.0 (1.06, 0.80 — 1.33)</td>
</tr>
<tr>
<td>No. GQ D5 embryos</td>
<td>0.4</td>
<td>0.4 (0.97, 0.60 — 1.34)</td>
<td>0.6 (1.64, 0.90 — 2.38)</td>
</tr>
</tbody>
</table>

# = Mean difference (OR, 95% CI)
pregnancy loss. BMI only differed from %BF in PPV of LGA infants (>4000g) where BMI was 12.7% and %BF was 9.35%.

CONCLUSIONS: To our knowledge, this is the first study to prospectively follow infertile patients and compare BMI to %BF in their predictive values on pregnancy outcomes. No differences were noted in the PPV of BMI versus %BF with regard to miscarriage rates or preterm delivery. BMI had a higher PPV than %BF in predicting LGA infants. Given that measurement of %BF through BIA has been previously validated in other fields of medicine, our findings suggest that BMI measures up to %BF as a successful approximation of patients’ adiposity, and can be confidently used for counseling at-risk obese patients undergoing IVF.

SUPPORT: None.

P-269 Tuesday, October 15, 2019 6:30 AM

LIFESTYLE MODIFICATIONS IN MALE PARTNERS OF SUBFERTILE COUPLES IN WHICH THE SPOUSE IS OBESE IMPROVES THE CHANCES OF THE COUPLE TO CONCEIVE. Matea Belan, MSc, a Belina Carranza-Mamane, MD, a Youssef AinMElk, MD, a Marie-Hélène Pesant, MD, a Karine Duval, PhD, a Farrah Jean-Denis, MSc, a Marie-France Langlois, MD, a Jean-Patrice Baillargeon, MD, a Reine Pesant, MD, a Karine Duval, PhD, a Farrah Jean-Denis, MSc, a Marie-France Langlois, MD, a Jean-Patrice Baillargeon, MD a Research Center of the Centre Hospitalier Universitaire de Sherbrooke, Sherbrooke, QC, Canada; bUniversité de Sherbrooke, Sherbrooke, QC, Canada; cUniversité de Sherbrooke - Department of Obstetrics and Gynaecology, Sherbrooke, QC, Canada; dUniversité de Sherbrooke, Department of Medicine, Sherbrooke, QC, Canada.

OBJECTIVE: To evaluate the impacts of an exposition of male partners of infertile couples to a lifestyle intervention, already targeted to their spouse with obesity, on fertility, anthropometric and lifestyle outcomes; and 2) to assess whether lifestyle and anthropometric changes in all male partners were associated to a conception.

DESIGN: Cross-sectional study, imbricated into a randomized controlled trial targeting the female spouses with obesity and infertility, including 97 infertile heterosexual subfertile couples.

MATERIALS AND METHODS: Male spouses were considered exposed to the intervention (Exp; n = 41) if their spouse was randomized in the intervention group according to the randomized controlled trial, or not exposed (NExp; n = 34) if the spouse was randomized in the control group. The NExp group followed the standard care for infertile, as the Exp group had access to the intervention targeting their spouse (individual sessions and group sessions). Lifestyle habits and anthropometry were assessed for both partners at 12 and 18 months, or at beginning and at 26 weeks of pregnancy. We pre-sent mean differences between the last available evaluation visit and the initial visit. Student’s tests were used to compare means, chi-squared tests for proportions and Spearman’s coefficients for correlations.

RESULTS: A total of 75 men (77%) had at least one follow-up research visit. Male partners participated little to the intervention targeting their spouse. There were no statistically significant differences for anthropometric and lifestyle changes between groups. When comparing couples with a conception and those without, independently of the exposition to the lifestyle intervention, men who conceived (n = 40) had lost significantly more weight (+2.38 kg ± 4.44 vs -0.08 kg ± 4.88, p = 0.026) and ate more fruits/day (+0.09 ± 0.67 vs 0.28 ± 0.65, p = 0.016) than men who did not conceive (n = 35). Weight loss remained significantly associated to a conception even after correcting for the weight loss of their spouse. Results were similar when assessing only couples in which both partners were obese (n = 36). Moreover, in these couples, we found significant associations between both partners’ changes in weight (r = 0.41; p = 0.012), and in nutritional quality (healthy eating index; r = 0.41, p = 0.013).

CONCLUSIONS: Exposing male partners to a lifestyle intervention targeting their spouse with obesity was not sufficient to improve their lifestyle. Nevertheless, our study shows that male partners of women with obesity and infertility, who lose weight or increase their daily consumption of fruits, increase the chances of their couple to conceive. Moreover, these male partners, who obese, tend to modify their weight and nutritional quality in parallel with their spouse. Therefore, engaging more actively male partners in the lifestyle intervention that is already indicated for their spouse with obesity can potentially further improve the couple’s fertility.

SUPPORT: None.

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IMPACT OF BMI ON PREGNANCY OUTCOMES WITH RESPECT TO DIFFERENTIAL TSH LEVELS. Maria Bustillo, M.D., a Ineabell Collazo, B.S., b Jessica Lapalme Ricard, B.S., b Juergen Eissermann, M.D., a Nicholas Hondon, B.S., a Himanshu Arora, Ph.D., b ‘IVFMD, South Florida Institute for Reproductive Medicine, MIAMI, FL; cUniversity of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: Serum thyroid-stimulating hormone (TSH) levels are routinely screened in women with infertility because thyroid disease may exert negative effects on ovulation and menstrual function. Women with clinical hypothyroidism (TSH levels > 4 uIU/mL) are treated with thyroid replacement. However, it is unclear whether subclinical hypothyroidism, defined as TSH levels > 2.5 uIU/mL (and < 4 uIU/mL) can affect pregnancy outcome. In the present study, we evaluated the IVF treatment/pregnancy outcomes with respect to BMI in euthyroid women and in those with subclinical hypothyroidism.

DESIGN: A retrospective study of 1,160 IVF cases.

MATERIALS AND METHODS: Patients were categorized into three groups. Group 1, euthyroid, consisted of 919 women, had pre-IVF TSH levels < 2.5 uIU/mL. Group 2 included 74 women with subclinical hypothyroidism, who were not treated. Group 3 included 167 women who were treated. All the patients were subgroup based on their BMI (≥ 25 or < 30). All women underwent standard IVF protocols following usual individualized practice in our IVF clinic.

RESULTS: Table below shows the classification of patients with respect to their pregnancy outcomes, by BMI levels, BMI and treatment respectively.

<table>
<thead>
<tr>
<th>BMI Category</th>
<th>Pre, TSH&lt;2.5, BMI &lt;30</th>
<th>Pre, TSH&lt;2.5, BMI ≥30</th>
<th>Pre, TSH&gt;2.5, Non Treated BMI &lt;30</th>
<th>Pre, TSH&gt;2.5, Non Treated BMI ≥30</th>
<th>Pre, TSH&gt;2.5, Treated BMI &lt;30</th>
<th>Pre, TSH&gt;2.5, Treated BMI ≥30</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of Patients</td>
<td>%</td>
<td>Mean Age</td>
<td>No of Patients</td>
<td>%</td>
<td>Mean Age</td>
<td>No of Patients</td>
</tr>
<tr>
<td>Not Pregnant</td>
<td>177*</td>
<td>22.7</td>
<td>35.1</td>
<td>32</td>
<td>22.7</td>
<td>35.7</td>
</tr>
<tr>
<td>Pregnant</td>
<td>601</td>
<td>77.2</td>
<td>34.6</td>
<td>109</td>
<td>77.3</td>
<td>36.4</td>
</tr>
<tr>
<td>Sab</td>
<td>92</td>
<td>11.8</td>
<td>34.8</td>
<td>15</td>
<td>10.6</td>
<td>39.3</td>
</tr>
<tr>
<td>BIOCHEM</td>
<td>69</td>
<td>8.9</td>
<td>34.4</td>
<td>19</td>
<td>13.5</td>
<td>36.4</td>
</tr>
<tr>
<td>DELIVERED</td>
<td>439</td>
<td>56.4</td>
<td>34.3</td>
<td>74</td>
<td>52.5</td>
<td>35.9</td>
</tr>
<tr>
<td>ECTOPIC</td>
<td>1</td>
<td>0.1</td>
<td>35.0</td>
<td>1</td>
<td>0.7</td>
<td>34.0</td>
</tr>
<tr>
<td>Total</td>
<td>778</td>
<td>100.034.5+/-.0.8</td>
<td>141</td>
<td>100.035.8+/-.5.3</td>
<td>63</td>
<td>100.033.6+/-.4.3</td>
</tr>
</tbody>
</table>

* p = 0.013
The overall pregnancy rate was significantly lower in untreated women with SClhypoT with BMI < 30 compared to Euthyroid with BMI < 30 (p = 0.013). However treated women with SClhypoT with BMI < 30 showed no significant differences compared to Euthyroid with BMI < 30 (p = 0.391).

CONCLUSIONS: Our findings suggest that irrespective of BMI, subclinical hypothyroidism may impact IVF success and pregnancy outcomes. Low dose thyroid supplementation may be beneficial. Further studies are ongoing considering parameters such as the presence of TPO antibodies and specific treatment strategies.

SUPPORT: This work was supported in part by the IVFMD, South Florida Institute for Reproductive Medicine.

P-271 Tuesday, October 15, 2019 6:30 AM

THE EFFECT OF BODY MASS INDEX (BMI) ON INTRATERINE INSEMINATION (IUI) CYCLE SUCCESS. Rachel M. Whynott, M.D., a Karen M. Summers, MPH CHES, b Amy E. Sparks, Ph.D. c

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Inclusion: IUI patients from 7/2009 - 12/2018. Exclusions: if weight (wt) or pregnancy outcome unavailable, or if BMI < 18.5 (due to low n), for a total of 1319 patients and 3244 IUI cycles. Primary outcome was clinical pregnancy (CP) by BMI, defined as intrauterine pregnancy (IUP) with heartbeat (HB) on ultrasound (US). Secondary outcomes were live birth (LB), multiple gestation (MG), and abnormal pregnancy (AP) defined as +hCG without an IUP with HB at US. Chi-square was used to compare outcome data between groups. Generalized estimating equations were used to examine relationships between individual factors and outcome of CP. Initial odds ratios (OR) were calculated for all hypothesized individual factors: maternal age, smoking, gravity, parity, diagnosis, antral follicle count (AFC), cycle order, and treatment cycle type. Age and factors meeting criteria of p < 0.25 were entered into regression model. Through an iterative process of variable selection, covariates were removed from model if they did not meet significance of α = 0.1 or were not found to change any remaining parameter estimate by >15%. After the iterative process of deleting, refitting, and verifying, each variable not selected for inclusion in the original multivariate model was added back one at a time, with any significant at α = 0.1 retained.

RESULTS: Factors retained in final model for BMI and CP included: AFC (OR 1.02 (1.00-1.03) p = 0.007), smoking (OR 0.51 (0.28-0.94) p = 0.030), endometriosis (OR 0.47 (0.25-0.91) p = 0.026), age (OR 0.99 (0.96-1.02) p = 0.514), and treatment cycle type (p = 0.007). When accounting for these factors, BMI 25-29.99 were more likely to have a CP compared to BMI 18.5-24.99 (OR 1.42 (1.04-1.95) p = 0.029). BMI ≥ 30 did not affect CP rates (OR 1.21 (0.83-1.66) p = 0.245).

CONCLUSIONS: After controlling for potential confounders, patients BMI 25 - 29.99 are more likely to have CP with IUI compared to normal BMI. A BMI ≥ 30 does not have an impact on IUI CP rate or LB at a clinic requiring BMI < 50. However, women BMI ≥ 30 are more likely to have AP which is consistent with prior studies in spontaneous and in vitro fertilization pregnancies.

SUPPORT: None.

TABLE 1. IUI pregnancy rates by BMI.

<table>
<thead>
<tr>
<th>BMI 18.5-24.99</th>
<th>BMI 25-29.99</th>
<th>BMI ≥ 30</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CP (n=3329)</td>
<td>192/1545 (12%)</td>
<td>115/813 (14%)</td>
<td>128/886 (14%)</td>
</tr>
<tr>
<td>AP (n=3329)</td>
<td>52/1545 (3%)</td>
<td>38/813 (5%)</td>
<td>53/886 (6%)</td>
</tr>
<tr>
<td>LB (n=3244)</td>
<td>146/1521 (10%)</td>
<td>72/788 (9%)</td>
<td>77/854 (9%)</td>
</tr>
<tr>
<td>MG (n=355)</td>
<td>13/157 (8%)</td>
<td>6/91 (7%)</td>
<td>10/99 (10%)</td>
</tr>
<tr>
<td>Multiple Delivery (n=312)</td>
<td>8/150 (5%)</td>
<td>5/77 (7%)</td>
<td>9/79 (11%)</td>
</tr>
</tbody>
</table>

CONCLUSIONS: A growing body of evidence has demonstrated that diet, irrespective of maternal BMI, influences fertility, pregnancy outcomes, and newborn health. In order to identify women for wellness interventions in the preconception period, it is necessary to understand local context. In this cohort of reproductive age women in St. Louis, we describe dietary patterns that are associated with obesity, but not with markers of ovarian reserve. Future research is needed to elucidate the relationship between diet and markers of ovarian reserve.

SUPPORT: Research reported in this publication was supported by the National Center For Advancing Translational Sciences of the National Institutes of Health under Award Numbers and KL2 TR000450 and TL1TR002344. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.
A NOVEL GNRH ANTAGONIST PROTOCOL BY SWITCHING ANTAGONIST TO PROVERA TO PREVENT PREMATURE LUTEINIZING HORMONE SURGE WHEN PATIENTS TURNED OUT TO BE AT HIGH RISK OF OVARIAN HYPERSTIMULATION SYNDROME (OHSS) DESPITE “INTENSIVE” LUTEAL SUPPORT WITH HCG IS ASSOCIATED WITH DECREASED LIVE BIRTH (LB) IN WOMEN AT HIGH RISK FOR OVARIAN HYPERSTIMULATION SYNDROME (OHSS) DESPITE “INTENSIVE” LUTEAL SUPPORT WITH INTRAMUSCULAR PROGESTERONE (IMP). Laura A. Bishop, MD,1,2 Natalie Clark Stentz, MD, MSCE,1 Micah J. Hill, DO,1 Kate Devine, MD,1 Saisoa Torrealday, MD,1 Eric A. Widra, MD,1 Alan H. DeCherney, MD,2 Frank E. Chang, MD,2 NNIH, Bethesda, MD;3Shady Grove Fertility, Atlanta, GA;4National Institute of Child Health and Human Development, NIH, Bethesda, MD;5Shady Grove Fertility, Washington D.C., DC;6 Walter Reed Military Medical Center, Bethesda, MD;7SG Fertility, Washington, DC;8Shady Grove Fertility, Rockville, MD.

OBJECTIVE: To determine if the absence of hCG for luteal support results in reduced LB rates from IVF with fresh embryo transfer (ET) when “intensive” luteal support with IMP is given after GnRH agonist (GnrHa) trigger.

DESIGN: Retrospective Cohort Study

MATERIALS AND METHODS: Fresh autologous IVF cycles from 2014-2017 with ≥24 oocytes retrieved were analyzed. Patients who did not undergo a fresh ET and those who received both hCG and GnRHa to trigger oocyte maturation were excluded. HCG trigger patients received luteal support with 100mg vaginal progesterone three times a day starting the day after retrieval. The same luteal support was used following GnRHa trigger if 1500 IU hCG was administered post retrieval. If OHSS risk was assessed as unacceptable high, hCG was held following GnRHa trigger and “intensive” luteal

TABLE 1. Characteristics of G2 v G1

<table>
<thead>
<tr>
<th>Single GnrHa</th>
<th>Double GnrHa</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(G1, n = 1394)</td>
<td>(G2, n = 498)</td>
<td></td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>35.4±4.7</td>
<td>35.4±4.5</td>
</tr>
<tr>
<td>Maximum E2 (pg/mL)</td>
<td>3592.6±1451.0</td>
<td>3713.8±1056.8</td>
</tr>
<tr>
<td>LH (mIU/mL)</td>
<td>101.6±47.4</td>
<td>101.4±50.8</td>
</tr>
<tr>
<td>Oocytes Retrieved</td>
<td>19.4±9.6</td>
<td>20.5±10.5</td>
</tr>
<tr>
<td>Mature Oocytes</td>
<td>15.1±8.0</td>
<td>15.9±8.3</td>
</tr>
<tr>
<td>Retrieved</td>
<td>Incidence of OHSS</td>
<td>10.0% (140/1394)</td>
</tr>
<tr>
<td>Use of Cabergoline</td>
<td>10.8% (151/1394)</td>
<td>9.8% (49/498)</td>
</tr>
</tbody>
</table>

WITholding luteal HCG is associated with decreased live birth (LB) in women at high risk for ovarian hyperstimulation syndrome (OHSS) despite “intensive” luteal support with intramuscular progesterone (IMP).
support with 50mg daily IMP was administered starting the day after retrieval. All patients received 2mg twice daily oral estradiol starting the night of retrieval. Multivariable logistic regression was used to compare laboratory and pregnancy outcomes in patients receiving hCG trigger (control) to those with GnRHa trigger with and without post retrieval hCG. Adjusted models accounted for age, BMI, number of embryos transferred, embryo quality, and serum progesterone level on day of trigger. Greater efficiency and receiver operator curves were used to determine if serum estradiol and progesterone concentrations on the day of trigger were associated with LB in each treatment group.

RESULTS: 984 autologous IVF cycles met inclusion criteria, distributed as follows: 235 hCG trigger, 236 GnRHa trigger with hCG post retrieval, and 454 GnRHa trigger with no hCG post retrieval. GnRHa trigger patients were older, had a higher peak estradiol level, more embryos available for vitrification, and fewer embryos transferred (P<0.001) compared to hCG trigger. Patients without hCG exposure had lower clinical pregnancy (CP) (42% vs 52%, P = 0.01) and LB (35% vs 44%, P = 0.01) rates compared to those using hCG trigger in both analysis models. Patients with GnRHa trigger who received post retrieval hCG had similar CP (56%, P = 0.43) and LB (46%, P = 0.42) to the hCG trigger cohort. There were no statistically significant differences in biochemical pregnancy, spontaneous abortion, and ectopic pregnancy. Patients without hCG exposure had lower rates of OHSS (<1%, P < 0.001) compared to hCG trigger (11%) and GnRHa patients (6%). LB did not vary by peak serum estradiol in any treatment arm.

CONCLUSIONS: Patients receiving GnRHa trigger who did not receive hCG post retrieval had lower CP and LB rates from fresh ET despite “intensive” luteal support. This was largely due to implantation failure as pregnancy loss was similar in all treatment groups. Adjusted analysis demonstrated that higher peak serum estradiol levels in the GnRHa without hCG group did not mediate this effect. Post retrieval hCG was associated with LB outcomes equivalent to hCG trigger, but at the cost of increased OHSS relative to the no hCG group. These data suggest when hCG luteal support cannot be given due to high OHSS risk, a freeze all strategy should be strongly considered.


P-276 Tuesday, October 15, 2019 6:30 AM
MATERNA L AND FETAL OUTCOMES AFTER OVARIAN HYPERSTIMULATION SYNDROME: A ROCHESTER EPIDEMIOLOGY PROJECT (REP) STUDY
Ajeeta Sanghani, MD, MZA Razaq Khan, MD, Maryama Ismail, BS, Mayo Clinic Rochester, MN.
OBJECTIVE: The objective of this study was to determine the effect of ovarian hyperstimulation syndrome (OHSS) on maternal and fetal outcomes.

DESIGN: This was a retrospective cohort design.

MATERIALS AND METHODS: IRB approval was obtained. Using the Rochester epidemiology project, residents of Olmsted County and the surrounding 9 counties with OHSS after in vitro fertilization were identified between 1995 and 2017. Matched controls were then screened as matches on age, parity, and cause of infertility. Two controls were identified for each patient with OHSS. Patients were included if they had a pregnancy lasting ≥ 20 weeks gestation after the diagnosis and treatment of OHSS. Background maternal and pregnancy outcomes were collected via chart review. Data was then analyzed using a t-test and ANOVA.

RESULTS: Patients with and without OHSS did not differ on BMI, number of stimulation days, amount of gonadotropin use. Patients with OHSS has significantly more follicles (p<0.0001) and more oocytes (p<0.0001) as well as a higher peak estradiol (p=0.004) [table 1]. Rates of intrauterine fetal death, gestational diabetes, placental abruption, deep venous thrombosis, pulmonary embolism, gestational hypertension, number of liveborns, infant birthweight, and use of antenatal steroids did not differ between the groups. One and 5 minute Apgars did not differ between the two groups either [table 1].

CONCLUSIONS: The incidence of OHSS after assisted reproduction is approximately 3%. OHSS did not affect maternal or neonatal outcomes in a subsequent pregnancy in our report. Further analyses are underway to determine if these differences persist in women who have a fresh transfer after OHSS diagnosis compared to those that undergo freeze all of embryos with a planned frozen embryo transfer.

P-277 Tuesday, October 15, 2019 6:30 AM
PREDICTION OF SEVERE OVARIAN HYPERSTIMULATION SYNDROME IN WOMEN UNDERGOING IN VITRO FERTILIZATION USING DAY 3 ESTRADIOL LEVELS, COLLECTED OVA, AND THE NUMBER OF FOLLICLES
Ivan Madrazo, MD,† Ginna Milena Ortiz, MD,ª Juan José Suárez, MD,ª Josue J. Hidalgo, MD,ª Monserrat Fabiola Vélez, MD,ª Esther López-Bayghen, PhD ‡Ingenes Mexico, Mexico City, DF, Mexico; Affiliation not provided; †Centro de Investigación y Estudios Avanzados IPN, México, EM, Mexico.

OBJECTIVE: Ovarian hyperstimulation syndrome (OHSS) is a potentially life-threatening iatrogenic condition that can occur during in vitro fertilization (IVF). The worst outcome is hydrothorax, hypovolemia, higher risk of deep venous thrombosis and oliguria. With severe OHSS patients are required to postpone embryo transfer for an undetermined amount of time. Patients in whom patients at high risk of developing OHSS is mainly based on serum estradiol (E2) levels, but other factors, such as female age, BMI, ovarian volume, antral follicle count (AFC), and polycystic ovary syndrome, are speculated to be predictive. Here, we aimed to determine if E2 levels at Day 3 and its fold change at day ten as well as antral follicle count and ova collected are predictive factors for severe OHSS.

METHODS: Retrospective and control studies.

MATERIALS AND METHODS: Patient chart review was performed between January 2008 and December 2017 at Ingenes in Mexico City. Three hundred twenty-seven women were selected. E2 >3000 ng/L usually on the last day of stimulation (day 10 with three 18 mm-follicles) was defined as OHSS (n=151). CULDOSCENTESIS was performed on a patient when upon clinical assessment patient presented features such as nausea, vomiting, oral intolerance and ascites identified by endovaginal ultrasound and abdominal ultrasound (renal and hepatic areas with visible ascites) that do not respond to conservative management (n=55 severe OHSS). Predictability was evaluated by measuring the area under the receiver-operating characteristic (AUC). Differences between groups were determined by t-test.

RESULTS: The OHSS positive group, when compared to the non-OHSS group, was higher with respect to E2 Day 3 levels (150±230 v 250±177 ng/L), E2 fold change (20±1.5 v 32.2±29.1), AFC (11.6±8.5 v 18.2±9.1), and Ova collected (10±1.64, 21±1.90, p<0.0001). E2 Day 3 levels (AUC=0.76, 95% CI: 0.71-0.82), E2 fold change (AUC=0.71, 95% CI: 0.65-0.77), AFC (AUC=0.75, 95% CI: 0.70-0.81), and Ova collected (AUC=0.85, 95% CI: 0.81-0.89) were predictive of OHSS. For CULDOSCENTESIS, E2 Day 3 levels (190±221 v 223±158 ng/L) were not different between the subjects who received culdocentesis, whereas the E2 fold change (24.5±26.6 v 32.9±28.8, p=0.038), AFC (13.7±9.0 v 19.8±8.9, p<0.0001), and Ova collected (13.7±8.9, 23.3±8.1, p<0.0001) were higher. Interestingly, all variables were predictive of subjects who would qualify for cULDOSCENTESIS (E2 Day 3 levels: AUC=0.63, 95% CI: 0.55-0.70; E2 fold change: AUC=0.63, 95% CI: 0.55-0.71; AFC: AUC=0.74, 95% CI: 0.68-0.80; and Ova collected: AUC=0.80, 95% CI: 0.75-0.85).

CONCLUSIONS: Here, we demonstrate the E2 levels, as well as the ova production parameters, are indicators of IVF patients who could develop severe OHSS and may require culdocentesis.

SUPPORT: Conacyt-A1 250768.

TABLE 1. Demographic and Result Data of OHSS and Control Cases

<table>
<thead>
<tr>
<th>Variable (mean)</th>
<th>Control (144)</th>
<th>OHSS (72)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>32</td>
<td>31.9</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>24.9</td>
<td>25.8</td>
<td></td>
</tr>
<tr>
<td>Gonadotropin</td>
<td>1868</td>
<td>1860</td>
<td></td>
</tr>
<tr>
<td>Days of stimulation</td>
<td>11.7</td>
<td>11.4</td>
<td></td>
</tr>
<tr>
<td>Follicles</td>
<td>25</td>
<td>35</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>Oocytes</td>
<td>15</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Peak E2</td>
<td>2243</td>
<td>3149</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>Days at delivery</td>
<td>264</td>
<td>260</td>
<td></td>
</tr>
<tr>
<td>Hypertension*</td>
<td>33</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Gestational diabetes*</td>
<td>10</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Placental abruption*</td>
<td>12</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Antimal steroid use*</td>
<td>10</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Intrauterine fetal demise*</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Number of live infants</td>
<td>1.3</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>Birthweight</td>
<td>2996</td>
<td>2895</td>
<td></td>
</tr>
<tr>
<td>1 minute Apgar</td>
<td>7.7</td>
<td>7.2</td>
<td></td>
</tr>
<tr>
<td>2 minute Apgar</td>
<td>8.7</td>
<td>8.4</td>
<td></td>
</tr>
</tbody>
</table>

*=number of cases

e216 ASRM Abstracts
OBJECTIVE: The aim of this study was to clarify the effectiveness and optimal dose of chlormadinone acetate (CMA) as progestin-primed ovarian stimulation (PROS).

DESIGN: This study was a prospective study conducted at Kyono ART Clinic Takanawa in Japan from August 2018 to April 2019 and performed with the consent of the Kyono ART Clinic Ethical Committee.

MATERIALS AND METHODS: Study 1: The subjects were classified into two groups. In both groups, either FSH/HMG was administered on day 3. Group A comprised 32 cycles (32 patients) using 12mg CMA from day 3; group B comprised 28 cycles (28 patients) using 0.25mg GnRH antagonist when mean dominant follicle diameter reached 14 mm. All embryos were cryopreserved at the blastocyst stage for later transfer. Study 2: The optimal dose of CMA (12mg, 6mg, 4mg, and 2mg) was examined. Study 3: Premature LH surge was not observed (0/32) in group A, whereas it was observed in 21.4% of cases (6/28) in group B; however, ovulation was not observed in either groups. Clinical outcomes in groups A and B were as follows: mean number of oocytes retrieved, 13.4±7.0 vs. 15.4±9.9; fertilization rate, 80.2% vs. 76.7%; blastocyst rate, 55.3% vs. 51.1%; good blastocyst rate, 43.6% vs. 44.0%; clinical pregnancy rate, 58.3% (7/12) vs. 62.0% (8/13); ongoing pregnancy rate, 50.0% (6/12) vs. 50.0% (6/12); miscarriage rate, 14.3% (17/12) vs. 16.7% (2/12). Thus, there were no significant differences between the two groups. Study 2: Premature LH surge was not observed: 0% (0/12), 0% (0/21), 0% (0/32), 0% (0/32) in CMA 2mg, 4mg, 6mg, and 12mg, respectively.

CONCLUSIONS: To our knowledge, this study is the first report of CMA worldwide. PROS using CMA completely inhibited premature LH surge and clinical outcomes equal to those of GnRH antagonist treatment. CMA is oral medicine, cheaper and effective as PROS, and 2mg CMA may be the optimal dose. Further studies are needed.

P-278 Tuesday, October 15, 2019 6:30 AM

EFFECTIVENESS AND OPTIMAL DOSE OF CHLORMADINONE ACETATE (CMA) AS PROGESTIN-PRIMED OVARIAN STIMULATION. Airi Kobayashi, RN, Emiko Funahashi, RN, Chiharu Tanaka, RN, Sachiko Nonaka, RN, Atsuko Tanaka, RN, Marina Kiuchi, RN, Yumi Suzuki, Medical doctors clark, Chiyori Kuma, BS, Mizuho Takahashi, BS, Noriyuki Okayama, M.Sc., Nobuya Aono, Ph.D., Toshihiro Tai, M.D., Ph.D., Mayumi Toya, M.D., Ph.D., Hideki Igarashi, M.D., Ph.D., Suguru Kikuchi, M.D., Ph.D., Tomoko Hashimoto, M.D., Ph.D., Koichi Kyono, M.D., Ph.D., Kyono ART Clinic Takanawa, Tokyo, Japan; Kyono ART clinic, Human Ovarian-tissue Preservation Enterprise (HOPE), Tokyo, Japan.

OBJECTIVE: To determine whether administration of 2 mature follicles and trigger administration with CMA 2mg from day 3, 1 day beyond in 1334 (16.7%) cycles, and 2 days beyond in 121 (1.5%) cycles. Univariate analysis demonstrated differences in age, antral follicle count, peak estradiol, gravity, and trigger type. After controlling for these confounders, no significant association was observed for continuing COH beyond visualization of ≥ 2 mature follicles and MII rate (OR 1.01 [95% CI 0.90-1.13]), fertilization rate (OR 0.98 [95% CI 0.88-1.10]), blastulation rate (OR 0.97 [95% CI 0.87-1.08]), or euploidy rate (OR 0.90 [95% CI 0.78-1.04]). A sub-analysis was performed for SART age group E, which also showed no differences in cycle outcomes when COH was extended.

CONCLUSIONS: In the largest study of GnRH antagonist protocol IVF cycles looking at oocyte developmental competence when trigger was delayed in the presence of ≥ 2 mature follicles, we demonstrated no significant difference in rates of maturation, fertilization, blastulation, and euploidy, even in patients >42 years old. Our study suggests that continuing COH up to 2 days in select patients does not negatively affect outcomes. While reassuring, the effects of COH prolongation on genomic and non-genomic factors must be investigated. Well-controlled prospective studies assessing CPR and LBR will be needed before we can definitively quantify the limits around optimal COH duration.


P-279 Tuesday, October 15, 2019 6:30 AM

CIRCULATING MicroRNA LEVELS AS PREDICTOR OF OVARIAN RESPONSE IN WOMEN UNDERGOING CONTROLLED OVARIAN STIMULATION. Maria Gabriela Mulato, BSc, Daniela Paes de Almeida Ferreira Braga, PhD, Amanda Souza Setti, MSc, Assumpito Iaconelli, Jr., MD, Edson Borges, Jr., PhD, Murilo Vieira Geraldo, PhD, UNICAMP, Campinas, Brazil; Fertility Medical Group / Sapientiae Institute, Sao Paulo, Brazil.

OBJECTIVE: The primary objective of individualization of assisted reproduction treatments is to offer every woman the best treatment tailored to her unique characteristics. However, the success of individualized controlled ovarian stimulation (COS) depends on finding a reliable method for predicting ovarian response to stimulation. Therefore, the goal for the present study was to identify circulating microRNAs (miRNAs) biomarkers of the response to COS.

DESIGN: Cohort study.

MATERIALS AND METHODS: For the present study, 90 serum samples were collected prior to COS for intracytoplasmic sperm injection (ICSI). Samples were collected in a private university-affiliated IVF center, between January 2017 and January 2018, and were split into three groups, depending on the patient’s response to COS: Poor Response Group: <4 retrieved oocytes (PR group, n=30), Normo Response Group: ≥4 and <12 retrieved oocytes (NR group, n=30), and Hyper Response Group: ≥12 retrieved oocytes (HR, n=30). Samples were used for two experimental sets. For the first experimental set, 5 samples from each group were pooled together and used to identify aberrantly expressed miRNAs in experimental groups, by using a large-scale microRNA expression analysis platform. For the second experimental set, 25 samples from each group were individually analyzed and the expression of specific miRNAs, determined by the first step, was investigated.

RESULTS: Twenty two miRNAs presented a twofold increase level in the PR or HR groups when compared with the NR group. From those miRNAs, 9 presented poor dissociation curves and were excluded from further analysis. Based on the quality of the amplification, observed in the manual analysis, the detection pattern in the experimental groups, and literature data, three miRNAs with exclusive detection in the HR group (miR-181d-5p, miR-221-3p and miR-92a-1-5p) and two miRNAs with exclusive detection in the PR group (miR-891a-5p, miR-99a-3p, miR-223-5p and...
miR-200c, let-7d-3p and miR-150-5p) were selected for a subsequent validation set. The results showed that the serum levels of miR-181d-5p was also positively correlated with the number of aspirated follicles (p<0.0001), number of retrieved oocytes (p<0.0001), and number of mature oocytes (p=0.0002).

CONCLUSIONS: The quantification of miR-181d-5p prior to the COS may discriminate patients who will respond in an exacerbated manner to those who will respond insufficiently to the COS. The use of this tool associated with other previously described parameters may allow the individualization of the treatment, increasing treatment success while decreasing patients’ risks and physical, emotional and economic burden.


P-281 Tuesday, October 15, 2019 6:30 AM

PHYSICIANS SHOULD AVOID CHANGING A PATIENT’S OVARIAN STIMULATION PROTOCOL FOR THE PURPOSE OF IMPROVING LABORATORY OUTCOMES. Kaitlyn Wald, MD, Eleni A. Greenwood, MD, MSc, Marcelle I. Cedars, MD, Mitchell P. Rosen, MD, HCLD. University of California San Francisco, San Francisco, CA.

OBJECTIVE: Providers consider a number of factors when selecting a stimulation protocol and may switch protocols when a patient has a suboptimal stimulation or laboratory outcome. We sought to determine whether providers’ choice in stimulation is associated with laboratory outcomes.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: IVF cycles from 1/2010 to 3/2019 were reviewed. Cycles were categorized as: (1) E2 priming antagonist (2) Antagonists +/- OCP priming (3) Long luteal (4) Lupron stop (5) Flare. Mini-stimulations were excluded. Laboratory outcomes for first stimulations only and repeated cycles within a patient were compared. For first stimulation cycles, linear and logistic regression were used. For repeated cycles, those who completed the same stimulation were compared to those who changed, using cluster analyses for pairwise comparison. A subgroup of patients who had a low blast progression in their first cycle was also analyzed. Outcomes were adjusted for number of eggs collected and patient age.

RESULTS: 5209 patients underwent ovarian stimulation for IVF. When comparing between stimulation types, fertilization rate, blast progression and euploid rate were not statistically different. 2477 of these patients underwent a second cycle: 50% repeated the same and 50% completed a different protocol. The fertilization rate and blast progression were not statistically different between those who repeated the same protocol and those who changed. There was a statistically significant improvement in eggs collected, usable embryos and euploid rate for those who repeated the same stimulation, after adjustment (table). Of those with low blast progression in the first cycle, a significant improvement occurred in the second cycle, however, repeating the same protocol resulted in a slightly greater improvement (coefficient 0.03 (0.01-0.04)).

CONCLUSIONS: All conventional ovarian stimulation protocols result in comparable laboratory outcomes. By enlarge, the variations seen from cycle to cycle within a patient cannot be explained by stimulation type. If anything, there is a subtle benefit to staying with the same protocol, for reasons yet to be determined, but likely inherent to the patient. Until these factors are further understood, physicians should avoid changing stimulation protocols for the purpose of improving laboratory outcomes.
OBJECTIVE: This study compared handling errors and preference ratings before and after use of four currently available r-hFSH pen injectors tested by women with infertility and fertility nurses.

DESIGN: This was a simulated use study comparing the GONAL-f® (Merck KGaA, Germany), Bemfola® (Gedeon Richter PLC, Hungary), Rekovelle® (Ferring Pharmaceuticals Ltd, UK) and Ovaleap® (Teva BV, The Netherlands) pen injectors in Germany, Poland and the UK.

MATERIALS AND METHODS: Injector-naive women with infertility and injector-experienced fertility nurses tested pen injectors with masked labels in a randomized testing order. Simulated injections were made into a foam pad following the instructions for use (IFU) and injectors were rated before and after use. Handling errors were noted by the moderator during the study. After the study, errors were grouped according to severity and use steps indicated in the IFU. Ordinal or Poisson linear mixed models were applied, adjusted for injector and testing order with an unstructured correlation matrix between measures (or non-convergence, non-parametric or normal approximation to the Poisson methods). All analyses were exploratory by nature without any correction for multiplicity.

RESULTS: A total of 120 women with infertility and 60 fertility nurses participated. All participants tested GONAL-f® and Bemfola injectors. Besides GONAL-f®, other participants tested either Rekovelle® (71 women: 30 nurses) or Ovaleap® (49 women: 30 nurses) injectors. Before simulated use, mean ratings from women with infertility were similar between the GONAL-f® and other pen injectors. After use, the ratings from women were higher for GONAL-f® vs other pen injectors (p<0.001 for all comparisons). Fertility nurses rated the GONAL-f® injector higher than the other pen injectors both before and after simulated use, with the difference in ratings larger after simulated use (p<0.01 for all comparisons vs GONAL-f®). Adjusted rates of total handling errors for both women with infertility and fertility nurses were lower with the GONAL-f® pen injector (p<0.001 for all comparisons vs GONAL-f®). Adjusted rates of total handling errors (95% CI) for women with infertility were 0.31 (0.16, 0.45), 1.30 (1.00, 1.60), 1.19 (0.71, 1.66) and 1.64 (1.06, 2.37) for GONAL-f®, Bemfola, Rekovelle and Ovaleap injectors, respectively. For fertility nurses, corresponding adjusted rates vs GONAL-f® were 1.02 (0.84, 1.20), 1.64 (1.41, 1.87), 2.07 (1.68, 2.45) and 3.16 (2.50, 3.81) with GONAL-f®, Bemfola, Rekovelle and Ovaleap injectors, respectively. For fertility nurses, corresponding adjusted rates were 0.31 (0.16, 0.45), 1.30 (1.00, 1.60), 1.19 (0.71, 1.66) and 1.64 (1.06, 2.21), respectively. The most difficult use-steps (i.e. during which most errors were recorded with all pen injectors) were "priming" and "giving the injection". Significantly lower error rates were recorded during these use-steps indicated in the IFU. Ordinal or Poisson linear mixed models were applied, adjusted for injector and testing order with an unstructured correlation matrix between measures (or non-convergence, non-parametric or normal approximation to the Poisson methods). All analyses were exploratory by nature without any correction for multiplicity.

CONCLUSIONS: In this study, the GONAL-f® injector was rated significantly higher than other pen injectors after use. This may be a result of more handling errors, including those that may affect treatment outcomes, observed with the Bemfola, Rekovelle and Ovaleap pen injectors.

SUPPORT: Funded by Merck KGaA, Darmstadt, Germany.

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**FERTILITY & STERILITY**

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**P-284 Tuesday, October 15, 2019 6:30 AM**

**EFFECT OF VARIANT B LH POLYMORPHISM (RS1800447) IN AN EGYPTIAN IVF POPULATION ON OVARIAN RESPONSE IN ASSISTED REPRODUCTION.**

Mohamad Ghanem, MD,a 
Mohamed Abohashem, MD,b 
Nessma Ahmed Noesser, MD,b 
Nawal A. Ghareeb, MD,c 
Reham M. El-farahaty, MD,c 
Adel Althropady, ms,c 
Mansoura Integrated fertility center, Mansoura, Egypt; cMansoura Faculty of medicine, Mansoura, Egypt; cclinical pathology department, faculty of medicine, Mansoura university, Mansoura, Egypt; cAffiliation not provided.

OBJECTIVE: Existing evidence supports the association between specific gonadotropins and their receptor single nucleotide polymorphism (SNP) and poor ovarian response (POR). Many SNPs have been identified in the LHβ gene. The most commonly studied is rs1800447 (Trp8Arg), which seems to vary among ethnic groups. We aimed to assess frequency of this SNP among our population and its association with ovarian response (OR): gonadotropin dose and number of eggs retrieved.

DESIGN: retrospective

MATERIALS AND METHODS: We included 181 IVF females in Mansoura Integrated Fertility Centre. Ovarian stimulation was conducted using either GnRH antagonist or agonist protocol with recombinant FSH. Total gonadotropin dose and number of oocytes retrieved were evaluated. DNA was extracted from peripheral blood leucocytes followed by analysis of genetic polymorphism by PCR-RFLP technique for rs1800447 (Trp8Arg).

RESULTS: Patients were grouped according their codon 8 genotype into TT, TC, CC groups. The groups showed no significant differences in female age, BMI, duration and causes of infertility. Although OR was lower in the CC genotype, the differences were not significant (small subgroup numbers). POR (number of eggs retrieved <4) was significantly higher in CC genotype compared to other genotypes. The frequency of homozygous genotype (CC) among poor responders 7/23 (30.7%) was three times higher than among normal responders 14/144 (9.7%) implying significantly higher risk of POR (OR 4.063, 95% CI 1.428 - 11.56, p = 0.012).

CONCLUSIONS: Our results showed that among a cohort of Egyptian infertility women the frequency genetic variants of V-LHB (p.Trp8Arg, c.rs1800447) is 53.5% for all C alleles and 13.8% for CC genotype and that variant CC is significantly associated with POR compared with other genotypes with the odds ratio of developing POR 4.063, 95% CI (1.428 to 11.56) p = 0.012. This means that genotyping for this variant among IVF women can help planning ovarian stimulation protocol to circumvent the risk of POR.

REFERENCES


P-285 Tuesday, October 15, 2019 6:30 AM

EFFECT OF OVARIAN STIMULATION OF OOCYTE DONORS ON IN-VITRO FERTILIZATION OUTCOMES. Heather S. Hipp, MD, Audrey J. Gaskins, Sc.D., Zsofia Peter Nagy, MD, PhD, Sarah M. Capelouto, MD, Daniel B. Shapiro, MD, Jessica B. Spencer, MD, MSC, Emory University, Atlanta, GA; Reproductive Biology Associates, Atlanta, GA; The University of Texas, Southwestern Medical Center, Dallas, TX.

OBJECTIVE: To determine the effect of ovarian stimulation in oocyte donors on in-vitro fertilization (IVF) outcomes for recipients.

DESIGN: Retropective cohort study of data from a frozen donor oocyte bank from 2008 to 2015.

MATERIALS AND METHODS: A total of 350 oocyte donors underwent 553 ovarian stimulation cycles with an antagonist protocol. Mature oocytes were vitrified and later warmed in individual cohorts among 989 unique recipients who underwent 1745 embryo transfer cycles. The associations between ovarian stimulation characteristics and rates of oocyte warm survival, fertilization, and usable embryos (combination of number of embryos transferred and cryopreserved for future use) per oocyte warmed as well as the odds of live birth per embryo transfer cycle were modeled using cluster-weighted generalized estimating equations adjusted for donor age, body mass index (BMI), race, retrieval year, and recipient age (live birth only).

RESULTS: The donors were 21-32 years old with BMI <30 kg/m². Per stimulation cycle, the median number of oocytes retrieved was 30 (range: 9-95). The majority of recipients, 78.6%, had 6-8 donor oocytes warmed. Mean (standard deviation) percentage of oocytes that survived warm, were successfully fertilized and were usable was 93.6% (11.5%), 79.8% (18.2%) and 53.9% (21.8%) respectively. Donors with more oocytes retrieved had a lower percentage of usable embryos per oocyte warmed (<15: 62.5% [95% Confidence interval (CI) 52.7-71.4], 15-30: 58.9% [95% CI 55.0-62.6], 31-50: 53.6% [95% CI 49.6-57.5], >50 52.0% [95% CI 46.0-57.9]). Of the transfers, 856 (49.1%) resulted in a live birth. There was no difference in the probability of live birth according to number of oocytes retrieved in a donor. For example, the adjusted odds of live birth among recipients was 0.93 (95% CI 0.67, 1.31) if the donor had >50 oocytes retrieved compared to 15-30 oocytes retrieved.

CONCLUSIONS: Oocyte donors represent an excellent model to determine the impact of ovarian stimulation on IVF outcomes given a relatively uniform uterine environment. Although high donor oocyte yield results in more oocytes available, there are less usable embryos per oocyte warmed as number of retrieved oocytes increases. These differences in early outcomes, however, do not translate into differences in live birth rate.

SUPPORT: REDCap grant support at Emory was provided through UL1 TR000424.

P-286 Tuesday, October 15, 2019 6:30 AM

THE IMPACT OF FOLLISTATIN HORMONE ON OVARIAN RESPONSE. Yahia Mohamed El-Faisal, M.D., M.Sc.; Alaa Amer, B.Sc.; Mohamed A. Aboughar, M.D.; Gamal Serour, M.D.; Ragaa Mansour, M.D., Ph.D.; Cairo University, Cairo, Egypt; The Egyptian IVF-ET center, Maadi, Cairo, Egypt; Cairo University, Egyptian IVF center, Cairo, Egypt.

OBJECTIVE: We aimed in this study to find the role of serum level of Follistatin in the process of folliculogenesis. Noticing the variability of Follistatin levels between women, we wanted to uncover a modifying role that Follistatin plays, resulting in a variable individual ovarian response.

DESIGN: A Prospective cross-sectional observation study, including 200 women undergoing an IVF program with the long stimulation protocol in the Egyptian IVF Center in Maadi, Cairo, Egypt.

MATERIALS AND METHODS: Patients were matched regarding age, BMI, ovarian reserve (based on AMH and AFC) and HMG initial doses (150-225iu/day). Serum Follistatin was measured in the blood sample withdrawn from the patient 12-14 days after starting the GnRHa, to test for pituitary down-regulation, prior to HMG administration. Two primary parameters were set. Parameter 1: the time needed to reach a satisfactory initial response (Point A set as: “the number of days needed by the patient to reach at least 2 follicles on each side with a minimum of 12 mm diameter”). Parameter 2 was set as “the time needed to reach mature Graafian follicles (Point B set at: 20 mm follicular diameters or more and concomitant Estradiol levels corresponding to at least 200 pg/ml per follicle”).

RESULTS: Patients were divided into four groups based on their Follistatin levels, ranging between the minimal and the maximal readings recorded in our study, using an increment of 1000 pg/ml between each group (Group 1: 0-1000, Group 2: 1001-2000, Group 3: 2001-3000, Group 4: 3001-4000 ng/ml). By 7 days of HMG stimulation 100% of Group 1 reached Point A, this was achieved in 64.1%, 38.2% and 0% in Groups 2, 3&4 respectively. By Day 9 stimulation 100% of Group 2, 91% of Group 3 and only 10.5% of Group 4 reached Point A. Point B was reached in Group 1 after 8 days in 82.1% and 100% after 10 days. At 12 days of stimulation the percentage of those who reached Point B was 92.2% in Group 2, 4.5% in Group 3 and 0% in Group 4. In that last group, 73.7% of patients needed 16 days to reach Point B, with a remaining 26.3% needed 18 days or more to reach it. Using Pearson’s correlation, a strong positive correlation was found between serum Follistatin levels and Parameter 1 & 2 (r=0.899 & 0.91, respectively). The correlations between Follistatin and Age, BMI and AMH were statistically insignificant.

CONCLUSIONS: In this study, serum Follistatin levels had a clear effect on ovarian response. The detected inverse correlation between Follistatin levels and the ovarian response time suggests a role of serum Follistatin levels assessment prior to starting an ovarian stimulation protocol. Follistatin could act as a reliable independent predictor of the magnitude of ovarian response in cases undergoing controlled ovarian hyperstimulation for IVF. This could be used to properly tailor the dose for those patients, reducing the need for dose modification and subsequently duration of stimulation. It could equally help to predict OHSS or slow response.

SUPPORT: None.

P-287 Tuesday, October 15, 2019 6:30 AM

ORAL OVULATION INDUCTION MEDICATIONS VERSUS GONADOTROPINS FOR UNEXPLAINED INFERTILITY: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS. Jessica R. Zolton, DO, Peter G. Lindner, M.D., Nancy Terry, B.S., M.L.S., Alan H. DeCherney, MD, Micah J. Hill, DO, National Institute of Child Health and Human Development, NIH, Bethesda, MD; Walter Reed National Military Medical Center, Bethesda, MD; NIH, Bethesda, MD.

OBJECTIVE: To compare live birth and multiple gestation in gonadotropins versus oral ovulation induction agents for patients with unexplained infertility.

DESIGN: Systematic review and meta-analysis

MATERIALS AND METHODS: A systematic review of PubMed and Embase was performed for RCTs comparing gonadotropins versus clomiphene citrate (CC) or letrozole in IUI cycles for patients diagnosed with unexplained infertility. Primary outcomes were live birth and multiple gestation. Random effects models were used for all comparisons, due to clinical heterogeneity or I² > 50%. Primary meta-analysis was performed on an intent-to-treat and per patient basis, with sensitivity analyses of per protocol, per cycle, and fixed effects models performed.

RESULTS: Eight total trials were identified that met inclusion criteria and constituted 2,989 patients undergoing 6,590 cycles. One study reported a significant increase in live births and multiple gestations with gonadotropins in comparison to letrozole and CC. All other studies compared CC and gonadotropins. Three of these studies found no difference in live birth or multiple gestations. One study found a lower live birth rate with CC but no difference in multiple gestations. Moderate heterogeneity was suggested by the Q test (Q=0.08) and the I² index (I²=53%) for live birth comparisons. The overall likelihood of live birth was not significantly increased in patients randomized to gonadotropins (RR 1.10, 95% CI 1.00-1.21, P=0.05). Similarly, the risk of multiple gestations was not significantly increased in patients assigned gonadotropins (RR 1.09, 95% CI 0.97-1.21, P=0.15). The number needed to treat with gonadotropins was 15 to have 1 additional live birth. For every 1 additional live birth from
gonadotropins, an additional 0.88 twin pregnancies occurred. Singleton birth per cycle was similar between the two groups. The results did not change in per protocol, per cycle, or per cycle effect model sensitivity analyses.

CONCLUSIONS: Gonadotropin use in women with unexplained infertility did not increase the likelihood of live birth. For every birth gained with the use of gonadotropins, an almost identical increase in the risk of twins occurs. The randomized data do not support the use of gonadotropins for superovulation in women with unexplained infertility.

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OVULATION RATE WITH LETROZOLE STAIR-STEP PROTOCOL AND IN SUBSEQUENT LETROZOLE CYCLE.

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OBJECTIVE: Stair-step (SS) protocols have been successfully used for anovulatory women who fail to ovulate with the initial dose of clomiphene citrate (CC), with the additional benefit of decreased time to ovulation and increased ovulation rates compared with more traditional protocols. Letrozole is now considered first-line therapy for ovulation induction (OI). However, ovulation rate with the letrozole SS protocol has never been reported. We sought to determine the effectiveness of the letrozole SS protocol for inducing ovulation, as well as the ovulation rate in the subsequent cycle with the letrozole dose that achieved ovulation through SS.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Anovulatory patients who underwent OI using the letrozole SS protocol at our center between 2013-2019 were included for analysis. Baseline and cycle characteristic data was collected from our electronic medical record. Ovulation was confirmed by positive result on urinary ovulation predictor kit, serum LH level >20 IU/mL or the presence of a follicle >15 mm on ultrasound. Ovulation rate was the primary outcome. Student’s t-test and chi squared test was used for continuous and categorical variables, respectively. A p-value of 0.05 was considered statistically significant.

RESULTS: Of 108 patients who underwent letrozole SS for OI, 83.3% (90/108) of patients became ovulatory. 38.9% (35/90) patients ovulated with the 5 mg dose and 61.1% (55/90) ovulated with the 7.5 mg dose. 88.9% (80/90) of patients became ovulatory. 38.9% (35/90) patients ovulated with the 7.5 mg dose and 61.1% (55/90) ovulated with the 10 mg dose. There was a 4.5% increase in the ovulation rate with the letrozole SS protocol compared to the initial dose of clomiphene citrate (88.9% vs 84.4%).

CONCLUSIONS: A single dose protocol with Letrozole in an OI/IIU cycle may be considered as an alternative to standard five day dosing protocols with potential for improved compliance and similar reproductive outcomes.

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PHASE 4, NON-INTERVENTIONAL, OPEN LABEL STUDY EVALUATING DOZING CHARACTERISTICS AND OVARIAN RESPONSE USING THE REDESIGNED FOLLITROPIN ALFA PEN INJECTOR IN ASSISTED REPRODUCTIVE TECHNOLOGIES (ART) TREATMENT IN ASIA: IMPROVE STUDY.

Bum Chae Choi, MD, PHD,a,b Canquan Zhou, MD,a,b Hong Ye, MD,a,b Sun Yun, M.D.,b Ying Zhong, Doc-tor,a,b Fei Gong, PhD,a,b Nadezda Abramova, MD, PhD,a Salvatore Longobardi, MD,a,b Teoman Ulas, MD,a,b Thomas D’Hooghge, MD, PhD,a Creation and Love Women’s Hospital, Gwang-ju, Korea, Repub-lic of (South);a First Affiliated Hospital, Sun Yat-sen University, GuangZhou, Guangdong, China; aChongqing Maternity and Child Healthcare Hospital, Chongqing, China; aCenter for Reproductive Medicine, Ren Ji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China; aChengdu Jinjiang District Maternal and Child Health Hospital, Chengdu, China; aReproductive and Genetic Hospital of CITIC-Xiangya, Changsha, Hunan, China; aMerck Healthcare KGaA, Darmstadt, Germany; aMerck Pte Ltd, Ascent, Singapore.

OBJECTIVE: Assess if use of a redesigned pen injector (RPI) for follitropin alfa (GONAL-f,a,b Merck KGaA, Darmstadt, Germany) with a small dose dial (12.5IU) allows greater treatment individualization, measured as reduction in the total dose (IU) of recombinant human follicle stimulating hormone (rhFSH) used per oocyte retrieved, in a subgroup of ART patients (pts) at risk for ovarian hyperstimulation syndrome (OHSS).

DESIGN: Phase 4, comparative study of pts receiving in vitro fertilization / intracytoplasmic sperm injection in an observational prospective cohort (PC) vs an historical cohort (HC).

MATERIALS AND METHODS: The PC included pts (20-40 yrs; BMI <30 kg/m2) using the RPI at 14 sites (Korea, Vietnam, Indonesia and China (N=1783; assessed 09/14-07/16)). The HC was from a Phase 4 study (EMR760023522) in a comparable Asian population using other injection devices (OID; N=1419; assessed 06/09-02/12). In the PC, pts followed either an agonist or antagonist protocol; rhFSH fine dose adjustment with the RPI was allowed at each stage. In the HC pts followed an agonist protocol; rhFSH dose adjustment with OID was allowed at each stage. The primary endpoint of amount of rhFSH (IU) administered per oocyte retrieved was assessed in a pt subgroup at high risk for OHSS, identified from pt characteristics (BMI, age) and biomarkers (anti-Müllerian hormone, antral follicle count, basal FSH and luteinizing hormone [LH], and estradiol [E2]) and propensity matched between the PC (N=123) and HC (N=123). The sensitivity analysis only included pts receiving agonist protocol (N=123 matched pts, each cohort). Secondary outcomes and safety (OHSS and all adverse events [AES]) were assessed in the total population.

RESULTS: Pt characteristics were comparable between cohorts. In the PC, 62.5% (1115/1783) of pts received an agonist protocol, 37.0% (659/1783) an antagonist protocol (0.5% [9/1783] were on both other). All pts in the HC received an agonist protocol. Mean amount (SD) of rhFSH in IU administered per oocyte retrieved (matched population) was significantly lower in the PC vs HC (132.5 [85.2] vs 332.7 [371.6]; p<0.0001; sensitivity analysis: [127.5 [81.6] vs 332.7 [371.6]; p<0.0001]). LH level (SD) in IU/L between Day 6 and 8, and E2 level (SD) in pg/mL on the day of human chorionic gonadotropin administration was higher in the PC vs HC (LH: 6.71 [69.2] vs 1.63 [1.5]; E2: 4058.3 [2663.5] vs 3291.8 [2313.9]). Mean (SD) total live birth rate (LBR), multiple gestation (MG), and miscarriage (SAB). Student’s t test, chi square, and Fisher’s exact statistic analysis were utilized where appropriate.

RESULTS: Of a total of 586 patients, the 1D group had 302 patients and the 5D group had 284 included in the study. There was no difference in smoking status, primary vs secondary infertility, or total motile concentration (TMC). Comparing 1D to 5D, there was a statistically significant, though not clinically relevant difference in both age and BMI (31 yrs vs. 31.8 yrs, p=0.03; 26.2 vs. 27.4, p=0.02), respectively. There were no differences between 1D and 5D in PR (14.2% vs 11.6%), LBR (9.6% vs 7%), MG (16.2% vs 13.8%), or SAB (16.2% vs 13.8%).

CONCLUSIONS: A single dose protocol with Letrozole in an OI/IIU cycle may be considered as an alternative to standard five day dosing protocols with potential for improved compliance and similar reproductive outcomes.
rhFSH dose in IU was lower in the PC vs HC (1848.4 [700.5] vs 2237.8 [772.6]; p < 0.001); clinical pregnancy rate was improved in the PC vs HC (per embryo transfer cycle: 50.3% vs 40.7%; per initiated cycle: 35.3% vs 37.8%). OHSS incidence was significantly lower in the PC vs HC (1.5% [27/183] vs 4.0% [57/1419]; p = 0.001); most events were mild/moderate. 5.0% [89/1783] of patients had ≥1 AE and 1.9% [33/1783] of patients had ≥1 serious AE in the PC.

CONCLUSIONS: Pts using the RPI required a significantly lower rhFSH dose per oocyte retrieved vs pts using OI in this Asian population. Clinical outcomes were improved and OHSS incidence was significantly lower in the PC vs HC.

SUPPORT: Merck KGaA, Darmstadt, Germany.

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USE OF LUTEINIZING HORMONE SUPPLEMENTATION FOR OVARIAN STIMULATION IN IVF/ICSI CYCLES OF WOMEN WITH GOOD OVARIAN RESERVE.

Liang Hsuan Chen, MD, Tzu-Hsuan Chin, MD, Ya-Chiung Hsu, MD, Shang Yu Huang, MD, Hsing-Tse Yu, MD, Hsien-Ming Wu, MD, PhD, Chia-Lin Chang, MD, Hong-Yuan Huang, MD, Shang Yu Huang, MD, Hsing-Tse Yu, MD, An accurate definition of the LH threshold in GnRH antagonist cycles may contribute to the discussion of which subgroups of women may benefit from adjuvant LH therapy.

OBJECTIVE: To declare current evidence exploring the added value of LH supplementation to GnRH antagonist cycles in women with good ovarian reserve.

DESIGN: We conducted a retrospective analysis exploring the benefit for pregnancy achievement of LH supplementation to GnRH antagonist cycles in women with AMH level over 5ng/mL.

MATERIALS AND METHODS: A total of 255 women with AMH ≥ 5 undergoing IVF/ICSI using a GnRH antagonist protocol was included. Of these, 148 were received treatment with recombinant FSH (r-FSH) + human menopausal gonadotrophin (HMG) and 107 with r-FSH alone through the ovarian stimulation.

RESULTS: We observed a significantly lower serum LH levels at the beginning of cycle, the day of GnRH antagonist administration and the day of oocyte triggering in the combination of r-FSH+HMG group. The treatment days and total gonadotropin dose was significantly higher in r-FSH+HMG group compared with r-FSH alone group. Nevertheless, there were no significant differences between the two groups with respect to the number of oocytes retrieved, maturation, fertilization, and blastocyst formation rate. The OHSS occurred 8% of the r-FSH+HMG group, whereas 8% OHSS developed in the r-FSH alone group. There were no difference in pregnancy outcome between the groups.

CONCLUSIONS: LH supplementation to r-FSH following GnRH antagonist protocol in women with good ovarian reserve does not seem to significantly augment serum E2 level on the trigger day and further pregnancy outcome in patient with good ovarian reserve.

In ovulatory women (11,449 cycles), LTZ use was associated a similar CPR (17.2% CC vs 15.5% LTZ, p = 0.168) and a similar multiple pregnancy rate (22.0% CC vs 20.3% LTZ p = 0.423) when compared to CC. Increased CC dosing from 50 to 100 mg decreased the chance of clinical pregnancy (CC50 (18.2%) vs CC100 (16.3%), p = 0.014) while increasing the chance of multiple pregnancy (CC50 (19.8%) vs CC100 (25.7%), p = 0.004). Increased LTZ dosing above 2.5 mg did not increase the chance of IUP (p = 0.354) but an increase from 2.5 to 5 mg did increase the chance of multiple pregnancy (LTZ 2.5 (7.7%) vs LTZ (22.8%), p = 0.040).

In women with ovulatory dysfunction (4,004 cycles), LTZ was associated with a decreased likelihood of multiple pregnancy compared to CC among those with a clinical IUP (20.3% CC vs 12.5% LTZ p = 0.001). Increasing doses of CC or LTZ were not associated with an increased chance of pregnancy or risk of multiple pregnancy.

In ovulatory women (11,449 cycles), LTZ use was associated a similar CPR (17.2% CC vs 15.5% LTZ, p = 0.168) and a similar multiple pregnancy rate (22.0% CC vs 20.3% LTZ p = 0.423) when compared to CC. Increased CC dosing from 50 to 100 mg decreased the chance of clinical pregnancy (CC50 (18.2%) vs CC100 (16.3%), p = 0.014) while increasing the chance of multiple pregnancy (CC50 (19.8%) vs CC100 (25.7%), p = 0.004). Increased LTZ dosing above 2.5 mg did not increase the chance of IUP (p = 0.354) but an increase from 2.5 to 5 mg did increase the chance of multiple pregnancy (LTZ 2.5 (7.7%) vs LTZ (22.8%), p = 0.040).

In women with ovulatory dysfunction (4,004 cycles), LTZ was associated with a similar CPR compared to CC (22.8% LTZ vs 21.0% CC, p = 0.271) with a significantly decreased risk of multiple pregnancy (6.5% LTZ vs 15.6% CC, p = 0.002). Increasing dose was not associated with increased multiples for either CC or LTZ.

CONCLUSIONS: To maximize clinical pregnancy rates while minimizing the chance of multiples in CO-IUI cycles, medication and dose should be chosen carefully. LTZ vs CC had similar pregnancy rates in the overall population. In ovulatory women, consideration should be given to starting CC at 50mg, as higher doses were associated with an increased risk of multiple pregnancy.
gestation without improvement in CPR. Patients with ovulatory dysfunction may benefit from lower multiple pregnancies with LTZ utilization.

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DO INFERTILE PATIENTS WHO TEST POSITIVE FOR GROWTH DIFFERENTIATION FACTOR 9 (GDF9) POLYMORPHISM C447T EXHIBIT AN ALTERED RESPONSE TO CONTROLLED OVARIAN STIMULATION (COH)? Jenna Friedenthal, MD,† Dmitry Gounko, MA,† Joseph A. Lee, BA,† Teresa A. Cacchione, MS, CGC,† Alan B. Copperman, MD,‡ †Icahn School of Medicine at Mount Sinai, New York, NY; ‡Reproductive Medicine Associates of New York, New York, NY.

OBJECTIVE: GDF9 is a protein coding gene responsible for promoting granulosa cell proliferation while inhibiting FSH-induced steroidogenesis [1]. GDF9 also potentiates the final stages of follicle growth and supports metabolic cascades such as steroid biosynthesis. Single nucleotide polymorphisms (SNPs) in GDF9 are associated with an increased risk for primary ovarian insufficiency and diminished ovarian reserve [2]. Fertilome®, a multigene panel test, reports GDF9 SNPs as part of a multigene targeted sequencing panel and is often suggested in poor responding patients. We sought to evaluate ovarian stimulation outcomes in patients who tested positive for the GDF9 SNP C447T.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The study included patients at a single academic center who underwent COH and Fertilome® testing from 2016 to 2018. Cases included patients who screened positive for the GDF9 SNP C447T. Control cases included patients who screened negative. Patients testing positive for a Fragile X premutation or abnormal karyotype were excluded. Our primary outcome was number of oocytes retrieved. Secondary outcomes were number of metaphase II (MII) oocytes, number of fertilized oocytes, blastulation rate, and euploidy. Data were analyzed using student’s t-test, with p < 0.05 considered significant.

RESULTS: A total of 96 patients who underwent 214 COH cycles and Fertilome® testing were assessed in the study. A total of 80 patients (170 cycles) tested positive for the GDF9 SNP C447T, while 16 patients (44 cycles) tested negative for the GDF9 SNP. Although there was a difference in BMI between groups (23.59 vs 21.42, P = 0.0005), no differences in age or AMH were observed. We demonstrated no differences in the total number of oocytes retrieved or MII oocytes. Last, there was no difference in the fertilization, blastulation, or embryo euploidy between groups.

CONCLUSIONS: A majority of patients who experienced poor response to IVF stimulation tested positive for the GDF9 SNP C447T. However, the presence of the SNP did not affect oocyte retrieval count or MII maturation. Thus, although the GDF9 gene may be important in follicular development and maturation, detection of SNP C447T is not associated with worse outcomes during COH. Patients can be reassured that testing positive for the SNP C447T does not translate to impaired ovarian stimulation and oocyte retrieval outcomes.

REFERENCE

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OOOCYTE RECRUITMENT OF PATIENTS SUBMITTED TO THE NEW OVARIAN STIMULATION REGIMEN USING PROGESTIN TO BLOCK THE LH SURGE. Michelli Saemi Tanada, BSc, Elen Souto Vieira Porto, BSc, Ivan Henrique Yoshida, BSc, MSc, Renato de Oliveira, MD, PhD, Emerson Barchi Cordts, MD, MSc, Caio Parente Barbosa, MD, PhD. Instituto Ideia Fertil de Saúde Reproductiva, Santo André, Brazil.

OBJECTIVE: To evaluate the recruitment and oocyte maturity of a new low cost and easy administration ovarian stimulation regimen, which uses progestin as an alternative to the GnRH analogue.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: It was analyzed 100 patients who underwent Assisted Human Reproduction between June 2018 to January 2019. Of those patients, 50 used the progestin protocol as an alternative to the GnRH analogue, to suppress the premature LH surge during the follicular phase. The other 50 patients used the standard protocol with antagonist. The total number of oocytes retrieved and the classification for maturity and viability were analyzed between the groups. Variables such as age and body mass index (BMI) were considered as well. The qualitative variables were presented by absolute and relative frequency and the quantitative variables by means of a 95% confidence interval, using a normality test of the Shapiro-Wilk data (p < 0.05). The Mann-Whitney test and Chi-square test were used to compare the variables according to the two induction protocols. The Chi-square test was used for the comparative analysis of the BMI. For all analyzes, the level of significance was p < 0.05. The statistical program used was Stata version 11.0.

RESULTS: No statistically significant results were found in relation to the number of oocytes retrieved in the conventional ovarian stimulation cycles with antagonist compared to the cycles using progestin to block the LH surge (283 versus 247, p = 0.54). Similarly, there was no difference in the degree of oocyte maturation (mature 79.72% / 77.43%, immature 13.52% / 16.68%), altered, degenerated or oocytes with ruptured zona pellucida (2.54% / 2.19%, 1.13% / 1.88%, 3.10% / 2.82%, p = 0.88). The body mass index (BMI) was also evaluated without significant differences after analysis (p = 0.07). When separated by age (up to 37 years and ≥ 38 years), the groups also did not present statistically significant differences in any of the analyzed variables.

CONCLUSIONS: The use of progestin in the induction protocols to block the LH surge seems to be an option in the substitution of GnRH analogues, since it presented similar results, more accessible cost and a route of administration more comfortable for the patients.

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COMPARISON OF TRADITIONAL AND STEP UP PROTOCOLS WITH LETROZOLE. Shelin Tsai, MD, Stephanie Smeltzer, MD, Thomas M. Price, MD. Division of Reproductive Endocrinology and Infertility, Duke University Medical Center, Durham, NC.

OBJECTIVE: To compare time to ovulation between traditional and step up protocols with letrozole.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Patients were identified through Duke Fertility Center’s Intrauterine Insemination database, which stores information about each ovulation induction cycle including patient’s age, body mass index (BMI), last menstrual period, trigger date, and outcomes. The electronic medical record was used to obtain missing data points. Patients receiving ovulation induction with letrozole for ovulatory dysfunction between January 1, 2010 and March 3, 2018 were included. Patients were excluded if they received gonadotropins or if they switched to a different ovulation induction agent. In the traditional protocol, patients had an increase in letrozole dose following spontaneous menstruation or medroxyprogesterone-one-induced withdrawal bleed if there were no follicles at 16mm or greater on ultrasound by cycle day 20. Patients were excluded if they delayed starting a cycle with the increased dose. In the step up protocol, patients had an immediate increase in letrozole dose by cycle day 20 at the latest if no developing follicle was detected. A separate cohort of those who underwent a step up protocol with clomiphene was also included for comparison. The primary outcome was time to ovulation, defined as the number of days between the last menstrual period and the detection of a follicle at 16mm or greater on ultrasound. A secondary outcome was clinical pregnancy. Student’s t-test or Wilcoxon rank sum test were used to compare variables. Statistical analyses were conducted using R version 3.5.1 (Vienna, Austria).

REFERENCE

REFERENCES


SUPPORT: None.

FERTILITY & STERILITY®
CONCLUSIONS: In unslected patients using corifollitropin alfa, the ultrashort GnRHa protocol needed low dose of additional gonadotropin and fewer injections but produced similar pregnancy outcomes than antagonist protocol did, suggesting that the ultrashort GnRHa protocol could be an alternative.

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FLEXIBLE VERSUS FIXED GONADOTROPIN RELEASING HORMONE ANTAGONIST (GNRH-A) STARTING DAY DURING CONTROLLED OVARIAN HYPERSTIMULATION FOR IN VITRO FERTILIZATION (IVF): A SYSTEMATIC REVIEW & META-ANALYSIS.

Clara Q. Wu, M.D., Cheng Wei Xiao, M.D., Paul Claman, M.D., Doron Shumorgun, M.D., Ottawa Fertility Centre, Ottawa, ON, Canada.

OBJECTIVE: To obtain the up-to-date evidence on fertility outcomes when comparing flexible and fixed start gonadotropin releasing hormone antagonist (GnRH-ant) protocols during controlled ovarian hyperstimulation for In Vitro Fertilization (IVF).

DESIGN: This study is a systematic review and meta-analysis of published randomized controlled trials (RCT). A systematic search of the literature, using keywords GnRH antagonist, fixed, flexible, pregnancy, and live birth, was performed across the Cochrane Library, EMBASE, and MEDLINE databases from 1996 to January 2019.

MATERIALS AND METHODS: Studies were selected for inclusion in the systematic review and meta-analysis if they were 1) RCTs, 2) that compared flexible versus fixed start GnRH antagonist protocols, 3) reported IVF outcomes, 4) on patients who were normo-responders. Data involving patient characteristics, IVF protocols, and fertility outcomes were extracted independently by two reviewers. Collected variables include IVF protocol used; total gonadotropin dosage; median estradiol level on day of GnRH-ant start; number of oocytes retrieved; fertilization rate; number of good quality embryos; clinical pregnancy rates; premature LH rises and cycle cancellation. Study quality assessment was performed using the Cochrane Collaboration's tool for assessing risk of bias in randomized trials.

RESULTS: Six hundred and thirty-eight articles were identified through database searches and five full text RCTs (701 IVF cycles) were included in our analysis. There is no statistically significant difference in clinical pregnancy rates between flexible and fixed GnRH-ant protocols (OR = 0.74, 95% CI = 0.53-1.03, p = 0.07) with a trend towards higher clinical pregnancy rate in the fixed GnRH-ant protocol. There is no significant difference in total oocytes retrieved between the flexible and fixed GnRH-ant protocols (Pooled mean difference = 1.02, 95% CI = -0.09-2.12, p = 0.07). There is a trend towards lower total gonadotropin dosage used in the flexible GnRH antagonist protocol (Pooled mean difference = -124.18, 95% CI = -325.36-76.99, p = 0.23); however, the difference is not statistically significant. There is no difference in the incidence of premature LH surge between the two protocols (OR = 1.11, 95% CI = 0.56-2.18, p = 0.76).

CONCLUSIONS: There is insufficient evidence to demonstrate whether flexible and fixed GnRH-ant protocols yield different IVF outcomes.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Ultrashort (n = 135)</th>
<th>Antagonist (n = 110)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>37.04 ± 4.28</td>
<td>36.56 ± 4.26</td>
<td>0.382</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>21.69 ± 2.95</td>
<td>22.24 ± 3.55</td>
<td>0.189</td>
</tr>
<tr>
<td>AMH (ng/mL)</td>
<td>2.58 ± 1.92</td>
<td>2.19 ± 2.21</td>
<td>0.142</td>
</tr>
<tr>
<td>Stimulation days</td>
<td>10.30 ± 1.52</td>
<td>8.88 ± 1.30</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>No. of OPD visits before triggering</td>
<td>2.04 ± 0.74</td>
<td>1.70 ± 0.64</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Additional FSH dosage (IU)</td>
<td>637.78 ± 537.63</td>
<td>802.95 ± 435.97</td>
<td>0.101*</td>
</tr>
<tr>
<td>No. of shots before triggering</td>
<td>6.63 ± 1.88</td>
<td>8.62 ± 2.81</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>LH (mIU/mL) before triggering</td>
<td>1.12 ± 0.77</td>
<td>4.12 ± 6.81</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td>Premature LH surge rate %</td>
<td>0% (0)</td>
<td>5.45% (6)</td>
<td>0.006**</td>
</tr>
<tr>
<td>Max. E₂ level (pg/mL)</td>
<td>2333.87 ± 1441.06</td>
<td>1903.43 ± 1028.72</td>
<td>0.009**</td>
</tr>
<tr>
<td>No. of oocytes retrieved</td>
<td>12.52 ± 8.12</td>
<td>9.40 ± 7.03</td>
<td>0.022**</td>
</tr>
<tr>
<td>MII rate (%)</td>
<td>73.38 ± 20.45</td>
<td>68.40 ± 15.01</td>
<td>0.642</td>
</tr>
<tr>
<td>Fertilization rate (%)</td>
<td>71.99 ± 16.92</td>
<td>71.41 ± 20.69</td>
<td>0.821</td>
</tr>
<tr>
<td>Blastocyst rate (%)</td>
<td>33.81 ± 31.96</td>
<td>21.05 ± 31.26</td>
<td>0.002**</td>
</tr>
<tr>
<td>Pregnancy rate (%)</td>
<td>37.04</td>
<td>43.64</td>
<td>0.294</td>
</tr>
<tr>
<td>Clinical pregnancy rate %</td>
<td>25.19</td>
<td>34.55</td>
<td>0.110</td>
</tr>
<tr>
<td>Live birth rate (%)</td>
<td>19.26</td>
<td>30.00</td>
<td>0.051</td>
</tr>
<tr>
<td>Cumulative pregnancy rate (%)</td>
<td>47.24</td>
<td>51.38</td>
<td>0.527</td>
</tr>
<tr>
<td>OHSS rate (%)</td>
<td>1.48</td>
<td>0</td>
<td>0.200</td>
</tr>
</tbody>
</table>
OBJECTIVE: Poor ovarian response (POR) is an increasingly common indication for IVF, accounting for 31% of cycles in the USA in 2016, compared to 12% in 2005. These patients are especially challenging as POR results in higher rate of cycle cancellation, lower number of embryos available for transfer, and overall lower pregnancy rates. Autologous platelet-rich plasma (PRP) is rich in growth factors and cytokines and has been used as an agent that induces tissue regeneration. PRP also promotes follicle development in vitro and two studies reported a total of 7 cases of POR, where PRP was utilized. The aim of the current study was to investigate whether intraovarian injection of autologous PRP is associated with improved ovarian reserve and IVF outcomes in patients with POR.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Reproductive age women diagnosed with POR based on American Society for生殖 Endocrinology and with a history of at least one prior failed IVF cycle were recruited for the study between December 15, 2018, and April 15, 2019. Antral follicle count (AFC), serum anti-mullerian hormone (AMH), and early follicular phase serum follicle stimulating hormone (FSH) levels were determined at baseline. Autologous blood obtained from peripheral vein was used to prepare PRP following standard protocols. PRP injection was performed under sedation anesthesia, using a 35 cm 17 gauge needle trans-vaginal ultrasound guidance. On the 2-4th days of the first three menstrual cycles following the procedure, AFC, AMH, and FSH levels were re-assessed. Patients with at least one antral follicle were started on ovarian stimulation for IVF-ICSI, followed by embryo banking at cleavage stage for PGT-A. Markers of ovarian reserve (AFC, FSH, AMH) and IVF outcome parameters (number of MII oocytes, 2PN and cleavage stage embryos) were followed and compared to previous cycle.

RESULTS: At the time of this submission, a total of 152 patients (mean age ± SD: 39.3 ± 5.6) with the diagnosis of POR were included in the study. PRP treatment resulted in higher AFC (6.2 ± 2.8 vs 2.6 ± 1.6; p<0.001) and AMH (0.54 ± 0.30 vs 0.41 ± 0.28; p=0.001, respectively), and lower FSH (17.5 ± 4.7 vs 20.3 ± 5.4; p<0.001) levels. Number of MII oocytes, 2PN and cleavage stage embryos were also increased following the PRP procedure (4.2 ± 2.9 vs 2.5 ± 1.9; 3.8 ± 2.6 vs 2.2 ± 1.7; 3.4 ± 1.8 vs 2.0 ± 1.6, respectively; p<0.001 for all). In 43 patients (12.5%), no changes were observed in AFC after the PRP procedure. Another 43 patients (25.3%) failed IVF due to stimulation failure, fertilization failure, or arrested embryo development. In 87 patients (60.3%), at least one cleavage embryo was obtained and embryo banking was achieved. In addition, three patients (1.9%) had spontaneous pregnancies in the first or second cycle after the PRP procedure that are ongoing.

CONCLUSIONS: Intraovarian injection of autologous PRP might be an alternative experimental treatment option for women with poor ovarian response to stimulation. Whether this treatment is clinically effective will need to be further investigated using a prospective randomized controlled clinical trial design.
TABLE 1. Clinical outcome of laparoscopic ovarian surgical activation

<table>
<thead>
<tr>
<th>Patients (n=60)</th>
<th>Growing follicle number</th>
<th>Number of retrieved oocytes (mean +SD)</th>
<th>Fertilization rate (% n)</th>
<th>D3 8cell stage rate (% n)</th>
<th>Clinical pregnancy rate (% n)</th>
<th>Miscarriage rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>within four months until operation*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-op (203 cycles)</td>
<td>1.34±1.03a</td>
<td>1.13±0.98b</td>
<td>57.7 (79/137)</td>
<td>25.6 (33/129)</td>
<td>0b (0/23)</td>
<td>0.05</td>
</tr>
<tr>
<td>Post-op (216 cycles)</td>
<td>2.81±2.02a</td>
<td>1.53±1.39a</td>
<td>68.2 (163/239)</td>
<td>40.6 (95/234)</td>
<td>17.1 (12/70)</td>
<td>58.3% (7/12)</td>
</tr>
</tbody>
</table>

(a-a’, b-b’, c-c’, d-d’: p<0.05, t-test, c-c’, d-d’: p=0.05, Chi-squared test) * including cycles without operation due to small number

CONCLUSIONS: Our procedure significantly increased the number of growing follicles with increase in viable embryos, resulting in twelve successful clinical pregnancies and five babies. Also, it might improve embryo quality based on disruption of Hippo signaling pathway.

P-301 Tuesday, October 15, 2019 6:30 AM

APPLICATION OF CONTROLLED OVARIAN HYPER-STIMULATION WITH AGONIST-ANTAGONIST PROTOCOL IN POSEIDON GROUP 3 AND GROUP 4 PATIENTS WITH DIMINISHED OVARIAN RESERVE.

Rui Yang, Doctor; Xiaoguo Du, Master; Liuxie Chen, M.D.; Xinna Chen, Professor. *Peking University Third Hospital, Beijing, China; **Affiliation not provided.

OBJECTIVE: By comparing standard antagonist regimen and agonist-antagonist protocol (AAP regimen), a combination of a microdose flare-up GnRH agonist with a GnRH antagonist in POSEIDON group 3 and group 4 patients with diminished ovarian reserve, this article aims to study if AAP regimen could improve the clinical outcomes in low prognosis patients.

DESIGN: This is a retrospective study.

MATERIALS AND METHODS: The clinical data of 646 cycles of prospective poor ovarian response POR patients (POSEIDON group 3 and 4) who received in vitro fertilization and embryo transfer (IVF-ET) in Peking University Third Hospital Reproductive medical center from January 2016 to May 2018 were retrospectively analyzed. The total number of APP cycle was 323, and the control group was selected from the database with 1:1 matching of prospective low prognosis patients (POSEIDON group 3 and group 4) with similar age and approaching date of oocyte retrieval. Patients' general information, ovarian hyperstimulation indices and clinical outcomes were studied.

RESULTS: AAP group had fewer antral follicle count (3.04±2.05 vs. 3.84±2.17, p = 0.05) and similar AMH level (0.62±0.64 and 0.63±0.49, p > 0.05) compared with control group. AAP group had shorter (8.84±2.59 vs. 10.31±2.23, p = 0.015) and lower dosage (2754.18±973.37 vs. 3246.7±1044.20, p<0.05) of Gn using, and had similar number of oocytes obtained compared with control group (4.06±2.89 vs. 4.16±2.65, p=0.649). Under the same proportion of fertilization schemes (routine or ICSI methods), AAP group had higher fertilization rate (74.1% vs. 69.1%, p=0.004) and good quality embryo rate (62.6% vs. 56.9%, p=0.014), and ultimately had higher embryo implantation rate (22.3% vs. 15.8%, p=0.020) and cumulative clinical pregnancy rate (32.5% vs. 22.9%, p=0.018).

CONCLUSIONS: For POSEIDON patients with low prognosis and poor ovarian reserve, controlled ovarian hyperstimulation with agonist-antagonist protocol had better clinical outcomes compared with conventional antagonist regimen.

SUPPORT: None.

P-302 Tuesday, October 15, 2019 6:30 AM

CONVENTIONAL PROTOCOL VERSUS MINIMAL OVARIAN STIMULATION IN PATIENTS WITH POOR PROGRESSIVE PROGNOSIS ACCORDING TO POSEIDON CRITERIA.

Mauro Corzollina, M.D.; Gustavo N. Cecchino, M.D.; Nicolas Garrido, PhD; Fundación IVI, Valencia, Spain; IVIRMA Madrid, Madrid, Spain; IVI Foundation, IIS La Fe, Valencia, IIS, Spain.

OBJECTIVE: to analyze whether minimal ovarian stimulation (MOS) is as effective as conventional controlled ovarian stimulation (COS) for patients belonging to different groups according to the Poseidon criteria.

P-303 Tuesday, October 15, 2019 6:30 AM

THE EFFECTIVENESS OF TRANSDERMAL TESTOSTERONE GEL 1% (ANDROGEL) FOR POOR RESPONDERS UNDERGOING IN VITRO FERTILIZATION.

Anjali Chaudhary, MD DNB. CONSULTANT AAROGYA HOSPITAL, Delhi, India.

OBJECTIVE: To investigate the effectiveness of treatment with transdermal testosterone gel (TTG) 1% (androgel) before ovarian stimulation (COS) using GnRH antagonist in low responders undergoing IVF/intracytoplasmic sperm injection (ICSI).
DESIGN: prospective randomized controlled trial.

MATERIALS AND METHODS: A total of 60 low responder, who were defined as patient who failed to produce <3 follicles with a mean diameter of < 16 mm with the result that <3 oocytes were retrieved despite the use of a high gonadotropin dose in a previous failed IVF/ICSI cycle from 1.1.18 to 31.3.19 (15 months). Patient were randomized into TTG pretreatment group and control group. For TTG pretreatment group, 12.5mg TTG were applied daily for 21 days in the cycle preceding COS for IVF.

RESULTS: There were no differences in patients characteristics between the two group. Total dose of FSH used were significantly fewer in the TTG pretreatment group than in the control group. The number of oocytes retrieved , mature oocytes, fertilized oocytes, and good quality embryos were significantly higher in the TTG pretreatment group. Embryos implantation rate and clinical pregnancy rate per cycle also were significantly higher in the women pretreated with TTG. No patient reported adverse effects attributed to TTG use.


PREIMPLANTATION GENETIC TESTING

P-305 Tuesday, October 15, 2019 6:30 AM

IMPACT OF PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) ON GESTATIONAL CARRIER (GC) CYCLES IN THE UNITED STATES.

Reeva B. Makhlani, MD, a Madeline Coulter, BA, a Jeffrey Thorne, MD, a Chantal Bartels, MD, a John Nulsen, MD, a Lawrence Engmann, MD, a Claudio Benadiva, MD, a Grow R. Daniel, MD, a Center for Assisted Reproductive Services, University of Connecticut School of Medicine, Farmington, CT, bCenter for Advanced Reproductive Services, University of Connecticut School of Medicine, Farmington, CT.

OBJECTIVE: We analyzed the SART registry to determine the impact of PGT-A on GC in vitro fertilization (IVF) cycles in the United States.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: SART data was analyzed from 4,470 autologous IVF cycles that used a GC between 2014-2016. Cycles were excluded if donor oocytes were used, multicellular embryo(s) was transferred or embryo transfer was not attempted. The cycles were separated into four groups determined by use of PGT-A and number of embryos transferred as follows: (A) PGT and single embryo transfer (SET); (B) PGT and multiple embryo transfer (MET); (C) no PGT and SET (D) no PGT and MET. The primary outcome was live birth rate (LBR). Secondary outcomes were clinical pregnancy rate (CPR), clinical loss rate (CLR) and multiple pregnancy rate (MPR). One-way ANOVA or Student’s t test and X² tests were used to compare continuous and categorical variables, respectively. Multivariate logistical regression was done to control for potential confounders. A p-value of 0.05 was considered statistically significant.

RESULTS: Groups significantly differed in terms of intended parent (IP) age, GC age, IP BMI, smoking status and parity. In MET groups, significantly fewer embryos were transferred when PGT was used (Group B: 2.0 ± 0.2 v. Group D: 2.1 ± 0.4, p<0.01). When comparing groups by number of embryos transferred (A to C, B to D), LBR and CPR were significantly higher with PGT. MPR was significantly lower with SET. After controlling for potential confounders, a significant difference in LBR remained among groups (p<0.01). Of potential confounders, only IP age was significantly predictive of live birth (OR 0.9574, 95% CI 0.9453 - 0.9697, p<0.01).

CONCLUSIONS: This study shows that euploid SET does not compromise LBR and significantly reduces MPR. It highlights an opportunity to increase GC safety as well as widen access to this already restricted service.

SUPPORT: None.

FERTILITY & STERILITY®
NGS EUPLOID EMBRYOS HAVE HIGHER DELIVERY RATES THAN THOSE DIAGNOSED AS EUPLOID BY ACGH/SNP. Caroline McCaffrey, Ph.D., David H. McCulloh, Ph.D., Xinjian He, MS, Patty Ann Labella, BS, Melicia Clarke-Williams, BA, Mary Elizabeth Fino, MD, James A. Grifo, MD, PhD, NYU Langone Fertility Center, New York, NY.

OBJECTIVE: To review outcomes of all STEET procedures based on PGT-A platform used to determine Ploidy status.

DESIGN: Retrospective review of all STEET procedures over an 8 year period at a single center.

MATERIALS AND METHODS: More than 3200 STEET procedures performed over an 8 year period (2011 to 2018) at a single center were reviewed based on the PGT-A platform (NGS, aCGH or SNP) utilized. Our main outcome measures were: Implantation Rate (IR), Clinical Preg rate (FH) and Live Birth (LB) rate. Only embryos reported as euploid were included in the analysis- embryos reported as mosaic or those not yielding a result were omitted. Statistical significance was determined using contingency X² with 1 degree of freedom.

RESULTS: TABLE 1. Comparison of STEET outcomes depending on PGT-A Platform

<table>
<thead>
<tr>
<th>NGS¹</th>
<th>aCGH + SNP²</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average age at Freeze</td>
<td>36.60±4.34</td>
<td>36.54±4.60</td>
</tr>
<tr>
<td>Implantation rate (sacs/embryo)</td>
<td>70.1% (1330/1897)</td>
<td>62.4% (858/1375)</td>
</tr>
<tr>
<td>Clinical Preg rate (FH/embryo)</td>
<td>66.7% (266/1897)</td>
<td>55.9% (768/1375)</td>
</tr>
<tr>
<td>SAB/ Clin Preg</td>
<td>10.3% (87/845)</td>
<td>12.6% (97/770)</td>
</tr>
<tr>
<td>Live Births³ (Live born/embryo)</td>
<td>61.7% (750/1216)</td>
<td>53.2% (657/1235)</td>
</tr>
</tbody>
</table>

1 Only included FETs of embryos with NGS performed in the Fresh IVF cycle.
2 SNP cases were included with aCGH due to low number
3 Live Birth rate calculated through 2017 only (results for 2018 cycles pending)

STEET following PGT-A via NGS resulted in a significantly higher IR compared to aCGH /SNP combined (70.1% vs 62.4%). Similarly, ongoing Pregnancy rates and LB rates were significantly improved when NGS was utilized vs aCGH or SNP. SAB rates were not significantly different between platforms but all methods reduced SAB rates compared to age matched controls without PGS (18%) ¹ (Ref 1).

CONCLUSIONS: STEET results in high IR, high clinical pregnancy rates and high LB rates across all age groups. However, with advances in PGT-A platforms we can continue to improve outcomes and increase safety of ART by maximizing the potential of every ET procedure. With continuing development of PGT-A platforms and interpretation methods used to determine ploidy we can further improve outcomes and safety by transferring a single embryo with the highest implantation potential every time.

REFERENCE
SUPPORT: None.

P-308 Tuesday, October 15, 2019 6:30 AM

BLASTOCYST CONVERSION RATE AND PLOIDY IN TRANSLOCATION CARRIERS. Iris Insohga, MD, MBE, Andrea Lanes, PhD, Ann M. Thomas, PhD, Lori J. Dobson, MS, LCCG, Elizabeth S. Ginsburg, MD, Catherine Racowsky, PhD, Elena Yanushpolsky, MD, Brigham & Women’s Hospital, Boston, MA.

OBJECTIVE: To determine if women intending to undergo in vitro fertilization (IVF) with preimplantation genetic testing for structural rearrangements (PGT-SR) have a poorer rate of blastocyst conversion and an increased risk of aneuploidy compared to patients undergoing IVF with PGT-A (PGT for aneuploidy).
TABLE 1. Comparison of laboratory outcomes and ploidy results following blastocyst biopsy for patients using PGT-A versus PGT-SR

<table>
<thead>
<tr>
<th>Variable</th>
<th>PGT-A</th>
<th>PGT-SR</th>
<th>aRR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>% 2PN/MII</td>
<td>39% ± 6</td>
<td>36% ± 6</td>
<td>Referent: PGT-A</td>
</tr>
<tr>
<td>% Blastocysts/2PN</td>
<td>66% ± 10</td>
<td>60% ± 10</td>
<td>Referent: PGT-A</td>
</tr>
<tr>
<td>% D5 Biopsied/Total blastocysts</td>
<td>67% ± 7</td>
<td>62% ± 7</td>
<td>Referent: PGT-A</td>
</tr>
<tr>
<td>% D6 Biopsied/Total blastocysts</td>
<td>46% ± 33</td>
<td>38% ± 30</td>
<td>Referent: PGT-A</td>
</tr>
<tr>
<td>% Euploid blastocysts</td>
<td>42% ± 33</td>
<td>29% ± 23</td>
<td>Referent: PGT-A</td>
</tr>
<tr>
<td>% Blastocysts with no result</td>
<td>4% ± 13</td>
<td>2% ± 5</td>
<td>Referent: PGT-A</td>
</tr>
</tbody>
</table>

DESIGN: Retrospective cohort study.
MATERIALS AND METHODS: Autologous cycles with the intent of pursuing PGT-A or PGT-SR with biopsy on either day 5 or 6 were identified from all IVF cycles performed in our program from 1/2012 to 10/2018. Outcome variables assessed included fertilization rate (%2PN/MII), blastocyst conversion rate (% total blastocysts/2PN), proportion of biopsiable blastocysts (% blastocysts of adequate quality for biopsy on days 5 or 6/total blastocysts), % euploid embryos, and % embryos with inconclusive biopsy results. GEE modeling was used to control for patients with more than one cycle during the study period. Rate ratios (RR) were calculated using a Poisson regression with offset model with PGT-A cycles as the referent group, adjusted for patient age, total number of mature oocytes, BMI and intracytoplasmic sperm injection (ICSI).

RESULTS: 566 cycles from 388 patients were included (462 PGT-A and 104 PGT-SR cycles). Demographic information and cycle characteristics were similar between groups in terms of age, AMH, and day 3 FSH, with small differences in BMI and use of ICSI. The laboratory outcome data are shown in the Table 1.

Blastocyst conversion rate was statistically significantly higher in the PGT-SR group, although there was no difference between groups in the percentage of blastocysts biopsied on either day 5 or day 6, or the percentage of biopsies that were noninformative. Of note, in the PGT-A group, 42% of biopsied embryos were euploid, compared to only 29% in the PGT-SR group (aRR 0.86; 95% CI 0.73-1.00).

CONCLUSIONS: Although translocation carriers have superior blastocyst development and a similar percentage of embryos available for biopsy compared to PGT-A testers, this group had fewer euploid blastocysts available for transfer. These findings should be helpful in counseling patients with structural rearrangements.

P-310 Tuesday, October 15, 2019 6:30 AM

THE IDENTIFICATION OF CHROMOSOME DELETIONS IN TROPHECTODERM BIOPSIES IS SIGNIFICANTLY REPRESENTATIVE OF THE ENTIRE BLASTOCYST. Lauren Henry, BS, Rachel S. Mann, BS, MS, Susanna McReynolds, PhD, Nathan McCubbin, BS, Taylor Jarvis, BS, William B. Schoolcraft, MD, Mandy G. Katz-Jaffe, Ph.D., Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: Chromosome deletions are often random de novo events during gametogenesis and have clinically recognizable genetic syndromes with characteristics including developmental delay, intellectual disability and dysmorphic traits. They occur at a frequency of 0.5% in prenatal testing and are present in 1/700 newborns. The aim of this study was to evaluate the clinical efficacy of diagnosing chromosome deletions in blastocyst trophectoderm (TE) biopsies.

DESIGN: Prospective blinded study
MATERIALS AND METHODS: A total of 54 transferrable quality blastocysts (≥ Grade 3BB) with chromosome deletions were identified for re-analysis with patient consent (mean maternal age = 36.7 ± 4.2 years; mean paternal age = 37 ± 5.1 years). Each blastocyst was separated into three distinct sections that were blinded and individually re-analyzed using the equivalent VeriSeq™ next generation sequencing (NGS) platform (Vitrolife). All analyses were performed at the same, single genetics laboratory as the original TE biopsy testing. After un-blinding, the data was compiled, identi-
TABLE 1. Pregnancy outcome comparison in IVF patients with PGT vs no PGT

<table>
<thead>
<tr>
<th></th>
<th>No PGT</th>
<th>PGT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of eSETs</td>
<td>31670</td>
<td>39228</td>
</tr>
<tr>
<td>Live birth rate per transfer</td>
<td>47.0%</td>
<td>42.5%</td>
</tr>
<tr>
<td>Term delivery</td>
<td>88.6%</td>
<td>89.3%</td>
</tr>
<tr>
<td>Pre-term delivery</td>
<td>9.4%</td>
<td>8.8%</td>
</tr>
<tr>
<td>Very pre-term delivery</td>
<td>2.0%</td>
<td>1.8%</td>
</tr>
</tbody>
</table>

X² tests for trend analysis of term, pre-term and very pre-term delivery: FET vs ET (P = 0.04), FET/PGT vs ET (P < 0.0001) and FET/PGT vs FET (P = 0.02).

Regional Hospital, Brandon, FL; "University of South Florida Department of Obstetrics and Gynecology, Tampa, FL.

OBJECTIVE: To study the effects of PGT on pregnancy outcomes in patients undergoing IVF with elective single embryo transfer (eSET).

DESIGN: Retrospective cohort study associated with mosaic embryo transfer (MET), determine which parameters predict MET success, and compare MET outcomes to single thawed euploid embryo transfer (STEET).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All STEET cycles after in vitro fertilization, trophectoderm biopsy, and preimplantation genetic testing for aneuploidy (PGT-A) by next-generation sequencing were identified as controls. Cases included all MET cycles. Statistical analysis included chi-square, with p < 0.05 considered significant.

RESULTS: A total of 645 PGT-A frozen embryo transfer cycles occurred during the selection period. STEET occurred in 569 cycles (mean age = 35.8), and MET occurred in 70 cycles (mean age = 39.6) with 76 embryos. 47 embryos were diagnosed as segmental mosaic (SM) and 29 embryos were diagnosed as whole chromosome mosaic (WCM, including monosomies and trisomies). 28/47 (59.6%) SM embryos and 10/29 (38.5%) WCM embryos implanted, compared to 408/569 (71.7%) euploid embryos. The ongoing pregnancy/live birth rate was significantly higher in SM embryos (22/47; 47.4%) with 76 embryos.

CONCLUSIONS: This preliminary study shows that mosaic embryos have a similar kinetic behavior with the cut-off values considered to establish the mosaicism degree. Our results suggest that kinetic variations between euploid and low-degree mosaics, and between aneuploid and high-degree mosaics, may be subtle or even non-existent. These findings recall the importance of a critical interpretation of any mosaics data, especially when working with limited sample sizes.

SUPPORT: Research supported by CDTI n. 20190022.
Materials and methods: The incidence of chromosomal abnormalities ranged from 34.6% to 82.5% and the mean number of blastocysts per cycle varied from 5.7 to 19. In the younger versus oldest patients, respectively. To estimate the minimal number of blastocysts and cycles needed to obtain a euploid embryo at each age group, these empirical data were used. To compute the expected number of SETs to be performed, a hypergeometric probability distribution was applied, using the probability-weighted average of all possible values. To obtain the final value, we applied a smooth method, computing running medians of odd span (J.H. Friedman and W. Stuetzle, Technical report, 1982). This calculation was performed starting from the minimal number of expected blastocysts at each age category.

Results: A summary of the results is presented in Table 1 according to maternal age in years (OD means ovum donation). Each row represents the frequency of euploid blastocysts, the mean number of blastocysts per cycle, the minimum number of blastocysts and stimulation cycles needed to obtain a euploid embryo and expected number of SETs needed to transfer a euploid embryo if PGT-A would not have been performed.

Conclusions: This mathematical model shows the potential benefits of selecting the euploid embryo in the first set in PGT-A, compared to standard set in which embryo selection is performed according to morphological criteria. These data as well as the number of cycles needed to obtain an euploid embryo according to the female age are valuable information for reproductive counselling.

Reference


Support: None.

Objective: To assess the ability of a computing tool based on artificial vision and machine learning to predict aneuploidy for single blastocyst pictures.

Design: Double blind, prospective, longitudinal cohort study.

Materials and methods: A self developed computing tool (CT) with artificial vision and machine learning capabilities was tested for its ability to segment images, extract features of each segment, and to predict aneuploidy on digital images of blastocysts collected between October 2018 and February 2019 from a single IVF center. All embryos were subject to embryo biopsy for PGT-A analysis with next generation sequencing (NGS). Pictures from all embryos were taken before trophectoderm biopsy. Results were assessed using a confusion matrix: PGT-A results matched against CT’s predictions. Technicians performing biopsy and PGT-A providers were blind to CT’s predictions. Mathematicians feeding information to our CT were also blind to PGT-A results until analysis was performed.

Results: A total of 241 blastocysts were analyzed with the use of our artificial vision and machine learning computing tool. Positive predictive value for aneuploidy was 79.5%, sensitivity of 70.1%, specificity of 73.2% and accuracy of 71.4%. FI Score was 74.5%. Negative Predictive Value, which is the ability of the algorithm to predict euploidy, was 62.3%.

Conclusions: Sensitivity, specificity and accuracy with our current Artificial Vision and Machine Learning tool is not yet comparable to embryo biopsy and NGS for euploidy prediction and, at this stage, are not ready to substitute what is still considered the gold standard for aneuploidy screening. However, a positive predictive value for euploidy estimated at 72% is for now good enough to guide embryologists during the embryo selection process in those cases where PGT-A was not performed. Further studies with a larger image database are already underway aiming to improve predictive capabilities of our software.

Table 1.

| OD  | ≤27 | 28  | 29  | 30  | 31  | 32  | 33  | 34  | 35  | 36  | 37  | 38  | 39  | 40  | 41  | 42  | 43  | ≥44 |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Frequency of euploid embryos | 0.6 | 0.7 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.6 | 0.5 | 0.5 | 0.5 | 0.4 | 0.3 | 0.3 | 0.2 | 0.2 | 0.2 | 0.2 |
| Minimum number of blastocysts to obtain a euploid embryo | 2   | 2   | 2   | 2   | 2   | 2   | 2   | 2   | 2   | 2   | 2   | 3   | 3   | 3   | 4   | 4   | 4   | 4   |
| Mean number of blastocysts | 5.7 | 4.9 | 4.8 | 4.8 | 4.7 | 4.7 | 4.5 | 4.2 | 4.1 | 3.9 | 3.7 | 3.4 | 3.2 | 3.0 | 2.8 | 2.6 | 2.4 | 2.3 | 1.9 |
| Minimum number cycles to obtain a euploid embryo | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 1   | 2   | 2   | 2   | 3   |
| Expected number of SET to transfer an euploid embryo | 1.5 | 1.4 | 1.3 | 1.5 | 1.5 | 1.5 | 1.5 | 1.6 | 1.6 | 1.7 | 1.7 | 2   | 2   | 2.2 | 2.5 | 3   | 3.3 | 3.8 | 4   |
they mainly confirm the initial results. Counting them as concordant leads to concordances 99.6% for Di, 95.9% for An, and 88.2% for Mo per chromosome. Rebiopsies of inner cell mass were clinically concordant for 100% of the blastocysts (biopsy result of ICM agreed with the clinical result of “euploid” or “not euploid”).

CONCLUSIONS: Despite small number of biopsied cells (required to avoid damage to the blastocyst) and mosaicism (demonstrated by rebiopsy specimens) the excellent chromosomal concordance for rebiopsy specimens (99.6% and 95.9%) and clinical concordance for ICM biopsies (100%) indicate that TE biopsy/NGS provides excellent accuracy in its assessment of ploidy. Within this non-randomly selected subset of blastocysts, mosaics detected in the clinical biopsy outnumbered mosaics detected only by rebiopsy 2.25:1 (18:8).

SUPPORT: None.

P-316 Tuesday, October 15, 2019 6:30 AM

A UNIVERSAL SINGLE TUBE PCR-BASED LIBRARY PREPARATION FOR PGT-A ALLOWING CROSS-PLATFORM NGS SEQUENCING. Melinda Jane Jasper, PhD,a Steven Anthony Myers, PhD,b Kimberly Warren, B Tech,c (Hons),d Lann Tay, B Sc,e Sandra Protopsaltis, Associate Diploma Medical Laboratory Science,f gPerkinElmer Health Sciences (Australia) Pty Ltd, Thebarton, SA, Australia; hAffiliation not provided; iPerkinElmer Health Sciences, Adelaide, SA, Australia.

OBJECTIVE: There are several methods to prepare trophectoderm biopsy samples for Preimplantation Genetic Testing for Aneuploidy (PGT-A) by Next Generation Sequencing (NGS). Most methods use a two-step approach of Whole Genome Amplification (WGA) followed by library preparation. However, combining WGA with library preparation by utilising PCR-based library preparation approaches offers several advantages over traditional two-step methods, including protocol time efficiencies and reduced hands-on time. In addition to these advantages, a novel combined approach developed based on the PerkinElmer DOPify® WGA kit offers the capability for cross-platform sequencing validation of a single biopsy.

DESIGN: Here we describe the development of a novel PGT-A approach which allows PCR-based library preparation of trophectoderm biopsies for cross-platform NGS using either Illumina® or Ion Torrent® sequencing technology.

MATERIALS AND METHODS: Five-cell samples representative of trophectoderm biopsies were manually sorted from aneuploid cell lines (Coriell Institute) and euploid lymphocytes. Cell lysis and WGA were performed using a modified DOPify® kit protocol (PerkinElmer) followed by incorporation of Illumina®-specific adapter sequences and unique indexes in a single tube. Amplified, indexed 5-cell samples were purified, quantified then pooled before 48 sample multiplex and 1x75bp read length sequencing on the MiSeq® Instrument (Illumina). Sequencing data was analysed for correct sequencing of the blastocyst using the PG-Seed® software (PerkinElmer).

RESULTS: A total of 105 5-cell samples were processed. Three samples were excluded from final analysis due to weak amplification (2.8%) with a further five samples failing to pass quality control checks (4.8%). The 48 sample multiplex generated an average of 510,000 reads per sample with 98.9% of reads mapping to hg19. All samples that passed quality control metrics displayed the expected karyotype when analysed with the PG-Find software. The PCR-indexing protocol took on average 4.5 hours (2.5 hours hands on) to process 48 samples from sample receipt to NGS instrument loading.

CONCLUSIONS: This novel PCR-indexing workflow provides rapid, scalable and economical sequencing for PGT-A and provides the capability for cross-platform sequencing validation of a single embryo biopsy for PGT-A. This flexible workflow allows customisable throughput and tailorable resolution to detect smaller segmental aberrations.

SUPPORT: None.

TABLE 1.

<table>
<thead>
<tr>
<th>All Patient Ages</th>
<th>2PN</th>
<th>1PN</th>
<th>0PN</th>
<th>Sig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional insemin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number Blasts Bx’d</td>
<td>11287</td>
<td>428</td>
<td>31</td>
<td></td>
</tr>
<tr>
<td>Ratio XX:XY (%)</td>
<td>47.52</td>
<td>61.39</td>
<td>64.36</td>
<td></td>
</tr>
<tr>
<td>ICSI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number Blasts Bx’d</td>
<td>3864 (34%)</td>
<td>113 (26%)</td>
<td>11 (35%)</td>
<td></td>
</tr>
<tr>
<td>Ratio XX:XY (%)</td>
<td>2189 (33%)</td>
<td>29 (38%)</td>
<td>35 (24%)</td>
<td></td>
</tr>
<tr>
<td>Conventional insemin+ ICSI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IR (sac/ ET) (%)</td>
<td>x/1809 (68%)</td>
<td>x/40 (60%)</td>
<td>x/10 (80%)</td>
<td></td>
</tr>
<tr>
<td>Ratio XX:XY</td>
<td>50.50</td>
<td>86.14</td>
<td>54.46</td>
<td></td>
</tr>
<tr>
<td>LB/ ET with known outcome (%)</td>
<td>52%</td>
<td>44%</td>
<td>66%</td>
<td></td>
</tr>
<tr>
<td>LB Ratio XX:XY</td>
<td>362:394</td>
<td>11.5</td>
<td>4.2</td>
<td></td>
</tr>
</tbody>
</table>

Of 11726 embryos biopsied from conventional insemination, 4% developed from 1PN. Less than 1% was from 0PN. Of 6553 ICSI embryos biopsied, 1% was from 1PNs, 2% were from 0PNs. Of the 11 XX 1PN LB N 10 (10/17) are from insemn, 1 (1/6) from ICSI. Of the 4 XX 0PN LB N LB insemn, 1 (1/1) is from ICSI.
OBJECTIVE: Next generation sequencing (NGS) provides evidence of mosaicism in the blastocyst stage embryo. Mosaic profiles are often graded as low or high to denote levels of risk. Here we assess mosaicism as it pertains to specific chromosomes and determine rates of high and low level mosaicism for individual chromosomes.

RESULTS: Of the 6525 samples that underwent PGT-A testing 931 (14%) displayed whole aneuploid mosaicism. High and low level mosaicism was observed in 47% and 53% of the samples respectively. Mosaicism and high level mosaicism in chromosome 22 occurred at a higher rate than other chromosomes, while mosaicism rates were lowest in chromosomes 12 and 17.

TABLE I.

<table>
<thead>
<tr>
<th>Chromosome</th>
<th>Mosaicism</th>
<th>High</th>
<th>Low</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>37</td>
<td>4.0%</td>
<td>15</td>
<td>40.5%</td>
<td>22</td>
</tr>
<tr>
<td>2</td>
<td>40</td>
<td>4.3%</td>
<td>20</td>
<td>50.0%</td>
<td>20</td>
</tr>
<tr>
<td>3</td>
<td>35</td>
<td>3.8%</td>
<td>18</td>
<td>51.4%</td>
<td>17</td>
</tr>
<tr>
<td>4</td>
<td>59</td>
<td>6.3%</td>
<td>32</td>
<td>54.2%</td>
<td>27</td>
</tr>
<tr>
<td>5</td>
<td>39</td>
<td>4.2%</td>
<td>21</td>
<td>53.8%</td>
<td>18</td>
</tr>
<tr>
<td>6</td>
<td>40</td>
<td>4.3%</td>
<td>21</td>
<td>52.3%</td>
<td>19</td>
</tr>
<tr>
<td>7</td>
<td>33</td>
<td>3.5%</td>
<td>7</td>
<td>21.2%</td>
<td>26</td>
</tr>
<tr>
<td>8</td>
<td>49</td>
<td>5.3%</td>
<td>20</td>
<td>40.8%</td>
<td>29</td>
</tr>
<tr>
<td>9</td>
<td>33</td>
<td>3.3%</td>
<td>5</td>
<td>24.2%</td>
<td>25</td>
</tr>
<tr>
<td>10</td>
<td>39</td>
<td>4.2%</td>
<td>20</td>
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<td>19</td>
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<tr>
<td>11</td>
<td>34</td>
<td>3.7%</td>
<td>15</td>
<td>44.1%</td>
<td>25</td>
</tr>
<tr>
<td>12</td>
<td>21</td>
<td>2.3%</td>
<td>8</td>
<td>38.1%</td>
<td>13</td>
</tr>
<tr>
<td>13</td>
<td>48</td>
<td>5.2%</td>
<td>20</td>
<td>41.7%</td>
<td>28</td>
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<tr>
<td>14</td>
<td>36</td>
<td>3.9%</td>
<td>15</td>
<td>41.7%</td>
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<tr>
<td>15</td>
<td>39</td>
<td>4.2%</td>
<td>19</td>
<td>48.7%</td>
<td>20</td>
</tr>
<tr>
<td>16</td>
<td>37</td>
<td>4.0%</td>
<td>17</td>
<td>48.9%</td>
<td>20</td>
</tr>
<tr>
<td>17</td>
<td>21</td>
<td>2.3%</td>
<td>10</td>
<td>47.6%</td>
<td>11</td>
</tr>
<tr>
<td>18</td>
<td>47</td>
<td>5.0%</td>
<td>25</td>
<td>53.2%</td>
<td>21</td>
</tr>
<tr>
<td>19</td>
<td>56</td>
<td>6.0%</td>
<td>33</td>
<td>58.9%</td>
<td>23</td>
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<tr>
<td>20</td>
<td>30</td>
<td>3.2%</td>
<td>11</td>
<td>36.7%</td>
<td>19</td>
</tr>
<tr>
<td>21</td>
<td>51</td>
<td>5.5%</td>
<td>26</td>
<td>51.0%</td>
<td>25</td>
</tr>
<tr>
<td>22</td>
<td>68</td>
<td>7.3%</td>
<td>45</td>
<td>66.2%</td>
<td>23</td>
</tr>
<tr>
<td>X</td>
<td>33</td>
<td>3.5%</td>
<td>15</td>
<td>30.3%</td>
<td>23</td>
</tr>
<tr>
<td>Y</td>
<td>6</td>
<td>0.6%</td>
<td>1</td>
<td>16.7%</td>
<td>7</td>
</tr>
</tbody>
</table>

CONCLUSIONS: Bridging the gap between preimplantation genetics and prenatal cytogenetics has the potential to be a powerful tool for clinicians treating infertile couples. The literature has reported that mosaicism is clinically relevant. This report evaluates the rates of mosaicism for individual chromosomes providing a basis on which to correlate the incidence of preimplantation mosaicism in specific chromosomes with mosaicism observed in prenatal samples. Additionally, the data highlights the putative uneven distribution of mosaicism in male and female samples.

P-319 Tuesday, October 15, 2019 6:30 AM

RATES OF EMBRYONIC MOSAICISM ARE CONSISTENT AMONGST EMBRYOLOGISTS PERFORMING OR LOADING TROPHECTODERM BIOPSIES FOR PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY. Emily K. Osman, MD, Shelby A. Neal, MD, Ashley W. Tieg, MD, Brent M. Hanso, MD, Julia G. Kim, MD, MPH, Jason M. Franaasi, MD, Richard Thomas Scott, Jr., MD, IVI-RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: The introduction of next-generation sequencing (NGS) for preimplantation genetic testing for aneuploidy (PTG-A) has led to increased detection of mosaicism and segmental errors. It has been suggested that the incidence of such abnormalities varies between reference laboratories where the biopsy is analyzed. Additionally, the technical aptitude of the embryologist performing or handling the biopsy specimen may contribute to mosaicism, segmental errors, and “no call” outcomes including nonconcurrent or unamplified results.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Patients undergoing in vitro fertilization (IVF) cycles with PGT-A at a single center were included. Embryos were cultured to the blastocyst stage and biopsies were performed on days 5, 6 or 7. PGT-A was performed using the NeXCCS NGS platform. An embryo was designated as mosaic if the DNA copy number ranged from 0.3 to 0.7. Segmental errors were defined as chromosomal duplications or deletions that were ≥ 5 Mb. A chi-squared analysis was utilized to compare the primary outcome of mosaicism and secondary outcomes of segmental errors and “no call” results between embryologists. An alpha error <0.05 was considered significant. Given the large sample size, differences <2% were determined to be clinically irrelevant despite statistically significant.

RESULTS: Four embryologists performed a total of 30,899 embryo biopsies and 6 individuals loaded biopsy specimens into designated tubes. PGT-A results of embryologists performing the biopsy were listed in Table I. Given the immense sample size, all biopsy results varied statistically by embryologists. Variation in PGT-A results can be attributed to differences in reference laboratories. With increasing utilization of PGT worldwide, reproducible results are critical for optimizing clinical outcomes during IVF cycles.

Table I. Rates of mosaicism, segmental errors and “no call” results based on embryologist performing the biopsy.

<table>
<thead>
<tr>
<th>Embryologist</th>
<th>Mosaicism %</th>
<th>Segmental Error %</th>
<th>“No Call” %</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>986/15803</td>
<td>6.6</td>
<td>136/15803</td>
</tr>
<tr>
<td>B</td>
<td>428/99969</td>
<td>4.3</td>
<td>86/99969</td>
</tr>
<tr>
<td>C</td>
<td>209/3754</td>
<td>5.6</td>
<td>39/3754</td>
</tr>
<tr>
<td>D</td>
<td>83/1373</td>
<td>6.1</td>
<td>13/1373</td>
</tr>
<tr>
<td>All</td>
<td>1607/30899</td>
<td>5.2</td>
<td>3124/30899</td>
</tr>
</tbody>
</table>

WITHDRAWN

P-320

P-321 Tuesday, October 15, 2019 6:30 AM

IN VITRO FERTILIZATION (IVF) WITH PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) IS NOT COST EFFECTIVE TO ACHIEVE A LIVE BIRTH COMPARED TO IVF ALONE IN DONOR OOCYTE CYCLES. Maria Facadio Antero, MD, Bhuchitra Singh, M.D., MPH, MS, Megan E. Gornet, MD, William G. Kearns, MD, PhD, Valerie L. Baker, MD, Mindy S. Christianson, MD, John Hopkins University School of Medicine, Lutherville, MD; Johns Hopkins School of Medicine, Baltimore, MD; John Hopkins University School of Medicine.
OBJECTIVE: The process of using donor oocyte can be costly for patients and in some cases it is not covered by insurance. For some patients, oocyte donation comes as their last resort after they have exhausted their financial limit. Optimizing every aspect of oocyte donation is important not only to improve outcomes but also reduce cost to patients. Preimplantation genetic testing for aneuploidy (PGT-A) has been shown to be cost effective in certain subpopulations of infertile patients undergoing IVF [1,2]. The objective of this study is to determine whether IVF with PGT-A is cost effective to achieve a live birth compared to IVF alone in donor oocyte cycles.

DESIGN: Cost-effectiveness study

MATERIALS AND METHODS: A decision analytic model was constructed using TreeAge Pro 2019 (TreeAge Software Inc, Williamstown MA) to compare the cost of IVF with PGT-A versus IVF alone to achieve a live birth. The model assumed donor oocytes were obtained from healthy females younger than 30 years old, with laboratory evidence of normal ovarian reserve, and no infertility diagnosis. The model analyzed a hypothetical single fresh oocyte donor IVF cycle with PGT-A versus IVF alone and followed the progression of a single embryo through the different decision nodes. Cost estimates of relevant clinical events and incorporated probabilities were based on data from published literature including the Society for Assisted Reproductive Technology (SART) database. Cost data was converted to 2018 US dollars. The primary outcome was the cost to achieve a live birth using IVF with PGT-A for donor egg cycles compared to IVF alone, and Monte Carlo sensitivity analyses were performed to assess for model robustness.

RESULTS: The model demonstrates IVF with PGT-A on average costs $37,940 to achieve a live birth with a donor oocyte cycle across all combined age groups. In base-case analysis, IVF with PGT-A did not increase the overall effectiveness of increasing live birth rate at an additional cost of $4650. This yielded an incremental cost-effectiveness ratio (ICER) of - $1142.66; IVF alone with donor eggs had a net monetary benefit (NMB) of $124,044 per live birth rate. The ICER was above the willingness to pay cost of $40,000 for achieving one live birth assuming the live birth rate of 61.3% per live birth rate. The ICER was above the willingness to pay cost of $40,000 for achieving one live birth assuming the live birth rate of 61.3% and $37,940 per cycle for this patient population. Monte Carlo simulations demonstrated that IVF+PGT-A is not cost-effective in nearly all iterations at an acceptability cut off of $40,000.

CONCLUSIONS: This model suggests that the addition of PGT-A to IVF in donor oocyte cycles is not cost effective compared to IVF alone over a wide range of probabilities and costs. To better understand the dynamics of cost effectiveness in this population, the willingness to pay per live birth should be refined or the motivation to pay for PGT-A needs to be further investigated.

REFERENCES

P-322 Tuesday, October 15, 2019 6:30 AM

THE COST-EFFECTIVENESS OF PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A): AN ANALYSIS OF 153,865 SART CYCLES. Malinda S. Lee, MD, MBA, Katherine T. Lofgren, MPH, Ann M. Thomas, PhD, Andrea Lanes, PhD, Randi H. Goldman, M.D., Elizabeth S. Ginsburg, M.D., Mark D. Hornstein, M.D., Brigham and Women’s Hospital, Boston, MA; 1Harvard University, Cambridge, MA; 2Northwell Health Fertility, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY.

OBJECTIVE: To determine the cost-effectiveness of PGT-A at cycle start for the treatment of infertility in the United States

DESIGN: Retrospective analysis of linked cycles from 1/2014–12/2016 from the Society for Assisted Reproductive Technology Clinic Outcomes Reporting System (SART CORS) applied to a decision analytic model.

MATERIALS AND METHODS: All first fresh autologous cycles of women undergoing IVF between 1/2014–12/2015 plus linked FET cycles from 1/2014–12/2016 were included. Banking, frozen egg, PGT-M and PGT-SR cycles were excluded. Cycles were categorized by intent to perform PGT-A.

Clinical and cost outcomes of IVF compared to IVF with PGT-A were estimated using a decision analytic model. Transitions between treatment stages relied on probability estimates from SART CORS. Patients progressed through the model until they achieved a live birth, exhausted their embryos or at one year after stimulation. Two payer perspectives were considered: patient and societal. Expected costs accounted for age-specific projections from SART CORS, such as number of embryos biopsied and total gonadotropin use.

RESULTS: 114,182 fresh and 39,683 linked FET cycles were included. Of fresh cycles, 18,470 (16.2%) planned PGT-A and 95,712 (83.8%) did not. Across all age groups, non PGT-A cycles used more gonadotropin, had fewer embryos, and had higher cancellation and failed fertilization rates, suggesting that patients utilizing PGT-A represent a more favorable prognosis group. Cumulative live birth (CLBR) and twin live birth rates (TLBR) per cycle start are presented. From the patient perspective, costs incurred with PGT-A were higher in every age group when compared to IVF alone (differential $4,551–5,137). From the societal perspective, costs incurred with PGT-A were lower in the <35 age range (~$4,233), equivalent at age 35, and higher at every other age ($955–6,905).

CONCLUSIONS: From the societal perspective, IVF with PGT-A can be cost-effective for certain ages. From a patient perspective, IVF with PGT-A is costlier at every age. Up to age 35, at which CLBR are equivalent between IVF with and without PGT-A, PGT-A incurs an additional cost to the patient of $4,551–4,742.
Preimplantation genetic testing for monogenic diseases (PGT-M) is the process in which embryos created via in vitro fertilization (IVF) are tested for diseases like SCID; unaffected embryos may then be selected for transfer. In the United Kingdom, this technology is available to couples with SCT; in the United States, it is not routine. In our center, the costs of IVF with PGT-M (IVF+PGT-M) to avoid the birth of a child with SCID outweigh the lifetime medical costs of a person with SCID is unknown.

MATERIALS AND METHODS: We conducted a decision analytic model using TreeAge Pro 2019 (TreeAge Software Inc, Williamstown, MA) for couples known to both have SCT, attempting to conceive, with natural concurrence (NC) versus IVF+PGT-M. The primary outcome variable was quality adjusted life years (QALYs) for children born with or without SCID. The model incorporated probabilities and cost estimates of relevant clinical events using data from published literature. The total cost for each potential child included the cost of conception, lifetime medical care, and future potential income. We assumed all patients undergoing IVF+PGT-M also test embryos for aneuploidy (PGT-A); data were thus derived for euploid embryo transfers for all IVF+PGT-M patients. To determine whether IVF+PGT-M is cost effective, we calculated the incremental cost effectiveness ratio (ICER). Here, the ICER is defined as the ratio of the difference between the per patient per QALY costs of IVF+PGT-M compared with NC. Costs were converted to 2018 U.S. dollars. To examine the impact of changes in model input parameters, a sensitivity analysis was performed. We assumed a willingness to pay of $30,000 which is equal to the average cost to conceive a healthy child. Incremental cost effectiveness ratio (ICER) is defined as the ratio of the difference between the per patient per QALY costs of IVF+PGT-M compared with NC. We assumed all patients undergoing IVF+PGT-M also test embryos for aneuploidy (PGT-A); data were thus derived for euploid embryo transfers for all IVF+PGT-M patients. To determine whether IVF+PGT-M is cost effective, we calculated the incremental cost effectiveness ratio (ICER). Here, the ICER is defined as the ratio of the difference between the per patient per QALY costs of IVF+PGT-M compared with NC. Since our center does not recommend following such transfers in the world.1 Since our original report with collaborating colleagues from 2 centers in 2015 where we reported 5 normal pregnancies,1 we counselled 38 patients who moved their embryos to CHR. Among those, so far 22 have elected to have a transfer, with 7 (26.9%) achieving clinical pregnancy; 3/7 miscarried (42.8%); 1 was aneuploid pregnancy, 1 was 46XX, with maternal contamination ruled out and a third is currently pending a genetic result. Three pregnancies delivered normal offspring. Most IVF centers were cooperative in transferring embryos, though one transfer only occurred after the couple engaged a lawyer.

CONCLUSIONS: Here reported pregnancy and live birth rates are slightly lower than we reported in our initial studies and others reported,6 but patients here were much older (44.2 ± 4.4 years). Considering age, the miscarriage rate was actually relatively low, confirming earlier reports. Since some of the original clinics had asked PGT-A laboratories not to report “mosaicism,” accurate separation of “mosaic” and “aneuploid” was not possible. Current definitions, based on percentages of aneuploid DNA within a single cell, has shown that trophoderm biopsy, however do, anyhow, have an empiric basis.3 Here presented data, therefore, suggest that, due to still excellent, pregnancy and delivery chances, embryos with alleged lethal aneuploid DNA should not be disposed. Because of downstream self-correction of human embryos, even intrauterine transfer of non-lethal “abnormalities” may have to be considered when no other embryos are available for transfer.

REFERENCES

SUPPORT: Intramural funds from The Center for Human Reproduction and grants from The Foundation for Reproductive Medicine.

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CLINICAL OUTCOMES OF SINGLE EMBRYO TRANSFER WITH MOSAIC: MOSAIC OR LOW-GRADE MOSAIC? MOSAIC OR LOW-GRADE MOSAIC EMBRYO: DOES IT MATTER?1-5

Pin-Yao Lin, MD,a Maw-Sheng Lee, MD, PhD,b En-Hui Cheng, PhD,b Chung Shan Medical University, Taichung, Taiwan; Taichung, Taiwan; Lee Women’s Hospital, Taichung, Taiwan.

OBJECTIVE: Preimplantation genetic testing (PGT-A) with the use of the high resolution next-generation sequencing (hr-NGS) that can detect mosaicism in excess of 20%. The 20-80% range as mosaic and transferred with caution, only in absence of euploid embryos. These cut-off level is an ongoing debate. Despite recent reports suggested low-grade mosaic embryos transfer (<50%) could result in healthy newborn as euploid embryo, very little is known about outcomes of high-grade (>50%) mosaic transfer. The aim of the study is to investigate whether high-grade mosaic embryos were capable of implanting and leading to ongoing pregnancies.

DESIGN: Retrospective analysis of the clinical outcome of single embryo transfer (IVF-ET) with low-grade mosaic embryos (30%-40% abnormal cells in the trophectoderm biopsy) and high-grade mosaic embryos (50%-80%) abnormal cells in the trophectoderm biopsy) as diagnosed with the use of hr-NGS.

MATERIALS AND METHODS: 108 Single embryo transfers with mosaic blastocyst were transferred at in Lee Women’s Hospital from July of 2016 through December of 2017. SET cycles of 83 low-grade mosaic embryos and 25 high-grade mosaic embryos were analyzed retrospectively. Mosaic levels and clinical outcomes were evaluated in this study.

Chromosomal abnormality of biopsied trophectoderm cells was analyzed by NGS (VeriSeq PGS-MSEQ, illumina). Before implantation, we counseled patients on the potential consequences of transferring a mosaic embryo and obtained the informed consent from each patient. After implantation, we analyzed the association between conditions of the mosaic blastocyst and pregancy outcomes of the SET for each patient. In order to confirm the condition of fetal chromosomes, NIPS or karyotyping were performed when patients were pregnant more than 10 weeks.

RESULTS: Our results of low-grade mosaic SET vs. high-grade mosaic SET: comparable implantation rate (51.8% vs. 43.83 vs 52%, 13.25; p=0.99), ongoing pregnancy rate (47%; 39/83 vs 36%/925 vs p=0.33) and live birth rate (44.5%, 37/83 vs 36%/925; p=0.45) between two groups. However, significantly higher elevation rate in the high-grade mosaic SET (5.1%, 2/39 vs. 30.7%, 4/13; p=0.012) There was also no statistical difference was observed in the average gestational weeks at delivery (38.3±1.6 vs. 38.6±2.1 weeks;p=0.53) and average birth weight (3015±507 vs. 3058±507;p=0.73).Transferring of mosaic embryo with different chromosomal numbers did not affect the implantation rate and clinical outcomes.

Sets of different mosaic types (whole chromosomal or segmental chromosomal abnormality) and grade of mosaicism had no obvious impact on clinical outcomes in our study. The results of NIPS or karyotyping of prenatal diagnosis in all pregnant were normal.
CONCLUSIONS: The findings of this study are valuable for understanding the clinical results after SET with low/high-grade level mosaic embryos. We demonstrated that the high-grade mosaic embryos have the probability of resulting in implantation and healthy newborn but with higher abortion rate than low-grade mosaic embryos.

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CLINICAL EXPERIENCE FOLLOWING PGT ANALYSIS OF 38,000 CONSECUTIVE EMBRYOS USING A FAST-SEQS NGS-BASED ASSAY. Dana Neitzel, MS, CGC, Kristina Robinson, PhD, Lauren Walters-Sen, PhD, Jocelyn Leahey, MS, CGC, Charlene A. Alouf, PhD, Nicole Faulkner, PhD. Invitae, San Francisco, CA.

OBJECTIVE: To report our clinical experience utilizing a FAST-SeqS NGS-based PGT assay, including aneuploidy rates and outcome data.

DESIGN: Patients undergoing IVF may elect to pursue preimplantation genetic testing for aneuploidy (PGT-A) to identify euploid embryos, with the goal of increasing pregnancy and live birth rates while reducing multiple gestations and time to pregnancy. Preventing transfer of embryos with chromosomal abnormalities is essential to improving PGT-derived pregnancy outcomes.

MATERIALS AND METHODS: Trophectoderm samples were analyzed using our modified FAST-SeqS method and associated bioinformatics pipeline. FAST-SeqS can accurately detect whole chromosome and segmental aneuploidies (≥ 10 MB), whole genome uniparental isodisomy (WG-UPiD or haploidy), all forms of triploidy, other polyploidies, and many instances of single chromosome UPiD.1-3 The likelihood of transfer and aneuploidy rates, stratified by egg age, fertilization type, day of biopsy, and clinical indication were assessed.

RESULTS: The dataset consisted of 138,643 embryos from 29,624 cycles. Egg age ranged from 18-55 years (mean of 35). The average number of biopsy samples per case was 4.5. Of resulted samples, 56% were euploid; 77% of all cycles had at least one euploid embryo (Table 1). As previously reported, the only factors affecting aneuploidy rates were egg age and day of biopsy.3-5 Excluding embryos from known translocation carriers, 10% of embryos had a segmental abnormality, 32% were observed in conjunction with at least one whole chromosome abnormality. Segmental changes were seen in all chromosomes and the rate was independent of egg age.

Out of 75,726 samples analyzed with our SNP enhancement, 1.6% were polyploid. These polyploidies consisted of 924 triploid, 164 haploid/WG-UPiD and 154 tetraploid, many of which would have been misclassified as euploid or mosaic with other NGS-based assays.5,6 The likelihood of transfer and aneuploidy rates, stratified by egg age, fertilization type, day of biopsy, and clinical indication were assessed.

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CONCLUSIONS: The majority of patients in this dataset had at least one euploid embryo for transfer. Consistent with previous reports, an age-related decline in euploidy was observed, and segmental aneuploidy was independent of age.5,6 Our data, stratified by egg age and number of embryos tested, is a valuable counseling tool for patients considering PGT-A.

REFERENCES

PREIMPLANTATION GENETIC TESTING FOR ANEUPOIDY (PGT-A) AND TECHNOLOGY PLATFORM: DOES PLATFORM INFLUENCE EUPLOID CALL RATES AND/OR SUBSEQUENT PREGNANCY OUTCOMES? Eleni A. Greenwood, MD, MSc, Charles E. McCulloch, PhD, Kaitlyn Wald, MD, Salustiano Ribeiro, MSc, Phil Marsh, BS, Marcellle I. Cedars, MD, Mitchell P. Rosen, MD, HCLD, University of California San Francisco, San Francisco, CA; UCSF, San Francisco, CA; University of California San Francisco, San Francisco, CA; University of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA.

OBJECTIVE: With the evolution in technology platforms for PGT-A over the past decade, benefits to genetic testing companies include increased speed and reduced expense. Whether benefits have concurrently accrued to patients in terms of pregnancy outcomes is unclear. We sought to 1) compare euploid call rates by technology platform, and 2) determine whether pregnancy outcomes after single embryo transfer (SET) of a euploid blastocyst varied as a function of platform.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: Trophectoderm biopsies for PGT-A at a single academic center between 2010-2019 were reviewed. Grade BB or better (Gardner criteria) blastocysts are biopsied on day 5 or 6 at our institution. Euploid call rates (euploid results per biopsied blastocysts) were compared among three technology platforms: single nucleotide polymorphism array (SNPa), array comparative genome hybridization (aCGH) and next generation sequencing (NGS), provided by two major commercial laboratories. Total euploid blastocysts generated per cycle were also compared. Mosaicism was masked. Generalized linear models were used to adjust for age and number of eggs collected, and account for the clustered nature of the data. We similarly compared rate of live birth or ongoing pregnancy following SET of a euploid blastocyst, between technology platforms.

RESULTS: 8,759 blastocyst biopsies were generated from 1,253 patients over 1,873 IVF cycles. Euploid call rates were lowest among SNPa and highest among aCGH cycles (Table). Controlling for age and number of oocytes collected, compared to SNPAs, aCGH cycles had 28% increased odds of euploid calls (OR 1.28, 95% CI 1.13, 1.44, p<0.001). NGS also had higher euploid call rates vs SNPa (OR 1.15, 95% CI 1.01, 1.31, p=0.03). aCGH vs NGS had similar euploid call rates (p=0.18). Total euploid blasts per cycle differed by technology platform (p=0.01), as aCGH yielded more euploid blastocysts than SNPa cycles, controlling for age and number of oocytes collected.

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<table>
<thead>
<tr>
<th>Age (years)</th>
<th># eggs collected/ cycle</th>
<th>Euploid***</th>
<th>Aneuploid Undetermined Pregnant after SET*</th>
<th>Live birth/ Ongoing pregnancy after SET*</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;35</td>
<td>37.9(4.0)</td>
<td>17.9(0.3)</td>
<td>42.1%</td>
<td>56.0%</td>
</tr>
<tr>
<td>35-37</td>
<td>37.8(4.0)</td>
<td>16.0(8.8)</td>
<td>46.1%</td>
<td>52.7%</td>
</tr>
<tr>
<td>38-40</td>
<td>37.7(3.9)</td>
<td>17.4(9.4)</td>
<td>44.2%</td>
<td>54.2%</td>
</tr>
<tr>
<td>41-42</td>
<td>37.7(3.9)</td>
<td>17.4(9.4)</td>
<td>44.2%</td>
<td>54.2%</td>
</tr>
<tr>
<td>43-44</td>
<td>37.7(3.9)</td>
<td>17.4(9.4)</td>
<td>44.2%</td>
<td>54.2%</td>
</tr>
<tr>
<td>All</td>
<td>37.9(3.9)</td>
<td>17.4(9.4)</td>
<td>44.2%</td>
<td>54.2%</td>
</tr>
</tbody>
</table>

Mean (SD) or %
*p=NS
**p=0.01
***p<0.001

SUPPORT: Invitae

TABLE 1. Likelihood of Euploid Embryos

<table>
<thead>
<tr>
<th>Age</th>
<th>% of PGT cycles with at least 1 euploid embryo</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1-3 embryos</td>
</tr>
<tr>
<td>1-3 embryos</td>
<td>84%</td>
</tr>
<tr>
<td>35-37</td>
<td>81%</td>
</tr>
<tr>
<td>38-40</td>
<td>73%</td>
</tr>
<tr>
<td>41-42</td>
<td>57%</td>
</tr>
<tr>
<td>&gt;42</td>
<td>33%</td>
</tr>
<tr>
<td>All</td>
<td>59%</td>
</tr>
</tbody>
</table>
CONCLUSIONS: Euploid call rates differ as a function of PGT-A technology platform after adjusting for age and eggs collected. However, these differences do not seem to translate into different pregnancy outcomes after SET of a "euploid" blastocyst. Further investigation should attempt to reconcile these differences and clarify if and how advances in PGT-A technology platforms translate to patients.

RESULTS: Two hundred forty-two embryos were warmed and biopsied or rebiopsied, and 78% of surviving embryos (200/258) were able to be biopsied or rebiopsied due to degeneration or arrest prior to re-expansion. Samples were sent to a third-party testing laboratory for PGT-A testing via aCGH, SNP array or NGS.

OBJECTIVE: To examine whether Artificial Intelligence (AI) algorithms and computer vision technology can non-invasively identify embryos with key morphological features associated with abnormalities of chromosome 21 and 16.

MATERIALS AND METHODS: Approximately 2,000 static 2D images of Day 5 blastocysts with related pregnancy and pre-implantation genetic testing for aneuploidy (PGT-A) outcomes were assessed. Images were divided into three groups: training, validation, and blind test sets. Two AI models were trained, validated, and tested on embryo images by a further blind set test of 461 images with known PGT-A outcomes.

RESULTS: Our results show a high level of accuracy with the use of AI in detecting embryological morphological changes associated with additions to chromosome 21 or an additional full copy of the chromosome. A blind data set of 54 images achieved an accuracy of 81.5%. To expand the model to include all abnormalities of chromosome 21, we achieved an accuracy of 71% from 214 images. This reduction in accuracy is most likely the result of increased morphological variability between embryos with different abnormalities of chromosome 21. Using the same methodology, an accuracy of 73.1% was obtained when we were able to determine abnormalities of chromosome 21 and 16.

CONCLUSIONS: Embryonic chromosomal abnormalities are known to lead to implantation failure, pregnancy loss, severe chromosomal diseases (e.g. Down and ATR-16 syndromes) and have recently been associated with developmental disorders including Autism. One of the major limitations of PGT-A analysis by traditional genetic analysis is the presence of chromosomal mosaicism within the developing embryo. Recent advances in non-invasive embryo ploidy determination by either morphokinetic analysis by time-lapse imagery or cell free DNA isolation from either spent conditioned culture medium or blastocoel fluid have shown promise, but concordance studies have shown otherwise. This study presents, for the first time, that AI can non-invasively determine whether certain morphological features of a Day 5 blastocyst are associated with specific chromosomal abnormalities of human embryos. Additional studies and analyses are under way.

### Table 1

<table>
<thead>
<tr>
<th>1st Biopsy</th>
<th>Rebiopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total # of patients</strong></td>
<td>48</td>
</tr>
<tr>
<td><strong>Average Age</strong></td>
<td>35.3</td>
</tr>
<tr>
<td><strong>Warmed</strong></td>
<td>242</td>
</tr>
<tr>
<td><strong>Survival</strong></td>
<td>232</td>
</tr>
<tr>
<td><strong>Biopsied</strong></td>
<td>178</td>
</tr>
<tr>
<td><strong>Euploid</strong></td>
<td>110</td>
</tr>
<tr>
<td><strong>Aneuploid</strong></td>
<td>56</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>12</td>
</tr>
</tbody>
</table>

*Other = 9 mosaic, 2 no DNA amplification, 1 no call

*Other = 1 mosaic, 1 no DNA amplification
way to increase specificity and explore other chromosomal abnormalities by including larger data sets

REFERENCES

SUPPORT: None.

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IF ANY MOSAICISM IS IDENTIFIED IN THE TROPHOCTEORODERM, THERE IS A 26% CHANCE OF MOSAICISM BEING PRESENT IN THE INNER CELL MASS; A CLINICAL PARADIGM, DO YOU TRANSFER MOSAIC EMBRYOS?

Paul Robert Brezina, M.D., Kyle J. Tobler, MD, Kamaria C. Cayton Vaught, MD, Anil K. Dubey, PhD, Louisville, MD; Womack Army Medical Center, Fort Bragg, NC; Johns Hopkins University School of Medicine, Baltimore, MD; Johns Hopkins University School of Medicine, Providence, RI.

OBJECTIVE: To determine the correlation of mosaicism identified in the trophocoeptoderm (TE) to the rate of mosaicism within the inner cell mass (ICM).

DESIGN: Prospective

MATERIALS AND METHODS: 78 patients (631 embryos) underwent IVF and PGT-A was performed. All patients underwent IVF due to repeat pregnancy loss, previous unsuccessful IVF cycles, decreased ovarian reserve or unexplained infertility between 2012 and 2016. Embryos were first biopsied at the cleavage stage and if aneuploid, remained in culture to the blastocyst stage. At the blastocyst stage of development, the ICM and TE were separated and blindly analyzed. Molecular karyotypes were performed by enhanced next generation sequencing (NGS) using a Personal Genome Machine (PGM) or S5. By deep sequencing and proprietary algorithm’s, we can detect mosaicism at approximately the 10% level. This sequencing provided a minimum of over 3.5 million reads with a median sequencing fragment of 186bp.

RESULTS: 55% (350/631) of cleavage stage embryos were aneuploid. Of these, 37% (131/350) differentiated to the blastocyst stage. 26% (34/131) of these embryos were found to have mosaicism within both the TE and ICM.

CONCLUSIONS: Our results indicate that using an enhanced NGS technology, a significant percentage (26%) of embryos with detectable levels of mosaicism as determined by PGT-A in the TE population will be associated with mosaicism within the ICM as well. Clinically, an aneuploid mosaic fetus may result in a live birth with significant mental and physical deficits. Given this risk, we strongly recommend that the transfer of mosaic embryos only be considered as a last resort for very poor prognosis patients following comprehensive informed consent by a geneticist.

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PRE-IMPLANTATION GENETIC TESTING (PGT-A) USING FAST-SEQS NGS OF IN VIVO CONCEIVED BLASTOCYSTS RECOVERED BY UTERINE LAVAGE. Charlene A. Afouf, PhD, Sam Najmabadi, MD, Steven T. Nakajima, MD, John E. Buster, MD, Nicole Faulkner, PhD, Invitae, San Francisco, CA; Center for Reproductive Health & Gynecology, Beverly Hills, CA; Stanford University School of Medicine, Stanford, CA; Professor Emeritus of Obstetrics and Gynecology, Brown University, Providence, RI.

OBJECTIVE: To report the chromosomal characterization of in vivo conceived embryos utilizing a FAST-SeqS NGS-based PGT-A assay

DESIGN: Reported rates of euploidy per oocyte age differ amongst fertility programs. The most striking range reported, with a relatively homogenous group of oocyte donors, suggests that stimulation, culture conditions and manipulation may impact ploidy.1 IVF/PGT-A reduces the transfer of abnormal embryos but may be cost prohibitive even with minimal stimulation. A preliminary report demonstrated success with retrieving in vivo created embryos for PGT-A using a patented uterine lavage system2. In vivo culture would reduce the financial burden and the potential untoward effects of the in vitro environment.

MATERIALS AND METHODS: Twenty women underwent ovulation induction and donor insemination, with uterine lavage 5 days later, as previously described.2 The study had IRB approval and oversight by the Ministry of Health. TE biopsy was performed after lavage or following in vivo culture demonstrations.

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Total # embryos at lavage (day 5)</th>
<th>Day 5 Grade</th>
<th>Day 6 Grade</th>
<th>Bx Day</th>
<th>Interpretation</th>
<th>Misc Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>186</td>
<td>4</td>
<td>6 cell frag</td>
<td>3CC</td>
<td>6</td>
<td>Aneuploid</td>
<td>del(1)(q41)</td>
</tr>
<tr>
<td>187</td>
<td>11</td>
<td>4AA</td>
<td>6AA</td>
<td>6</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>192</td>
<td>3</td>
<td>12 cell, vac</td>
<td>4AB</td>
<td>6</td>
<td>Mosaic</td>
<td>trisomy 22(mos)</td>
</tr>
<tr>
<td>197</td>
<td>4</td>
<td>3AB</td>
<td>4AB</td>
<td>6</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>193</td>
<td>1</td>
<td>10 cell, vac</td>
<td>3CC</td>
<td>6</td>
<td>Mosaic</td>
<td>del(4q32) (mos)</td>
</tr>
<tr>
<td>185</td>
<td>2</td>
<td>2 (early)</td>
<td>6BB</td>
<td>6</td>
<td>Aneuploid</td>
<td>Monosomy 13</td>
</tr>
<tr>
<td>196</td>
<td></td>
<td>morula</td>
<td>3CC</td>
<td>6</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>200</td>
<td>5AA</td>
<td></td>
<td></td>
<td>5</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>202</td>
<td>2</td>
<td>6CC</td>
<td></td>
<td>5</td>
<td>Normal</td>
<td></td>
</tr>
<tr>
<td>199</td>
<td>1</td>
<td>5BB</td>
<td></td>
<td>5</td>
<td>Normal</td>
<td></td>
</tr>
</tbody>
</table>
vitra culture. Biopsies were analyzed using Invitae’s FAST-Seq S NGS/bioinformatics pipeline which detects whole chromosome and segmental aneuploidies (≥10 MB). Whole genome uniparental isodisomy (WG-UPiD or haploidy), all forms of triploidy, and most single chromosome UPiD are also identified from NGS.

RESULTS: Thirty-five viable embryos were recovered from 15 patients. Five blasts were biopsied on day 5 and 13 biopsied on day 6 from 10 patients total. Mean egg age for the resulting biopsied embryos was 26 (range 21-30). In all (n=18), 12 embryos (67%) were euploid, 4 were aneuploid (22%) and 2 mosaic (5.7%). Of interest, all 5 embryos biopsied on day 5 were euploid regardless of grade: the day 6 aneuploidy rate was 46%. Additionally, the euploid rate for egg age (<= 30) and the mosaic rate are consistent with Invitae’s internal data (68% and 5%-7%, respectively). Uterine lavage is an effective alternative to IVF for the recovery of viable embryos for PGT-A. Additional studies are planned to confirm these findings.

REFERENCES

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PGT-A (PREIMPLANTATIONAL GENETIC SCREENING) IN PATIENTS WITH PARTIAL X MONOSOMY USING OWN OOCYTES: IS A SUITABLE INDICATION? Juan Giles, M.D., Ph.D., a, b Amparo Mercader, Ph.D., b Carmen Rubio, Ph.D., c Carmen Vidal, M.D., Ph.D., b Lucia Alegre, Ph.D., a Martina Trabalon, M.D, Ph.D., a Marcos Meseguer, Ph.D., a IVI-IVM Valencia, Valencia, Spain; a IVI-IVM Valencia, Valencia, Spain; a IVI-IVM Valencia, Valencia, Spain; a IVI-IVM Murcia, Murcia, Spain; a IVI-IVM Global, Valencia, Spain; a IVI-IVM Murcia, Murcia, Spain; a Tel Aviv, Israel.

OBJECTIVE: Evaluate the reproductive outcome of preimplantational genetic diagnosis (PGT-A) in patients with mosaic Turner’s syndrome (MTS) using own oocytes, compared to mosaic and pure Turner syndrome (PTS) using ovum donation (OD).

DESIGN: Retrospective cohorts study from January 2011 until December 2017, scrutinizing >120,000 IVF cycles from 14 infertility clinics in Spain, searching for pure or mosaic TS, confirmed by the karyotype.

MATERIALS AND METHODS: University-affiliated private-infertility centre. 67 PGT-A in MTS patients (FISH/arrays-NGS), on which 65 controlled ovarian hyperstimulation cycles (COH) were performed, and embryo transfers (ET) performed in 32. As well, 165 women belonged to the OD-MTS or PTS group, with 157 cycles and 156 ET. RESULTS: Mean age and body mass index was 38,ly(37-38,7) vs.37,8y(37-38,7), 24.6kg/m²(23.4-25.8) vs.23.6kg/m²(22.9-24,2) for PGT-A (MTS and OD/MTS/PTS) respectively, without significant differences found.

The mean number of oocytes MII retrieved/received, for PGT-A in MTS and OD (MTS and PTS) respectively were 10.56 (9.84-11.27) and 9.32 (8.43-10.22); embryos transferred 1.5(1.3-1.7) and 1.79(1.69-1.89); implantation rate per ET 22.5% (8.5-36.5) in PGT-A and 35.19% (28.52-41.36) in OD, not reaching statistical significance, but showing differences.

Pregnancy rates tended to be higher but not significant (p=0.27) in OD 52.6 %95CI(60.4-44.4) vs. PGT-A 41.9 %95CI(24.8-59.0), while miscarriage rates remained statistically comparable, although with a noticeable higher rate when using donated oocytes, being OD 42.3% 95CI(31.5-52.3) vs. PGT-A 10.3% 95CI(0.3-26.8), resulting in live-birth rates of OD 28.84%95CI (7.1-21.7), higher than observed for PGT-A 21.87%95CI(7.5-36.1).

CONCLUSIONS: The retrospective nature of this study may be a reason for caution. Despite being the largest sample size ever reported with PGT-A in MTS the number of patients included is still low. Subsequently, the conclusions reached should be taken carefully until a larger body of evidence will be available.

Oocyte donation (OD) seems to be the best reproductive option in female who are missing one of the X chromosomes, with or without mosaicism present.

Nevertheless, based on the previous data, PGT-A is a valid therapeutic option in patients with mosaic Turner’s syndrome (MTS) using own oocytes and OD should not necessarily be recommended directly as the treatment of choice.

REFERENCES

P-333 Tuesday, October 15, 2019 6:30 AM

OBJECTIVE: The absence of standardised culturing conditions or molecular testing methodologies, including whole genome amplification (WGA) used for non-invasive preimplantation genetic testing of spent embryo culture media for aneuploidy (NI-PGT-A) may explain the variable rates of
concordance reported between the spent embryo culture media and embryo biopsy results to-date. Culture conditions impact the accumulation of embryonic and contaminating DNA in spent embryo culture media and optimisation of either the culturing conditions, molecular testing methodologies, or both, should yield the highest level of concordant results for NI-PGT-A.

DESIGN: This study examined rates of ploidy concordance between spent embryo culture media and embryo biopsies to evaluate the impact of culture conditions on NI-PGT-A results.

MATERIALS AND METHODS: Spent embryo culture media was collected from single embryo culture droplets following biopsy of the embryo for PGT-A then stored at -20°C with ethics approval. Equivalent volumes of spent embryo culture media samples from 10μl-60μl culture droplets, from either continuous (n=4 labs) or two-step cultures (n=4 labs) were whole genome amplified using DOPify® kit reagents (PerkinElmer). WGA DNA yield was assessed by gel electrophoresis and high sensitivity quantification using a Qubit® instrument (Thermo Fisher® Scientific). Next generation sequencing libraries were generated according to the PG-Seq™ kit 48 sample protocol and sequencing was performed on an MiSeq® instrument (Illumina®). Data was bioinformatically aligned to hg19, and WGA DNA yield, NGS metrics, and whole chromosome aneuploidy concordance with the PGT-A result for the embryo biopsy were determined.

RESULTS: Whole genome amplification using the DOPify® kit reagents resulted in the amplification of 78-100% of spent embryo culture media samples (WGA failure rate 0-22%). Ploidy concordance with the embryo biopsy ranged from 29-75% for autosomal chromosomes and 47-94% for sex chromosomes using a single-step culturing system (n=4), compared with concordance rates of 67-90% and 50-97% respectively when media was changed during the 5-6 day culture (n=4). DNA yield was not affected by embryo culture media droplet volume, or continuous or two-step culture. Sex chromosome concordance varied between individual labs, suggesting that embryological processes are important in NI-PGT-A testing. Further statistical analysis during the ongoing larger scale collaborative study will determine quality control parameters for acceptance of NI-PGT-A results.

CONCLUSIONS: Successful NI-PGT-A using spent embryo culture media will possibly require specific culturing conditions and/or specialised molecular methodologies for accurate and representative amplification and testing of the embryonic DNA. In a step toward this, we identified that renewing culture media during IVF improves overall concordance rates between the embryo biopsy and spent embryo culture media for NI-PGT-A.

P-335 Tuesday, October 15, 2019 6:30 AM
APPLYING WHOLE GENOME NEXT GENERATION SEQUENCING (NGS) ANALYSIS OF PRODUCTS OF CONCEPTION (POC) AFTER EMBRYO TRANSFER. Siwei Chen, MD, a Rina Abramov, MSc, b Ran Antes, PhD, c Valeriy Kuznetsov, PhD, d Svetlana Madjunkova, MD, e Clifford Lawrence Librach, MD, e Create Fertility Centre, Toronto, ON, Canada; eCreAte fertility centre, Toronto, ON, Canada; eCreAte Fertility Centre, Toronto, ON, Canada.

OBJECTIVE: Genetic assessment of tissue from products of conception (POC) can elucidate the reason for miscarriage in approximately 50-70% of first trimester miscarriages. Assessment of the fetal chromosomal composition may be very helpful in counselling and management of patients experiencing miscarriages, especially after IVF, or in patients with recurrent pregnancy losses. However, obtaining fetal tissue from early miscarriages is often compromised by maternal cell contamination (MCC). Here we present the results from assessing early POC samples (<10 GW) after IVF single embryo transfer, controlling for MCC, using whole genome NGS at the CreAte Fertility Centre.

DESIGN: A retrospective study.

MATERIALS AND METHODS: POC samples (n=294) (Jan, 2016-Apr, 2019) from early pregnancy losses after IVF treatment were obtained by suction D&C collection. Four representative samples of fetal tissue and/or chorionic villi were separated from decidual tissue and blood using a dissecting microscope. A maternal/paternal blood sample was obtained for DNA extraction to test for MCC. MCC was determined using analysis of short tandem repeats-STRs (AmpFLSTR Identifier Plus kit) of maternal and fetal DNA (tDNA). After confirmation of fetal DNA origin, whole genome NGS was carried out using VeriSeq kit. GeneMapper (Applied Biosystems) and BlueFuse Software4.4 (Illumina) were used to analyze the STR and NGS data.

RESULTS: In total, we analyzed 294 POC samples (8.45±1.8 weeks) from patients undergoing IFV. Overall, mean maternal age was 36.8±8.5 years, DNA confirmed by STR MCC analysis was obtained from 45.6% (n=134) of the samples. NGS analysis for chromosomal aberrations showed the highest level of concordant results (134/134) of the POC samples were euploid (46, XX n=37; 46, XY n=29). 14.2% of IDNA samples (19/134) were from euploid embryos tested by NGs for aneuploidy at blastocyst stage. All these 19 POC samples were confirmed to be euploid and 100% sex concordant with preimplantation result. Aneuploidy was detected in 46.3% (62/134) [trisomy- T16,12.9% ;T21, 12.9% ; T22, 11.3%; T15,9.7%; T20, 6.5%; T14, 4.8%; T3 and T18, 3.2% ; 1.6% of each T9,T12,T14,T13, T15,T16,T5,15, T15+22, T17, X monosomy – X, 17.7%, and 4.8% were triploid (69.XXY). Mosaicism was detected in 4.5% (6/134): ((-X;0,6%),(+X,60%, 1/6); (-Xp11.1-q21.33, 36Mb, 60%, -Xq21.33-qter, 40%, 1/6); (-Y,60%;1/6); (+8,50%,+9,50%, 1/6);(+1,2q,30%, 1/6)).

CONCLUSIONS: MCC is high in POC samples from early pregnancies and controlling for it is warranted. NGS results from euploid embryo transfers were fully concordant with PGT-A results. Establishing STR MCC and NGS analysis of POC on a larger scale would improve diagnostic accuracy, and could aid in patient counselling and management.

SUPPORT: Create Fertility Centre.

P-336 Tuesday, October 15, 2019 6:30 AM
RETROSPECTIVE EVALUATION OF PGD-HLA CASES FOR DIVERSE GENETIC DISEASES. Gamze Bilgili, MSc, a Tolga Ecemis, MD, a Hasan Huseyin Kazan, MSc, a Yaman Saglam, MD, b, Department of Physiology, Faculty of Medicine, Gazi University, Ankara, Turkey; cEcemis Clinics, Ankara, Turkey; dDepartment of Biological Sciences, Middle East Technical University, Ankara, Ankara, Turkey; dDepartment of Medical Genetics and Biology, Maltepe University, Istanbul, Turkey.

OBJECTIVE: The combination of preimplantation genetic diagnosis (PGD) with human leukocyte antigen (HLA) matching has appeared as a remarkable tool for the therapy of single-gene or acquired diseases in affected individuals. The technique (PGD-HLA) provides the parents who have affected child with disease-free and HLA-matched embryos that are compatible with the affected child, offering an unaffected newborn and a donor for affected child.

DESIGN: The present retrospective evaluation covers 64 couples who had undergone 131 PGD cycles in total for both HLA matching and elimination of the mutation(s) associated with different diseases, including acute lymphoblastic leukemia (n=2), aplastic anemia (n=1), Diamond-Blackfan anemia (n=2), Fanconi anemia (n=2), Griscelli syndrome (n=2), Hermansky-Pudlak syndrome (n=1), hyper IgE syndrome (n=1), hyper IgM syndrome (n=3), myelodysplastic syndrome (n=1), Morquio syndrome (n=1), severe combined immunodeficiency (n=1), thalassaemia (n=55), Wiskott-Aldrich syndrome (n=1), chronic granulomatous disease (n=1) and amyotrophic lateral sclerosis (n=1).

MATERIALS AND METHODS: Oocytes were picked up by antagonist protocol. After in vitro fertilization (IVF), eight blastomeres were analyzed for wild type cells by the gene- and HLA-linked STR markers as well as linkage analysis at day three, and normal and HLA-compatible cells were transferred to the mother via frozen embryo transfer (FET).

RESULTS: Amongst the total embryos (n=1217), 250 embryos (20%) were wild type in terms of scanned mutation(s) and 206 embryos (17%) were found to be HLA-matched. 125 embryos in total were transferred and 33.8% clinical pregnancy rate per transfer was achieved.

CONCLUSIONS: The present study underlines the importance and efficacy of PGD-HLA method in the treatment of related diseases.

DOES PGT WITH FRESH EMBRYO TRANSFER AFFECT PERINATAL OUTCOMES?: AN ANALYSIS OF THE 2014 AND 2015 SART DATA. Kristin Van Heer- tum, MD, a Channing Burks, MD, a Kerry S. Flannagan, PhD, a Sunni L. Mumford, PhD, a Alexandra C. Purdue-Smith, PhD, a James Goldfarb, MD, MBA, a Rachel S. Weinerman, MD, a University Hospitals Fertility Center/Case Western Reserve University, Beachwood, OH; bEpidemiology Branch, DIPHR, NICHD, NIH, Bethesda, MD; cNICHD, Bethesda, MD; dOH.
RESULTS: The mean age of the no biopsy patients (N = 52,754) and biopsy patients (N = 1,003) was 33.9 and 35.2 years, respectively (p = 0.01). Compared to patients whose embryos were not biopsied, patients whose embryos were biopsied were significantly more likely to have a clinical pregnancy (61.2 vs. 57.3%, adjusted relative risk (aRR) 1.16, 95% confidence interval (CI) 1.07, 1.26) and live birth (54.4 vs. 48.4%, aRR 1.17, 95% CI 1.07, 1.26) and pregnancy (61.2 vs. 57.3%, adjusted relative risk (aRR) 1.16, 95% confidence interval (CI) 1.07, 1.26) and live birth (54.4 vs. 48.4%, aRR 1.17, 95% CI 1.07, 1.26). In the biopsy group, there were no differences seen in perinatal outcomes compared to the non-biopsy group. Low birth weight (LBW) was the primary outcome.

CONCLUSIONS: Evaluating the subset of patients whose had fresh embryo transfers following PGT allows for the assessment of the effects of PGT itself without the confounding effects of embryo cryopreservation. While there was a difference seen in the incidence of LGA babies, there were otherwise no differences seen in perinatal outcomes between fresh transfer with and without embryo biopsy. Future studies should assess potential etiology for the observation of an increase in LGA babies following fresh transfer after embryo biopsy.

SUPPORT: None.

**P-338 Tuesday, October 15, 2019 6:30 AM**

**MOSSIC EMBRYO DIAGNOSIS CORRELATED WITH ABNORMAL 15Q DUPLICATION SYNDROME IN OFFSPRING.** Emily L. Mounts, MS, CCCa; Shiliou Olive Zhu, MScb; Rebecca K. Sanders, PhDb; Alison Coates, PhDb; John S. Hesla, MDa; cOMR Fertility, Portland, OR; CooperGenomics, Los Angeles, CA.

OBJECTIVE: Outcome data from the practice of mosaic embryo transfer has to date not suggested an association with adverse postnatal outcomes. The objective of this case review was to determine whether a chromosomal duplication syndrome, discovered in a phenotypically abnormal child who was the product of euploid embryo transfer, could be retrospectively identified in full or mosaic form using an updated PGT-A platform.

MATERIALS AND METHODS: A 29yo G1P1 female patient with ovarian factor infertility and her male partner, who had oligospermia, underwent IVF/PGT-A via next-generation sequencing (VeriSeq PGS, Illumina Inc). 5/7 embryos were diagnosed as euploid and FET of two euploid male embryos resulted in the birth of healthy twin boys. By 8 months of age one twin had failed to meet his developmental milestones, developed marked obesity, and had abnormally low growth hormone and insulin levels.

RESULTS: Multiplex ligation-dependent probe amplification (MLPA) and methylating testing was performed to evaluate for Prader-Willi syndrome (caused by 15q11.2-13 paternal deletions) on the affected boy. This testing incidentally diagnosed an extra paternal copy of 15q11.2-q13. Chromosomal microarray [Dian Dianalysis] confirmed a 5.76Mb duplication at 15q11.2-q13.1. The boy was diagnosed with 15q duplication syndrome, a highly variable condition associated with developmental delays, autism spectrum disorders, and a phenotype influenced by parental origin of the duplication (maternal vs paternal). Retrospective analysis of his PGT-A results was requested per clinic protocol. Review of archived profile images of the original NGS data [BlueFuse Multi, Illumina] from the two male embryos reaffirmed the original interpretations of euploid males. Preserved amplified DNA from both embryos was reanalyzed using NGS and PGTAi [CooperGenomics proprietary algorithm]. This algorithm detected a high-level mosaic (57%) 6Mb duplication on 15pter-q13.3 in one embryo, demonstrating that this finding was detectable by PGT-A using an updated platform with a revised algorithm and increased resolution. Additionally, two separate and larger segmental mosaic abnormalities were identified upon reanalysis of preserved amplified DNA from the affected boy and his healthy twin brother, respectively; the former was not confirmed on postnatal CMA. The

**ABNORMAL 15Q DUPLICATION SYNDROME IN Mosaic EMBRYO DIAGNOSIS CORRELATED WITH ABOormal 15Q Duplication SYNDROME IN OFFSPRING.** Emily L. Mounts, MS, CCCa; Shiliou Olive Zhu, MScb; Rebecca K. Sanders, PhDb; Alison Coates, PhDb; John S. Hesla, MDa; cOMR Fertility, Portland, OR; CooperGenomics, Los Angeles, CA.

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patient’s three remaining euploid embryos were also then reanalyzed via PGT-A and 2/3 embryos were reaffirmed to be euploid. The third embryo was found to have the same 15pter-q13.1 duplication as the affected boy, also in the mosaic range (78%), suggesting that the variant may be inherited.

CONCLUSIONS: This may be the first case in which correlation between a mosaic PGT-A result and the same finding postnatally, in non-mosaic form and likely resulting in an abnormal phenotype, has been made. This case is highlights the significant challenges of predicting mosaic embryo transfer outcomes. Transfers of mosaic result embryos may not always result in binary outcomes, an essential consideration for genetic counseling of families considering this option.

P-339 Tuesday, October 15, 2019 6:30 AM
OUTCOMES OF A SIMPLIFIED MOSAIC RANKING SYSTEM
Andrijana Jovasevic, Bachelor of Science (Molecular Genetics and Biotechnology); Mark Livingston, Genea Deputy Medical Director, MB, Chb, FRANZCOG, CREI, MM; Maria Victoria Travera, MS, Med; Jolene Stockton, Bachelor of Science; Steve Grkovic, PhD; Steven J. McArthur, BSc, PLD (Harvard Business School); Genea, Sydney, NSW, Australia; Genea Sydney, Sydney, NSW, Australia.

OBJECTIVE: Investigating outcomes of transferring mosaic embryos according to a simplified classification system that replaced our more complex 1-9 ranking system.

DESIGN: Following previous implementation of a comprehensive mosaicism classification system, a review of our mosaic embryo outcome data, together with that of recent literature (Spinella et al 2018, and Munne et al 2017) was conducted. The goal was to introduce a more simplified classification system – using an A-D grading – which ranks mosaic embryos for clinical use (as per table below). The study included 158 single transfers of embryos (between April 2016 to February 2019) which exhibited a mosaic shift (ranging from 20-79%) using NGS technology.

TF-A = NAD (no abnormality detected) – first choice for transfer
TF-B = Noisy result/low level mosaicism (<40%) – second choice
TF-C = Mosaic (significant mosaicism detected (40–< 80%)) - third choice, further stratified by:
C1: -segmental -low risk chromosomes
C2: -high risk chromosomes TF-D: ABN (abnormal) – not available for transfer

MATERIALS AND METHODS: Mosaic embryos were separated into the above categories dependent on the percentage of mosaicism present in the sample and the chromosome involved, with only levels over 40% being reportable findings. This study retrospectively compared the positive bHCG and fetal heart (FH) outcomes for the TF-A, B and C groups. We also analyzed outcomes for whole chromosome mosaics compared to segmental mosaic findings.

RESULTS: We found that overall, TF-A group had the highest positive bHCG rates (62.9%) and FH rates (53.7%) followed by TF-B bHCG (57.6%) and FH rates (47.6%). TF-C had lower positive bHCG rates outcomes (44%) and FH rates (36%). Analysing TF-C (40-80% mosaics) in more detail we found that segmentals had higher bHCG and FH rates (69.2% and 61.5%) compared to whole chromosome mosaics (20% and 10%). Furthermore, irrespective of the mosaic percentage, all single segmentals (in the 20-80% range) had clearly better outcomes than multiple segmentals (bHCG: 63.3% vs 44.4% and FH: 48.3% vs 33.3%). In comparison low level segmental mosaics (<40%) had higher bHCG (58.9%) and FH (42.9%) rates compared to low level whole chromosome mosaics (44.8%) and (36.2%).

CONCLUSIONS: Overall the positive bHCG and fetal heart outcomes support the simplified classification system and the concept of preferentially transferring low level before high level whole chromosome mosaics in the absence of NAD embryos. Single segmental mosaic embryos have improved clinical outcomes compared to whole chromosome mosaic embryos and should be considered for preferential transfer ahead of other types of mosaic findings. Whole chromosome mosaics should be considered last choice.

P-340 Tuesday, October 15, 2019 6:30 AM
EVALUATION OF THE IMPACT OF THE PULLING AND FLICKING TROPHECTODERM BIOPSY PROCEDURES ON THE INTEGRITY OF THE BIOPSED CELLS AND THEIR CORRELATION TO PGT-A RESULTS
Marina Benavent, MSc; Maria Escriba, MSc; Clara Miret, MSc; Ivette Varell, MSc; Nuno Costa-Borges, PhD; Gloria Calderón, PhD; Juana Crespo, MD; Jose Teruel, MSc; Equipo Juana Crespo, Valencia, Spain; Embryotools, Barcelona, Spain.

OBJECTIVE: Blastocyst biopsy is currently the gold standard in PGT-A. However, because trophectoderm (TE) cell excision is technically challenging, results can vary depending on how the procedure is performed. To ensure successful results, it is important not only to avoid harming the blastocyst during the biopsy procedure, but also to ensure a minimal damage on the biopsied cells. In this study, we aimed to evaluate the impact of two different TE biopsy techniques (pulling and flicking) on the integrity of the biopsied cells and to correlate their status with the chromosome screening results of the two methods.

DESIGN: This is a retrospective observational study that includes the data analysis of 268 TE biopsies performed on blastocysts from 83 patients (mean age – 39.1 y/o) that underwent a PGT-A cycle between October 2018 and April 2019. Chromosome screening analysis were carried out by an associated genetics laboratory. Indications for PGT-A cycles included advanced maternal age, recurrent implantation failure, recurrent miscarriage and/or severe male factor.

MATERIALS AND METHODS: Trophectoderm biopsies were performed with the assistance of a dynamic laser. Assisted hatching was performed on Day 3 and 5 blastocysts with hatching cells not completely hatched were biopsied with the “pulling” or “flicking” techniques. In the pulling method, blastocysts were held firmly with the holding pipette and the biopsy needle used to pull TE cells away from the blastocyst, while laser pulses were applied. In the flicking method, laser pulses were used to allow TE cells to be drawn inside the biopsy pipette and subsequently the TE cells were excised with a quick movement of the biopsy pipette against the holding pipette. Biopsied cells were then photographed and classified according to their integrity status as follows: intact (A); partially lysed (B); completely lysed (C). After biopsy, the cells were washed and transferred into PCR tubes to be processed for chromosome screening by NGS. Statistical significance was assessed by Students t-test or Fisher’s exact test.

RESULTS: A total of 118 blastocysts were biopsied with the pulling method and 150 with the flicking technique and no differences were found in terms of mean age of the patients (39.5±1.1 and 38.5±3.2, respectively) or average number of laser pulses used (4.2±1.1 vs 3.9±0.9, respectively). Overall, the pulling technique resulted in higher (p = 0.0009) percentage of pieces graded as A (74.6%, n = 88) than the flicking method (54.7%, n = 82), but no differences were found among the two groups in terms of euploidy rates (28% and 36%, respectively). Regardless of the technique used, all cells grade C were majorly (80-100%) diagnosed as chromosomally abnormal compared to those that were classified as morphologically intact (43.9-62.5%) or partially lysed (52.4-62.5%).

CONCLUSIONS: These results indicate that the pulling and flipping techniques do not differ in terms of rates of chromosomally normal blastocysts as long as both procedures are applied correctly. The integrity of the cells seems to affect the results of aneuploidy rates, which might depend on blastocyst morphology.

SUPPORT: Institutional funding.

P-341 Tuesday, October 15, 2019 6:30 AM
DEVELOPMENT OF A NEXT GENERATION SEQUENCING METHOD (PGT-SR PLUS) TO DETERMINE CARRIER STATUS OF BALANCED TRANSLATION PATIENT EMBRYOS
Hua Jin, PhD; Hui Zheng, MA; Alysha Nicole Salsato, BS; Robert Snyder, BS; ManLi, MD, PhD, Lian Liu, MD; PacGenomics, Agoura Hills, CA.

OBJECTIVE: Currently, PGT-SR is the only PGT option in the United States for patients with a balanced translocation. While PGT-SR does
reliably screen for chromosomal copy number normal embryos and avoid the transfer of unbalanced translocation embryos, PGT-SR cannot determine the carrier status of embryos. Our objective is to develop a generic genome-wide next generation sequencing method (PGT-SR Plus) that can determine the carrier status of balanced translocation patient embryos, regardless of the type or location of translocation. This will allow patients the option to transfer embryos without the structural chromosomal abnormality.

**DESIGN:** Feasibility and validation study.

**MATERIALS AND METHODS:** The feasibility of the PGT-SR Plus method has been tested on 10 cases involving various chromosomes, including both Robertsonian and reciprocal translocations. Parental blood was collected to determine the balanced translocation allele. Then, PGT-SR was performed on all embryos to identify those with a normal chromosomal copy number. These identified embryos, along with one unbalanced embryo, were then tested with PGT-SR Plus. The unbalanced embryo is used as a reference for phasing the parental carrier’s balanced translocation allele. The carrier status of each embryo was then determined based on whether or not the embryo carries the parental balanced translocation allele.

**RESULTS:** All 10 translocation cases that have been tested with PGT-SR Plus have had definitive results for the carrier status of the balanced translocation embryos. 7 of these 10 cases were also tested on the illumina karyomapping microarray platform and the same carrier statuses were identified, indicating that our generic next generation sequencing method and bioinformatic analysis pipeline are encouraging for screening structural chromosomal abnormalities.

**CONCLUSIONS:** The next generation sequencing-based PGT-SR Plus is a promising method for determining the carrier status of balanced translocation patient embryos. As a generic method, it does not rely on the design of patient specific primers. It is applicable to all currently identified structural chromosomal abnormalities and is therefore very affordable.

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**P-342** Tuesday, October 15, 2019 6:30 AM

**IMPACT OF TROPHODERM BIOPSY FOR PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGT-A) ON EARLY BETA-HCG TRENDS IN SINGLE FROZEN EMBRYO TRANSFERS (FET) RESULTING IN LIVE BIRTH.** Laura Perez Soriano, BA, a Joshua Stewart, M.D., b Steven Spandorfer, M.D., b Zev Rosenwaks, M.D., b Weill Cornell Medical College, New York, NY; The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

**OBJECTIVE:** Newer techniques in PGT-A allow blastocyst biopsy removing 6-10 trophoderm cells for genetic analysis. As syncytiotrophoblasts produce beta-hCG, our objective was to determine the effect of trophoderm biopsy for PGT-A on early serum beta-HCG trends in pregnancies resulting in a singleton live birth.

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** All patients undergoing an FET cycle of a single blastocyst between January 2015 to December 2017 were analyzed. Cycles were divided into those with PGT-A and without. For PGT-A cycles, only euploid embryos were included. Inclusion criteria: 2 serum BHCG results obtained 2 days apart, delivery of a live singleton. Exclusion criteria: cycles utilizing donor oocytes, multiple gestation pregnancies. Primary outcomes were initial serum BhCG and 2-day increase in BhCG. Secondary outcomes were serum estradiol (E2) and progesterone (P4). Groups were further stratified by FET protocol, natural cycle or medicated.

**RESULTS:** 487 cycles met inclusion criteria, 279 with PGT-A and 208 without. There was no difference in mean initial BhCG or second serum BhCG levels between the cycles with PGT-A and those without PGT-A despite controlling for age and protocol. The median 2-day increase in BhCG was significantly higher in the PGT-A group versus the cycles without PGT-A (247.9% vs 238.9%, respectively, p = 0.02). There was no difference in the 2-day rise of serum E2 or P4 levels between the groups.

**CONCLUSIONS:** BhCG is commonly used as a marker of trophoblast differentiation and to assess pregnancy viability, but little is known about the impact of trophoderm biopsy on BhCG trends. Our results reveal no difference in initial BhCG between cycles with PGT-A and without. While there was a significantly greater 2-day increase in BhCG in the PGT-A group, the clinical relevance of this minimal difference is unclear. However, it is clinically reassuring that trophoderm biopsy does not impair BhCG rise. This contributes to previous studies that suggest trophoderm biopsy does not affect implantation or early pregnancy steroidogenesis, adding to the overall safety of PGT-A to achieve healthy pregnancies.

**REFERENCES**


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### Demographics

<table>
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<th>PGT (n = 279) Mean ± SEM</th>
<th>No PGT (n = 208) Mean ± SEM</th>
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<td>Age</td>
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<td>BMI</td>
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<td>AMH</td>
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<td>Mean Serum Hormone Levels (mIU/mL)</td>
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<tr>
<td>1st BhCG</td>
<td>275 ± 9.4</td>
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<tr>
<td>2nd BhCG</td>
<td>678 ± 25</td>
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<td>ns</td>
</tr>
<tr>
<td>2nd P4</td>
<td>26.5 ± 0.7</td>
<td>24.6 ± 0.7</td>
<td>ns</td>
</tr>
<tr>
<td>2-day % Increase in Hormone, Median (IQR)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BhCG</td>
<td>244 (220 – 277)</td>
<td>237 (209 – 260)</td>
<td>0.02</td>
</tr>
<tr>
<td>E2</td>
<td>112 (96 – 129)</td>
<td>112 (95 – 127)</td>
<td>ns</td>
</tr>
<tr>
<td>P4</td>
<td>100 (88 – 114)</td>
<td>97 (86 – 126)</td>
<td>ns</td>
</tr>
</tbody>
</table>

Differences calculated by Paired Student’s T-test or Wilcoxon rank sum tests.
OBJSCTIVE: To describe the anthropometric, hormonal and hematological characteristics of women undergoing in vitro fertilization (IVF).

MATERIALS AND METHODS: We report on a subgroup analysis of 10 women undergoing IVF from subjects prospectively enrolled in an IRB approved study of hemostatic balance. Samples were longitudinally collected during the follicular phase prior to the IVF cycle (V1), prior to commencing gonadotropins (V2), 30-90 minutes prior to oocyte retrieval (V3), and 14 days after oocyte retrieval (V4) with a subsequent fresh embryo transfer. Complete blood counts, progesterone (P4) and estradiol (E2) were assessed at all visits, body composition was evaluated by Dual Energy X-ray Absorptiometry at V1. Pregnancy was detected by serum hCG 14 days after retrieval and luteal support, V4. Women who conceived were compared with those who did not using two-sample t-tests and Wilcoxon tests; data presented as mean ± standard deviation with the significance threshold set at p < 0.05.

RESULTS: The mean age of subjects at retrieval was 32 ± 3.7 years, mean BMI 25.5 ± 3.9 kg/m², with no significant differences between women based on conception status. Half of the women conceived with the initial fresh IVF cycle. Women who conceived had a lower waist:hip circumference ratio (0.77 ±0.05) compared to those who did not (0.9 ±0.04), p = 0.003. There were differences in android tissue fat and android:gy努oid fat ratio based on conception status (not statistically significant). There were no other differences in body composition or bone mineral density age matched Z scores between groups.

E2 and P4 during the IVF cycle are shown in the table below. The mean P4 was higher in the not pregnant group at V3, and both E2 and P4 were significantly lower at V4. Total white blood cell, neutrophil and lymphocyte counts were higher in the pregnant group at V4. Higher E2 (p = 0.02), P4 (p = 0.02), lymphocyte % (p =0.02) and neutrophil % (p =0.02) were found at V4.

CONCLUSIONS: Hematological differences exist between women who successfully conceive following a fresh IVF cycle, as demonstrated by increases in neutrophil and lymphocyte counts in women who had a positive hCG versus those who did not conceive. There are also differences in estradiol and progesterone early when pregnancy is diagnosed. Waist hip ratio was inversely associated with pregnancy in this small sample, but there may also be differences in body composition not detected with this sample size. Our future studies may elucidate further metabolic and hematologic factors related to successful fresh IVF cycles.

NIH grant: #R61 HL141787-01


P-345 Tuesday, October 15, 2019 6:30 AM

ATYPICAL VAGINAL TEMPERATURE PATTERNS MAY IDENTIFY SUBTLE, NOT YET RECOGNIZED, CAUSES OF INFERTILITY.

Bradley S. Hurst, M.D., a

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OBJECTIVE: To determine if averaged nocturnal vaginal temperature measurements recorded during non-menstruation by use of the OvuSense system (OS), could describe atypical patterns potentially associated with reduced fertility.

DESIGN: Retrospective, longitudinal, comparative, observational study.

MATERIALS AND METHODS: 10,463 ovulatory cycles from 6,647 OS users aged 20 to 52 (if age provided), with cycle length 11 to 190 days (90% 22 to 47 days). Participants used OS vaginally at night to monitor core body temperature (temp), having voluntarily been asked to provide date of birth and identify how long they had been trying to conceive before OS use. OS produces a representative temp for each night of recordings taken every 5 minutes, which are then assessed with a proprietary moving averaged calculation to produce a “smooth” analysis curve. The main outcome measures were: proportion of normal and atypical OS temp patterns as classified by observation of the smooth curve and applied mathematical criteria, frequency of their occurrence, and associations between patterns.

RESULTS: Three novel atypical temp patterns were identified: (a) “Crash To Baseline” = first nightly averaged temp falls by >0.2 degrees Celsius (℃) to lowest cycle temp point (baseline) - in 1,481 cycles (14.2%) from 1,352 OS users (12.0%); (b) “False Start” = rise of >0.1 ℃ from baseline but instead a return to baseline temp followed by ovulation two or more days later in the cycle - 981 cycles (9.4%); 939 users (14.1%); (c) “Crash After Ovulation” = final temp >0.2 ℃ lower than the post ovulatory peak temperature - 1,259 cycles (12.0%); 1,062 users (16.0%). Additionally, Short Luteal Phase (SLP) (d) was noted with menstruation 9 or fewer days post-ovulation - 871 cycles (8.3%); 793 users (12.0%). SLP occurred combined with pattern (a), (b), or (c) 237 cycles (2.3%); 231 users (3.5%). SLP co-existed with (a)

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OBJECTIVE: This study aimed to establish an innovative system in which the molecular mechanisms of FSH-induced granulosa cell differentiation during ovarian follicle maturation could be studied.

DESIGN: In vitro studies of gene and protein expression were conducted in primary cultures of mural granulosa cells collected from women undergoing in vitro fertilization (IVF) at the University of Illinois Hospital.

MATERIALS AND METHODS: Mural granulosa cells collected from IVF patients were cultured in phenol-red-free media containing 2% serum for 0, 24, 48, or 72h. At these time-points, the cells were serum starved for 24h and then treated with FSH for 48h. Total RNA was isolated from these cells, and gene expression of key granulosa cell differentiation markers including Cyp19a1, Star, and P450scc was measured by quantitative RT-PCR. Additionally, total protein was isolated from these experimental groups and the expression of CYP19A1, Star, and P450SCC at the protein level was measured by Western blot. Differences between the means of different groups were analyzed by ANOVA or t-test and considered statistically significant at p<0.05.

RESULTS: After culturing cells in serum-containing media for at least 24h before serum starvation and FSH treatment, the expression of steroidogenic genes Cyp19a1, Star, and P450scc were reduced significantly, suggesting that under the culture conditions used mural granulosa cells de-differentiate and resemble undifferentiated granulosa cells. After treatment with FSH, the expression of Cyp19a1, Star, and P450scc increased significantly by 3.5, 2.5, and 3-fold respectively. The protein expression of CYP19A1, Star, and P450SCC was also increased significantly by 3.4, and 1.5-fold, respectively.

CONCLUSIONS: Mural granulosa cells from IVF patients cultured in serum for 24h followed by serum starvation respond to FSH with an increase in steroidogenic gene and protein expression, suggesting that cell culture in an experimental system can be used to study the molecular mechanisms of human granulosa cell differentiation in response to FSH in vitro.

SUPPORT: This work was supported by NIH grant number R01HD057110 (COS); SCB was supported by NIH training grant number T32HL07692.
133 cycles; 128 users, with (b) 155 cycles; 153 users, with (c) 7 cycles; 7 users. SLP co-existed with pattern (a) + (b) 33 cycles; 32 users, and as in low frequency with (a) + (c) 1 cycle; 1 user, and (b) + (c): 2 cycles; 2 users. Therefore 3.721 cycles exhibited one or more ‘atypical’ patterns (a), or (c) = 35.6%.

CONCLUSIONS: It is likely OS continuous vaginal temp patterns closely reflect luteal progesterone changes, hence describe subtle progesterone secretion or metabolism anomalies, which not yet have been recognized.

(a) suggests high progesterone early in the cycle, (b) suggests a small progesterone rise which does not result in a sustained ovulatory rise, but is followed by an ovulatory rise later in the cycle, and (c) would be expected to occur in women with PCOS, and further studies are planned to examine this within the OS population. (c) suggests that progesterone may fall sharply in some women before onset of menses, and it is possible that fertility may be impaired in these cycles. Relatively strong correlation between SLP and patterns (a), (b), and/or (c) indicates vaginal, core-body temp monitoring may represent a promising method of identifying previously undetectable causes of infertility in women with “normal” ovulation.

References:

SUPPORT: This study was financially supported by Fertility Focus Ltd.

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IGF-1 AND IGFBP-3 SERUM CONCENTRATIONS IN PATIENTS UNDERGOING PROGRAMMED FROZEN-TAHEAD EMBRYO TRANSFER OF EUPLOID PGT-A EMBRYOS. Robert Setton, MD, Antonia Athanasiou, MD, Dayton James, PhD, Steven Spandorfer, M.D., The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: IGF-1 has been shown to induce embryonic development in vitro, but at high concentrations exhibits toxic effects by decreasing embryonic glucose uptake. IGFBP-3 binds IGF-1, modulating its bioavailability and is essential to its function. Prior reports have associated elevated follicular phase IGF-1 with pregnancy loss in frozen-thawed embryo transfer in natural cycles (n-FET), but an association in programmed (p-FET) cycles or in the luteal phase has not been analyzed. We sought to determine whether serum levels of IGF-1 and IGFBP-3 correlate with the outcome of p-FET cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients who underwent p-FET of single, good quality (Grade ≥2BB), PGT-normal embryos were included in the study. GnRH-agonist suppression was started in the preceding luteal phase, overlapped with estradiol patches, and stopped with the start of progesterone. Serum samples were collected on cycle day 2 (CD2), the day of progesterone start (CDP4), and cycle days 28 (CD28) and 30 (CD30). Embryo transfer occurred on the 7th day of P4 administration. Serum levels of IGF-1 and IGFBP-3 were compared between those who did not achieve pregnancy, those who had a live birth, and those who had a pregnancy loss. Serum IGF-1 and IGFBP-3 levels were measured by chemiluminescent immunoassays using the Immulite 2000 XPI. Statistical analysis was performed using chi-square and Fisher’s exact test. P < 0.05 was deemed statistically significant.

RESULTS: A total of 102 patients who underwent p-FET of single euploid embryos over 2 years were analyzed. The mean age at retrieval was 35.7 ± 4.1 years, BMI 24.2 ± 4.8 kg/m2, gravity 1.8 ± 1.6, parity 0.4 ± 0.6 and peak endometrial thickness 9.7 ± 2.0 mm. 76.5% of patients were pregnant and 78.2% of those had a live birth. Among women who conceived, those who had a subsequent pregnancy loss had significantly higher serum IGF-1 levels on CDP4 and CD28 compared to those who achieved live birth when analyzing patients whose serum IGF-1 levels were above the mean value of IGF-1 level on CDP4 (136 ng/ml, p = 0.044) and CD28 (138 ng/ml, p = 0.007), and between patients with CD28 IGF-1 levels one standard deviation above the mean (≥ 160 ng/ml, p = 0.007). There was no significant difference in the serum levels of IGFBP-3 in any of the treatment cycle days.

CONCLUSIONS: In p-FET cycles with transfer of a single, euploid, high quality embryo, IGF-1 serum levels on day of progesterone start and CD28 are significantly higher in patients who subsequently had a pregnancy loss compared to those who had a live birth. This is in contrast to the findings of prior studies in n-FET.

Reference: None.

SUPPORT: None.

REPRODUCTIVE BIOLOGY - BASIC

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UPEREGULATION OF THE LONG NON-CODING RNA TUG1 INHIBITS GRANULOSA CELL APOPTOSIS AND AUTOPHAGY IN POLYCYSTIC OVARY SYNDROME BY REGULATING ERK/MAPK PATHWAY. Ying Li, M.D., Shi-ling Chen, Ph.D., Nanfang Hospital, Southern Medical University, Guangzhou, AP, China; Center for Reproductive Medicine, Department of Gynecology and Obstetrics, Nanfang Hospital, Southern Medical University, Guangzhou, China.

OBJECTIVE: Polycystic ovary syndrome (PCOS) is the most common cause of anovulatory infertility in women of reproductive age, and its etiology remains poorly understood. Evidence has indicated that the increase in granulosa cell (GC) proliferation is associated with PCOS. Altered activities of long non-coding RNAs (lncRNAs) have been associated with human diseases and development. TUG1 is a long non-coding RNA whose upregulation in PCOS patient and GC tumor-derived cell line, KGN, to investigate the role of TUG1 and its molecular mechanism in cell apoptosis and autophagy.

MATERIALS AND METHODS: GCs were collected from women with or without PCOS undergoing IVF or ICSI treatment. The PCOS diagnosis was based on the Rotterdam revised criteria, and control patients were limited to male factor or tubal disease and had a normal ovarian reserve. Quantitative real-time PCR was used to measure the differential expression levels of TUG1 between PCOS patients and controls. The receiver operating characteristic (ROC) curve was drawn to evaluate the diagnostic values of TUG1 in PCOS. In the KGN cell line, TUG1 was knocked down with locked nucleic acid GapmeRs. Cell counting kit-8 assays, ethynyl-2-deoxyuridine assays and flow cytometry were used to study the role of TUG1 in cell proliferation and apoptosis, and western blotting was performed to detect the potential underling mechanism.

RESULTS: We first found that TUG1 IncRNA expression levels in GCs from 58 PCOS patients and 58 controls. Also, TUG1 was knocked down in a human GC tumor-derived cell line, KGN, to investigate the role of TUG1 and its molecular mechanism in cell apoptosis and autophagy.

CONCLUSIONS: Our study first reported that the expression of TUG1 was significantly upregulated in PCOS GCs and was associated with the antral follicle count (R = 0.264, P < 0.01 versus control). The ROC curves illustrated strong separation between all the PCOS patients and the control group (AUC: 0.627; 95% CI: 0.526–0.728; P = 0.017). TUG1 was primarily localized in the nuclei of GCs. TUG1 knockdown in KGN cells inhibited cell proliferation and promoted cell apoptosis. In addition, TUG1 knockdown induced an increase in the protein levels of bax, bak, cleaved caspase-3, caspase-9, cleaved caspase-9, LC3B and phosphorylated ERK (p-ERK), and a decrease in the protein levels of bcl-2 and p62. Furthermore, inhibition of the ERK/MAPK pathway with U0126, the upregulation of p-ERK, bak, cleaved caspase-3, caspase-9, cleaved caspase-9, LC3B, and the downregulation of bcl-2 and p62 by the knockdown of TUG1 were all attenuated. Therefore, downregulation of TUG1 may promote cell apoptosis and autophagy by activation of the ERK/MAPK pathway.

CONCLUSIONS: Our study first reported that the expression of TUG1 was significantly higher in the PCOS group than that in the control group. TUG1 may inhibit cell apoptosis and autophagy in GCs through inhibition of the ERK/MAPK pathway and contribute to excess antral follicles.
TUG1 has potential diagnostic value in PCOS. Therefore, analysis of TUG1 and its molecular mechanisms of action provide new insights into the pathogenesis of PCOS.

SUPPORT: This work was supported by the National Natural Science Foundation of China (grant No. 81671524).

THE IMPACT OF BOTULINUM TOXIN A (BOTA) TREATMENT ON ENDOMETRIAL BLOOD FLOW. Yoon-Jung Kang, Ph.D., Sooyeim Kim, MD, Siwon Lee, MD, Hwag Kwon, MD, Ph.D., Jung-Jae Ko, Ph.D., Kyung-A. Lee, Ph.D., Hwa Seon Koo, MD. CHA University, Seongnam, Korea, Republic of (South); CHA Bundang Medical center, Seongnam, Korea, Republic of (South); Department of obstetrics and gynecology, Mound Sinai Medical Center, Miami Beach, FL; Fertility Center, Seongnam-si, Gyeonggi-do, Korea, Republic of (South).

OBJECTIVE: Most embryos produced in vitro fail to produce live offspring after transfer. There is a dearth of research activity addressing this problem despite the significant population of women suffering repeated failure of implantation after transfer of high-quality embryos. We hypothesize that a proportion of these failures arises due to failure of construction of functional endometrium with the proficient blood flow. We have investigated the impact of treatment with Botulinum toxin A (BoTA), which is widely used in the field of plastic and reconstructive surgery with the specific purpose of enhancement in wound healing, to induce endometrial angiogenesis to improve the endometrial blood flow and increase the vessel formation at the site of uterine cavity.

DESIGN: In vitro assessment of impact of BoTA treatment on endometrial epithelial and stromal cells using various types of cell-based assay. In vivo effect of intratraline injection of BoTA on endometrial angiogenesis by measuring CD31 expression.

MATERIALS AND METHODS: I in vitro: BoTA (0.5, 2, 10 IU/ml) was exposed to human endometrial epithelial carcinoma (Ishikawa) cells and stromal (CRL4003) cells in culture condition for 24h and 72h. Proliferation and migration of the 2 cell types were observed in response to BoTA treatment. Quantitative RT-PCR was used to quantify the expression levels of HIF1α and VEGFα, well-known surrogates of angiogenic effects. Data were normalized to β-actin mRNA and analyzed using the ordinary one-way ANOVA with Tukey’s multiple comparisons.

II in vivo: BoTA was injected to the intratraline cavity of female mice and uterine tissues were harvested at day 3 and 8. Changes in endometrial histology and CD31 immunoreactivity in response to BoTA treatment were examined to assess the levels of endometrial angiogenesis.

RESULTS: BoTA treatment enhances the capacity of proliferation of wound healing of both endometrial epithelial and stromal cells. QRT-PCR results revealed that soluble BoTA treatment induced integrin β3 (~3 fold) and IL-8 (~2 fold) mRNA in both endometrial epithelial (Ishikawa cells) and stromal cells (CRL4003). The expression levels of HIF1α (~1.5 fold, p < 0.001) and VEGFα (~4 fold, p < 0.001) were significantly increased in BoTA-treated Ishikawa cell compared to untreated group. In CRL4003 cells, Vimentin (~1.5 fold, p < 0.001) and IL-6 (~2.5 fold, p < 0.001) were significantly higher in groups with BoTA treatment compared to control group. Of note, little impact was observed in 10 IU BoTA-treated cells and no toxic effect was induced by BoTA treatment. Significantly, intratraline injection of BoTA induced higher expression of CD31 in uterine tissues compared to saline-treated group displaying higher numbers of blood vessel formation near uterine cavity.

CONCLUSIONS: Our findings indicate that BoTA treatment has a beneficial effect on reconstruction of functional endometrium prior to embryo implantation by increasing endometrial blood flow near the uterine cavity suggesting BoTA treatment as a potential therapeutic strategy for in vitro fertilization-embryo transfer (IVF-ET) cycles.
OBJECTIVE: Although organ-on-a-chip platforms to reproduce physiological functions have been developed in a variety of tissues, there have been only a few reports on ovary-on-a-chip platforms. The human ovarian follicle is the functional unit of an ovary which consists of granulosa and theca cells interacting in an intimate relationship to produce reproductive hormones such as estradiol and progesterone. The aim of this study was to develop a dynamic microfluidic, ovary-on-a-chip platform comprising of multilayered engineered follicles that could demonstrate ovarian endocrine function in vitro.

DESIGN: In vitro animal study.

MATERIALS AND METHODS: Granulosa and theca cells were isolated from the ovaries of 3-5 week old rats. After aggregation of cells into a spheroid shape, the engineered follicles were placed in a PDMS platform for structural support and dynamic microfluidics was constructed in a three-dimensional network of gelatin hydrogels fabricated with thermo-responsive sacrificial poly(N-isopropylacrylamide) microfibers. Two types of engineered follicles were crafted through forced aggregation of theca and granulosa cells; Bi-layered follicle with inner granulosa cells surrounded by outer theca cells (BF), and tri-layered follicle with a 5% matrigel basal membrane between the two cell layers (TF). Three dimensional static and dynamic cultures were observed for 30 days. The dynamic culture medium was continuously perfused at a flow rate of 7µL/min. Hormone secretion peaked at day 21 and remained elevated longer for dynamic TF without decrease as opposed to the dynamic BF which tapered off starting on day 15. The same was true for progesterone production. Progesterone secretion peaked at day 21 and remained elevated longer for dynamic TF compared to the dynamic BF. Hormone production, both 17β-estradiol and progesterone, remained uniformly stagnant without increasing during static culture and significantly lower compared to that of the dynamic culture. The dynamic TF produced 17β-estradiol for longer than that of the static culture up to the observed 30 days. Circularity was assessed to determine the effect of morphological factors on hormone secretion. F-actin staining to assess the overall shape and structure of the cells and live/dead assay to assess the cell viability were performed.

RESULTS: The structure and viability of engineered follicles were maintained for both the static and dynamic cultures up to the observed 30 days. The circularity of TF was maintained better than that of BF in both static and dynamic culture. The dynamic TF produced 17β-estradiol for longer without decrease as opposed to the dynamic BF which tapered off starting from day 15. The same was true for progesterone production. Progesterone secretion peaked at day 21 and remained elevated longer for dynamic TF compared to the dynamic BF. Hormone production, both 17β-estradiol and progesterone, remained uniformly stagnant without increasing during static culture and significantly lower compared to that of the dynamic culture. Statistically significant differences in testosterone levels were not observed among all static and dynamic cultures.

CONCLUSIONS: This microfluidic ovary-on-a-chip platform using engineered follicles with a matrigel basal membrane yielded better hormone secretion results. This platform may provide an opportunity to research ovarian physiology and to establish a novel ovary-on-a-chip platform comprising of multilayered engineered follicles that could demonstrate ovarian endocrine function in vitro.

THE IMPACT OF MULTIPLE-DOSE PACLITAXEL ON FERTILITY IN MICE AND THE PROTECTIVE EFFECT OF GONADOTROPIN REleasing HORMONE-AGONIST. Mengge Cui, Master Department of gynecological oncology, Tongji Hospital, Wuhan, China.

OBJECTIVE: Chemotherapeutic agents have numerous side effects. However, when used as paclitaxel, it can impair gamete quality in vitro.

MATERIALS AND METHODS: 1. Seven-week-old female ICR mice 2. 50 mg/kg paclitaxel (10 mg/kg paclitaxel 1 day before or an equal volume of vehicle was given intraperitoneally to 7-week-old female ICR mice. These mice were given 1 mg/kg GnRHa every day or normal saline for one estrous cycle before, during and another estrous cycle after chemotherapy. On the 1st, 6th, 11th or 16th day after the multiple-dose paclitaxel, the mice were managed in several ways: follicle counting (n=5/group/time point), acquisition of oocytes (n=5/group/time point) and immunofluorescence.

RESULTS: The follicle counting showed that paclitaxel only destroyed antral follicles for 2 estrous cycles after chemotherapies and induced increasing atretic follicles without affecting follicles in other stages. Add GnRHa to paclitaxel significantly reduced the amount of atretic follicles (30.60±5.50 versus 63.80±4.00, P < 0.05). Moreover, the ovarian stimulation was also performed to determine the duration of the gonadotoxicity after multiple-dose paclitaxel. The acquisition of MII oocytes in paclitaxel-only group was extremely less on the 1st and 6th day after the last dose of the treatment(D1: 1.00±0.00 versus 30.40±5.27, P < 0.01; D6: 17.20±4.25 versus 31.33±4.67, P < 0.05). Comparison to the control, mice, with the protection of GnRHa, ovulated even more MII oocytes on the 6th day after chemotherapies (46.80±3.44 versus 31.33±4.67, P < 0.05). And analyzed using a qPCR array. Isolated follicles were cultured with LMW-HA for 12 days. Follicle survival, growth, morphology, estradiol production and markers of gamete quality were assessed using brightfield microscopy.

RESULTS: Primary ovarian stromal cells treated with both concentrations of LMW-HA exhibited different expression of pro-inflammatory genes. Most notably, the coxin receptor Ccr3 (4.07 and 3.57-fold change following 10 µg/mL or 100 µg/mL treatment, respectively) and a suite of Ccr3-related, eosinophil activation genes (p = 0.044) were significantly regulated by LMW-HA. Interestingly, these findings were consistent with an age-dependent increase in ovarian stromal expression of Ccr3, a major CCR3 ligand (1.86-fold change, p = 0.0002). In follicle cultures, LMW-HA treatment did not affect follicle survival, growth, or morphology but the 100 µg/mL condition did significantly reduce estradiol production (p = 0.0098). With respect to gamete quality, follicles grown in 10 µg/mL LMW-HA produced a higher proportion of morphologically abnormal gametes relative to controls (50.7% vs. 17.1%, p = 0.0035). Strikingly, only 48.1% of morphologically normal gametes reached a mature metaphase-II (MI) stage (versus 90.0% of control normal gametes, p = 0.0213) and MII eggs had significantly smaller diameters (p = 0.0013). The 100 µg/mL LMW-HA produced more severely impaired gamete morphology, as 97.4% of gametes were abnormal (vs. 8.8% of controls, p < 0.0001). This was primarily due to premature oocyte meiosis resumption by day 10-12 of culture, ultimately leading to in vitro aging of the resulting MII eggs (p = 0.026).

CONCLUSIONS: Our data demonstrate that bioactive LMW-HA fragments may contribute to reproductive aging by driving an inflammatory stroma and impair gamete quality, while also releasing pro-inflammatory cytokine networks that may contribute to reproductive aging by driving an inflammatory stroma and impair gamete quality.
up to 2 estrous cycles after the last dose, the quantity of MII oocytes in all groups showed no statistical difference. Meanwhile, the morphology of oocytes was observed by immunofluorescence.

CONCLUSIONS: These results indicated that paclitaxel mainly impacted antral follicles and the gonadotoxicity lasted no more than 2 estrous cycles of mice. The protective effect of GnRHa on ovaries was significant. This study provides a laboratory evidence for the impact of paclitaxel and the effectiveness of GnRHa in clinical practice.

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ESTABLISHMENT OF DECREASED OVARIAN RESERVE MOUSE MODEL BY CONSECUTIVE SUPEROVULATION. Xiaowei Nie, M.D. Daorong Hou, Ph.D. Embryologist, NANJING, China.

OBJECTIVE: This study investigated the effect of consecutive superovulation on the ovaries and established a decreased ovarian reserve (DOR) model in mice.

DESIGN: One hundred fifty C57BL/6 female mice aged 7–8 weeks and thirty C57BL/6 female mice aged 44 weeks were used. The mouse POF model was induced by 5-15 consecutive superovulation treatments with pregnant mare serum gonadotropin (PMSG), human chorionic gonadotropin (HCG) and prostaglandin F2α (PGF2α). Normal adult mice were compared with mice displaying natural ovarian aging.

MATERIALS AND METHODS: The following serum biochemical parameters were measured: including follicle-stimulating hormone (FSH), luteinizing hormone (LH), progesterone (P), estradiol (E2), inhibit B (INH B), malondialdehyde (MDA), total superoxide dismutase (SOD) and glutathione peroxidase (GSHP) levels. Follicles were counted using H&E staining. Levels of 8-hydroxyguanosine (8-OHdG), 4-hydroxynonenal (4-HNE), Nitrotyrosine (NTY), anti-Mullerian hormone (AMH) and CDKN2A/p16 (p16) were detected using immunohistochemical staining. Reactive oxygen species (ROS) levels were measured using dihydroethidium (DHE) staining. Cell apoptosis was detected using an in situ TUNEL fluorescence staining assay. Levels of proteins involved in ROS-related pathways and the p16 protein were detected using Western blotting. Sod1, Sod2 and Sod3 mRNA levels were detected using quantitative polymerase chain reaction (Q-PCR). Oocyte quality was evaluated using in vitro fertilization (IVF) and zygote culture.

RESULTS: Consecutive superovulation groups presented lower P, E2, SOD, GSH-Px and INH B levels, significantly higher FSH, LH, MDA and ROS levels, and significantly fewer primordial follicles compared with the control group. Consecutive superovulation groups presented significantly increased levels of Sod2, 8-OHdG, 4-HNE, NTY, significantly increased levels of the SIRT1 and FOXO1 proteins, significantly increased levels of the senescence-associated protein p16, as well as decreased AMH, Sod1 and Sod3 levels and increased granulosa cell apoptosis compared with the control group.

CONCLUSIONS: Consecutive superovulation significantly decreased ovarian function and oocyte quality and increased oxidative stress and apoptosis in the ovary via a mechanism involving the p16 and SIRT1/FOXO1 signaling pathways. These findings suggest that consecutive superovulation may be used to establish a mouse model of ovarian aging.


SUPPORT: This work was supported by the National Natural Science Foundation of China (81774357, 81403426, 81674012).
configuration, which has been hypothesized to be critical for the ordered exodus of the paternal genome following fertilization. This model describes centromeres clustering in the center (chromocenter), with p- and q-chromosome arms stretching toward the nuclear periphery. However, we recently proposed a refined segmental model of sperm chromatin organization; to further investigate these findings and their relationship to the hairpin-loop model we examined the 3D configurations of chromatids in human sperm nuclei.

**CONCLUSIONS:** We report reproducible nonrandom hairpin-loop organization of chromatids that partially supports the proposed hairpin-loop model of organization. However, our findings do not support the existence of a centralized chromocenter(s) with 68.3% of investigated centromeres being more distally localized within the sperm nucleus than one (30.5%) or both (37.8%) of their respective chromosome arms.

**RESULTS:** Distinct reproducible chromosome-specific patterns of organization emerge. All chromatids were found to possess nonrandom radial organization (p < 0.05), with the exception of the chromosome 12 centromere. Chromosome arms were found to form discrete hairpin-loop configurations. However, different chromosomes were observed to preferentially form narrower or wider hairpin loops that were largely reproducible between the five subjects enrolled. We did not find evidence to support the existence of a centralized chromocenter(s) with 68.3% of investigated centromeres being more distally localized within the sperm nucleus than one (30.5%) or both (37.8%) of their respective chromosome arms.

**OBJECTIVE:** To examine the effect of maternal age on mitochondrial function and spindle formation in maturing oocytes, and to investigate whether in vitro treatment with mitochondria-targeted antioxidants (AOs) can reverse the impact of aging on oocyte quality.

**MATERIALS AND METHODS:** Cumulus-free oocytes were cultured in vitro for 14 h in M2 or M16 medium, or in the same medium containing H2O2 (25 μM) with or without AOs (experiment 1). In a separate experiment, oocytes from young and old mice were matured in vitro in the presence and absence of mitochondria-targeted AOs. At the end of the culture period mitochondria membrane potential (MMP) was measured by ratioing the fluorescence intensities of Tetramethylrhodamine methyl ester (TMRM), and MitoTracker green (MTG). Oocytes were fixed and labeled with the microtubules and DNA. ImageJ software was used to analyse spindle dimensions and chromosome alignment. Student's t-test was then used to compare between groups and a P value below 0.05 were considered statistically significant.

**RESULTS:** We find oxidative stress causes a decrease in MMP (P < 0.001) and an increase in the frequency of disrupted spindles and misaligned chromatids (P < 0.001). Co-treatment with H2O2 and AOs reversed the MMP and spindle disruption to control levels. Oocytes from old mice matured to the MII stage in vitro also showed decreased MMP and disrupted spindles. These age-related phenotypes were completely reversed by incorporating antioxidants in the culture media. Furthermore, for the first time we have performed live-cell ratiometric imaging of TMRM and MTG for the full time-course of maturation in young and old eggs. This study reveals that MMP increases significantly during IVM in young oocytes (P < 0.001) but not in old oocytes.

**CONCLUSIONS:** Oxidative stress and maternal age are both associated with decreased MMP and spindle disruption and chromosome misalignment. Time-lapse imaging suggests that mitochondria in young oocytes undergo an adaptive increase in MMP during IVM and that this capacity is lost in mitochondria of old oocytes. The compromised mitochondrial function in maternal aging and the ability of the mitochondria-targeted AOs treatment to mitigate against aging and oxidative stress-induced mitochondrial and spindle disruption, suggests that mitochondria may be a useful therapeutic target for improving oocyte quality.

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**P-357 Tuesday, October 15, 2019 9:30 AM**

**THE UBIQUINONE MITOCHONDRIA-TARGETED ANTIOXIDANT AMENDS THE EFFECT OF MATERNAL AGE ON OOCYTE SPINDLE FORMATION AND DEVELOPMENTAL COMPETENCE.**

**OBJECTIVE:** To examine the effect of maternal age on mitochondrial function and spindle formation in maturing oocytes, and to investigate whether in vitro treatment with mitochondria-targeted antioxidants (AOs) can reverse the impact of aging on oocyte quality.

**MATERIALS AND METHODS:** Cumulus-free oocytes were cultured in vitro for 14 h in M2 or M16 medium, or in the same medium containing H2O2 (25 μM) with or without AOs (experiment 1). In a separate experiment, oocytes from young and old mice were matured in vitro in the presence and absence of mitochondria-targeted AOs. At the end of the culture period mitochondria membrane potential (MMP) was measured by ratioing the fluorescence intensities of Tetramethylrhodamine methyl ester (TMRM), and MitoTracker green (MTG). Oocytes were fixed and labeled with the microtubules and DNA. ImageJ software was used to analyse spindle dimensions and chromosome alignment. Student's t-test was then used to compare between groups and a P value below 0.05 were considered statistically significant.

**RESULTS:** We find oxidative stress causes a decrease in MMP (P < 0.001) and an increase in the frequency of disrupted spindles and misaligned chromatids (P < 0.001). Co-treatment with H2O2 and AOs reversed the MMP and spindle disruption to control levels. Oocytes from old mice matured to the MII stage in vitro also showed decreased MMP and disrupted spindles. These age-related phenotypes were completely reversed by incorporating antioxidants in the culture media. Furthermore, for the first time we have performed live-cell ratiometric imaging of TMRM and MTG for the full time-course of maturation in young and old eggs. This study reveals that MMP increases significantly during IVM in young oocytes (P < 0.001) but not in old oocytes.

**CONCLUSIONS:** Oxidative stress and maternal age are both associated with decreased MMP and spindle disruption and chromosome misalignment. Time-lapse imaging suggests that mitochondria in young oocytes undergo an adaptive increase in MMP during IVM and that this capacity is lost in mitochondria of old oocytes. The compromised mitochondrial function in maternal aging and the ability of the mitochondria-targeted AOs treatment to mitigate against aging and oxidative stress-induced mitochondrial and spindle disruption, suggests that mitochondria may be a useful therapeutic target for improving oocyte quality.

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**P-358 Tuesday, October 15, 2019 6:30 AM**

**LOSS OF MITOCHONDRIAL FUSION PROTEIN MFN2 RESULTS IN A REPRODUCTION AGING PHENOTYPE WITH TELOMERE SHORTENING, REDUCED FERTILITY, AND ACCELERATED DEPLETION OF FOLLICULAR POOL.**

**OBJECTIVE:** Mitochondria change their shape through fusion and fission in order to adapt to their metabolic milieu and respond to environmental stress. Mitofusin-2 (MFN2) is a key regulatory protein in this process, mediating mitochondrial fusion and interaction with endoplasmic reticulum. The aim of the present study was to determine the role of MFN2 in female reproductive competence using a mouse model with oocyte-specific deletion of Mfn2.

**MATERIALS AND METHODS:** To evaluate fertility, mature (8-weeks-old) females were mated with adult WT males as indicated. RNA sequencing analysis was performed using pooled Mfn2+/+ and WT GV oocytes and secondary follicle enclosed oocytes (SFOs) (n=3 mice per group). Protein and mRNA expression were assessed using immunofluorescence and qRT-PCR, respectively. Telomere length was assessed using quantitative real-time PCR.

**RESULTS:** Mature female Mfn2−/− mice exhibited reduced fertility compared to WT females (5.21 ± 0.39 vs 7.63 ± 0.31 pups per litter, p < 0.001). They had decreased number of antral follicles (9.33 ± 2.33 vs 30.67 ± 1.67, P < 0.001), and generated a significantly lower number of GV oocytes (13.63 ± 2.03 vs 29.33 ± 0.67, P < 0.001). MII oocytes (10.58 ± 21.33 ± 1.20, P < 0.01), 2-cell embryos (8 ± 5.8 vs 20.33 ± 8.88, P < 0.001) and blastocysts (6.33 ± 0.88 vs 13 ± 0.58, P < 0.001). RNA-seq analysis revealed 363 and 1041 genes that were differentially regulated in young and old MFN2−/− ovaries (P < 0.01). Pro-apoptotic protein caspase 6 and COX5B expression was significantly increased in Mfn2−/− SFOs. Telomere length in Mfn2−/− GV oocytes was shorter compared to WT with decreased expression of telomerase protective protein TRF1. When we assessed changes in follicular pool across mouse reproductive lifespan, we found Mfn2−/− ovaries to have significantly lower number of...
primordial, secondary, and antral follicles at 6 months (p < 0.05), and dramatically decreased number of follicles at all stages at 12 months (p < 0.0001), compared to WT.

CONCLUSIONS: Targeted deletion of Mfn2 in oocytes results in female subfertility associated with impaired oocyte maturation and follicle development. Oocytes lacking MFN2 show shortened telomeres and increased apoptosis, resulting in compromised oocyte quality and accelerated follicle depletion, consistent with a reproductive aging phenotype.

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THE ROLE OF AKAP13 INHIBITORS AND ACTIVATORS AND MATRIX STIFFNESS IN HIPPO PATHWAY SIGNALING FOR PRIMORDIAL FOLLICLE ACTIVATION. Jacqueline Yano Maher, MD, MA, Md, Sorifual Islam, PhD, Szu-Chi Su, MS, James Segars, MD. Johns Hopkins University, School of Medicine, Baltimore, MD.

OBJECTIVE: Signaling pathways of primordial follicle activation are incompletely understood. Disruption of Hippo pathway signaling promotes gonadotropin independent follicle activation in granulosa cells. F-actin formation increases primordial follicle activation through Hippo signaling inhibition, and A-Kinase Anchoring Protein-13 (AKAP13) possesses a Rho- guanine exchange region (GERF) that promotes actin nucleation. Our objective was to test whether pharmacologic manipulation with AKAP13 inhibitor (A13) or AKAP13 activator (A02) affected Hippo signaling in a human granulosa cell line. Second, we tested whether activation of RhoA by manipulation of substrate stiffness affected Hippo signaling.

MATERIALS AND METHODS: Translational research using COV434 cells, derived from a human granulosa cell tumor.

CONCLUSIONS: Targeted deletion of AKAP13 inhibitors and activators and matrix stiffness in Hippo pathway signaling for primordial follicle activation is an important mechanism.

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CULTURE MEDIA WITH AND WITHOUT EXPOSURE TO HUMAN PREIMPLANTATION EMBRYOS CONTAIN EXTRACELLULAR VESICLES OF COMPARELABLE SIZE. Diego Marin, M.S., Emre Sevi, M.D., Richard Thomas Scott, Jr., MD IVI-RMA New Jersey, Basking Ridge, NJ.

OBJECTIVE: Extracellular Vesicles (EV) are cell-derived particles with a lipid bilayer membrane ranging in size from 30 to more than 1000 nm in diameter. EVs carry a variety of biomolecules and play pivotal roles in intercellular communication. It has been evidenced that EVs secreted by preimplantation embryos play a vital role in the embryo-endometrium crosstalk during implantation and could therefore become potential biomarkers for embryonic reproductive potential. This study aimed to develop and optimize an EV isolation protocol for spent culture media (SCM) of human IVF preimplantation embryos so as to characterize the embryonic EV population and their potential as reproductive biomarkers.

DESIGN: Experimental study.

MATERIALS AND METHODS: SCM microdrops (50 mL) were collected following 48 hours of embryo culture from day 3 to day 5 of development. Microdrops incubated under the same conditions in the IVF lab without embryo exposure were used as negative controls. Two methods were tested for EV isolation. 1) Size exclusion chromatography (SEC): 70 SCM microdrops were pooled for each sample (2 samples exposed to ~188 embryos each) and concentrated to ~180 mL using centrifugal filters prior to SEC (Izone). After SEC, 21 fractions of 200 mL were obtained from each sample. Fractions 3, 4, and 5, the most enriched in EVs, were further pooled and re-concentrated to ~180 mL. 2) Differential centrifugation: 30 SCM microdrops were pooled for each sample (3 samples exposed to ~100 embryos each). The 3 pooled SCM samples and other 3 non-pooled single embryo culture microdrops were subjected to three rounds of centrifugation at different g forces before a final 90 minutes ultracentrifugation at 100,000 g. Finally, transmission electron microscopy imaging was performed in all processed samples obtained using the 2 methods in order to visualize and analyze EV. Negative controls were processed similarly.

RESULTS: Using both SEC and differential centrifugation, spherical and highly electron-dense particles ranging from 22 to 159 nm were observed in both embryo SCM and embryo unexposed media samples. Size of nanoparticles isolated from pooled SEC fractions (3, 4 and 5) were comparable between SCM and negative control (Size: SCM = 57.05 ± 20.06 nm, NC= 44.47 ± 14.23 nm). In addition, differential centrifugation allowed for isolation and verification of EVs from single embryo culture microdrops, as well as from media unexposed to embryos.

CONCLUSIONS: SEC and differential centrifugation successfully isolated EVs from pooled and single embryo culture samples of human embryo SCM. Furthermore, presence of EVs was also evidenced in culture medium microdrops unexposed to embryos, which presented a size distribution comparable to the ones found in embryo SCM. These findings urge to conduct further research in order to shed light on the origin and possible effects of non-embryonic EVs in culture media, as well as the role of embryo-derived EVs during implantation and their potential as biomarkers.

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EFFECTIVENESS OF PLATELET RICH PLASMA ON PREVENTION OF CHLAMYDIA INDUCED HYDROSALPINX IN A MURINE MODEL. Sheena M. Rippentrop, MD, a Zhi Hao, PhD, b Chet Schwab, MD, c Randal D. Robinson, MD, d Guangming Zhong, MD, PhD, e University of Texas Health Science Center San Antonio, San Antonio, TX, c Chinese Society for Immunology, San Antonio, TX, a UT Health San Antonio, San Antonio, TX, e Univ of Texas Health Science Center San Antonio, San Antonio, TX.

OBJECTIVE: To test whether oviduct delivery of platelet rich plasma (PRP) can attenuate chlamydia induction of hydrosalpinx in a mouse model

DESIGN: Intravaginal instillation of CBA/J mice with C. muridarum can induce almost 100% bilateral hydrosalpinx, which was used as a hydrosalpinx induction model for comparing the effect of F platelet-rich hydrosalpinx development.

MATERIALS AND METHODS: A total of 16 CBA/J mice were infected intravaginally with a standard dose of C. muridarum, then PRP was instilled into one oviduct and a sham instillation with phosphate buffer solution was performed on the contralateral oviduct at the same time. Oviduct inflammation was induced in 4 groups of mice occurring on day 7 (D7), day 7 plus day 21 (D7/21), day 21 (D21), or day 14 plus day 21 plus day 28 (D14/21/28) after infection. Vaginal and rectal shedding were monitored in all mice. Mice were then sacrificed, and pathologic evaluation performed. Statistical analysis was performed using the Mann-Whitney test.

RESULTS: Oviduct instillation of PRP on day 21 with or without additional instillations was associated with a 41.5% reduction in degree of hydrosalpinx compared to sham instillation with an average hydrosalpinx score of
1.62 and 2.77 respectively (p=0.15). Instillation of PRP on D14/21/28 was associated with a 43% reduction of hydrosalpinx, average score 1.14 and 2 for sham (p=0.56). Oviduct installation of PRP on D21 alone was associated with a 50% reduction in degree of hydrosalpinx compared to sham instillation with an average score of 2 and 4 respectively. The average grade of inflammation on histopathology was 1.57 with any day 21 instillation vs 1.77 sham instillation (p=0.54). PRP instillation on D7 was not associated with reduction in degree of hydrosalpinx or grade of inflammatory infiltrate. No differences were observed in vaginal or rectal shedding of C. muridarum amongst the four groups.

CONCLUSIONS: Our results suggest that oviduct instillation of PRP was associated with a reduction in the degree of C. muridarum induced hydrosalpinx in CBA/J mice; however, this reduction was not statistically significant.

References:

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THE REGULATION OF ENDOPLASMIC RETICULUM STRESS IMPROVES THE DEVELOPMENT OF POST-OVULATORY AGED MOUSE OOCYTES. Isao Takehara, M.D., a Hideki Igarashi, M.D., Ph.D., b Kyoko Takahashi, M.D., a Gyozo Takahashi, M.D., a Michi Nishi, M.D., a Koki Matsuo, M.D., b Jun Kawagoe, M.D., Ph.D., a Satoru Nagase, M.D., Ph.D. a Yamagata University, Yamagata, Japan; b Kyono ART Clinic Takanawa, Tokyo, Japan.

OBJECTIVE: Endoplasmic reticulum stress (ER stress) is closely associated with several ageing-related diseases, such as neurodegenerative disorders, diabetes mellitus, arteriosclerosis and cancer. Similarly, ER stress in oocytes and preimplantation embryos may be involved in oocyte aging and affect embryo development. The aim of this study is to clarify the relationship of ER stress with the quality of aged oocytes and whether the regulation of ER stress improves the embryo development of aged oocytes.

DESIGN: Animal model study.

MATERIALS AND METHODS: Animals were treated in accordance with the NIH Guide for the Care and Use of Laboratory Animals, as approved by the Animal Care and Use Committee of Yamagata University. In this study, mouse oocytes were obtained from the oviduct at 14 hours and 20 hours post-6CG were designated as "fresh" and "aged" oocytes, respectively. We compared embryo development and GRP78 expression (a chaperone protein increased by ER stress) in fresh oocytes, aged oocytes and preimplantation embryos. To evaluate the regulation of ER stress on embryo development, mouse oocytes released from the oviduct at 14 hours and 20 hours post-hCG were designated as "fresh" and "aged" oocytes, respectively. Mouse oocytes were treated with salubrinal, a specific inhibitor of PERK pathway on ER stress, for 1 hour before IVF. Embryo development, expression of GRP78 and phospho-eIF2a levels (phosphorylated via the PERK pathway) and the rate of dead blastomeres in blastocysts were compared between aged oocytes and salubrinal-treated aged oocytes.

RESULTS: Aged oocytes showed lower fertilization rate and poor embryo development like ER stress-induced oocytes. Although GRP78 expression was significantly higher in aged oocytes than in fresh oocytes, salubrinal significantly lowered GRP78 and phospho-eIF2a levels and improved embryo development via decrease of dead blastomeres. Salubrinal treatment had no adverse effect on pups’ birth weight and the presence of congenital malformation, as well as no significant effect on the rate of live births. Pregnancy rate, however, was significantly higher in the salubrinal-treated group than in the aged group.

CONCLUSIONS: Present results show that ER stress contributed to oocyte aging and suppression of the ER-related PERK pathway by salubrinal significantly improved embryo development in post-ovulatory aged oocytes. Hence, regulation of ER stress might represent a promising therapeutic strategy to overcome poor oocyte quality.

P-364 Tuesday, October 15, 2019 6:30 AM
ABNORMAL PHOTOPERIOD EXPOSURE BEFORE PREGNANCY AFFECTS OFFSPRING LIPID METABOLISM IN SD RATS. Yanjun Yang, B.S.Med, Dan Zhang, MD, PhD, Juan Liu, Doctor, Mixue Tu, Doctor. Women’s Hospital, Zhejiang University School of Medicine, Hangzhou, China.

OBJECTIVE: Exposure to constant light or shift work impairs endogenous circadian rhythm, which can lead to metabolic diseases. Previous animal and human studies demonstrated that circadian rhythm disruption during pregnancy affects the long-term health of their progeny. But circadian rhythm disruption before pregnancy would have any effect on their offspring is not thoroughly studied. This study is designed to investigate the effects from maternal circadian disruption.

DESIGN: Randomized animal study.

MATERIALS AND METHODS: Eighteen 6-8 week-old adult female SD rats were exposed to abnormal photoperiod (18 h:16 h light/dark cycle) and control photoperiod (12 h:12 h light/dark cycle) for 4 months. Thereafter, rats were housed in control photoperiod, mated, gestated and reared their offspring. At the age of 20 weeks, offspring were sacrificed every 8 hours. Tissue and plasma were harvested.Data were analyzed with t-tests.

RESULTS: Exposure to abnormal photoperiod results in prolonged and irregular estrous cycles with pregnancy rate decreased (p<0.05). Their ovary weight decreased(p<0.01), less corpus luteum and more expanded follicles in ovary H&E stain slides. The offspring from abnormal photoperiod group not only had significantly body weight gain (male +43.1%, p<0.01; female +7.8%, p<0.05) but also higher body fat rate (female +10.1%, p<0.01). The circadian genes expression pattern in the liver were not consistent with control group. Serum LDL-c and HDL-c of female offspring elevated (p<0.05). Serum cholesterol and HDL-c of male offspring decreased (p<0.05).

CONCLUSIONS: Abnormal light-dark cycle induced maternal circadian rhythm disruption have an effect on offspring lipid metabolism disorder in rats. As shift work, artificial night lighting, jet lag are becoming increasingly prevalent. Our finding may have the implications for people to conceive and pay attention to offspring health.

SUPPORT: Grant support was provided by the National Key Research and Development Program of China (2019YFC1005003).

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CYTOKINE PROFILING REVEALS A UNIQUE INFLAMMING SIGNATURE IN HUMAN FOLLICULAR FLUID AND THE OVARY. Jordan H. Machlin, MS, a Seth J. Barishansky, MS, a Sharron LaChelle Manuel, MD, PhD, b Jian-Jun Wei, MD,a John Zhang, PhD,a Mary Ellen Pavone, MD, MSCI, a Francesca E. Duncan, PhD. a Northwestern University, Chicago, IL; b Northwestern University Professor of Pathology and Obstetrics and Gynecology, Chicago, IL.

OBJECTIVE: Reproductive aging in the ovary is characterized by a decrease in oocyte quality and quantity that leads to adverse reproductive outcomes such as infertility, miscarriages, and birth defects. Aging is associated with a general increase in damaging chronic inflammation termed “inflammaging.” The goal of our study was to determine how inflammaging impacts the ovary.

DESIGN: Translational.

MATERIALS AND METHODS: To examine whether inflammatory cytokines increase in the human ovary with age, we obtained human follicular fluid aspirated from the first follicle from the right or left ovary from 30 participants ranging in age from 27.7-44.8 years old undergoing oocyte retrieval. We performed cytokine antibody arrays on the follicular fluid which measured 98 unique cytokines. Cumulus cells that would have otherwise been discarded were obtained from women undergoing oocyte retrieval for
a non-cancerous diagnosis at Fertility and Reproductive Medicine (FRM) who were ≥ 18 years old and ≤ 30 kg/m². We performed immunoblot analysis on cumulus cells with a TGFβ3-specific antibody and normalized expression to the GAPDH signal. To investigate TGFβ3 expression in ovarian tissue, we generated a human ovarian Tissue Microarray (TMA) using samples from two reproductive research archives: the National Physician’s Cooperative (NPC) and the Northwestern University Reproductive Tissue Library (NU-RTL). The array contained cortical tissue samples from 60 participants in two cohorts of females: 22 months-20 years old and 39-58 years old. We performed immunohistochemistry on this array with the TGFβ3 antibody and quantified expression based on age and tissue sub-structures.

RESULTS: Of the 80 cytokines measured in the follicular fluid on the cytokine antibody array, 61 were above threshold. We plotted the cytokines by both chronologic age (years) as well as reproductive age (AMH) and found that six cytokines; IL-3, IL-7, IL-15, TGFβ1, TGFβ3, and MIP-1 showed a positive correlation with chronologic age but were negatively correlated with AMH. Thus these cytokines represent a unique inflammatory aging signature in the ovary. To validate these follicular fluid findings, we focused on TGFβ3 which is part of the transforming growth factor beta (TGFβ) family of proteins that has unique immunoregulatory properties. To validate that TGFβ3 expression increases with age, we examined two cellular compartments – the cumulus cells immediately surrounding the oocyte and the ovarian tissue microenvironment. We did not observe an age-associated increase in TGFβ3 expression in the cumulus cell samples, suggesting that the age-associated increase in this cytokine in follicular fluid was attributable to a different cellular source. Within the human ovary, TGFβ3 localized throughout the stroma, vasculature, and within follicles. Interestingly, we observed a significant age-associated increase in TGFβ3 expression in the ovary, specifically in samples enriched in stroma and vasculature.

CONCLUSIONS: Inflammaging is a hallmark of reproductive aging in human follicular fluid and ovarian-derived TGFβ3 is a central component of this signature.

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PREINCUBATION TIME CAN BE EFFECTIVE ON THE QUALITY AND FERTILIZATION POTENTIAL OF MOUSE MII OOCYTES. Fatemeh Mohammadladi, PhD, student. Zahra Zandieh, PhD, Faculty of Medicine, Iran University of Medical Sciences, Tehran, Iran (Islamic Republic of).

OBJECTIVE: It is demonstrated that non–optimal preincubation time in IVF/ICSI (in vitro fertilization/intracytoplasmic sperm injection) cycles can lead to reduction in the oocyte quality, regarding to oxidative stress condition and mitochondrial alteration, and consequently can decrease the oocyte fertilization potential. Nevertheless, there is not any explanation of standard preincubation time in ART (assisted reproductive technology) guidelines. Myo-inositol, as an antioxidant, exists naturally in the follicular fluid and is a marker of good quality in the oocytes. This study evaluated the oxidative stress condition, mitochondrial alterations and fertilization potential in mouse MII oocytes following 0, 4 and 8 hours preincubation time in the simple and myo-inositol supplemented media.

DESIGN: This was a basic experimental study that included 50 adult (6-8 weeks-old) female NMRI mice which underwent hormonal superovulation from 2018 to 2019.

MATERIALS AND METHODS: Cumulus Oocyte Complexes (COCs) which were retrieved from 6-8 weeks-old superovulated female NMRI mice were pooled and divided randomly in five experimental groups: (1) control (2) 4 hours preincubation in simple medium (3) 4 hours preincubation in 20 mmol/l of myo-inositol supplemented medium (4) 8 hours preincubation in simple medium (5) 8 hours preincubation in 20 mmol/l of myo-inositol supplemented medium. COCs in each group were denuded and intracellular Reactive Oxygen Species (ROS), glutathione (GSH), Mitochondrial Membrane Potential (MMP) and mitochondrial distribution were measured by a fluorometric assay. ATP content of oocytes also was measured using the ELISA method. Pronucleus formation was assessed for evaluation of oocytes fertilization potential.

RESULTS: Results showed that intracellular H2O2 and glutathione levels, mitochondrial distribution, mitochondrial membrane potential, ATP content, as well as fertilization rate were different between groups. Nonetheless, myo-inositol supplementation could improve levels of H2O2, glutathione, mitochondrial distribution, ATP content and fertilization rate. Unlike other variables, mitochondrial membrane potential of oocytes was not reduced after 4 hours of preincubation in either simple or supplemented medium, but 8 hours of preincubation time could decrease it significantly. Addition of myo-inositol to the medium could not ameliorate mitochondrial membrane potential in oocytes preincubated for 4 and 8 hours. While, ATP content did not decline in oocytes preincubated for 4 and 8 hours, supplementation of myo-inositol in medium could increase it in both groups.

CONCLUSIONS: Finally, the analysis addressed that 4 hours or more preincubation time can influence the oocyte quality related to alternation in H2O2, glutathione, mitochondrial integrity and mitochondrial membrane potential which ultimately leads to reduced oocyte fertilization potential. Supplementation of myo-inositol in medium improves the oocyte quality in comparison to the simple medium and saves 4 hours for preincubated oocytes.

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COLLAGEN AND HYALURONAN MATRICES UNDERGO AGERELATED CHANGES IN THE HUMAN OVARY. Sharon L. Manuel, MD, PhD, MS¹, Elena Antonova, PhD²,³, Jessica E. Hornick, PhD¹.¹Farners Amargant Riera, PhD,²,³ Jian-Jun Wei, MD,² Mary Ellen Pavone, MD, MSCL,¹ Michele T. Pritchard, PhD,¹ Francesca E. Duncan, PhD,²,³ Northwestern University, Chicago, IL;²Biological Imaging Facility Northwestern University, Evanston, IL;¹Research Associate Professor, Dept Molecular Biosciences Northwestern University, Evanston, IL;²Center for Reproductive Science, Northwestern University, Chicago, IL;¹Northwestern University Department of Pathology, Chicago, IL;²Department of Pharmacology, Toxicology, & Therapeutics, Kansas University Medical Center, Kansas City, KS.

OBJECTIVE: Female reproductive aging is characterized by a decrease in gamete number and quality, which contributes to infertility. The ovarian microenvironment in which gametes grow likely influences their development and quality, and we recently demonstrated a significant increase in age-associated fibrosis in the mouse ovarian stroma. Whether such stromal changes are conserved and occur in the human ovary is unknown. The objective of this study was to examine how collagen and hyaluronan (HA), two major extracellular matrix (ECM) components, change in the human ovary with age.

DESIGN: Translational.

MATERIALS AND METHODS: To examine age-associated collagen and HA content changes in the human ovary, we generated a tissue microarray (TMA) consisting of 1 mm human ovarian cortex cores from 60 individuals in four age cohorts, ranging in age from 1.8 – 58 years old. Sequential sections of the TMA were processed for hematoxylin & eosin (H&E) staining to assess tissue architecture, picrosirius red (PSR) staining to assess collagen I and III, and fluorescent-tagged HA binding protein (HABP) -mediated staining to assess HA levels. The PSR stained tissue was imaged by both light and polarized light microscopy, while HA was imaged using fluorescence microscopy. The percent area that was PSR or HA positive as well as the mean intensity (MI) were determined.

RESULTS: The amount of cortical collagen decreased between the 1.8 – 10-year-old cohort and the 11 – 20-year-old cohort (p = 0.0045) perhaps related to puberty onset. Collagen then increased between the 11 – 20-year-old cohort and the ≥51-year-old cohort, likely reflecting increased fibrosis (p = 0.0009). In contrast to collagen, there was an overall decrease in ovarian HA content between the young participants (1.8 – 20-years-olds) and the older participants (39 – 58-years-olds) (p < 0.0001). The ovarian cortex cores revealed considerable heterogeneity with some samples containing follicles, vasculature, and/or stroma. Therefore, we stratified our analyses by structural category. In the ≥51-year old cohort, we observed significant age-associated increased fibrosis in blood vessel-containing cores (p = 0.011 by percent area and p = 0.027 by MI) and stroma (p = 0.019 by MI) when compared to the 11 – 20-year-old cohort. Although fibrosis...
increased and overall HA levels decreased with age, there was no correlation between HA and collagen content on an individual core basis.

CONCLUSIONS: These studies demonstrate that the human ovarian cortical ECM undergoes significant changes with age, and that ovarian stromal fibrosis is a conserved mammalian aging hallmark. Cortical ovarian collagen content is high at age extremes, and likely reflects normal stromal composition during early development but age-related pathology with advanced age. HA shows an opposite pattern and decreases with advanced reproductive age. The precise interplay between the collagen and HA matrices is currently under investigation.

SUPPORT: Supported by: National Institute of Child Health and Human Development (R01HD093726).

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THE EFFECT OF AUTOPHAGY AFTER MOUSE OOCYTE ACTIVATION TEST.
Atsushi Yamamoto, MD, PhD, Naoki Yoshikawa, Bachelor of Medicine, Sae Onozuka, Bachelor of Agriculture, Akiyoshi Osaka, Bachelor of Medicine, Shin Oonota, Bachelor of Medicine, Toshiyuki Iwahata, MD, PhD, Yoshitoshi Kobori, MD, PhD, Kouhei Sugimoto, MD, PhD, Hiroshi Okada, MD, PhD, Dokkyo Medical University Saitama Medical Center, Koshigaya, Japan.

OBJECTIVE: Autophagy is a lysosome-mediated intracellular process for protein degradation and is induced in the situation of amino acid starvation and several biological stimulations to maintain the cytoplasmic homeostasis. And previous studies in the reproductive field have shown that autophagy after fertilization is essential in embryogenesis. Though in the male infertility field, there is the test named mouse-oocyte-activation test (MOAT) to check the human sperm function after fertilization, there are no reports about the relation between MOAT and autophagy induction and we check the relations.

DESIGN: Experimental Research.

MATERIALS AND METHODS: To collect MII oocytes, 8-10 weeks old female mice (C57BL/6) were superovulated. Oocytes were fertilized by in-tradition sperm in embryonic stage (ICSI) using 1 or 2 human sperm; MOAT or mouse sperm. After 5-hour incubation, embryos in parafomaldehyde and immunostained by microtubule-associated protein 1 light chain 3 alpha (LC3) which is the marker of autophagy. Then they were analyzed by fluorescence microscopy and LC3 puncta in each embryo were counted.

RESULTS: LC3 puncta were significantly detected in a human sperm injection more than in a mouse sperm injection. The number of puncta was almost the same in 1 sperm injection as in 2 sperm injections. The size of puncta was bigger in 1 sperm injection than in 2 sperm injections.

CONCLUSIONS: Autophagy was induced by xenogeneic sperm fertilization. The reason why autophagy was induced strongly in human sperm injection may be that the removal reaction of xenogeneic proteins occurs strongly, or that the volume of autophagy inducing factor is more in the human than in mice. LC3 puncta was bigger in two-sperm injection because the proteins to remove may be much more than in one-sperm injection. Though we have not check the phenomenon quantitatively and analyze the difference autophagic induction between normal and infertile man, to detect autophagic function we have to remove may be much more than in one-sperm injection. Though we have to remove may be much more than in one-sperm injection.

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FUNCTIONAL ACTIVITY OF MITOCHONDRIA IN AGED OOCYTES IS ASSOCIATED WITH CYTOSKELETON STABILITY IN MICE.
Jae Ho Lee, Ph.D., Hye Ran Lee, Ph.D., Bong Hwan Lee, Ph.D., Tae Ki Yoon, M.D., Ph.D., Sang Jin Lee, Ph.D., Yoon Hye Choi, Ph.D., Jih Yang Kim, MD, Ph.D., Hannah Kim, MD, Chanhong Park, MD, Ph.D., Soo Yeon Kim, MD, Mi Kyung Koong, MD, Ph.D., Jae Ho Lee, Ph.D., CHA Fertility Center, Seoul, Korea, Republic of (South); CHA University, Seoul, Korea, Republic of (South); CHA Fertility Center Seoul, Seoul, Korea, Republic of (South); CHA Fertility Center Gangnam Medical Center, Seoul, Korea, Republic of (South); CHA Bundang Medical Center, CHA University, CHA University, Seongnam-si, Gyeonggi-do, Korea, Republic of (South); CHA Fertility Center Gangnam Medical Center, Seoul, Korea, Republic of (South); CHA University, Seoul, Korea, Republic of (South); CHA Fertility Center Seoul Station, CHA University, Seoul, Korea, Republic of (South); CHA Fertility Center Seoul Station, Obstetrics and Gynecology, Seoul, Korea, Republic of (South); Department of Animal Biotechnology & Resources, Sahnmyook University, Seoul, Korea, Republic of (South).

OBJECTIVE: Dysfunctional mitochondria are strongly associated with oocyte quality and aging. However, cannot fully explain the decrease of mitochondrial activity in oocytes. Here, we studied dysfunctional mitochondria and assessed whether their functionality in aged oocytes was associated with cytoskeleton stability.

DESIGN: Experimental animal study.

MATERIALS AND METHODS: We performed time-lapse confocal live microscopy of mitochondrial motility in both young and aged oocytes. We then examined the association between cytoskeleton stability and mitochondrial motility with young oocyte, aged oocytes and 150mM cytochalasin B (CB)-treated young oocytes and analyzed the relationships between mitochondrial motility and functional activity including ATP production ratios.

RESULTS: Young oocytes showed dynamic mitochondrial motility and high ATP production levels during maturation, whereas aged oocytes did not. Cytoskeleton destabilization in CB-treated young oocytes led to a significant decrease in motility of mitochondria and to maturation ratios comparable to those of aged oocytes. Young oocytes present well development with microtubule formation in the ooplasm. But old oocytes have less development and thin microtubule formation in the ooplasm. Besides, 150mM cytochalasin B (CB)-treated young oocytes showed a lot of disconnected microtubule formation in the ooplasm like disassemble microtubule formation look like microtubule formation in the aged oocytes. It was shown that CB disturbed cytoskeleton formation in the oocytes. Therefore, low mitochondrial motility was associated with low ATP production ratios in CB-treated young oocytes and in aged oocytes.

CONCLUSIONS: In aged oocytes showed a loss of motility and poor ATP production ratios compared to young oocytes. These findings may be related to cytoskeleton stability with a loss of motility and poor ATP production ratios of mitochondria as observed in aged oocytes. Mitochondrial motility along the cytoskeleton may play an important role for the determination of oocytes quality, depending on age.

P-372 Tuesday, October 15, 2019 6:30 AM
ROLE OF VOLTAGE DEPENDENT N AND P/Q TYPE CALCIUM CHANNEL IN MOUSE EGG FERTILIZATION.
Sook Young Yoon, Ph.D., Jin Hee Eum, Ph.D., Misaeon Park, Master, Woo Sik Lee, M.D. Ph.D. Fertility Center of CHA Gangnam Medical Center, Seoul, Korea, Republic of (South); Affiliation not provided.

OBJECTIVE: During mammalian fertilization, phospholipase C zeta (PLCz) induces repetitive changes termed Ca2+ oscillations. Ca2+ oscillation triggers egg activation, including cortical granule (CG) exocytosis, reumption of second meiosis, block to polyspermy, and initiating embryonic development to the blastocyst stage. The sources of Ca2+ oscillations are calcium entry from endoplasmic reticulum through IP3 receptor and Ca2+ influx through Ca2+ channel on the plasma membrane. Ca2+ channels have been characterized into voltage-dependent Ca2+ channel (VDCs), ligand-gated Ca2+ channel, and leak-channel. VDCs expressed on muscle cell or neuron is specified into L, T, N, P, Q, and R type VDCs by their activation voltage dependence and thin microtubule formation in the ooplasm. But old oocytes have less develop...
decreased by Lat A treatment. N or P/Q type VDCC specific inhibitor, α-Conotoxin CVIB induced abnormal Ca2+ oscillation profiles in SrCl2 treatment. N or P/Q type VDCC were distributed on plasma membrane, not in cytoplasm in cortical cluster form.

CONCLUSIONS: (α-Conotoxin CVIB)-influx is essential for Ca2+-oscillation during mammalian fertilization. This Ca2+-influx may be controlled through the N or P/Q type voltage dependent Ca2+ channel. Abnormal VDCC expression of eggs could be tested in fertilization failure or low fertilization eggs in subfertility women. This research was supported by a grant from Republic of Korea NRF-2017 R1D1A1B03208155.

SUPPORT: This research was supported by a grant from Republic of Korea NRF-2017 R1D1A1B03208155.

P-373 Tuesday, October 15, 2019 6:30 AM

THE CHANGING OF CELL MODULATION VIA EPIDERMAL GROWTH FACTOR RECEPTOR IN HUMAN DECIDUAL StromAL CELLS. Kaori Goto, Ph.D., a Yasushi Kawano, M.D., Ph.D., a Yufuko Kai, M.D., a Hiroko Itoh, M.D., Ph.D., a Hisashi Narahara, M.D., Ph.D., a Takafumi Utsunomiya, M.D., Ph.D. aSt.Luke Clinic, Oita, Japan; bDepartment of Obstetrics and Gynecology, Faculty of Medicine, Oita University, Yufu, Japan.

OBJECTIVE: Human endometrial stromal cells (ESCs) undergo morphological and functional changes by growth factors and/or steroid hormones. Decidual cells are thought to be involved in the maintenance of pregnancy. The purpose of the present study was to clarify the physiological role of epidermal growth factor receptor (EGFR) in the regulation of the endometrial secretion of chemokines [interleukin (IL)-8, monocyte chemotactic protein (MCP)-1], matrix metalloproteinase (MMP-1), and VEGF in response to epiregulin (ER) was also evaluated. The regulation of EGFR in cultured ESCs/DSCs, the expression of EGFR mRNA and protein production were evaluated. The secretion of chemokine, MMP-1, and VEGF in response to epiregulin (ER) was also evaluated. The effects of ER on the motility with ESCs/DSCs were assessed by an in vitro wound repair assay. To investigate the expression of HOXA10 in cultured ESCs/DSCs, the expression of HOXA10 mRNA was investigated.

MATERIALS AND METHODS: Normal endometrial specimens were obtained from premenopausal patients who had undergone hysterectomies for subserosal leiomyomas. Normal ESCs were separated from endometrial tissue fragments by collagenase digestion. Decidualization of ESCs (DSCs) was induced by incubating subconfluent cells in media containing medroxyprogesterone acetate (MPA) and db-CAMP for 16 days. To investigate the regulation of EGFR in cultured ESCs/DSCs, the expression of EGFR mRNA and protein production were evaluated. The secretion of chemokine, MMP-1, and VEGF in response to epiregulin (ER) was also evaluated. The effects of ER on the motility with ESCs/DSCs were assessed by an in vitro wound repair assay. To investigate the expression of HOXA10 in cultured ESCs/DSCs, the expression of HOXA10 mRNA was investigated.

RESULTS: According to the real-time quantitative PCR (RT-PCR) analysis, EGF/EGFR mRNA expression levels on day 4 after decidual stimulation appeared to be higher than those on day 0. At 8 days after stimulation, the production of EGFR protein was higher than those on day 0. The productions of IL-8 and MMP-1 increased in the DSCs with the addition of ER. The wound repair of the DSCs was significantly enhanced compared to that of the ESCs. When ER was added, the wound repair was more enhanced. According to the RT-PCR analysis, HOXA 10 mRNA expression levels on day 12 decidual stimulation appeared to be higher than those on day 0. However, the downregulation of HOXA 10 in the DSCs were expressed on day 16.

CONCLUSIONS: Our results suggest that cell function is changed by decidualization in association with increasing EGFR expression. The up-regulation of EGFR accompanied with decidualization may contribute to have some influence on maintenance of pregnancy.

Reference: None.

SUPPORT: None.

TABLE 1. Results

<table>
<thead>
<tr>
<th>TP73 (rs3765730) Genotypes</th>
<th>GG</th>
<th>GA</th>
<th>AA</th>
<th>P</th>
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<tbody>
<tr>
<td>n</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cycles</td>
<td></td>
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</tr>
<tr>
<td>Age (years)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>AMH (ng/ml)</td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AFC (n)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total dose rFSH (UI)</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Follicles (n):Total</td>
<td></td>
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<tr>
<td>Follicles (n):≥ 18 mm</td>
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<td></td>
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<tr>
<td>Retrieved oocytes (n):Total</td>
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<td></td>
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<td></td>
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<tr>
<td>Fertilization rate</td>
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<tr>
<td>Implantation rate</td>
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<tr>
<td>Pregnancy rate/patient</td>
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<td>Pregnancy rate/transfer</td>
<td></td>
<td></td>
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</tbody>
</table>

Values within rows with the same superscript letter were significantly different

Vol. 112, No. 3, Supplement, September 2019
cycles. Homozygosity of the A allele was associated with significantly better results. The identified SNP may provide an additional tool to test patients for ovarian response and thus help in the individualization of ovarian stimulation protocols. To the best of our knowledge, this is the first study associating this SNP and ovarian response.

SUPPORT: Merck Grant for Fertility Innovation (GFI-2014).

P-375 Tuesday, October 15, 2019 6:30 AM

SEQUENTIAL CLINICAL MANIPULATIONS OF EMBRYOS RESULTS IN ALTERATIONS IN EXPRESSION OF GENES INVOLVED IN INNATE IMMUNITY, APOPTOSIS, AND MITOCHONDRIAL FUNCTION. Kristin Van Heurtem, MD,a Lisa Lam, BS,b Michael J. Cartwright, MS,b Brian Richardson, BS,b Mark Cameron, PhD,b Sam Mesiano, PhD,b Rachel S. Weinerman, MDa University Hospitals of Cleveland/Case Western Reserve University, Beachwood, OH;Afiliation not provided.

OBJECTIVE: Although data do not suggest a decreased clinical pregnancy rate with single blastocyst (blast) vitrification (vit) or blast biopsy, vit before and after biopsy has been shown to compromise embryo survival, suggesting a greater impact of cryoprotectants following trophectoderm biopsy. There are also little data on the long-term safety of embryo vit. Clinical studies suggest differences in perinatal outcomes between babies born following fresh and frozen embryo transfer (FET), with higher rates of preterm birth (PTB) and pre-eclampsia (P-E) after FET, and higher rates of low birthweight (LBW) after fresh transfer. In this study, we aim to identify specific genes affected by blast vit and biopsy that may account for these phenotypic differences.

DESIGN: Laboratory research.

MATERIALS AND METHODS: Female mice were superovulated with 5 IU PMSG and 5 IU hCG and mated with male mice. Blasts were flushed on E3.5 and divided into four groups: no manipulation (g2), single vit/thaw (g3), double vit/thaw (g4), and single vit/thaw plus biopsy and revived and thawed (g5). 3 sets of 15 blasts per group were pooled for RNA extraction. Low input libraries were made using Takara SMART-Seq v4 and Illumina Nextera XT kits. RNA-Seq was performed on an Illumina NextSeq 550 (75 base pair, paired-end, 30 X 106 reads/sample). Differentially expressed genes (DEGs) were determined by two group t-tests (P ≤ 0.05) and organized into top enrichment pathways by P value (P ≤ 0.05) and organized

RESULTS: The MMP9 p.Glutamine(Gln)279Arginine(Arg)(rs17576) polymorphism was identified. Women with the Gln/Gln genotype had significantly poorer ovarian reserve indicators (lower levels of AMH and AFC), poorer ovarian response to FSH, and poorer clinical outcomes (implantation rate). Table 1 presents a summary of the results

CONCLUSIONS: The MMP9 p.Gln279Arg polymorphism was associated with ovarian reserve and seemed to have affected ovarian response to FSH and the clinical outcomes of IVF/ICSI cycles. Homozygosity of the Gln allele was associated with significantly poorer results. The identified SNP might provide an additional tool to test patients for ovarian response and thus help in the individualization of ovarian stimulation protocols.

SUPPORT: Merck Grant for Fertility Innovation (GFI-2014).

MATERIALS AND METHODS: This study encompassed 135 women submitted to IVF/ICSI cycles.

The enrolled individuals met the following inclusion criteria: age ≤ 37 years; normal karyotype; having two ovaries as evinced in ultrasound examination; no history of ovarian surgery, endometriosis, hydrosalpinx, infection, or endocrine disorders.

DNA extracted from peripheral blood was sequenced on MiSeq(Illumina) to find single nucleotide polymorphisms (SNPs) in the MMP9 gene. SNPs were identified using the TruSeq Custom Amplicon (TSCA) Panel (Design/Studio Illumina).

The findings from sequencing were associated with age, anti-Müllerian hormone (AMH) levels, antral follicle counts (AFC), total dose of recombinant FSH (r-FSH), follicle size, number of retrieved oocytes, and clinical outcome of IVF/ICSI cycles.

OBJECTIVE: To investigate a possible association between an MMP9 gene polymorphism and ovarian response after IVF/ICSI.

RESULTS: Table 1. Results

TABLE 1. Results

<table>
<thead>
<tr>
<th>Gln/Gln</th>
<th>Gln/Arg</th>
<th>Arg/Arg</th>
<th>P</th>
<th>Gln/Gln</th>
<th>Gln/Arg+Arg/Arg</th>
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<td>33.4±3.1</td>
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<td>15.8±9.2</td>
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<td>10.8±7.3</td>
<td>15.5±10.3</td>
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<td>5.9±4.0</td>
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<td>8.5±6.5</td>
<td>0.58</td>
<td>5.9±4.0</td>
<td>8.1±6.6</td>
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<td>55.8%</td>
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<td>46.3%</td>
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<td>39.8%</td>
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<td>39.8%</td>
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THE MATRIX METALLOCYRPROTEASE-9 (MMP9) P. Gln279Arg POLYMORPHISM IS ASSOCIATED WITH OVARIAN RESERVE AND OVARIAN RESPONSE DURING IVF/ICSI TREATMENT. Laura D. Vagnini, B.Sc.a Claudia G. Petersen, Ph.D.b Ana Lucia Mauri, B.Sc.b Adriana Renzi, Ph.D.b Bruna Petersen, B.Sc.b Mariana Mattila, B.Sc.b Juliana Ricci, R.N.c Felipe Dieamant, M.D.„ Joao Batista A Oliveira, M.D.„ Ph.D.b Ricardo L. Baruffi, M.D., Jose G. Franco Jr., M.D., Ph.D.b Paulista Center for Diagnosis, Research and Training, Ribeirao Preto, Brazil; Center for Human Reproduction Prof. Franco Jr. Paulista Center for Diagnosis, Research and Training, Ribeirao Preto, Brazil; Center for Human Reproduction Prof. Franco Jr, Ribeirao Preto, Brazil.

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CONCLUSIONS: The MMP9 p.Gln279Arg polymorphism was associated with ovarian reserve and seemed to have affected ovarian response to FSH and the clinical outcomes of IVF/ICSI cycles. Homozygosity of the Gln allele was associated with significantly poorer results. The identified SNP might provide an additional tool to test patients for ovarian response and thus help in the individualization of ovarian stimulation protocols.

SUPPORT: Merck Grant for Fertility Innovation (GFI-2014).

The MATRIX METALLOCYRPROTEASE-9 (MMP9) P. Gln279Arg POLYMORPHISM IS ASSOCIATED WITH OVARIAN RESERVE AND OVARIAN RESPONSE DURING IVF/ICSI TREATMENT. Laura D. Vagnini, B.Sc.a Claudia G. Petersen, Ph.D.b Ana Lucia Mauri, B.Sc.b Adriana Renzi, Ph.D.b Bruna Petersen, B.Sc.b Mariana Mattila, B.Sc.b Juliana Ricci, R.N.c Felipe Dieamant, M.D.„ Joao Batista A Oliveira, M.D.„ Ph.D.b Ricardo L. Baruffi, M.D., Jose G. Franco Jr., M.D., Ph.D.b Paulista Center for Diagnosis, Research and Training, Ribeirao Preto, Brazil; Center for Human Reproduction Prof. Franco Jr. Paulista Center for Diagnosis, Research and Training, Ribeirao Preto, Brazil; Center for Human Reproduction Prof. Franco Jr, Ribeirao Preto, Brazil.

OBJECTIVE: To investigate a possible association between an MMP9 gene polymorphism and ovarian response after IVF/ICSI.
OBJECTIVE: The studied polymorphism was used to assess the ovarian stimulation. The mean age of the oocyte donors included in the study was 29.3 ± 3.5 years. The mean AMH level was 4.54 ± 2.35 pmol/L and the mean number of antral follicles count was 19.1 ± 2.8. We performed a linear regression, taking into consideration confounding factors such as age, smoking, BMI, and AMH. Regarding the number of retrieved oocytes, we found statistically significant differences for the ESR1 SNP (19.3 ± 8.9 for TT vs. 15.3 ± 6.2 for CC/CT, p = 0.027) and ESR1 (TA)n STR (19.1 ± 8.3 for TT vs. 17.7 ± 6.2 for >17 repeats, p = 0.020). When we combined both genotypes, the haplotype analysis showed that women who carries CC or CT in the ESR1 gene and at position -397T>C (rs2234693) with a number of repeats greater than 17 showed 12 retrieved lower oocytes (14.0 ± 5.6) than the other genotypes (p = 0.001). Regarding AMHR2, we observed an association with the length of stimulation (9.1 ± 1.4 for AA vs. 9.7 ± 1.3 for AG/GG, p = 0.021) and gonadotropin received (2050 ± 319 for AA vs. 2188 ± 299 for AG/GG, p = 0.017). No significant association among genotype, retrieved oocytes and ovarian stimulation was observed for LHCR, CYP19A1, AMH, SHBG, AR and both of GDF-9 SNPs (p > 0.05).

CONCLUSIONS: We reported that polymorphisms in the ESR1 and AMHR2 genes showed a clear association with the number of retrieved oocytes and ovarian stimulation because young women with normal ovarian function. This prospective randomized study includes 12 healthy, normoovulatory, caucasian egg donors genotyped for six SNPs present in ESR1, AMH, AMHR2, GDF-9 and LHCRG and four STRs present in ESR1, SHBG, CYP19A1 and AR. All donors followed a standard ovarian stimulation protocol using a daily dose of 225 UI of either uFSH or rFSH.

TOWARDS PERSONALISED REPRODUCTIVE MEDICINE: SCREENING FOR GENETIC VARIANTS AND ITS INFLUENCE IN CONTROLLED OVARIAN STIMULATION. Belen Lleido, PhD, Laura Blanco, MSc, Jose A. Ortiz, PhD, Ruth Morales, PhD, Jaime Guerrero, MSc, Ana Fabregat, PhD, Joaquín Llacer, PhD, Rafael Bernabeu, Ph D M D In-stuto Bernabeu, Alicante, Spain.

Where does extra X in Klinefelter Syndrome come from? Atsushi Tanaka, M.D., Ph.D.,a Motoi Nagayoshi, M.D.,a Izumi Tanaka, Ph.B.,a Takashi Yamaguchi, M.D., Ph.D.,a Motoharu Ohno, M.D.,a Seiji Watanabe, Ph.D.b aSaint Mother Hospital, Kitakyushu, Japan;bHirosaki University Graduate School of Medicine, Hirosaki, Japan.

OBJECTIVE: It has been reported that the incidence of sperms with disomic XY is higher in the testis tissue smear of KS patients and these sperms are the cause of KS. However some papers report the maternal origin. So we performed this study to investigate the origin of extra X in Klinefelter Syndrome (KS).

DESIGN: Cytogenetic analysis in KS patients and their parents.

MATERIALS AND METHODS: Blood samples from 29 KS patients were used for X-chromosome short tandem repeats (STR) analysis. The STR analysis also included data of the parents of the KS patients (24: both parents, 5: mother only, 0: father only) from January 2015 to March 2019. This study was conducted with the informed consent of all participating patients and approved by The Institutional Review Boards of the Saint Mother Obstetrics and Gynecology Clinic and adhered to JCMIR criteria UMIN Clinical Trial Registry was UMIN00002452.

RESULTS: Blood samples of 29 KS patients and one of both of their parents were used to determine the origin of the extra X chromosome using X-chromosome haplotype markers (short tandem repeats of 12 loci), according to the method by Shrivastava et al. With DNA extracted from the samples, multiplexed PCR amplifications of the 12 X-STR loci and AMELOGENIN were conducted using an Investigator Argus X-12 Q5 Kit (Quigen, Germany). The data obtained was analyzed with GeneMapper ID software.

RESULTS: X-chromosomal STR DNA profiles were compared among KS patient and their parents. In 13 of the 29 KS patients, both 2 chromo- somes were maternal origin, showing that an extra X chromosome was left in an oocyte as a result of chromosomal non-disjunction at the 1st (4/13) or 2nd (9/13) meiotic division. In 15 patients, X-chromosomes were inherited from parents, suggesting that fertilization of XY-sperm is the cause of KS.

CONCLUSIONS: Although the sample number applied for X-chromosomal STR DNA profiling is not enough, the present data may indicate that contribution of XX oocyte to the production of XXX embryos is greater than XY sperm. Namely, a XX oocyte penetration by a Y sperm is the main cause of KS. Cytogenetic analysis with smear of testicular cell mixture that was used in the studies may overestimate chromosomal abnormality.

P-375 Tuesday, October 15, 2019 6:30 AM

BREAKPOINT MAPPING UNCOVERING ABOUT 1.32% OF APPARENT BALANCED RECIPROCAL TRANSLOCATION (ABRT) CARRIERS EXISTING CRYPTIC COMPLEX CHROMOSOMAL STRUCTURAL VARIATIONS IN PREIMPLANTATION GENETIC TESTING (PGT). Shimin Yuan, Master, Yue-qi Tan, Doctor, Reproductive and Genetic Hospital of Citic-Xiangya, Changsha, China.

OBJECTIVE: To identify precise breakpoints, evaluate the reproduction-related risks and guide the following PGT treatment, high resolution breakpoint mapping was performed in ABRT carriers indicated by G-banding. DESIGN: A single-center, descriptive research.

MATERIALS AND METHODS: A large sample of 833 cases with ABRT who planned to accept PGT treatment were recruited in this study. For these patients, the approach of the next-generation sequencing following microdissection (MirosSeq) of the junction region in the derivative chromosomes, and linkage analysis of the adjacent single nucleotide polymorphisms (SNPs) were performed to distinguish the carriers from noncarriers in balanced embryos. For some cases with unbalanced chromosome rearrangement in the breakpoint region, SNP-array and fluorescence in situ hybridization (FISH) techniques were further used to determine the accurate karyotype.

RESULTS: In the 833 cases with ABRT, we found 11 cases (1.32%) carried cryptic complex chromosomes. In 10 cases, we found 3 balanced reciprocal translocations and 8 balanced ones in which 2 cases carried both inversion and translocation. In these 11 cases, 5 cases related to 3 chromosomes with 4 to 21 breakpoints and 6 cases involved 2 chromosomes with 3 to 6 breakpoints. It is noteworthy that there were two cases exhibited rare chromosomal aneuploidy, including chromothripsis and chromoplexy. Fortunately, two couples have been both successfully transplanted a normal normal.
embryo and given birth to a healthy child, and the remaining nine cases are undergoing PGT treatment.

CONCLUSIONS: In this large-scale analysis of ABRT, high resolution breakpoint mapping precisely characterized these breakpoints and uncovered 1.32% of the ABRT carriers existed cryptic complex chromosomal rearrangements. These data suggests that high resolution breakpoint mapping used in PGT can improve the accuracy of evaluating the reproduction-related risks and avoid genetic risks for the ABRT carriers.

SUPPORT: This study was supported by the National Key R&D Program of China 2018YFC1003100 (L.H.) and 2016YFC1002006 (G.L.), National Natural Science Foundation of China 81873478 (L.H.) and Merck Serono China Research Fund for Fertility Experts.

P-380 Tuesday, October 15, 2019 6:30 AM

SINGLE CELL GENE EXPRESSION OF HUMAN PU-BERTAL TESTIS DEVELOPMENT. Jingtao Guo, PhD,ª Xichen Nie, BS,º Douglas T. Carrell, PhD,ª James Hotaling, MD,a Bradley R. Cairns, PhD,a University of Utah School of Medicine, Andrology and IVF Laboratories, Salt Lake City, UT; ³Huntsman Cancer Institute, Salt Lake City, UT; ¹University of Utah School of Medicine Andrology and IVF Laboratories, Salt Lake City, UT; aHoward Hughes Medical Institute, Department of Oncological Sciences and Huntsman Cancer Institute, University of Utah School of Medicine, Salt Lake City, UT.

OBJECTIVE: We investigated the molecular mechanism underlying human testis development during puberty by single cell RNA-seq profiling.

DESIGN: We derived single cell suspensions using the testicular biopsies from 4 juvenile donors (7-14 years old) and performed single cell RNA-seq profiling and analysis.

MATERIALS AND METHODS: We performed scRNA-seq profiling of whole testis tissues from juvenile donors (two technical replicates for each donor): one 7-year old (≈3000 cells), one 11-year old (≈3000 cells), one 13-year old (≈3000 cells), one 14-year old (≈3000 cells). This yielded a dataset composed of≈12000 single cell transcriptomes. We compared the current data set with the single cell transcriptome from the young adult (~25 years old) and infant (~1 year old) male donors described in our previous work. We performed dimension reduction and clustering analysis using Seurat and SDA programs, and utilized known markers to help deduce cell identities. We further performed differential gene expression and gene ontology analysis to study the gene expression programs that display differential gene expression dynamics.

RESULTS: We found that spermatogonial stem cells (SSCs) commit to spermatogenesis in two sequential phases: mitotic differentiation (involving proliferation and metabolic changes) followed by subsequent commitment to meiosis, which may be induced by testosterone and activin signals. Remarkably, the early SSCs (marked by PIWIL4, TSPAN33 and many other genes) were pre-determined during infancy (~1 year old), and persisted in adults. Regarding the somatic niche, we identified a common pre-pubertal cell precursor for Leydig and Myoid cells, and revealed pathways for pubertal differentiation, including the insulin signaling pathway. We have confirmed critical roles of testosterone in promoting germ cell development and maturation in vitro. Importantly, we have developed a culture system that maintains human seminiferous tubule in vitro for three weeks.

CONCLUSIONS: The current study provided the first single cell transcriptomic atlas for pre- and peri-pubertal testis development, and uncovered many important signaling pathways that may regulate both germ cell and somatic cell maturation during human puberty, which could be critical for initiation and maintenance of spermatogenesis. This can be applied to an in vitro culture system to help drive and maintain in vitro spermatogenesis using testicular tissues from prepubertal boys undergoing cytotoxic chemotherapy.

P-382 Tuesday, October 15, 2019 6:30 AM

LUTEAL PHASE-DERIVED OOCYTE-CUMULUS COMPLEXES: GENE EXPRESSION AND MITOCHON-DRAL DNA COPY NUMBER. Bella Martazanova, PhD,a Nona Mishieva, PhD,a Anna Korolkova, MD,a Khava Bogatyreva, PhD,a Maria Veykova, PhD,a Anastasia Kirillova, PhD,a Olga Burmenskaya, PhD,a Aydar Abubakirov, PhD,a Reproductive endocrinology, Moscow, Russian Federation; bEmbriologist, Moscow, Russian Federation; cGenetic, biology, Moscow, Russian Federation.

OBJECTIVE: The double stimulation (DuoStim) became a new approach for poor responder management. However, luteal phase stimulation-derived (LPS) oocytes require further investigation. One of the methods to determine oocyte quality is investigation of the cumulus cells (CCs), which surround the oocyte and are pivotal in determining oocyte developmental competence. Several studies have revealed certain CCs genes that are correlated with oocyte competence and embryo development; also there are data, which shows that mitochondrial DNA (mtDNA) copy number is positively linked with embryo quality. However, gene expression and mtDNA quantification in CCs of LPS derived oocytes after the DuoStim approach still has not been investigated.

DESIGN: A total of 39 patients with a reduced ovarian reserve were included in the study. Inclusion criteria: age <43 years; AMH <1.2 ng/mL; AFC <6; basal FSH ≥ 11 IU/mL. Exclusion criteria: uterine fibroids ≥4 cm, deep endometriosis, cancer, BMI ≥29 kg/m², smoking, severe male infertility. Gene expression was assessed in a total of 169 CCs. 20 CCs were excluded: 4 due to mRNA impairment and 16 due to immature oocytes. A total of 149 CCMs were divided into two groups: group 1 included 55 follicular phase-derived oocytes from 15 patients and group 2 included 94 LPS-derived oocytes from 24 patients.

MATERIALS AND METHODS: The expression levels of HAS2, VCAN, ALCAM, PTGS2, GREM1, ITFPA, TRPM7, SDC4, CALM2, SPBS2, TP5313, PGR, PFK, and mtDNA were assessed using quantitative polymerase chain reaction. Statistical analysis – the Mann-Whitney test, t-test, the chi-squared test; p<0.05 was considered to be statistically significant.

RESULTS: CCs gene expression was similar between the groups. However, a significant increase in the mRNA levels of VCAN (15.542±6.8 vs.

FERTILITY & STERILITY® e257
OBJECTIVE: To report ordering patterns within and outside of ACOG BEST PRACTICE CARRIERS’ GUIDELINES. We evaluated the impact of the ‘‘tandem reflex’’ strategy on turnaround-time and maximization of detection of at-risk couples. 

RESULTS: The tandem reflex strategy reduced the average wait time for a couple to receive a full couple-based carrier screening report to approximately 15 days after submission of the partner's sample. The tandem reflex strategy also reduced the average time for a sequentially tested couple to receive a full couple-based carrier screening report to approximately 34 days after submission of the female partner's sample. The tandem reflex strategy also reduced the average time for a sequentially tested couple to receive a full couple-based carrier screening report to approximately 34 days after submission of the female partner's sample.

CONCLUSIONS: The tandem reflex strategy should be implemented to improve detection of at-risk couples and reduce the average time for a couple to receive a full couple-based carrier screening report.

Keywords: Carrier screening, tandem reflex strategy, improved detection of at-risk couples, reduced average time for a couple to receive a full couple-based carrier screening report.
TABLE 1. Summary of Ordering Patterns & Positive Rates

<table>
<thead>
<tr>
<th>Panel</th>
<th>REI</th>
<th>ObGyn</th>
<th>MFM</th>
<th>GC</th>
<th>Other</th>
<th>% of all orders</th>
<th>Positive Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>288 gene panel with 13 add-on genes</td>
<td>16%</td>
<td>21%</td>
<td>0%</td>
<td>18%</td>
<td>9%</td>
<td>15%</td>
<td>77%</td>
</tr>
<tr>
<td>288 gene panel</td>
<td>36%</td>
<td>27%</td>
<td>66%</td>
<td>53%</td>
<td>53%</td>
<td>41%</td>
<td>65%</td>
</tr>
<tr>
<td>46 gene panel</td>
<td>13%</td>
<td>10%</td>
<td>9%</td>
<td>3%</td>
<td>16%</td>
<td>12%</td>
<td>44%</td>
</tr>
<tr>
<td>3 gene panel</td>
<td>12%</td>
<td>24%</td>
<td>14%</td>
<td>3%</td>
<td>13%</td>
<td>14%</td>
<td>15%</td>
</tr>
<tr>
<td>Other: ACOG/ACMG ethnicity-specific genes</td>
<td>14%</td>
<td>7%</td>
<td>4%</td>
<td>2%</td>
<td>4%</td>
<td>9%</td>
<td>22%</td>
</tr>
<tr>
<td>Other: All other combinations</td>
<td>9%</td>
<td>11%</td>
<td>7%</td>
<td>21%</td>
<td>6%</td>
<td>9%</td>
<td>Varies</td>
</tr>
</tbody>
</table>

Total | 7729 | 3106 | 446 | 903 | 4275 | 16459 | 51% |

**P-385 Tuesday, October 15, 2019 6:30 AM**

**THE PROLONGED DISEASE STATE OF INFERTILITY IS ASSOCIATED WITH BLASTOCYST IMPRINTED EPIGENETIC DYSREGULATION.**

Michelle M. Denomme Tignelli, PhD, William B. Schoellerf, MD, Mandy G. Katz-Jaffe, Ph.D., Colorado Center for Reproductive Medicine, Lone Tree, CO.

**OBJECTIVE:** Epidemiological studies suggest that the disease state of infertility may play a role in the observed increased incidence of rare imprinting disorders in children born following infertility treatment. Imprinting disorders frequently arise from epigenetic dysregulation at imprinting control regions (ICRs). Examples include loss of imprinted DNA methylation at the KvDMR ICR in ~50% of children with Beckwith-Wiedemann Syndrome, and loss of methylation at the H19 ICR in ~45% of children with Russell-Silver Syndrome. The purpose of this study was to examine the association between duration of infertility and DNA methylation at four ICRs in euploid blastocysts.

**DESIGN:** Research study.

**MATERIALS AND METHODS:** Surplus cryopreserved euploid blastocysts of transferable quality (grade ≥ 3BB; n=58) were donated with IRB approval and patient consent. Blastocysts were subdivided into four groups based on duration of infertility, classified as number of months of reported primary infertility prior to the oocyte retrieval that resulted in a live birth [Fertile Control; 0 months, donor oocyte/donor sperm (n=14); Infertile Short: 12-24 months (n=14); Infertile Intermediate: 36-48 months (n=14); Infertile Long: ≥ 60 months (n=16)]. Female age was restricted to ≤ 39 years. Infertility diagnoses were equally varied among the test groups. Euploid blastocyst DNA was isolated (QiAamp DNA Micro Kit; Qiagen) and bisulfite converted (EZ DNA Methylation-Direct Kit; Zymo Research) prior to PCR amplification and pyrosequencing (PyroMark Q24 Advanced system; Qiagen). Statistical analysis included Student’s t-test and one-way ANOVA where appropriate, with significance at p<0.05.

**RESULTS:** Extended durations of infertility ≥ 36 months (Infertile Intermediate + Infertile Long; mean=65 months) showed significant alterations in blastocyst imprinted DNA methylation, with a decrease in methylation marks when compared to short durations ≤ 24 months (Fertile Control + Infertile Short; mean=10 months). The ICRs for KvDMR (39% Extended Infertility vs. 48% Short Infertility; p<0.05), H19 (29% Extended Infertility vs. 41% Short Infertility; p<0.05), and MEST (40% Extended Infertility vs. 49% Short Infertility; p<0.05) showed significant hypomethylation, while SNRPN/trended downward without significance. Infertility diagnoses, blastocyst grades, and total doses of recombinant follicle stimulating hormone during ovarian stimulation where comparable across the groups.

**CONCLUSIONS:** This novel study is the first to report evidence that altered blastocyst imprinted methylation correlates with prolonged infertility. The prevalence of ICR hypomethylation was significant in euploid blastocysts derived from patients with an extended duration of infertility ≥ 36 months. Ongoing studies will investigate whether the underlying infertility leads to epigenetic errors, or if the methylation alterations themselves are perpetuating the duration of infertility? Our results contribute towards the identification of a mechanistic link between imprinted epigenetic dysregulation and infertility as a prolonged disease.

**SUPPORT:** None.
TUBB8 demonstrated that there is evidence of association with ‘ovarian reserve’, ‘ovarian response to stimulation’ (examined in 34% (n=99/291) of assessed genetic studies), with strong or moderate evidence of association with ‘implantation’, ‘implantation failure’ and ‘pregnancy loss after IVF’.

OBJECTIVE: Empty follicle syndrome (EFS) is the complete failure to retrieve oocytes from mature follicles after ovarian stimulation for in vitro fertilization. “Genuine” (GEFS) occurs without any human or pharmaceutical error during the ovarian stimulation process and its existence has been a question in the research community until LHCGR and ZP3 were identified as causative genes. Even so, it is still unclear what happens to these patients’ oocytes, and the pathogenesis of GEFS remains obscure. Most GEFS cases, additionally β-hCG or repeated controlled ovarian hyperstimulation (COH) by different protocols do not succeed in oocyte recovery, and use of donor oocytes have been proposed as the only viable alternative approach. Our study aimed to identify novel pathogenic variants (PVs) causing EFS and dissect follicular development in EFS patients.

METHODS: Seven cases with non-pregnant cycles were enrolled, and their genomic sequences were analyzed. The new phenotype of human ZP in the absence of ZP1 protein was detected in two cases. The PVs in ZP1 were verified using the zebrafish model system. The PVs were classified into four types: nonsense, frameshift, splicing and small deletions. The PVs were further analyzed using the ClinGen scoring system and imprinted ZP1 PVs were identified.

RESULTS: We identified several novel ZP1 PVs causing EFS and female infertility in a recessive genetic mode, and for the first time present surrounding growing oocytes. However, this thin ZP was defective in normal cumulus-oocyte complex organization during antral folliculogenesis, present surrounding growing oocytes. However, this thin ZP was defective in normal cumulus-oocyte complex organization during antral folliculogenesis, present surrounding growing oocytes. However, this thin ZP was defective in normal cumulus-oocyte complex organization during antral folliculogenesis.

CONCLUSIONS: We identified several novel ZP1 PVs causing EFS and female infertility in a recessive genetic mode, and for the first time present surrounding growing oocytes. However, this thin ZP was defective in normal cumulus-oocyte complex organization during antral folliculogenesis.

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ANALYSIS OF ACCESSIBLE CHROMATIN LANDSCAPE IN THE INNER CELL MASSES OF HUMAN BLASTOCYSTS USING ATAC-SEQ.

Min Yang, PHD,a Xin Tao, PHD,b Tianhua Zhao, PHD,a Can Dai, Ph.D.a Yongzhe Chen, Ph.D.,b Ge Lin, M.D., Ph.D.4 Reproductive and Genetic Hospital of CITIC-Xiangya, Changsha, China; 3Central South University, Changsha, China; 4Reproductive and Genetic hospital of CITIC-Xiangya, Changsha, China.

OBJECTIVE: The chromatin accessibility landscape during the early-stage embryo development, especially the early lineage specification, has not yet been delineated in human preimplantation embryos, mainly due to the assay limitation. We optimized the Assay for Transposable-Accessible Chromatin using sequencing (ATAC-seq) for low DNA input with the aim of exploring the chromatin


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ZPI PATHOGENIC VARIANTS CAUSE ‘GENUINE’ EMPTY FOLLICLE SYNDROME: EVIDENCE FOR THE EXISTENCE OF AN INTACT OOCYTE AND A ZONA PELLUCIDA IN FOLLICLES UP TO EARLY ANTRAL STAGE.

Can Dai, Ph.D.,a Yongzhe Chen, Ph.D.,b Ge Lin, M.D., Ph.D.4 Reproductive and Genetic Hospital of CITIC-Xiangya, Changsha, China; 3Central South University, Changsha, China; 4Reproductive and Genetic hospital of CITIC-Xiangya, Changsha, China.

OBJECTIVE: Empty follicle syndrome (EFS) is the complete failure to retrieve oocytes from mature follicles after ovarian stimulation for in vitro fertilization. “Genuine” (GEFS) occurs without any human or pharmaceutical error during the ovarian stimulation process and its existence has been a question in the research community until LHCGR and ZP3 were identified as causative genes. Even so, it is still unclear what happens to these patients’ oocytes, and the pathogenesis of GEFS remains obscure. Most GEFS cases, additionally β-hCG or repeated controlled ovarian hyperstimulation (COH) by different protocols do not succeed in oocyte recovery, and use of donor oocytes have been proposed as the only viable alternative approach. Our study aimed to identify novel pathogenic variants (PVs) causing EFS and dissect follicular development in EFS patients.

METHODS: Seven cases with non-pregnant cycles were enrolled, and their genomic sequences were analyzed. The new phenotype of human ZP in the absence of ZP1 protein was detected in two cases. The PVs in ZP1 were verified using the zebrafish model system. The PVs were classified into four types: nonsense, frameshift, splicing and small deletions. The PVs were further analyzed using the ClinGen scoring system and imprinted ZP1 PVs were identified.

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CONCLUSIONS: We identified several novel ZP1 PVs causing EFS and female infertility in a recessive genetic mode, and for the first time present surrounding growing oocytes. However, this thin ZP was defective in normal cumulus-oocyte complex organization during antral folliculogenesis.
remodeling pattern in human preimplantation embryos and revealing the epige-
netic regulation of inner cell mass (ICM) and trophectoderm (TE) differentiation.

MATERIALS AND METHODS: The whole ICM and partial TE were bio-
preserved from eight 6-8 cell-stage embryos. DNA obtained from lysed samples was tag-
tagged using Nextera Trn transposase and purified by phenol-chloroform extraction.
PCR was conducted using Phusion high-fidelity PCR master mix (NEB) with customized index adapter oligos. AMPure XP magnetic beads (Beck-
hamp Coulter) were used for Library purification. Sequencing was performed on Illumina NextSeq 550 with paired-end 150 bp reads. Sequencing reads were aligned to human genome reference Hg19 using Bowtie2. All PCR duplicates, mitochondrial, unmapped and non-uniquely mapped reads were removed. Peaking calling was conducted using MACS2 and visualizations of the peaks in a genomic context were generated. ChiPseeker was used for peak annotation and differential ATAC-seq peaks analysis was conducted by DiffBind. The ATAC peak distribution differences were analyzed using both Fisher’s exact and Chi-squared test.

RESULTS: The assay for ATAC-seq was optimized and validated to obtain high-quality data using small sample input (10-30 cells). The ATAC-seq result of each sample for both ICM and TE groups showed a highly reproduc-
able pattern. A large fraction of the ATAC seq peaks were located in the pro-
moter and distal intergenic regions in both ICM and TE, which is consistent with previously published data from animal models. Transcription factor binding sites (TFBS) are often accessible in the active genes and not uni-
formly distributed over the promoter region. Our data showed that ATAC peak distributions of the promoter regions (<1kb) and distal regions vs other regions were significantly different between ICM vs TE samples (P<0.01). We detected that higher percentage of accessible binding loci were located within 1kb of the transcription start site in ICM compared to TE (P<0.01). However, higher percentage of accessible regions were de-
tected in the distal region of TE compared to ICM. In addition, 8 differential peaks with the FDR<0.05 between ICM and TE were detected and these 8 accessible locations were identified in ICM samples.

CONCLUSIONS: This is the first study to compare the landscape of the accessible chromatin between ICM and TE of human preimplantation em-
broies, which unveiled chromatin-level epigenetic regulation of cell lineage specification in early embryo development.

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AN OVARIAN COMPONENT INVOLVED IN SUBFER-
TILITY OF THE NSMF KO MOUSE. Erica Louden, M.D. Ph.D., Lynn Chorich, B.S., M.S., Lawrence Layman, M.D., Augusta University, Augusta, GA.

OBJECTIVE: Genetic approaches in humans with gonadotropin releasing hormone (GnRH) deficiency causing normosmic hypogonadotropic hypogo-
adotropism (NHS) and Kallmann Syndrome (KS) are important to un-
derstand normal reproduction. NSMF (NMDA receptor synaptophysin,
signaling & neuronal migration factor), formerly known as NELF (nasal em-
bryonic LHRH factor), gene mutations have been identified in humans with either NHL/KS. However, the phenotype of the Nsmf knockout (KO) mouse is less severe than the human. The Nsmf KO female have reduced numbers of GnRH neurons and delay in vaginal opening, but normal puberty and sub-
fertility. We previously showed Kiss1 mRNA expression was increased in the hypothalami of KO animals and that pituitary gonadotropin responses were not different in wild type (WT) vs Nsmf KO mouse. Our objective in this study was to identify cell types that express Nsmf in the ovary and determine if the subfertility in the female Nsmf KO mouse has a gonadal component.

DESIGN: NSMF protein cellular localization was determined in the WT mouse ovary. Kiss1 and Kiss1r mRNA expression was characterized in the KO mouse in 8 and 18 week old ovaries, and ovarian responses to gonadotropins were studied in 3 week old Nsmf KO mice in the diestrus phase.

MATERIALS AND METHODS: Heterozygous Nsmf mice were bred to homozygosity. Ovaries from KO vs WT mice were sectioned and prepared for immunohistochemistry (IHC) using a monoclonal anti-NSMF antibody. RNA extracted from ovaries of KO and WT animals were subjected to RT-
qPCR for Kiss1 and Kiss1r expression. The ΔΔCt, cycle of threshold, method was used to calculate relative gene expression of Nsmf KO vs control using Gapdh expression for normalization. To determine the ovarian response to go-
adotropins, WT and KO mice 3 weeks of age were superovulated using PMSG and ICG. Mice were sacrificed and oocytes were removed from the ovi-
ducts and counted. Differences were analyzed using the Mann-Whitney U test.

RESULTS: Our preliminary findings demonstrate Nsmf mRNA expression in the ovary, and IHC studies and serum gonadotropins after ovarioctomy are ongoing. Kiss1r expression is unchanged in Nsmf hypothyalamus and ovary, but Kiss1 was upregulated in the hypothalamus and the ovary. Preliminary data suggests that oocyte numbers were modestly decreased in the KO (~16/ovary) vs WT (30/ovary), but maturity has not been assessed yet.

CONCLUSIONS: A hypothalamic component appears to be involved in the subfertility of the Nsmf KO mouse, as demonstrated by a decreased num-
ber of GnRH neurons as well as our finding of increased Kiss1l expression in the hypothalamus of Nsmf KO mice, which we hypothesize is a compensatory increase secondary to deficient NSMF. Therefore we sought to characterize Kiss1 and Kiss1r expression in the ovary. Kiss1r expression was unchanged, but there was a significant increase in Kiss1l, which is known to be expressed in granulosa cells in mice. We also demonstrated Nsmf expression in the WT ovary. The reduced number of oocytes in the Nsmf KO mouse supports an ovarial role for NSMF in the subfertility of the Nsmf KO mouse.

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PRO-APOPTOTIC GENE EXPRESSION IN BLASTO-
COEL FLUID FROM EUPLOID DAY-5 EMBRYOS IS
ASSOCIATED WITH NEGATIVE PREGNANCY OUT-
cOMES. Deepthi M. Athavale, B.S., Alyssa Barré, B.S., Allison C. Kranjak, B.S., Arnav Lal, M.D., Jonathan L. Blalock, B.S., Shawn Zimmerman, Ph.D., HCLD, R. Arthur Chang, Ph.D., HCLD, ELD, Randolph D. Robinson, M.D., J. David Wining, Ph.D., HCLD, William E. Roudesh, Ph.D., Renee J. Chosid, Ph.D., University of South Carolina School of Medicine Greenville, Greenville, SC; Vios Fertility Institute, Swansea, IL; University of Texas Health Science Center, San An-
tonio, TX; UT Health San Antonio, San Antonio, TX; Atlantic Reproduc-
tive Medicine Specialists, Raleigh, PA.

OBJECTIVE: The identification of molecular markers for use during selec-
tion of embryos for intrauterine implantation can enhance in vitro fertilization-
embryo transfer success rates. Assessing apoptotic gene expression in blastocoe-
l fluid-conditioned media from human embryos with known ploidy and implanta-
tion status provides the opportunity to study patterns and processes occurring during early embryo development. Apoptosis occurs during preimplantation development and may serve to selectively eliminate aneuploid cells from the developing embryo thereby enhancing implantation potential. Therefore, apoptotic remnants (i.e. mRNAs) may reside within the embryo’s blastocoe-
fluid and vary in relation to the embryo’s implantation potential. This study compared apoptotic gene expression in blastocoeel fluid-conditioned media using Real-Time PCR from euploid embryos with known implantation outcomes.

DESIGN: Retrospective analysis of day-5 euploid blastocoeel fluid apoptotic gene expression and implantation outcome.

MATERIALS AND METHODS: Blastocoeel fluid-conditioned media (25μL) was collected following trophectoderm (TE) biopsy of ICSI-gener-
dated day-5 blastocysts. Biopsied TE cells were sent for preimplantation ge-
etic testing for aneuploidy using NEGS. The blastocoeel fluid-conditioned media from 10 euploid embryos (6 that implanted; 4 that did not implant) were subjected to ICSI. Treatment prior to CDNA synthesis before as-
sessing gene expression via RT-PCR using TaqMan Fast Array-Human Apoptosis plates (assessing 92 apoptosis associated genes).

RESULTS: Of the 92 genes analyzed, CASP7 and MCL1 gene expression were only detected in euploid embryos that successfully implanted. Conversely, expression of TNFRSF25 and BCL2.L11 genes were only detected in euploid embryos that failed to implant. Several other apoptotic genes (BAD, BCL2.L13, BCAF31, NOD1 and CARD18) were expressed more often in em-
broies that failed to implant versus those that successfully implanted.

CONCLUSIONS: This study poses that specific apoptotic remnants (mRNAs encoding apoptotic genes) may represent a molecular indicator of euploid em-
bryo future implantation potential. Specifically, we detected the expression of seven pro-apoptotic genes associated with negative implantation outcomes. Apoptosis is initiated within the developing embryo in response to the presence of aneuploidy and/or ROS-induced damaged cells. Our results suggest that altered cells may still reside within some euploid blastocysts, thus initiating apoptosis. Evidence of apoptotic cell elimination may be detected by expression of pro-apoptotic genes found within the blastocoeel fluid.

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FRAGILE X CARRIER SCREENING ACCOMPANIED
BY GENETIC CONSULTATION HAS CLINICAL UTIL-
ITY IN POPULATIONS BEYOND THOSE RECOMMEND-
ED BY GUIDELINES. Katie A Johansen Taber, Ph.D., Jeraldine Lim-Harashima, MS, CGC, Harris Naemi, BS, Jim Goldberg,
OBJECTIVE: To determine the clinical utility of FXS carrier screening by analyzing actions among FMR1 premutation carriers who do and do not meet American College of Medical Genetics and Genomics (ACMG) or American College of Obstetricians and Gynecologists (ACOG) criteria for testing.

Fragile X syndrome (FXS) is the most common inherited form of intellectual disability, with 1:1515 women carrying an FMR1 premutation that confers elevated risk for FXS in offspring. ACMG and ACOG recommend FMR1 carrier screening only in women with a family history of FXS, intellectual disability suggestive of FXS, or fragile X-related disorders. Screening is also recommended for those undergoing fertility evaluation. Offering screening for FMR1 to all women who are pregnant or considering pregnancy has been resisted in part due to questions about the clinical utility of screening. Concerns have also been raised about the ability to adequately counsel large numbers of screened women about the complex inheritance patterns and the wide range of phenotypes associated with FXS.

DESIGN: Retrospective survey of couples at increased risk for a pregnancy affected by FXS.

MATERIALS AND METHODS: FMR1 premutation carriers identified by expanded carrier screening (ECS) between September 2015 and December 2017 were invited to respond to a survey about their actions following receipt of the test result.

RESULTS: A total of 122 FMR1 premutation carriers responded to the survey. Providers recommended screening for 77% of patients, while 23% of patients had requested screening themselves. 79% of screening occurred in females that did not meet the ACMG/ACOG family history criteria, and 52% occurred in those who did not meet the ACMG/ACOG fertility evaluation criteria. 99% of those screened had received post-test genetic consultation.

Among 73 FMR1 premutation carriers screened preconceptionally, 74% planned or considered actions that reduce the risk of having an affected pregnancy, including in vitro fertilization with preimplantation genetic testing for monogenic conditions (52%), prenatal diagnosis when pregnancy occurred (25%), use of a gamete donor (6%), avoiding pregnancy (6%), and adoption (4%). A family history of FXS increased the likelihood of pursuing risk-reducing actions, but undergoing fertility evaluation did not. Among 49 FMR1 premutation carriers screened prenatally, 41% planned or pursued prenatal diagnosis. Neither family history nor undergoing fertility evaluation had a significant effect on the decision to undergo prenatal diagnosis.

CONCLUSIONS: Providers recommended, and patients desired, FMR1 carrier screening regardless of whether the patient met current ACMG/ACOG screening criteria. Patients who did not meet screening criteria took action to reduce the risk of having an affected pregnancy to nearly the same extent as those who did meet criteria. Nearly all patients made reproductive and pregnancy management decisions informed by genetic consultation. These results support offering FMR1 carrier screening to all women who are pregnant or considering pregnancy.

SUPPORT: This analysis was fully funded by Myriad Women’s Health.

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THE EXPRESSION OF HUMAN ENDGENOUS RETROVIRUS SYNCYTIN IN HUMAN ANEUPLOIDY ARE INSUFFICIENT COMPARED TO EUPLOIDY.
Daxia Luo, MD, Fang Wang, PhD, Isaac J. Chamani, B.A., David H. McCulloh, Ph.D., Caroline McCaffrey, Ph.D., David L. Keefe, M.D. New York University School of Medicine, Department of Obstetrics and Gynecology, New York, NY; New York University School of Medicine, New York, NY; NYU Langone Health, New York, NY; New York Langone Health, NYU Fertility Center, New York, NY.

OBJECTIVE: Retrotransposons are a group of abundant, repetitive sequences, which originated from ancient retroviral infections of our ancestral genomes. They are silenced by epigenetic marks throughout most of life, but become activated during early embryo development, with reprogramming of the epigenome. Some retrotransposons play regulatory roles during early development. Non-Long Terminal Repeat (LTR) retrotransposons (e.g. L1) regulate gene expression during early mouse development. LTR retrotransposons, such as the human endogenous retrovirus HERV-W and HERV-FRD (Syncytin-1 and Syncytin-2), mediate placenta. We hypothesized that aneuploidy, which disrupts implantation, would affect expression of retrotransposons during early human development.

DESIGN: Prospective laboratory study.

MATERIALS AND METHODS: Blastocytes donated by patients who underwent IVF/PGT-A at NYU Langone FC were thawed, stripped of zona pel}

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A STEP TOWARD GENE REMODELING OF MAMMALIAN SPERMATOZOA BY CRISPR-Cas9.

OBJECTIVE: To identify the optimal conditions to carry out genomic remodeling of mammalian spermatozoa using CRISPR-Cas9.

DESIGN: Mouse spermatozoa with and without in vitro decondensation were transfected with a CRISPR ribonuclease-protein (RNP) targeting exon 10 of the Stra8 gene in chromosome 6. The cleavage site was designed for noninnovative gene repair by homologous recombination. The success of editing at the target site was measured by mismatch cleavage assay.

MATERIALS AND METHODS: Epididymal spermatozoa were retrieved from one B2D6F1 mouse. Half of the sample was resuspended in mHTF, and the remaining was incubated with 46 µM hEparin and 10 mM GSH at 37 °C and 5% CO2 for 30 minutes to decondense the DNA. Purified Cas9 and a custom Stra8 gRNA were pre-complexed for 10 minutes. In both the decondensed and untreated conditions, a CRISPR group was electroporated with the RNP and a negative control was electroporated without. The Neon Transfection System (ThermoFisher Scientific) was used at 1100 Volts, 30 milliseconds, and 1 pulse, based on our preliminary research. After 30 minutes at room temperature, samples were processed for analysis by the GeneArt Genomic Cleavage Detection kit. In brief, DNA was extracted from the cells and a 500-bp region around the CRISPR target site was amplified by PCR. The presence of mismatches at the cleavage site due to indels causes two fragments to appear in gel electrophoresis as opposed to one band of uncleaved DNA.

RESULTS: The raw morphological sample yielded a concentration of 30 million, 0.75 ml, and 76% motility. An aliquot was processed by microfluidic selection for a final sample of 8 million, 1.0 ml, and 89% motility. After the decondensation process, motility decreased to 72%, compared to 85% in the untreated sample. Immediately after electroporation, the motility of the negative controls dropped to an average of 60%, while that of the CRISPR samples decreased to an average of 37%. Finally, the gel analysis revealed 11% cleavage efficiency in the CRISPR population without decondensation, and 18% in the decondensed sample.

CONCLUSIONS: Our results indicate that we were able to cleave genomic DNA in the final exon of the Stra8 gene in up to 18% of spermatozoa. The addition of a brief decondensation treatment proved to be beneficial. While this assessment took into consideration the entire population of electroporated spermatozoa, it would be interesting to observe the proportion of successful transfection in spermatozoa that retained motility.
Semen parameters including volume (2.9 ± 0.2 ml), mean sperm zona-adhesion was 128 sp/mm², etc.

OBJECTIVE: The aim of this study was to observe the effect of the cumulus extracellular matrix on the sperm zona-adhesion rate in healthy fertile men.

DESIGN: Comparison of the zona-adhesion rate between spermatozoa treated with cumulus extracellular matrix and non-treated spermatozoa.

MATERIALS AND METHODS: The cumulus matrix proteins used in this study were isolated from 150 cumulus complexes that were obtained from 16 donors during oocyte retrieval procedures. The cumulus cells and their extracellular matrix were separated by pipetting followed by centrifugation. The protein content in the pool of isolated cumulus matrixes (CM) was measured by Bradford method. Semen samples were obtained from 30 normozoospermic donors. After sperm washing, the motile spermatozoa were isolated by swim-up and diluted to 0.5 x 10⁶ cells/ml. Each sample was divided into four aliquots and incubated with (1) 0.5 mg/ml CM, (2) 1.25 mg/ml CM, (3) 2.5 mg/ml CM and (4) wash medium for 30 min at 37°C. The zona-adhesion rate was evaluated by counting the adhered spermatozoa to immobilized acid-solubilized zona pellucidae from healthy donors. Results are presented as number of adhered spermatozoa per 1 mm² of the immobilized surface (sp/mm²). Statistical analysis was performed with paired t-test using IBM SPSS Software ver.21.

RESULTS: The zona-adhesion rate of the untreated spermatozoa was 81 ± 17 sp/mm² (Mean ± SD) and ranged between 54 sp/mm² and 116 sp/mm². CM treatment of the spermatozoa dose-dependently and significantly increased the zona-adhesion rate in every patient (p < 0.05). When spermatozoa were treated with 2.5 mg/ml CM, 1.25 mg/ml CM and 0.625 mg/ml the mean sperm zona-adhesion was 128 ± 28 sp/mm², 107 ± 37 sp/mm² and 99 ± 27 sp/mm², respectively.

CONCLUSIONS: The results from this study show the important role of the cumulus matrix in the preparation of the spermatozoa before meeting the oocyte and confirm that the cumulus effect should be considered during sperm processing for ICSI.

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VARICOCELE DIMINISHES SPERM CAPACITATION FUNCTION AND THE CHANCES OF GENERATING A PREGNANCY. Philip Xie, B.S.⁷, Alessandra Parrella, M.S.c, Alexander J. Travis, VMD, PhD,⁴ Zev Rosenwaks, M.D.,⁴ James A. Khashian, M.D.,² Gianpiero D. Palermo, M.D., Ph.D.⁵ "The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY; °Cornell University, Ithaca, NY; †Weill Cornell Medicine, Department of Urology, New York, NY.

OBJECTIVE: To determine whether varicocele can adversely affect sperm capacitation and therefore the probability of generating a pregnancy (PGP).

DESIGN: In 8 consenting men with grade 2 varicoceles or larger, we assessed functional semen characteristics by using Cap-ScoreTM to measure the percentage of sperm that can capacitate, and calculated the related PGP calculation. Ten men with normal semen parameters, no varicoceles, and proven fertility served as a control. Cap-Score was determined in a blind determination. Test-samples were compared to controls using paired t-tests.

RESULTS: In all experiments, Cap-Score was greater for control-CAP when compared to control-NC (p < 0.05). No differences were observed between the control-CAP and the test-CAP for any dilution (1:1 ratio: 39.7 ± 0.04 vs 40.1 ± 0.03 sp/mm², 1:6 ratio: 32.0 ± 0.04 vs 34.0 ± 0.03 sp/mm², p = 0.33; 8.5 ratio: 36.0 ± 0.02 vs 34.2 ± 0.01 sp/mm², p = 0.50).

CONCLUSIONS: A good capacitation response was observed in the controls for all experiments, suggesting proper stimulus by the CAP condition. The ratios of semen:TXY were mimicked with typical ejaculate volumes, such that a constant volume of extender could potentially be utilized in an at home semen collection kit that maintains sperm capacitation ability. Addition of a fixed volume of TYB to varying ejaculate volumes would limit user input. Similar Cap-Score values between the control-CAP and test-CAP, no matter the ratio, indicates that ejaculates can be maintained overnight in varying concentrations of TYB with minimal impact on next day function. At home sample collection could lessen the burden of processing samples at clinics with limited resources. It could also encourage pursuit of workup by men whose main barrier is privacy in producing samples at clinics or bringing them to clinics. It could also broaden the geographical availability of sperm function tests to those living far from clinics, and reduce financial burdens associated with travel and time away from work.

SUPPORT: Androvia LifeSciences.

P-398 Tuesday, October 15, 2019 6:30 AM

IMPACTS OF TEST (TES AND TRIS) YOLK BUFFER AND COOLING ON THE ABILITY OF HUMAN SPERM TO CAPACITATE. G. Charles Ostermeier, PhD; Alexander J. Travis, VMD, PhD; Androvia LifeSciences, Mountainside, NJ; The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: Studies across several mammalian species show that Gαs localization patterns are indicative of capacitation at the single cell level. The Cap-Score™ Male Fertility Assay reports the proportion of sperm displaying Gαs localization consistent with capacitation. Using clinical pregnancy outcomes, Cap-Score was previously shown to prospectively predict a man’s fertility and the relationship between Cap-Score and a man’s probability of generating a pregnancy was established. TEST (TES and Tris) yolk buffer (TYB) can prolong the fertilization capacity of sperm. Here, we evaluated whether incubation in TYB overnight at a cool temperature affected human sperm capacitation.

DESIGN: To evaluate the impact of semen extension with TYB and cooling on sperm capacitation, ejaculates were split into control and test samples for a repeated measure design.

MATERIALS AND METHODS: Studies approved by WIRB (20152233). Semen was collected, liquefied and split into control and test samples. Control samples were processed normally for Cap-Score. Test samples were extended in TYB at 1:1 (n=3); 1:6 (n=5) or 8.5 (n=5; volume ratio of semen:TYB) and cooled overnight in a Styrofoam box with an ice pack. The next day, samples were washed, exposed to non-capacitating (NC) or capacitating (CAP); conditions for 3 hrs, and then fixed overnight before Cap-Score determination. Test-samples were compared to controls using paired t-tests.

RESULTS: In all experiments, Cap-Score was greater for control-CAP when compared to control-NC (p < 0.05). No differences were observed between the control-CAP and the test-CAP for any dilution (1:1 ratio: 39.7 ± 0.04 vs 40.1 ± 0.03 sp/mm², 1:6 ratio: 32.0 ± 0.04 vs 34.0 ± 0.03 sp/mm², p = 0.33; 8.5 ratio: 36.0 ± 0.02 vs 34.2 ± 0.01 sp/mm², p = 0.50).

CONCLUSIONS: A good capacitation response was observed in the controls for all experiments, suggesting proper stimulus by the CAP condition. The ratios of semen:TYB were chosen to mimic typical ejaculate volumes, such that a constant volume of extender could potentially be utilized in an at home semen collection kit that maintains sperm capacitation ability. Addition of a fixed volume of TYB to varying ejaculate volumes would limit user input. Similar Cap-Score values between the control-CAP and test-CAP, no matter the ratio, indicates that ejaculates can be maintained overnight in varying concentrations of TYB with minimal impact on next day function. At home sample collection could lessen the burden of processing samples at clinics with limited resources. It could also encourage pursuit of workup by men whose main barrier is privacy in producing samples at clinics or bringing them to clinics. It could also broaden the geographical availability of sperm function tests to those living far from clinics, and reduce financial burdens associated with travel and time away from work.

SUPPORT: Androvia LifeSciences.

RELATIONSHIP AMONG INTRACELLULAR SUPEROXIDE DISMUTASE ACTIVITY, GLUTATHIONE PEROXIDASE ACTIVITY, MOLITILITY AND MORPHOLOGY IN HUMAN SEMEN. Lucezara Vasilev Jelezarski, PhD; Dimitar Parvanov, PhD, Vilyana Georgieva, MSc, Rumiana Ganeva, MSc.
OBJECTIVE: Oxidative damage by reactive oxygen species (ROS) is one of the main causes for sperm dysfunction. Important components of the anti-oxidative defense systems are the superoxide dismutase (SOD) and glutathione dismutase (GPx). Therefore, our objective was to examine the relationship among sperm SOD activity, sperm GPx activity, sperm motility and morphology in human spermatozoa.

DESIGN: Prospective study.

MATERIALS AND METHODS: Sixty four patients aged between 26 and 39 years were selected. Samples were collected by masturbation after sexual abstinence for 3-5 days. After semen liquefaction, semen analysis was performed (concentration, progressive motility and non-strict morphology) according to WHO 2010 guidelines. Sperm SOD and GPx activities were determined using Ransod and Ransel diagnostic kits (Randox Laboratories Ltd., Antrim, UK). An aliquot of the corresponding sperm suspension (20 x 10^6 sperm/mL) was centrifuged at 600 x g for 5 minutes and the supernatant was discarded. The remaining pellet was treated with 0.5 mL of 0.1% Triton X-100 in PBS and vortex-mixed three times for 20 seconds followed by centrifugation at 1,000 x g for 5 minutes. Aliquots of the supernatant were added to the wells of the microplate and the assay was performed according to the manufacturer’s instructions. The supernatant was discarded and the pellet was treated with 0.5 mL of 0.1% Triton X-100 in PBS, vortex-mixed three times for 20 seconds, and centrifuged at 1,000 x g for 5 minutes. Aliquots of the supernatant were added to the wells of the microplate and the assay was performed according to the manufacturer’s instructions. Statistical analysis was performed by Spearman’s correlation test using SPSS v.21 (IBM Corp., Armonk, NY, USA). Descriptive parameters and patient characteristics were reported as mean ± SD and median. P ⩽ 0.05 was considered statistically significant.

RESULTS: The determined SOD activity ranged between 0 and 1415 U/10^6 spermatozoa with a mean of 131.82 ± 242.11 U/10^6 spermatozoa and a median of 56.64 U/10^6 spermatozoa. The observed GPx activity ranged from 0.2 to 111.57 U/10^6 spermatozoa with a mean of 5.12 ± 14.57 U/10^6 spermatozoa and a median of 1.67 U/10^6 spermatozoa. There was a significant but low positive correlation between sperm SOD and GPx activities (R = 0.27; p = 0.04). Sperm SOD activity did not correlate significantly with sperm motility and morphology. In contrast, sperm GPx activity showed a significant negative correlation with the progressive motility (R = -0.48; p < 0.01) and negative correlation with the sperm morphology (R = -0.49; p < 0.01).

CONCLUSIONS: Intracellular sperm GPx activity seem to be linked more strongly to the sperm motility and morphology parameters rather than the sperm SOD activity. Among the studied group the lower sperm motility and poor sperm morphology were associated with relatively high GPx activity.

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DURAMYCIN DISRUPTS SPERM MOTILITY AND IN VITRO FERTILIZATION (IVF). Devang Sharma, MD, Claudia M. Rival, PhD, Sarah C. Krzastek, MD, Jeffrey J. Lysiak, PhD, Ryan P. Smith, MD, NICHD’s Reproductive Medicine Network, University of Virginia, Charlottesville, VA.

OBJECTIVE: The aim of our study was to investigate effects of phosphatidylethanolamine (PtdE) on mouse epididymal sperm and to evaluate the effect of Duramycin, a broad-spectrum antibiotic commonly used in animal husbandry and a compound used to detect PtdE in cell membranes, on sperm progressive motility and fertilization capacity in IVF.

DESIGN: Capacitated caudal epididymal sperm were isolated from mice and either untreated or incubated with Duramycin. Sperm progressive motility and sperm cell death were assessed. Additionally, sperm were used for IVF and the percentage of resultant two-cell embryos was analyzed.

MATERIALS AND METHODS: Caudal epididymal sperm were isolated from > 10 week-old C57BL/6 mice. To detect PtdE, capacitated sperm were incubated with biotinylated Duramycin for 30 minutes, followed by streptavidin conjugated with Texas Red, mounted, and analyzed via fluorescent microscopy. Sperm progressive motility was assessed after a 30 minute incubation with 0.1 – 2 μM Duramycin or control DMSO. The effect of Duramycin on sperm motility during IVF was evaluated with 7AAD (necrosis) and staining of cleaved caspase-3 (CC3; apoptosis) by immunofluorescent microscopy. Sperm progressive motility was assessed after a 30 minute incubation with 0.1 – 2 μM Duramycin or control DMSO. The effect of Duramycin on sperm death was evaluated with 7AAD (necrosis) and staining of cleaved caspase-3 (CC3; apoptosis) by immunofluorescent microscopy. During IVF, sperm untreated or incubated with 2 μM Duramycin were used to inseminate oocytes isolated from super-ovulated C57BL/6 female mice. After 24 hours, the percentage of resultant 2-cell embryos was analyzed.

RESULTS: PtdE exposure was detected exclusively on the midpiece of mouse sperm. The fertilization rate of oocytes inseminated with untreated sperm was ~75%, while it was completely abolished (0%) when sperm were pre-incubated with 2 μM Duramycin. Sperm progressive motility was completely disrupted by 0.25 – 2 μM Duramycin and dramatically reduced with 0.1 μM Duramycin (% of motile sperm – Control: ~56%; Duramycin 4.2%). Sperm death increased after incubation with Duramycin (% of CC3+ sperm – Control: 2.3 ± 2.3, Duramycin: 13.8 ± 4.4), while CC3+ cells were not detected.

CONCLUSIONS: Duramycin significantly impaired sperm motility even at very low concentrations. This may explain the incapacity of the Duramycin-treated sperm to fertilize oocytes. Duramycin did induce cell necrosis on a fraction of sperm; however, this cannot explain the complete disruption of sperm motility. Since Duramycin binds the sperm midpiece where PtdE is exposed, it is possible that Duramycin disturbs mitochondrial activity depleting sperm energy and leaving the sperm immotile but alive. Environmental toxins have been implicated as a powerful contributor to the published widespread decline in semen parameters. The frequent use of Duramycin in agriculture portends frequent human exposure with unknown health and fertility consequences. Future studies are needed to examine the presence of Duramycin in our food chain.
THE EFFICACY OF OXIDATION REDUCTION POTENTIAL (ORP) IN MALE INFERTILITY AND ITS RELATIONSHIP WITH SEMINAL LEUKOCYTE CONCENTRATION. Shinnosuke Kuroda, M.D., Teppi Takeshima, M.D., Yasushi Yumura, Ph.D., Yokohama City University, Medical Center, Yokohama, Japan.

OBJECTIVE: Reactive oxygen species (ROS) in semen has been reported to have negative effect to male fertile capacity, and recent studies reported the efficacy of oxidation-reduction potential (ORP) which reflects the balance of oxidants and antioxidants in semen. The source of ROS in semen is considered as immature spermatozoa and seminal leukocytes, but the detail is still unknown. The aim of this study is to evaluate the relationship between the concentration of seminal leukocytes and oxidative stress level using ROS, ORP.

DESIGN: Retrospective study.

MATERIALS AND METHODS: Between April 2018 and March 2019, 29 infertile males who visited Reproduction Centre of Yokohama City Medical Center were enrolled. All patients underwent semen analysis and measurement of ROS and ORP levels. The ROS level in semen was measured using Monolight 3010 TM Luminometer and the ORP level was measured using MIOXSYS System TM. The concentration of peroxidase-positive leukocytes were evaluated using myeloperoxidase staining (Endtz test). The relationship between ROS levels, ORP levels, the concentration of leukocytes and semen parameters were evaluated using correlation analysis. RESULTS: The sperm concentration and motility were 39.6±36.6×10⁶/mL, 30.0±18.9 %, respectively. The total ROS level was 9328.9 (±18851) Relative Light Units, and the ORP level was 46.1±38.7 mV. The ROS level was significantly correlated with ORP level (r=0.79, p<0.01). The concentration of leukocytes measured by Endtz test was positively correlated with both ORP level (r=0.46, p=0.023) and ROS level (r=0.82, p<0.01). ORP level was negatively correlated with sperm concentration (r=-0.41, p=0.026), while ROS level didn’t show significant correlation with every semen parameters.

CONCLUSIONS: To our knowledge, this is the first study that showed the significant correlation between ORP levels and seminal leukocytes concentration. Our study suggested that peroxidase-positive leukocyte is one of the main source of ROS in semen. Although ROS was strongly correlated with sperm concentration (r<0.41, p<0.023), while ROS showed no significant correlation with every semen parameters.

P-802 TUESDAY, OCTOBER 15, 2019 6:30 AM

ANDROGENS NEGATIVELY AFFECT CILIARY FUNCTION AND ALTER GENE EXPRESSION IN THE HUMAN FALLOPIAN TUBE. Tia Jackson-Bey, MD MPH,¹ Angela Russo, Ph.D.,³ Alexandra N. Young, B.S., B.A.,³ Joanna E. Burdette, Ph.D.³ 'University of Illinois at Chicago, College of Medicine, Chicago, IL; 'University of Illinois at Chicago, College of Pharmacy, Chicago, IL.

OBJECTIVE: To evaluate the impact of androgen exposure on human fallopian tube epithelium in relation to ciliary function and gene expression.

DESIGN: Translational research.

MATERIALS AND METHODS: We exposed human fallopian tube epithelium to either a hormonally physiologic (low testosterone) or hyperandrogenic (high testosterone) culture media for 7-14 days. The hyperandrogenic media was characterized by twice the concentration of testosterone (2nM) than in the physiologic media (0.8 nM). After 7 days, cilia were imaged with spinning confocal microscopy to capture ciliary beating. The cilia beating frequency was then quantified using Fiji Image J software. After 14 days, gene and protein expression was assessed via immunohistochemistry staining, qualitative PCR, RNA sequencing and ELIZA. Parallel experiments were conducted in static conditions, with the tissue on porous wells partially submerged in culture media that was exchanged every 2-3 days, as well as in microfluidic “organ on a chip” devices, in which fresh media is dynamically circulated through, and waste removed from, wells containing the human fallopian tube epithelium in culture media.

RESULTS: After 7 days, a difference was seen in the rate of ciliary beating frequency as detected by spinning disk confocal microscopy. Human fallopian tube epithelium exposed to high testosterone had a decreased rate of cilia beating compared to human fallopian tube epithelium exposed to the low testosterone media. Further, at differing testosterone concentrations, the ciliary beating frequency exhibited a dose-response decrease as concentration of testosterone increased. Changes in genes that regulate cilia structure and function were found after 14 days. RNA sequencing showed that amongst other genes, FOXL1, SAA2, and DNAH5 were down-regulated and MAP2 and CNTN4 were up-regulated respectively in the high testosterone group. These genes play major roles in ciliary motility and structure. Genes involved in hormonal signaling, including ZBTB16, were also found to be elevated in the human fallopian tube epithelium exposed to high testosterone on RNA sequencing. Immunohistochemistry staining showed that the androgen receptor was up-regulated and became localized to the nucleus in the high testosterone group, while estrogen receptor expression was reduced. qPCR also showed androgen and estrogen receptors to be up and down regulated in the high testosterone environment, respectively. In addition, qPCR showed down-regulation of OVGP1, an estrogen regulated epithelial glycoprotein important for reproductive function, and up-regulation of ZBTB16, an androgen target gene involved in cell cycle regulation. ELIZA showed decreased VEGF in the high testosterone conditions.

CONCLUSIONS: These novel findings demonstrate that elevated androgen exposure alters cilia expression and function in the human fallopian tube. These ex-vivo experiments may add to our understanding of the mechanisms of subfertility and reproductive health risks in women with living with hyperandrogenic disorders, such as PCOS, obesity and androgen producing tumors.

SUPPORT: The study PI is part of a NIHES UG3 ES029073

P-803 TUESDAY, OCTOBER 15, 2019 6:30 AM

MIR-297 REPRESSIONS THE EXPRESSION OF PROGESTERONE RECEPTOR AND DECIDUALIZATION IN EUTOPIC ENDOMETRIUM IN INFERTILE WOMEN WITH ENDOMETRIOSIS. Wei Huang, Ph.D. M.D., Tingting Liu, M.D. West China Second University Hospital of Sichuan University, Chengdu, China.

OBJECTIVE: Progesterone resistance is one of the epigenetics affecting the decreased endometrial receptivity and implantation failure in endometriosis-associated infertility. Altered miRNAs expression plays an important role in the pathophysiology of endometriosis. Our previous study demonstrated that miR-297 was overexpressed in the mid-secretory eutopic endometrium in the endometriosis group compared with control. We performed our study to explore the regulation of miR-297 on the aberrant progesterone receptor expression and impaired decidualization in the endometrial stromal cells from eutopic endometrium of women with minimal or mild endometriosis.

DESIGN: Human tissue study.

MATERIALS AND METHODS: We performed our study to explore the regulation of miR-297 on the aberrant progesterone receptor expression and impaired decidualization in the endometrial stromal cells from eutopic endometrium of women with minimal or mild endometriosis. Eutopic endometrial tissues from infertile endometriosis patients (n = 20) and normal patients (n = 19) were collected in vitro analysis. Endometrial stromal cells were isolated and transfected with miR-297 mimic or miR-297 inhibitor or the respective controls. Gene expression regulation was examined by real-time quantitative PCR, Western blot and luciferase reporter assay. Artificial decidualization assay was performed to investigate the role of miR-297 during decidualization in vitro.

RESULTS: Eutopic endometrial tissues from infertile endometriosis patients (n = 20) and normal patients (n = 19) were collected in vitro analysis. Endometrial stromal cells were isolated and transfected with miR-297 mimic or miR-297 inhibitor or the respective controls. Gene expression regulation was examined by real-time quantitative PCR, Western blot and luciferase reporter assay. Artificial decidualization assay was performed to investigate the role of miR-297 during decidualization in vitro. The expression of progesterone receptor especially progesterone receptor B were decreased after transfected with miR-297 mimics and increased in the controls. Moreover, miR-297 overexpression inhibited miR-297 inhibited the decidualization of endometrial stromal cells in vitro.

CONCLUSIONS: Our study demonstrated the regulation of miR-297 on the blunted PR expression is direct.

SUPPORT: National Natural Science Foundation of China (No.81370693)
INHIBITION OF BOTH DNA METHYLTRANSFERASES AND HEDGEHOG SIGNALING SUPPRESSES THE PHENOTYPE OF HUMAN UTERINE LEIOMYOSARCOMA CELLS, Natalia Garcia, MSc, Ayman Al-Hendy, MD PhD, Leonardo Tomiatti da Costa, MSc, Kaíta Candido Carvalho, PhD, Qiwei Yang, PhD "University of Illinois at Chicago, Chicago, IL; "University of Sao Paolo, Sao Paulo, Brazil.

OBJECTIVE: Uterine leiomyosarcoma (LMS) is the most common of uterine sarcoma, it is a rare and aggressive tumor with poor prognosis. Our group described previously that the hedgehog (HH) signaling was activated in LMS, which contributed to its aggressive phenotype. However the mechan-ism by which HH activation in LMS is largely unknown. The objective of this work was to characterize the genetic and epigenetic mechanism in HH signaling and evaluate the anti-HH effect of DNA methyltransferase inhibitor (DNMTi) alone or in combination with GLI inhibitor (GLIi) on LMS.

DESIGN: Laboratory research studies using human uterine smooth muscle (UTSM), LMS cells and LMS patient samples.

MATERIALS AND METHODS: LMS cells were used to evaluate the mRNA and protein expression of DNMT1, 3a, 3b, PTCH1, SMO and SUFU mutations were evaluated in 7 LMS patients from 3 different Brazilian institutions (CEP 477/15) using next generation sequencing Ion AmpliSeq (Thermo Fisher Scientific). The percentage of PTCH1 methylation was determined by EpiTect Methyl II PCR array (Qiagen) in LMS cells. Proliferation, migration, invasion and apoptosis assays were performed to evaluate the inhibitory effect of DNMTi (2 μM of 5-aza-2'-deoxycytidine) alone or in combination with GLIi (15 μM of Gant61) during 72 hours. The statistical analysis was performed using GraphPad Prism 5. Significance was accepted for p<.05.

RESULTS: No hot spot mutations on PTCH1, SMO and SUFU sequences were detected in LMS patient samples. Uregulation of DNMT1, 3a and 3b mRNA and protein was observed in LMS compared to UTSM cells. The percentage of PTCH1 DNA methylation in LMS was 2.3%. Treatment with DNMTi decreased the expression of DNMT1, 3a and 3b and DNA methyl-ation of PTCH1 to 1%. Although inhibition of DNMT did not change PTCH1 gene expression, significant downregulation of GLI1 was observed in LMS cells (p<.05). The DNMTi in combination with GLIi (Gant61) ex-hibited decreased SMO and GLI1 protein expression (p<.05), and supressed GLI1 nuclear translocation. Moreover, the combination treatment showed more inhibitory effects on proliferation, migration, invasion and induced apoptosis in LMS cells (p<.05).

CONCLUSIONS: Our study demonstrates for the first time that although genetic mutations of key HH members are not observed, DNA methylation is tightly linked with LMS phenotype via HH signaling. Notably, a combined treatment of DNMTi and GLIi exhibits a more robust inhibitory effect on LMS phenotype. Further understanding the mechanism of HH pathway in LMS may lead to development of a novel treatment strategy for this aggressive cancer.

SUPPORT: Support: FAPESP 2017/24448-1, 2015/23482-6, 2015/21068-8; ROI ES028615; U54 MD007602

P-806 Tuesday, October 15, 2019 6:30 AM

INTRATERINE INSEMINATION CYCLES: CHARACTERISTICS ASSOCIATED WITH LIVE BIRTH AND THRESHOLDS FOR INEFFECTIVE AND FUTILE CARE, Alessandra J. Ainsworth, MD, Emily P. Barnard, DO, Sarah Baumgarten, MD, PhD, Camden Lopez, MS, Amy Weaver, MS, Zaraq Khan, MD Mayo Clinic, Rochester, MN; University of Pittsburgh School of Medicine, Pittsburgh, PA.

OBJECTIVE: This study aimed to identify intrauterine insemination (IUI) cycle characteristics associated with live birth and to define ineffective and futile care guidelines.

DESIGN: This retrospective cohort study evaluated couples pursuing IUI at Mayo Clinic from 1/2005 to 9/2017. Couples using fresh partner ejaculate were included. Female age, ejaculate and inseminate parameters, and ovarian stimulation type were evaluated for association with live birth, defined as birth after 24 weeks gestation. Outcomes were evaluated per cycle, rather than per patient.

MATERIALS AND METHODS: Univariate and multivariable logistic regression models were fit to evaluate the association of cycle characteristics with probability of live birth. Models were fit using generalized estimating equation methodology with an exchangeable correlation structure to account for the correlation between cycles involving the same patient. Ineffective and futile care were defined as live birth <5% and 0%, respectively, consistent with ASRM guidelines.

RESULTS: A total of 2912 IUI cycles were included for 1117 women. No live births were reported in women 43 years of age or older. Initial analysis identified a threshold of live birth >5% for inseminate motility of 70%. Multivariable analysis restricted to women under 43 years of age, type of ovarian stimulation, age, and inseminate motility were significantly associated with higher odds of live birth. Rates of live birth per combination of aforementioned factors are presented in Table 1. Cate-gories with less than 10 subjects were considered inconclusive, rather than ineffective.

CONCLUSIONS: Female age and inseminate motility were found to be primary contributors to live birth rate. Ineffective care was noted with low motility (<70%) in the inseminate even for women aged 35-37. Increasing female age, above 37, compounded by low motility met criteria for futile care. Both pre- and post-treatment components should be reviewed for counsel-ing and appropriately directed care.
ogy, utilization of these frozen gametes is low. Disposition preferences will become increasingly important as this patient population ages and meets their reproductive goals. Formalized research protocols need to be established to accommodate this anticipated increase in oocytes available for research.

P-807 Tuesday, October 15, 2019 6:30 AM

OOCYTE DISPOSITION PREFERENCES: PLANNING FOR THE FUTURE. Anne Hutchinson, M.D., Rafael Confino, BS, John Zhang, PhD, Angela K. Lawson, Ph.D., Mary Ellen Pavone, MD, MSCI Northwestern University, Chicago, IL.

OBJECTIVE: To characterize the frozen oocyte disposition preferences of patients undergoing medical and social fertility preservation

DESIGN: Descriptive Study

MATERIALS AND METHODS: This descriptive study was performed using data collected between 2011 and 2018 in the Division of Reproductive Endocrinology and Infertility at Northwestern University. Demographic and cycle information was collected for each patient. Medical diagnosis was collected for each medical fertility preservation patient. Medical and social fertility preservation (FP) patients were distinguished based on documentation in their initial consult note in the electronic medical record. Disposition options included: disposal, donation to research, or donation to a specified third party which was decided at the time of initial consent and scanned into the patient chart. The demographic parameters were compared between the two groups using chi-squared analysis.

RESULTS: 578 oocyte vitrification cycles were identified between 2011 and 2018. 15 cycles were noted to have no documented disposition preference and were excluded from the analysis. 143 cycles corresponded to medical FP patients and 435 to social FP. Medical FP patients were more likely to be under the age of 35, have a higher BMI, and have had a prior live birth. In both groups, the most commonly selected option was donation to research (48.3% social, 48.3% medical), followed by donation to a specified third party (27.4% social, 28.7% medical) and finally disposal of oocytes (41.6% social, 48.3% medical), followed by donation to a specified third party (27.4% social, 28.7% medical) and finally disposal of oocytes (48.3% social, 48.3% medical), followed by donation to a specified third party (27.4% social, 28.7% medical) and finally disposal of oocytes (48.3% social, 48.3% medical) and disposal of oocytes (48.3% social, 48.3% medical) and disposal of oocytes (48.3% social, 48.3% medical) and disposal of oocytes (48.3% social, 48.3% medical) and donation to research (22.8% social, 17.5% medical).

CONCLUSIONS: Our data shows that oocyte disposition choices are similar in patients undergoing oocyte vitrification for medical and social indications. Both groups most commonly elect donation to research, followed by donation to a specified third party. Disposal of oocytes was the least common disposition choice for both groups. While oocyte vitrification is a relatively new technology, utilization of these frozen gametes is low. Disposition preferences will be under the age of 35, have a higher BMI, and have had a prior live birth. In both groups, the most commonly selected option was donation to research (48.3% social, 48.3% medical), followed by donation to a specified third party (27.4% social, 28.7% medical) and finally disposal of oocytes (22.8% social, 17.5% medical).

TABLE 1. Comparison of patients across low-normal BMI to Morbid obesity (BMI Class II)

<table>
<thead>
<tr>
<th>Pre-operative Demographics</th>
<th>Low-Normal BMI (n=1042)</th>
<th>Morbidly Obese (BMI&gt;30) (n=280)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black race</td>
<td>266 (25.5)</td>
<td>168 (60.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Diabetes with pharmacotherapy</td>
<td>12 (1.51)</td>
<td>30 (10.7)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Hypertension with pharmacotherapy</td>
<td>37 (3.6)</td>
<td>81 (28.9)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>ASA Class III/IV</td>
<td>32 (3.1)</td>
<td>119 (42.5)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Surgical and post-operative characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal Myomectomy</td>
<td>472 (45.3)</td>
<td>160 (57.1)</td>
<td>0.002*</td>
</tr>
<tr>
<td>Inpatient Recovery</td>
<td>498 (47.8)</td>
<td>169 (60.4)</td>
<td>0.002*</td>
</tr>
<tr>
<td>Total Surgery Time (min)</td>
<td>131.9 ± 76.7</td>
<td>157.3 ± 84.9</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Length of Hospital stay</td>
<td>1.0 (0.0-14.0)</td>
<td>2.0 (0.0-31.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Unplanned Hysterectomy at time of Myomectomy</td>
<td>30 (2.9)</td>
<td>20 (7.1)</td>
<td>0.0009*</td>
</tr>
</tbody>
</table>

1 Chi-Square n(%)  
2 t-test mean(Standard deviation), Mann-Whitney U-test Median(Range)
DETECTION OF THE FERTILE WINDOW USING A WEARABLE MEDICAL DEVICE AND THE CALENDAR METHOD: A COMPARATIVE STUDY. Evangelia Mourtiki, MS,⁎ Aljosa Bilic, MSc,⁎ Brianna M. Goodale, PhD,⁎ Gyorgyi Hamvas, MSc,⁎ Catrin Argyle, BSc, MSc,⁎ Mohamed Shilaaih, PhD,⁎ Brigitte Leeners, Dr. Prof⁎ Ava AG, Zurich, Switzerland; University Hospital Zurich, Zurich, Switzerland.

OBJECTIVE: While many women rely on the calendar method to detect their fertile window and prevent or aid conception, recent advances in wearable sensor technology and artificial intelligence suggest a wrist-worn medical device could provide women with an accurate, individualized prediction.

In this study, we compare the accuracy and precision of these two methods in identifying the six-day fertile window.

DESIGN: Retrospective analysis of data from a clinical sample

MATERIALS AND METHODS: Thirty-four conception-seeking women enrolled in a trial to test the performance of a wrist-worn medical device in detecting physiological changes across the menstrual cycle. Participants wore the Ava Fertility Tracker nightly while sleeping for up to a year. Via three sensors, the Ava Fertility Tracker measures seven different biophysical parameters every 10 seconds including skin temperature and heart rate. Participants synchronized each morning with the complementary smartphone app, which relies on a machine learning algorithm to predict and detect the real-time fertile window. Participants also completed a daily diary entry about their activity in the last 24 hours and recorded whether they had received a positive urinary luteinizing hormone (LH) test each morning. Women had to be older than 18 years old, not currently taking hormonal birth control, and have regular cycles (defined as 24-35 days in length) in order to be included in our analyses. For each subject and each cycle, we retrospectively calculated the fertile window as would have been predicted by three different calendar methods: the Standard Days method, the Rhythm Method, and the Alternative Rhythm Method. Using the LH test result as an objective measure of ovulation, we compared the accuracy and precision of each calendar method to the algorithm-identified fertile window. We defined precision as the fraction of days which the method reported as fertile that aligned with the LH-detected fertile window and accuracy as the percentage of correctly classified fertile or infertile days overall.

RESULTS: The accuracy in identifying the fertile days for the wearable device was 88.1% (Standard deviation [SD] = 9.1%) compared to 76.8% (SD = 5.1%) for the Standard Days method, 69.2% (SD = 15.6%) for the Rhythm Method, and 67.6% (SD = 16.1%) for the Alternative Rhythm Method. Furthermore, the wearable fertility tracker had the highest precision of any of the methods analyzed (70.3%, SD = 21.9% v. 42.7%-47.7% for the calendar methods [SDs = 7.6%-13.0%]).

CONCLUSIONS: Despite the ease of use and straightforward calculations driving the calendar method, using a wrist-worn medical device that records multiple physiological parameters simultaneously provides a more accurate and more precise estimation of the fertile window. Our findings have implications for women across the reproductive lifespan; whether women are currently using birth control, taking the pill, or trying to conceive.

Cryo Tank Issues

Cryo tank failure at several US and Canadian IVF clinics has been reported in the news media recently. Hundreds of patient specimens were lost. Current Quality Control (QC) measures are typically to assess liquid nitrogen (LN₂) concentration and re-fill on a strict schedule. We wished to see what happens when a properly QC’d tank fails (defined as vacuum loss) to judge whether the ‘measure & fill’ approach was adequate.

Cryogenics and its consequences are of increasing concern.

MATERIALS AND METHODS: 12 retired various model cryogenic dewars (35L+Taylor-Wharton and 47L MVE) were filled with LN₂ to the neck of the tank per QC protocol. Each tank was fitted with temperature sensors at mid-level and the bottom of the canister. Furthermore a temperature probe was placed in the lid of the tank as well as the shoulder of the tank (near handle). 1mm holes were drilled either into the shoulder of the tank (external breach), or into the neck of the tank (internal breach). Temperatures were then taken from the time of the breach, and every 15 minutes thereafter until the tank was considered ‘failed’ (internal mid tank temperature rose above -150°C).

RESULTS: Boiling of the LN₂ was evident within 60 seconds of the breach regardless of tank model.

Upon vacuum breach of each tank the sound of vacuum loss was audible for up to 4 hours with external breaches.

Temperature of lid due to escaping cold LN₂ gas went below 5°C in the first 15 minutes of the breach regardless of model, and stayed below this level until the tank was considered failed (above -150°C)

Ice ‘crowning’ of the lid was only obvious with external breaches, but not so with internal breaches.

Time for tank to fail was dependent on tank model and type of breach.

Temperature of the external probe on the tank showed a drop in surface temperature, but this was dependent on type of breach and varied in time from when breach had occurred.

Time to tank failure depended on tank model and breach type, but for a minimum of 12hrs internal temperature were maintained above -150°C for all tanks tested.

Lid temperatures below 5°C were consistently observed until a tank’s internal temperature went above -150°C regardless of model or breach type.

CONCLUSIONS: Tanks that experience vacuum loss will almost immediately experience LN₂ boiling and emit a steady stream of cold LN₂ gas. Monitoring lid temperature twice daily could identify tanks that have lost vacuum. Using an infrared red gun to take the lid temperature of a cryo tank twice daily (a.m. & p.m.) would be a quick and convenient way to identify tanks that have lost vacuum, and that are compromised. Tank lid temperatures that deviate more than 20% from the mean of other tanks in the storage area should be evaluated for failure. Additionally tanks can be fitted with remote alarmed lid temperature sensors to detect temperature drops due to LN₂ boiling that would occur when a tank loses vacuum.

THE ANATOMY OF LIQUID NITROGEN (LN₂) CRYO DEWAR TANK FAILURES. Mitchel C. Schiewe, MS, PhD⁎, Shane Zozula, B.S., T.S. (ABB),⁎ Erica J. Behnke, PhD⁎, Jason Cowles, BA,⁎ Rob Manchise, BS,⁎ John B. Whitney, BS,⁎ Ovation Fertility, Newport Beach, CA; ⁎Ovation Fertility, Cincinnati, OH; ⁎Trust Gnosis, Brea, CA.

OBJECTIVE: The key factor in averting the catastrophic loss of precious gametes and embryos rests in the comprehensive implementation of quality management practices and the early detection of an unexpected failure event. The goal of our investigation was to simultaneously evaluate, interrupt and understand weight and temperature changes of induced dewar tank failures under continuous video surveillance over a 24h interval.

DESIGN: A prospective, observational study assessed a variety of induced tank failure events monitored by real-time video, weight determination and temperature measurements following an external or internal breach of their insulating vacuum. Our aim was to characterize the nature of different tank failures and determine what alarm indicators may best provide an early warning of a potentially catastrophic outcome.

MATERIALS AND METHODS: Using a novel Wi-Fi based, pressure sensitive weight cart devices (TrustGnosis; Brea, CA) and a hard wired temperature-based continuous monitoring alarm system (Xilinx, Netherlands), we prospectively correlated ‘alarm’ characteristics of several aged (>18 years old; n=6) 35-36L Taylor-Wharton dewar LN₂ storage tanks and one ‘recalled’ new Biocane 73L TS/Chart tank. We installed and drilled (1/16”) together vacuum port of the 73L dewar and two smaller tanks (35HC, 36VHC). In phase 2, we increased the external drill (ED) opening to 1/8” and 3/16” on two 35HC tanks, while two others (35HC) where drilled (1/4”) through their inner base seam (ID) into the vacuum space. An ANOVA regression model was used to correlate the relationship between weight and LN₂ levels.
RESULTS: The intentional destruction of all external dewar tanks created an aspiration noise as room air initially warmed the interstitial space outside the inner tank. Conversely, internal dewar tanks displayed overt bubbling of its inner liquid chamber and immediate LN vaporization (within 10 sec). LN vaporization occurring outside the cap and neck of the external dewar tank was also evident within 30 sec. An external thermocouple registered 5°C within 3 min. Ice was seen on the cap surface by 3 min, while gradual frost build-up occurred over several hours. icing and condensation on the tank walls was apparent early on and throughout failure. A 20% evaporation detected by weight took about 4h, while the first internal temperature alarm at -194°C did not occur until 5.5-6.5h. The ID tanks reached -170°C sooner (+14-15h) with 65-75% evaporation while the first internal temperature alarm at -194°C did not occur until 4.5-5.5h. The ID tanks reached -170°C sooner (+14-15h) with 65-75% evaporation while the first internal temperature alarm at -194°C did not occur until 4.5-5.5h. The ID tanks reached -170°C sooner (+14-15h) with 65-75% evaporation while the first internal temperature alarm at -194°C did not occur until 4.5-5.5h.
Rebecca Holmes, PhD, a TURE MEDIA IN A TIME-LAPSE INCUBATOR USING MEDIUM INCUBATION WITH SEQUENTIAL CULT-P-405

HSA alone. Source: SPS and SSS support better blastocyst development than native for the culture of human embryos, in which complex protein supplement alternative antioxidants, growth factors and fatty acids do not provide any additional benefit over HSA alone, although they are not detrimental to embryo development or quality. This novel protein supplement may be a viable alternative for the culture of human embryos, in which complex protein supplement such as SPS and SSS support better blastocyst development than HSA alone.

SUPPORT: None.

P-405 Wednesday, October 16, 2019 6:30 AM

COMPARISON OF HUMIDIFIED VERSUS NON-HUMIDIFIED INCUBATION WITH SEQUENTIAL CULTURE MEDIA IN A TIME-LAPSE INCUBATOR USING SIBLING OOCYTE SPLITS. Rebecca Holmes, PhD,a Jaime Weinberg, BS,a Laurie Kalaghan, BS,b Brett Goode, BS,b William B. Schoolcraft, MD, Jason E. Swain, PhD. aACRM Boston, Chestnut Hill, MA; bTexas Children’s Hospital, Houston, TX; cUniverse of the Western Cape, Bellville, South Africa.

OBJECTIVE: Many modern embryo culture incubators are non-humidified. Initial studies indicate that evaporation of culture media may occur in non-humidified culture environments, even under mineral oil. This evaporation may negatively impact embryo development and quality. Controlling for other variables in the culture system while trying to study the impact of humidity may be difficult. The objective of this study was to compare outcomes following sibling zygote splits in identical culture conditions, within the same incubator, utilizing a time-lapse system that permits both dry and humidified culture.

DESIGN: Prospective randomized trial.

MATERIALS AND METHODS: A total of 214 commercially obtained frozen mouse embryos (B6D2F1 & B6C3F1 hybrid) were thawed and cultured in One-Step medium with 10% Serum Protein Substitute using an Ultra-Low Co2 environment could enhance blastocyst development in terms of yield and quality blastocysts on day 5, 6 and overall on day 7 and than non-humidified culture. No differences in fertilization, good quality cleavage or total blastocyst development were apparent. Under the culture conditions used, evaporation may have occurred to compromise blastocyst quality, though this seems unlikely with media exchanges at 48h intervals based on prior studies within our laboratory. Results may vary with fewer media changes, in laboratories using single step media in an uninterrupted fashion, or if using differing amounts or types of mineral oil overlay.
blastocyst (HBB). The 2-cell stage was considered as time zero since the exact time of insemination was unknown. Time points were statistically compared between the two groups. Blastocyst development rates for both culture environments were also compared.

**RESULTS:** There were no statistically significant differences between the two groups in any of the time points measured up to the 8-cell stage. However, after the 8-cell stage, the 2% O₂ group showed significantly slower embryo development for each time point up to the hatching blastocyst stage. There was no difference in the blastocyst development rate between the 6% O₂ and 2% O₂ environments (99.1% vs 95.4%, P=0.099).

**CONCLUSIONS:** Culture of mouse embryos in a 2% oxygen environment did not show any improvement in blastocyst development. However, embryos cultured in 2% oxygen took significantly longer to reach the blastocyst stage than those cultured at 6% oxygen, and this delay became prominent after the 8-cell stage.

**P-407 Wednesday, October 16, 2019 6:30 AM**

**DOES SUPPLEMENTATION OF MEDIA WITH INSULIN OR INSULIN-LIKE GROWTH FACTOR 1 (IGF-1) ENHANCE MORPHOKINETICS OF MOUSE EMBRYO DEVELOPMENT?** Khalied Kaskar, MS, a Richard Cochran, PhD, a Daneeka P. Hamilton, MPH, a Amanda David, BS, a Ralf Henkel, PhD, b William Gibbons, MD, a Chellakkann Selvanesan Blesson, PhD, b Baylor College of Medicine, Houston, TX, bTexas Children’s Hospital, Houston, TX, bUniversity of the Western Cape, Bellville, South Africa.

**OBJECTIVE:** To evaluate if adding either insulin or insulin-like growth factor 1 (IGF-1) to culture medium improves mouse embryo development and time-lapse morphokinetics.

**DESIGN:** Prospective study.

**MATERIALS AND METHODS:** A total of 305 commercially obtained frozen mouse embryos (B6D2F1 & B6C3F1 hybrid) were thawed and cultured in 1 (One-Step medium only), 2 (One-Step medium with 100ng/mL insulin, and 3) One-Step medium with 100ng/mL IGF-1, using an EmbryoScope time-lapse incubator at 37°C, 5.5% CO₂, and 6.0% O₂. The EmbryoScope was set to record images of each embryo every 10 minutes for 6 days of culture. The following time points were annotated: 2cell (t2), 3cell (t3), 4cell (t4), 5cell (t5), 6cell (t6), 7cell (t7), 8cell (t8), start of compaction (tSC), morula (tM), start of blastulation (tSB), blastocyst (tB), expanded blastocyst (tEB) and hatching blastocyst (tHB). The 2-cell stage was considered as time zero since the exact time of insemination was unknown. All time points were statistically compared between each of the three groups with a P-value of <0.05 considered to be significant. Blastocyst development rates for each group were also compared.

**RESULTS:** A total of 304 blastocysts developed from the 316 embryos cultured, yielding an overall blastocyst development rate of 96.2%. When comparing the blastocyst development rate between the 3 groups, there were no significant differences between the One-Step and IGF-1 media groups (99.1% vs 96.2%). However, the insulin group showed significantly lower blastocyst rates when compared to the controls (93.3% vs 99.1%; P=0.02). There were no statistically significant differences in any of the time points measured between the One-Step, insulin and IGF-1 groups.

**CONCLUSIONS:** No beneficial effects were noted by adding insulin or IGF-1 to culture media for mouse embryo development. Mouse embryos cultured with insulin showed a lower blastocyst development rate compared to unsupplemented One-Step media. No differences were seen in any of the time-lapse morphokinetics parameters by supplementing media with either insulin or IGF-1. Ongoing studies using a different more sensitive strain of mouse embryos are underway to see if any subtle changes in morphokinetics may be detected.

**TABLE 1. Blastocyst development rates between two strains on mouse embryos cultured in One-step media, IGF-1 and insulin**

<table>
<thead>
<tr>
<th>Culture media</th>
<th>Strain 1 (B6D2F1 &amp; B6C3F1 Hybrid)</th>
<th>Strain 2 (C57BL-6N)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>One-Step (n=238)</td>
<td>99.1% (n=106) a</td>
<td>80.3% (n=132) b</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>IGF-1 (n=249)</td>
<td>96.2% (n=105)</td>
<td>74.3% (n=144)</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>Insulin (n=249)</td>
<td>93.3% (n=105) b</td>
<td>68.8% (n=144) b</td>
<td>P&lt;0.0001</td>
</tr>
<tr>
<td>P-value</td>
<td><strong>P=0.02</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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e271
OBJECTIVE: To evaluate whether an artificial intelligence (AI) framework can be used to classify between normally fertilized (2PN) and abnormally (non-2PN) fertilized embryos at the pronuclear (PN) stage.

DESIGN: Historical Prospective Cohort Study.

MATERIALS AND METHODS: Embryo images from a retrospective dataset recorded by multiple optical systems at 18 hours post-insemination (hpi) were utilized. The deep convolutional neural network (CNN) model was trained and tested, with a total of 3,469 embryos, to classify between 2PN (n = 2,893) and non-2PN (n = 576) embryos.

The training set contained 2,366 images (6.33 2PN:1 non-2PN) while the validation set contained 154 images (0.97 2PN:1 non-2PN) with a distribution aimed at minimizing training bias. During training, the dataset was augmented through randomized rotations of the images ranging from 0 to 359 degrees, which was done using OpenCV libraries (ver. 3.1.0). In each training batch, we used 16 unique images per class supplemented by augmented data for the training class. When all the images of a specific embryo class were used for CNN training, the same embryo class was shuffled randomly to create different batches, making every batch unskewed by repeating and augmenting the embryo images.

For the independent test set, we used 949 non-overlapping images (4.42 2PN:1 non-2PN), which were obtained from 100 patient cohorts.

RESULTS: Using annotated data of 2,366 inseminated oocytes, the CNN was trained and validated to categorize oocytes based on their fertilization outcomes. The CNN in classifying hypotetegytes based on their fertilization status at 18 hpi was evaluated using a test set of 949 pronuclear stage embryos from which two completely out-of-focus images were removed. The accuracy of the algorithm in 2PN and non-2PN embryo classification using the 947 embryos test set was 91.86% (CI: 89.94% to 93.53%).

A Distributed Stochastic Neighbor Embedding (t-SNE) was performed to visualize the separation of the dataset by the network in a 2D space. With the observation of good separation between the two classes, the network was further probed by mapping the final activation layers to visualize the saliency for identifying the pixels that are being utilized by the network. It was confirmed that the network focused on features pertaining to the embryo in its decision-making process.

For the given test set, the sensitivity and specificity of the algorithm in identifying 2PN embryos were 93.26% (CI: 91.21% to 94.96%) and 86.83% (CI: 81.42% to 91.14%), respectively. The positive predictive value and negative predictive value of the CNN were 96.24% (CI: 94.74% to 97.33%) and 78.07% (CI: 73.04% to 82.39%), respectively. The area under the curve (AUC) value, established through a receiver operating characteristic (ROC) analysis, was 0.90 (CI: 0.88 to 0.92).

CONCLUSIONS: Here, we report the development and evaluation of an AI-based approach for automated human embryo assessment and selection of normally fertilized embryos at the pronuclear stage with high accuracy. The network was further probed by mapping the final activation layers to visualize the saliency for identifying the pixels that are being utilized by the network. It was confirmed that the network focused on features pertaining to the embryo in its decision-making process.

SUPPORT: This work was partially supported by the Brigham Precision Medicine Developmental Award (Brigham Precision Medicine Program, Brigham and Women’s Hospital) and R01AI118502, R01AI138800, and R21HD092828 (National Institute of Health).

OBJECTIVE: To evaluate whether an artificial intelligence (AI) network could improve the consistency of morphologic embryo grading at the blastocyst stage and ultimately aid embryologists in embryo disposition decision making.

DESIGN: Prospective double blinded trial using a retrospective dataset.

MATERIALS AND METHODS: Using a dataset comprising of 3,469 embryos, the deep convolutional neural network (CNN) model was trained and tested to primarily classify between non-blastocysts and blastocysts using images of embryos captured at 113 hours post insemination (hpi). Using a blinded 742 embryo image dataset, we evaluated the grading tendencies of 7 embryologists qualitatively classifying day 5 blastocysts on a 5-grade system (poor, fair, good, great, and excellent). A coefficient of variation (%CV) was calculated to evaluate the variability across the 7 embryologists. Furthermore, we used a blinded 56 embryo image dataset to evaluate the disposition decisions (biopsy/cryopreservation (HQB) vs. discard (non-HQB)); HQB criteria: >3CC of 10 embryologists after rotating the embryo image 90 and 180 degrees. Consistency was defined as the percentage of cases where the disposition decision was unaffected by the rotation. For both tasks, we compared the degree of variability in the embryologists’ assessments to that of the CNN.

RESULTS: When qualitatively classifying day 5 blastocysts into a 5-grade system, embryologists exhibited a high degree of variability (%CV: 44.98%), implying significant variation in embryo quality assessment between the embryologists. When selecting day 5 blastocysts for biopsy or cryopreservation, embryologists had an average consistency of 52.14% (CI: 40.99% to 63.29%) and 57.68% (CI: 47.39% to 67.97%), respectively. The CNN outperformed the embryologists with a consistency of 83.95% and 83.92% (P < 0.05 for both), respectively. A Bonferroni alpha corrected an alpha coefficient of 0.0582 (CI: 47.39 to 67.97) for the embryologists and 1.00 (lower CI: 1.00) for the CNN. Of note, the recommended internal consistency range should be higher than 0.9 alpha coefficient in clinical settings.

CONCLUSIONS: The results of our study show a high degree of inter- and intra-embryologist variability in scoring day 5 blastocysts, likely due to the subjective nature of traditional morphology grading. This may ultimately lead to less precise disposition decisions and the recording of viable embryos. The application of an AI-based approach, as shown in our study, can introduce improved reliability and high consistency during the process of embryo selection and disposition, potentially improving outcomes in an embryology laboratory.

SUPPORT: This work was partially supported by the Brigham Precision Medicine Developmental Award (Brigham Precision Medicine Program, Brigham and Women’s Hospital) and R01AI118502, R01AI138800, and R21HD092828 (National Institute of Health).
accuracy of 94.0% (95% CI: 92.4-95.7%). A one sample t-test revealed that the system performed significantly (P<0.05) better than the embryologists in selecting two embryos for transfer among which at least one will eventually form a blastocyst. The accuracy of the CNN in selecting an embryo at 70 hpi, which developed into a high-quality blastocyst (HQB) for a single embryo transfer (SET), was 63.9% that is significantly higher (P<0.05) than the average accuracy of the embryologists (52.8%, 95% CI: 48.6-57.0%). The accuracy of the CNN in selecting an embryo at 70 hpi, which developed into HQB for a double embryo transfer (DET), was significantly higher (79.4%, P<0.05) compared to the embryologists with an average accuracy of 72.4% (95% CI: 70.7-74.0%)

CONCLUSIONS: Here, we reported an artificial intelligence-based approach for predicting the developmental fate of cleavage stage embryos. Our study shows that the developed CNN outperforms an embryologist’s morphologic assessment at 70 hpi in predicting blastocyst formation. Additionally, we demonstrated that this technology might be used to select embryos with the highest in vitro developmental potential. Utilization of artificial intelligence (AI) technologies in human IVF practices may allow for more objective/standardized methods for improving embryo selection.

Reference: None.

SUPPORT: Financial Support: A This work was partially supported by the Brigham Precision Medicine Developmental Award (Brigham Precision Medicine Program, Brigham and Women’s Hospital) and 1R01AI18502, R01AI138800, and R21HD092828 (National Institute of Health).

P-412 Wednesday, October 16, 2019 6:30 AM

THE APPLICATION OF MACHINE LEARNING METHODS TO EVALUATE PREDICTORS OF LIVE BIRTH IN PROGRAMMED THAW CYCLES. Denis Vaughan, MD, MRCPI,a Weiwei Pan, PhD,b Yaniv Yacoby, BA,c Emily A. Seidler, MD,c Angela Q. Leung, MD,d Finale Doshi-Velez, PhD,d Denny Sakkas, PhD,d Beth Israel Deaconess Medical Center, Boston, MA; Harvard Institute for Applied Computer Science, Cambridge, MA; Harvard University, Cambridge, MA; b Boston IVF, Waltham, MA.

OBJECTIVE: The utilization of frozen embryo transfers is increasing annually. The objective of this study was to investigate the utility of machine learning (ML) methods to weight predictors for positive pregnancy and live birth rate (LBR) in programmed thaw cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All first, autologous programmed thaw cycles (January 2014 to October 2017) were reviewed. Data was collected from both stimulated and subsequent frozen cycles. Each patient received estrogen replacement until endometrial thickness was deemed adequate (usually ≥8mm). Progesterone was prescribed with embryo transfer after 5 doses of progesterone supplementation.

For data analysis, we normalized the numerical variable and one-hot-encoded the categorical variables. For each outcome, a logistic regression model was fitted with ROCS regularization. The model test ROC was evaluated and averaged across 10 random training/test data splits. For each outcome, the top variables, most predictive across the 10 random splits are presented using regression coefficients (RC).

RESULTS: A total of 1726 cycles were available for analysis with 129 variables evaluated. The median age of the cohort was 34.3. The positive pregnancy rate among our cohort was 70% and the LBR was 47%. Top predictors for both models were shown in Table 1. The ROC for model fit for positive pregnancy and LBR was 0.65 and 0.73 respectively. Interestingly, both increasing age at oocyte retrieval and anti-mullerian hormone (AMH) level were weaker predictors for live birth (RC -0.5, 0.6 respectively) than those increasing age at oocyte retrieval and anti-mullerian hormone (AMH) level for both models are shown in Table 1. The ROC for model fit for positive pregnancy rate among our cohort was 70% and the LBR was 47%. Top predictors

Support: Darwin Technologies LTD.

OBJECTIVE: To build and to validate a computational tool aimed at reducing the subjectivity inherent to current embryo classification methods.

DESIGN: Data augmentation for building and initial validation of a neural network architecture using an embryo pictures’ bank.

MATERIALS AND METHODS: An Inception V3 deep convolutional neural network architecture was built and trained using a dataset containing 1,204 pictures of blastocyst obtained from 2 IVF centers and classified by an expert embryologist into three categories according to its developmental stage: (i) expanding, (ii) hatching and (iii) hatched. The dataset was increased to a total of 15,000 images using data augmentation techniques to assure that the network model is robust to translations and rotations. 12,000 images where employed training and the remaining 3,000 for validation through the computation of the weights of the neural network.

RESULTS: Once the network was trained, we used it to classify 56 images never seen before by the network. All 54 images were correctly classified by the network.

CONCLUSIONS: Results indicate the feasibility of employing deep learning techniques for the automatic and objective classification of blastocyst development stage which will pave the way for building computational tools that will aid the expert embryologist to define a ranking based on quantitative information.

SUPPORT: Darwin Technologies LTD.

P-414 Wednesday, October 16, 2019 6:30 AM

ARTIFICIAL NEURAL-NETWORK ANALYSIS COMBINED WITH TIME-LAPSE IMAGING PREDICTS EMBRYO ABILITY TO DEVELOP TO THE BLASTOCYST STAGE. Giovanni Coticchio, Ph.D.,a Raffaella Sciajno, B.Sc.,b Giulia Fiorentino, B.Sc.,b Federica Cavalera, Ph.D.,b Giovanna Nicora, B.Sc.,b Riccardo Belluzzi, Ph.D.,b Andrea Borini, M.D.,b Silvia Garagna, Ph.D.,b Maurizio Zacchetti, Ph.D.,b Baby - Family and Fertility Center, Bologna, Italy; University of Pavia, Department of Biotechnology ‘Lazzaro Spallanzani’, Pavia, Italy; University of Pavia, Department of Electrical- Computer and Biomedical Engineering, Pavia, Italy.

OBJECTIVE: To assess the potential of machine learning algorithms, implemented for image analysis at early developmental stages, to predict embryonic development to the blastocyst stage.

DESIGN: The ANN approach was undertaken to assess retrospectively the ability of human embryos to develop to the blastocyst stage. The analysis focused on 113 embryos generated in 32 IVF cycles, carried out between October 2015 and May 2018. Female age was 36.3±4.9 years. To minimise possible patient-based bias, cycles were recruited ensuring to have in the same cohort both embryos able to develop to the blastocyst stage and arresting at earlier stages.

CONCLUSIONS: The abundance of measurements related to infertility treatment is well suited for the application of ML. A clinician makes decisions based on knowledge and past experience which may bias the process and impact clinical outcomes. In our work, we already find that factors considered by clinicians to predict the outcome are not identical to those considered by our model. Validation and further development of ML models is ongoing.

SUPPORT: None.

REFERENCE: None.
MATeRIALs AND METHODS: Embryos were subject to time-lapse assessment to monitor development and perform trophoderm biopsy for preimplantation genetic testing of aneuploidy. Fertilisation was achieved by ICSI. Time-lapse monitoring started immediately after ICSI, with a 15 min interval between consecutive observations. Of 113 embryos analysed, 55 reached the blastocyst stage (BL-group) and 58 arrested sometime after the 2-cell stage (NoBL-group). ANN analysis was performed, at this stage, only during the first two cell divisions (175 frames; 2.625 min).

RESULTS: We developed a classification platform consisting of three main steps: 1) collection of time-lapse images of preimplantation, embryos; 2) evaluation of time-lapse sequence images of each embryo by a particle image velocimetry software that detects cytoplasmic movements; 3) finally, analysis of cytoplasmic movement patterns through an ANN that predicts developmental competence. Specifically, cytoplasmic movements of single embryos development were measured as multivariate time series and used to train and test a Long-Short Term Memory (LSTM) neural network. LSTM displayed the capacity to learn “long-term” temporal dependences of both BL- and NoBL-group and provide a classification when challenged blind. Following a ten-fold cross validation of the training set, the specific LSTM selected was trained with 90% of data and tested on the remaining. Thus, based on the analysis of the cytoplasmic movement occurring during the first two cell divisions of single blind embryos (test set), the trained LSTM reached an 82% classification accuracy in the prediction of development to the blastocyst stage.

CONCLUSIONS: This study represents an initial attempt to build up a robust system of classification of the quality of human preimplantation embryos totally automated from input to output. A three-steps workflow, combining time-lapse imaging, particle image velocimetry and artificial neural network (ANN) classification, predicts with high accuracy embryo ability to develop to blastocyst stage. Further refinement of the approach is expected to impact embryo assessment ability and improve efficiency in assisted reproduction treatments.

Reference: None.

SUPPORT: None.

P-415 Wednesday, October 16, 2019 6:30 AM

A MASSIVE EMBRYO MORPHOKINETICS COMPARISON SYSTEM IS ABLE TO SELECT EMBRYOS WITH HIGH IMPLANTATION POTENTIAL ENHANCING SINGLE EMBRYO TRANSFER POLICY. Lucia Alegre, PhD, a Raquel Del Gallego, PhD, a Lorena Bori Arnal, PhD, a Manuel Muñoz, MD, b Antonio Pellicer, M.D., Ph.D., c Marcos Meseguer, PhD, d IVIRMA Global, Valencia, Spain; e IVIRMA ALICANTE, Alicante, Spain; f IVI-RAIMA Valencia, Valencia, Spain; g IVIRMA Global, Valencia, Spain, Tel Aviv, Israel.

OBJECTIVE: To analyze the abilities of DANA automatic embryo selection software to interpret embryo morphokinetic parameters by massive comparison with a database of embryos with known implantation potential and generate a transfer order ranking in a single embryo transfer policy.

METHODS: DANA compares each cohort of embryos with a data cloud of KID (Known Implantation Data). This data cloud was performed from a retrospective analysis of 1021 KID embryos. For that, timings of embryo cleavage and cell cycle lengths were included in the DANA software. Morphokinetic parameters were arranged on a 2D graph and the software analysed the unit average distance (UAD) of the embryos to the centre of the cloud. We defined a category of TOP embryos with an UAD ≤ 0.5.

RESULTS AND METHODS: The percentage of twin gestation was calculated in our double embryo transfer cases comparing whether 1 or 2 of the transferred embryos had a high score in the Dana ranking. A total of 357 fresh cycles from infertile couples undergoing oocyte donation were included; 1562 embryos were analysed from which 536 were transferred, and 371 embryos achieved the status of KID embryos.

RESULTS: Therefore, we compared cases in which the two blastocysts transferred were ranked as TOP compared to those cases in which only 1 being TOP. The twin gestation rate was significantly higher in those cases in which the number of TOP embryos (UAD ≤ 0.5) transferred was 2 vs. 1% in one top group (P < .001).

CONCLUSIONS: In cases in which a double embryo transfer was performed, the twin gestation rate was significantly higher when the two embryos transferred were ranked as TOP by the software, reaching very high values. In consequence, the selection method presented, is a relevant strategy, to encourage single embryo transfer at least when two TOP blastocyst are available.

SUPPORT: The development of this publication was financially supported by CDTI research project IDI-20170310 from Spanish Government of Economy and competitiveness, a research grant from the Spanish Society of Embryology (SEF) and Merck S.L.U. (Spain), an affiliate of Merck KGaA, Darmstadt, Germany, through an independent medical writing grant.

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EFFECTS OF MEIOTIC SPINDLE IMAGING IN HUMAN OOCYTES FOLLOWING PIEZO-ICSI ON OOCYTE FERTILIZATION AND EMBRYO DEVELOPMENT. Kenichiro Hiraoka, Ph.D.a Takayuki Tatsumi, M.D., Ph.D., b Makiko Tajima, M.D., c Tomonori Ishikawa, M.D., d Kiyotaka Kawai, M.D. Ph.D. e Kameda IVF Clinic Makuhari, Chiba, Japan; f Comprehensive Reproductive Medicine, Tokyo Medical and Dental University, Tokyo, Japan; g Kameda IVF clinic Makuhari, Department of Reproductive Medicine, Tokyo, Japan; h Tokyo Medical and Dental University, Tokyo, Japan; i Kameda Medical Center, Kamogawa, Japan.

OBJECTIVE: Recent studies using polarized light microscopy have revealed a correlation between meiotic spindle imaging in human oocytes following intracytoplasmic sperm injection (ICSI) and fertilization rate. However, these studies have only assessed conventional-ICSI, in which a beveled and spiked micropipette is used to aspirate the cytoplasm and break the membrane before sperm are injected. To our knowledge, no studies have yet elucidated the relationship between meiotic spindle imaging in human oocytes following Piezo-ICSI, and fertilization or embryo development. In Piezo-ICSI the membrane is broken by applying a Piezo pulse, which produces ultra-fast submicron forward momentum using uniquely-shaped flat-tipped micropipettes with no bevel or spike. The objective of this study was to investigate the effect of meiotic spindle imaging in human oocytes following Piezo-ICSI on fertilization and embryo development.

DESIGN: Retrospective, case control.

MATERIALS AND METHODS: We retrospectively investigated 529 oocytes with the first polar body retrieved from 124 infertile couples (147 cycles; women’s average age, 37.8 ± 4.8; partner’s average age, 39.7 ± 4.8; expressed as the mean ± SD) who attended the Piezo-ICSI program at the Kameda IVF Clinic Makuhari between May 2016 and December 2018. Of these, 489 oocytes (92.4 %) with visible meiotic spindle comprised the Spindle (+) group, while 40 oocytes (7.6 %) not observed meiotic spindle comprised the Spindle (-) group. Meiotic spindle imaging was performed using polarized light microscopy, and the rates of oocyte survival, fertilization, good-quality day-3 embryos, blastocysts, and good-quality blastocysts were evaluated for both groups. Categorical values were compared using Fisher’s exact test. A P-value of < 0.05 was considered significant.

RESULTS: The fertilization rate of the Spindle (+) and Spindle (-) oocytes was 92.0 % (450/489) and 70.0 % (28/40), respectively. The rate of good-quality day-3 embryo formation by the Spindle (+) and Spindle (-) oocytes was 62.9 % (283/450) and 35.7 % (10/28), respectively. The rate of blastocyst formation by the Spindle (+) and Spindle (-) oocytes was 53.7 % (205/382) and 32.1 % (9/28), respectively. The rate of good-quality blastocyst formation by the Spindle (+) and Spindle (-) oocytes was 29.8 % (114/382) and 3.6 % (1/28), respectively. Significantly higher rates of fertilization, good-quality day-3 embryos, blastocysts, and good-quality blastocysts were obtained in the Spindle (+) group than in the Spindle (-) group.

CONCLUSIONS: To the best of our knowledge, this is the first study to evaluate the effect of meiotic spindle imaging in human oocytes following Piezo-ICSI on fertilization or embryo development. Spindle imaging (i.e. identifying oocytes with visible or not observed meiotic spindle) does influence the outcome of Piezo-ICSI in human oocytes, including fertilization and embryo development. Our results demonstrate that the combination of meiotic spindle imaging and Piezo-ICSI can increase the fertilization of viable oocytes without oocyte loss in human assisted reproductive technology.

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EFFECT OF DIFFERENT 6-DIMETHYLAMINOPURINE (6-DMAP) TREATMENTS ON REVERSIBLE ARRESTING OF MONO- AND TRIPRONUCLEAR EMBRYOS AT THE PROPRONUCLEAR STAGE. Nicola Graziani, M.D. a, b, PhD,a Ana González-Picazo, MSc,b Nuria Soler, MSc,a María José Escribá, PhD,a Xavier Vendrell, PhD,a Thamara Viloria, PhD,b IVIRMA-Valencia, Valencia, Spain; bIVI-Foundation, Instituto de e274 ASRM Abstracts Vol. 112, No. 3, Supplement, September 2019
OBJECTIVE: To determine the optimal values of 6-DMAP to synchronize human zona pellucida (ZP) stage (presumably at the G2-phase of the cell-cycle) without compromising subsequent development to blastocyst, as possible pre-treatment to enhance the natural DSB repair pathways in CRISPR-Cas9 technology.

DESIGN: This study utilized mono- (MPN; n=580) and tripolar pronuclei (TPN; n=261) human embryos. They were incubated for 6hrs in different 6-DMAP concentrations, in order to assess the arresting rate. After 6-DMAP treatment, zygotes were cultured to the blastocyst stage, in order to assess the effect of 6-DMAP on subsequent developmental competence.

MATERIALS AND METHODS: MPN and TPN zygotes were incubated in 0mM (control), 0.24mM or 0.48mM 6-DMAP, in GEMS medium (Genea Biomedx) for 6hrs at 37°C, 5%CO2 and 5%O2. Arresting rate was calculated as percentage of zygotes, blocked at PN stage when 6-DMAP treatment had finished. Then, MPN/TPN were cultured in a time-lapse incubator in 20μL GEMS for 5 days. Blastocyst rate was calculated as a percentage of blastocysts per number of pronuclear-arrested zygotes.

Morphokinetic variables included the precise occurrence time of pronuclear fading and cleavage (6hr after 6-DMAP treatment, t0).

RESULTS: Concerning MPN zygotes, higher arresting rates were observed in 0.60mM 6-DMAP groups (averaged: 86.1%) than in 0.24mM (44.4%; p<0.004). In 0.24mM and 0.48mM 6-DMAP groups, some zygotes exhibited an abnormal pronuclear fragmentation at the end of 6-DMAP treatment (27.8% and 7.1%, respectively). This event was never observed in 0.60mM or control groups. Morphokinetic analysis showed that regardless 6-DMAP concentration, PfN and cleavage occurred at comparable timings (averaged: 3.9h and 8.3h, respectively). Regardless of 6-DMAP concentration, arrested MPN cleaved (78.3%) and progressed to the blastocyst stages (18.2%) at comparable rates to controls (77.8%; p=0.3 and 18.6%; p=0.96, respectively).

As regards TPN zygotes, they were arrested at the pronuclear stage efficiently (averaged, 92.3%), regardless 6-DMAP concentration. No PN fragmentation was observed at any 6-DMAP concentration or controls. However, at 0.24mM and 0.48mM concentrations pronuclei faded significantly (4.5h) both than 0.60mM group did (2.8-8.0h vs. 1.6-4.0h; p<0.05). Further, the arresting rates were calculated as a percentage of zygotes, blocked at PN stage when 6-DMAP treatment had finished. Then, MPN/TPN were cultured in a time-lapse incubator in 20μL GEMS for 5 days. Blastocyst rate was calculated as a percentage of blastocysts per number of pronuclear-arrested zygotes.

MATERIALS AND METHODS: Tripolar (TPN) human embryos were used as retrospective data in this study. A deep neural network was developed and trained to predict fertilization in embryos at 18 hours post insemination (hpi) by evaluating the respective oocytes before fertilization.

The developed network was evaluated using another independent set of oocyte images with known fertilization outcomes. The system differentiated fertilized embryos primarily based on the number of pro-nuclei (2PN vs non-2PN). We probed if a deep neural network was able to identify enough features in oocytes to sufficiently differentiate between the developmental outcomes through a receiver operator characteristic (ROC) analysis. We also evaluated the networks predictive power.

RESULTS: The network was able to differentiate between the fertilization outcomes with an accuracy of 67.0% (95% CI: 63.4% to 70.4%). The AUC of 0.613 indicated through a ROC analysis confirmed that the network was able to differentiate between the outcomes with a reasonable degree of accuracy. After establishing that the neural network was able to differentiate oocytes based on their fertilization potential, we tuned the network to conservatively identify oocytes with the highest fertilization potential. In our evaluations, the network achieved a maximum predictive power of 86.0% (95% CI: 77.3% to 94.2%).

CONCLUSIONS: Our results suggest that a neural network can be used to help identify the highest quality oocytes objectively based on their fertilization potential. The high predictive power of the trained network can carefully select the oocytes with the promise of improving the patient prognosis.

SUPPORT: This work was partially supported by the Brigham Precision Medicine Developmental Award (Brigham Precision Medicine Program, Brigham and Women’s Hospital) and R01AI118502, R01AI138800, and R21HD092828 (National Institute of Health).

USE OF A SPECIFIC GRAVITY DEVICE TO PREDICT BLASTOCYST SEX. Alex L. Schaubhut, B.S.1, Caralynn Wessels, Ph.D.1, Samuel D. Pien, Ph.D.1, Lindsay L. Penrose, Ph.D.1, Texas Tech University, Lubbock, TX.2 Texas Tech University Health Sciences Center, Lubbock, TX.

OBJECTIVE: Previous research has demonstrated that a Specific Gravity Device (SGD) is useful in providing a noninvasive means of assessing embryo quality at various stages of development from zygote to blastocyst. Preliminary data suggested the system might also be useful for predicting embryo sex. The objective of the present study was to assess the predictive value of the SGD in determining embryo sex using a bovine model.

DESIGN: Lab-based trial of the SGD in predicting embryo sex.

MATERIALS AND METHODS: Bovine oocytes were collected from ex vivo ovaries and fertilized in vitro. Six hundred embryos developed into grade 1 or 2 blastocysts and were individually assessed in SGD. Embryo depositions were measured and recorded in seconds and then used in an Embryo Prediction Algorithm (EPA) to predict embryo sex. Sex of each embryo was also confirmed individually by Polymerase Chain Reaction (PCR). Comparisons were then made between EPA prediction and PCR values to assess the ability of the SGD to predict embryo sex.

RESULTS: PCR data were obtained on 463 of the 600 embryos and available for comparison with SGD predictions. The EPA demonstrated significant classification rates between sex for male and female embryos (P<0.001). Further, the EPA demonstrated 65.3-78.4% accuracy selecting for female embryos. These data suggest, with refinement, the SGD might provide a noninvasive means of predicting sex of preimplantation embryos.

CONCLUSIONS: The SGD can detect embryo sex based on differences in embryo buoyancy. Theoretically, the differences in the buoyancy of mammalian blastocyst embryos would be a reflection of differences in the chromosomal weight of X and Y chromosomes or developmental differences of male and female embryos. Data demonstrate a high degree of correlation between SGD and the PCR results suggesting the technology can provide a noninvasive means to differentiate female pre-implantation embryos without the use of pre-implantation genetic testing or sexed semen. On-going studies are assessing if improvements in the EPA will allow predictive values for male embryos as well. Identifying the sex of an embryo is important for family planning or for patients with sex-linked genetic diseases.

SUPPORT: The authors would like to thank the J.R. Simplot Company for funding of this project.
A CLINICAL MODEL PREDICTING SUPERNUMBERARY EMBRYOS IN WOMEN UNDERGOING FREEZE-ALL CYCLES UTILIZING SART CORS DATA

Yetunde O. Ibrahim, MD,a Greg Stoddard, MS,b Erica Johnstone, MDa Utah Center for Reproductive Medicine, Salt Lake City, UT; bAffiliation not provided; aUniversity of Utah, Salt Lake City, UT.

OBJECTIVE: The field of IVF has focused on embryo selection technology and multiple methods have been utilized including metabolomics, time lapse imaging and PGT-A. PGT-A was touted as the optimal method but it has recently come under scrutiny due to some evidence of euploid births from embryos found to be aneuploid on testing [1-3]. A selection method can only enhance the chances of success if we have a cohort of embryos to select from and yet, we have inadequate counseling tools for patients on their chances of having supernumerary embryos for a selection method to be applicable. We have identified factors predictive of having supernumerary embryos in freeze-all cycles. Therefore, we sought to create a clinical prediction model using those identified factors for clinical counseling.

DESIGN: Retrospective cohort study of women who underwent freeze-all cycles in 2014.

MATERIALS AND METHODS: Data were obtained from the Society for Assisted Reproductive Technology. We defined supernumerary as having two or more embryos cryopreserved. We utilized previously identified predictors and entered them into a logistic regression model presenting a receiver operating characteristic curve (ROC) for all predictors. Any predictor that did not alter the area under the curve for the ROC was removed from the prediction model. We then utilized methods described by Sullivan and colleagues [4] to modify the final model into a risk index. The number of points assigned to each significant covariate equaled its regression coefficient divided by the parameter estimated in the model with the smallest value rounded to the nearest whole number. The accuracy of the prediction model was then tested using an ROC.

RESULTS: Of 31,537 freeze-all cycles in 2014, 18,250 produced supernumerary embryos. We included 16,395 cycles into the logistic regression model after excluding cycles with missing AMH as this was a very strong predictor of the outcome. Table 1 demonstrates the points assigned to each significant covariate necessary for the ROC for the ROC was 0.84.

CONCLUSIONS: Age, AMH and number of eggs retrieved are necessary predictors for the model. The AUC for the ROC is considered excellent discrimination and therefore, this model can be used to counsel patients undergoing freeze-all cycles on their probability of having supernumerary embryos for a selection method to be applicable.

TABLE 1. Points assigned to each significant covariate

<table>
<thead>
<tr>
<th>Variable (Referent)*</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (&lt;35)</td>
<td>35 - 37</td>
</tr>
<tr>
<td></td>
<td>38 - 40</td>
</tr>
<tr>
<td></td>
<td>41 - 42</td>
</tr>
<tr>
<td></td>
<td>&gt; 42</td>
</tr>
<tr>
<td>AMH (1.0 – 3.0)</td>
<td>&lt;1.0</td>
</tr>
<tr>
<td></td>
<td>&gt;3.0</td>
</tr>
<tr>
<td># eggs retrieved (0 – 3)</td>
<td>4 - 8</td>
</tr>
<tr>
<td></td>
<td>9 – 13</td>
</tr>
<tr>
<td></td>
<td>14 - 20</td>
</tr>
<tr>
<td></td>
<td>21 - 45+</td>
</tr>
</tbody>
</table>

*Referent category is assigned zero (0) Points
*Scores = Score + 5 (automatically sets the minimum summative score to zero).

REFERENCES:

SUPPORT: None.

BLASTOCYST AND EMBRYO SCREENING SELECTION TOOL (BESST): AN ULTRAFAST NON-INVASIVE EMBRYO SELECTION TEST FOR USE IMMEDIATELY PRIOR TO EMBRYO TRANSFER

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OBJECTIVE: Development and implementation of a novel embryo selection workflow immediately prior to transfer during routine fertility cycles.

DESIGN: A scoring algorithm for the selection of embryos based on a mass spectral profile of culture media has been developed previously. Here the algorithm was adapted and optimized to be integrated into the current routine practices of a fertility centre in the USA. The applicability and advantages of using this workflow were analyzed retrospectively using post implantation data outcomes from the cohort.

MATERIALS AND METHODS: A total of 1190 embryo cell culture media were collected and frozen prior to implantation from a single IVF clinic in the USA between March 2014 and March 2018. Samples were stored in 50ul aliquots and subsequently 1 µl was applied directly onto prepared stainless-steel plates with α-Cyano-4-hydroxycinnamic acid matrix. After drying on a hot plate, the sample plate was loaded to a Shimadzu benchtop MALDI-ToF mass spectrometer. To score embryos, we used the Blastocyst and Embryo Screening and Selection Tool (BESST) software, previously installed on our instrument. This tool provides an embryo score from mass spectral features of between 0 and 5, with 5 being the best chance of implantation and ongoing pregnancy and 0 being the least.

RESULTS: The time responses of our workflow were monitored starting from sample preparation to embryo scores reporting for candidate embryos. The total time obtained ranged between 6 to 8 minutes, which is a reasonable time to give an informative response before embryo implantation. In each day, success showed substantial differences between embryos from the same cycle: indicating that some embryos had a greater chance of success when compared to others. Statistically, embryos selected with higher scores (>4) correlated with more cases of successful implantation and ongoing pregnancy with a positive predictive value of 76.9%. In comparison, those embryos with low scores (<1.5) poorly correlated with ongoing pregnancy outcome, predicting the chance of ongoing pregnancy of 35.7% or lower. In unsuccessful pregnancies, the tool was able to identify embryos from the same cycle with higher scores in comparison to the embryo transferred. This suggests that relying on BESST in these cases could have resulted in an implanted embryo and an ongoing pregnancy.

CONCLUSIONS: We have successfully implemented a fast scoring system for embryo selection that can be applied in any fertility clinic immediately prior to transfer. We further demonstrated that the integration of this workflow into current practices in fertility clinics may provide advantageous information that increases the chances of successful embryo implantation and ongoing pregnancy.

QUALITY EVALUATION OF DIRECT CLEAVAGE EMBRYOS AT THE FIRST DIVISION USING A COMBINED EARLY CLEAVAGE WITH AN EMBRYO MORPHOLOGICAL GRADING METHOD

Yumi Nagata, M.D., Ph.D.,a Hiroyuki Tomari, Ph.D.,b Sakis Gondo, M.D.,b Kensuke Saito, M.D.,b Kou Honjo, M.D.,b bIVF Nagata Clinic, Fukuoka, Japan; aAffiliation not provided.

OBJECTIVE: Several studies have reported a clear correlation between the occurrence of DC (divided into three or more cells) during the first division of an embryo and impaired embryo development potential in humans. In addition, it has also been reported that the pregnancy rate due to transfer of DC embryos that developed to blastocysts is similar to that of normalcleavage embryo transfer. However, only few studies have reported on methods for assessing DC embryo quality. In this study, we evaluated the quality of DC embryos using early embryo two-step evaluation (ETE) methods combining early cleavage and morphological grading.

DESIGN: This prospective observational study was performed in a single in vitro fertilization (IVF) center between 2015 and 2017. This study...
included patients undergoing IVF or intracytoplasmic sperm injection. All study participants provided informed consent and the study design was approved by the ethics committee of the IVF Nagata Clinic, Fukuoka, Japan.

MATERIALS AND METHODS: We analyzed 1,242 DC embryos with normal fertilization using a time-lapse incubator. We compared blastocyst formation rates between 3- and ≥4-cell groups during the first division. Ex.2: The two groups from Ex.1 were classified using ETBE methods. The blastocyst formation rates of each group were compared. Embryos were evaluated for EC at 27 hours after insemination and morphology was scored on day 2 (poor, ≥4 cells with ≥50% frag.; fair, ≥4 cells with <50% and ≥20% frag.; good, ≥4 cells with <20% frag. and equal blastomere).

RESULTS: Ex.1: Among the 1,242 DC embryos, 669 were in the 3-cell group and 573 were in the ≥4-cell group. The blastocyst and high-quality blastocyst formation rates were significantly higher (p<0.01) in the 3-cell group than in the ≥4-cell group (53.5% vs. 32.7%, 28.0% vs. 14.1%, respectively). Ex.2: Among the 669 embryos in the 3-cell group, 211 were in the EC-fair embryos, 141 were in the EC-poor embryos, 75 were in the late cleavage (LC)-fair embryos, and 242 were in the LC-poor embryos. Among the 573 ≥4-cell group, 102 were in the EC-fair embryos, 127 were in the EC-poor embryos, 90 were in the LC-fair embryos, and 254 were in the LC-poor embryos. The blastomeres of DC embryos were unequal and no embryo was evaluated as good. The blastocyst and high-quality blastocyst formation rates were significantly higher (p<0.05) in the EC-fair embryos of the 3-cell group than in the other groups (71.6% vs. 18.5%-57.8%, 44.1% vs. 5.1%-33.3%, respectively).

CONCLUSIONS: The EC-fair embryos of the 3-cell group had high blastocyst development ability for DC embryos. The results suggest that the detailed evaluation of DC embryos at the early embryonic stage is not only predictive of embryogenic potential, but also useful for the selection of embryos for early embryo transfer.

ART LAB - ICSI

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OBJECTIVE: We previously reported how the presence of the fertilization cone (FC) and cytoplasmatic wave (CW) can act as indicators for the necessity of early rescue ICSI after short-term insemination (ESHRE 2018). However, FC is present for only short durations. In addition, in some eggs it is difficult to identify CW due to cytoplasmatic texture. Consequently, such determinations, when based upon one observational time point under an inverted microscope, can sometimes be difficult. Thus, we investigated whether a time-lapse incubator (TL) that allows the observation of embryos over time improves the accuracy of diagnosis for FC and CW, which makes time-lapse observation very useful for determining fertilization signs.

RESULTS: Ex.1: Among the 1,242 DC embryos, 669 were in the 3-cell group and 573 were in the ≥4-cell group. The blastocyst and high-quality blastocyst formation rates were significantly higher (p<0.01) in the 3-cell group than in the ≥4-cell group (53.5% vs. 32.7%, 28.0% vs. 14.1%, respectively). Ex.2: Among the 669 embryos in the 3-cell group, 211 were in the EC-fair embryos, 141 were in the EC-poor embryos, 75 were in the late cleavage (LC)-fair embryos, and 242 were in the LC-poor embryos. Among the 573 ≥4-cell group, 102 were in the EC-fair embryos, 127 were in the EC-poor embryos, 90 were in the LC-fair embryos, and 254 were in the LC-poor embryos. The blastomeres of DC embryos were unequal and no embryo was evaluated as good. The blastocyst and high-quality blastocyst formation rates were significantly higher (p<0.05) in the EC-fair embryos of the 3-cell group than in the other groups (71.6% vs. 18.5%-57.8%, 44.1% vs. 5.1%-33.3%, respectively).

CONCLUSIONS: The EC-fair embryos of the 3-cell group had high blastocyst development ability for DC embryos. The results suggest that the detailed evaluation of DC embryos at the early embryonic stage is not only predictive of embryogenic potential, but also useful for the selection of embryos for early embryo transfer.

FERTILITY & STERILITY®

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SPERM DNA FRAGMENTATION REDUCES EMBRYO DEVELOPMENT AND ONGOING PREGNANCY IN COUPLES WITH NON-MALE FACTOR INFERTILITY UNDERGOING INTRACYTOPLASMIC SPERM INJECTION CYCLES. Matheus de Castro Azevedo, BSc, Bianca Ferrarini Zanetti, PhD, Daniela Paes de Almeida Ferreira Braga, PhD, Amanda Souza Setti, MSc, Assumputo Iaconelli Jr., MD, Edson Borges Jr., PhD, Fertility Medical Group, Sao Paulo, Brazil; Sapientiae Institute, Sao Paulo, Brazil; Fertility Medical Group / Sapientiae Institute, Sao Paulo, Brazil.

OBJECTIVE: Nearly 15% of infertile men have semen parameters within normal reference ranges, which underlines that there must be others subcellular or nuclear factors, which are not identifiable by conventional semen analysis, that may contribute to male infertility. The value of SDF testing to improve the determination of the reproductive status of men that has neither altered seminal parameter nor history of male factor infertility still has to be determined. The objective of this study was to investigate the possible implications of sperm DNA fragmentation (SDF) for the outcomes of intracytoplasmic sperm injection (ICSI) in couples with non-male factor infertility.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: This study included data from 475 non-male factor infertility ICSI cycles, performed from June/2016 to June/2017, in a private university-affiliated IVF center. The sample size calculation suggested that 416 cycles would be enough to demonstrate a 20% effect with 80% power and 5% significance level. Semen samples were evaluated for sperm count, motility, morphology and SDF. Sperm DNA Fragmentation was measured using a Sperm Chromatin Dispersion (SCD) test. Cycles were divided according to SDF index into two groups: low fragmentation index (≤30% SDF, n=433) and high fragmentation index (>30% SDF, n=42). Laboratory and clinical outcomes were compared between groups using generalized linear models with linear distribution followed by Bonferroni post hoc test, with adjustment for potential confounders.

RESULTS: Fertilization rate was similar between groups (≥30% SDF: 85.28±1.06% vs. <30% SDF: 90.68±3.61%, p=0.153). Significant lower rates of normal cleavage speed (≥30% SDF: 61.12±2.41% vs. <30% SDF: 72.53±1.24%, p=0.010), high-quality embryos on day three (≥30% SDF: 39.09±2.73% vs. <30% SDF: 58.83±7.59%, p=0.016) and high-quality blastocyst rate (≥30% SDF: 11.97±1.22% vs. <30% SDF: 30.09±2.39%, p<0.001) were observed in cycles with higher SDF. Implantation rate was significantly reduced in the SDF ≥30% group (33.24±1.66% vs. <30% SDF: 46.40±4.61%, p<0.001), despite the similar pregnancy rates (≥30% SDF: 30.40% vs. <30% SDF: 32.40%, p=0.862). A 2.5-fold increase in the miscarriage rate was observed in cycles with SDF above the established cutoff (≥30% SDF: 42.8% vs. <30% SDF: 16.8%, p=0.018).

CONCLUSIONS: High SDF index leads to poor embryo development, and reduced implantation and ongoing pregnancy in couples with non-male factor infertility. Sperm DNA fragmentation testing may reveal hidden sperm abnormalities in men who have been categorized into idiopathic infertility based on apparently normal standard sperm parameters, bringing additional information to sperm quality evaluation in men with unknown history of infertility.

Reference: None.

SUPPORT: None.

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EFFECT OF SPERM SELECTION TECHNIQUES ON HUMAN NEONATAL GENDER RATIO IN PATIENTS UNDERGOING ICSI. Khaled Mohamed Elqusi, BSc, Eman Mohamed Hassanen, BSc, Hanaa Ahmed Alkhader, MBbch, Hosam Zaki, MBbch, Msc, FRCOG, Ralf Henkel, PhD.
Ashok Agarwal, PhD. 2 Ganin Fertility Center, Cairo, Egypt; 3 Ganin IVF lab Director, Cairo, Egypt; 4 University of the Western Cape, Bellville, South Africa; 5 Cleveland Clinic, CLEVELAND, OH.

OBJECTIVE: To investigate the effect of commonly used sperm selection techniques, density gradient centrifugation (DGC), physiological ICSI (PICSI), and magnetic activated cell sorting (MACS), on the neonatal gender ratio of ICSI outcome.

DESIGN: Retrospective cohort study comparing the effect of sperm selection on gender ratio in three groups through statistical data analysis. ClinicalTrials.gov Identifier: NCT01922568.

MATERIALS AND METHODS: A total of 529 babies of known gender born out of 388 ICSI cycles between August 2016 and May 2018 at Ganin Fertility Center, Cairo, Egypt, were investigated for the gender ratio and then divided into three groups according to the sperm selection technique used before performing sperm injection: DGC (237 neonates out of 173 ICSI cycles), PICSI (147 neonates out of 109 ICSI cycles), and MACS (145 neonates out of 106 ICSI cycles). In PICSI and MACS groups, the sperm samples were processed by DGC prior to sperm selection. All embryos transferred were at the blastocyst stage. Power analysis was done by comparing the sex ratio of the neonates between DGC, PICSI and MACS. The chi-squared test for independent samples was chosen to perform the power analysis with \( p \) error level at 0.05. \( p \) values less than 0.05 were considered statistically significant. All statistical calculations were done using IBM SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA). A release 22 for Microsoft Windows.

RESULTS: Sperm selection using DGC, PICSI and MACS leads to different male ratios. The highest male ratio was observed in the MACS group (62.7%) compared to the DGC group (46.4%) (\( p = 0.002 \)) with statistical power of (76.5%). In contrast, there was no difference (\( p = 0.2 \)) between the PICSI group with a male ratio of (53.1%) and the DGC group (46.4%). The PICSI and MACS groups also did not differ significantly (\( p = 0.09 \)). Moreover, there was neither a significant difference in female gender (Mean\pm SD) between DGC (29.9\pm 5.2 yrs.), PICSI (29.9\pm 4.5 yrs.), and MACS (30.6\pm 4.8 yrs.) (\( p = 0.45 \)) nor in the male age of DGC (34.9\pm 6.4 yrs.), PICSI (36.2\pm 6.2 yrs.) and MACS (36.2\pm 7.7 yrs.) (\( p = 0.22 \)).

CONCLUSIONS: The use of MACS as sperm selection technique significantly alters the neonatal sex ratio at birth in favor of male offspring. Further investigations should be made on phospholipid phosphatidylserine externalization of MACS sperm during MACS sperm separation and it’s possible association with sex chromosome may provide some evidence for an association between semen quality and sex ratio of the offspring. To verify the outcome of higher male ratio in the PICSI group is needed, future studies with larger number of subjects are needed to compare PICSI with DGC.

SUPPORT: N/A.

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DAY 2 ICSI DOES RESULT IN GOOD QUALITY BLASTOCYST DEVELOPMENT AND PREGNANCY.

Rebecca Kile, MS. 1 Haleigh Silz, MS. 2 Sue McCormick, BS, 3 William B. Schoolcraft, MD, 4 Rebecca L. Krisher, PhD, 5 Colorado Center for Reproductive Medicine, Lone Tree, CO; 6 CCRM, Lone Tree, CO.

OBJECTIVE: Poor prognosis patients are often faced with negative IVF cycle outcomes, in which no or very few blastocysts are produced. Utilizing immature eggs recovered at oocyte retrieval may increase their chance of success. The aim of this study was to determine the efficacy of in vitro maturation of immature oocytes recovered in a standard IVF cycle, matured in vitro and fertilized with ICSI (D2, or rescue, ICSI), with respect to good quality blastocyst yield and establishment of pregnancy.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: After oocyte retrieval, cumulus oocyte complexes (COC) were denuded of cumulus cells. Mature oocytes (MII) were fertilized by ICSI (D1); immature oocytes at the germinal vesicle (GV) or metaphase I (MI) stage were placed into Oocyte Handling Medium for Maturation (OHM Mat) and incubated overnight. ICSI (D2) was performed on all oocytes that matured to MI. Zygotes (2PN) were cultured in sequential culture medium for 5-7 days when good quality blastocysts were biopsied for PGT-A and vitrified.

RESULTS: A total of 165 patient IVF cycles in 2018 in which D2 ICSI was performed were reviewed (average age 37.8 yrs.; range, 27-47). There were 2,101 oocytes retrieved; 1,325 (63.1%) were MII, 363 (17.3%) were MI, and 408 (19.4 %) were GV. After IVM, 527/771 oocytes matured (68.4%). ICSI on D1 resulted in higher (\( P < 0.01 \)) normal fertilization (63.3%) than on D2 (56.5%), and improved (\( P < 0.01 \)) cleavage (D1, 101.2%; D2, 85.9%). In total, 36 patients (21.8%) that underwent D2 ICSI produced a good quality blastocyst from eggs that were immature at retrieval. Total good quality blastocysts (\( \geq 3 BB \)) development (per 2PN) for Day 2 ICSI was 20.8% across all patients. Within patients that had blastocyst development from D2 ICSI eggs, there was no difference (\( P > 0.05 \)) in total blastocyst production per 2PN between D1 (52.0%) and D2 (53.5%), or in euploid blastocysts (D1, 47.5%; D2, 38.9%). Three D2 ICSI euploid blastocysts have been transferred into three individual patients, resulting in 1 negative hCG, 1 biochemical pregnancy, and one ongoing pregnancy. For two of these patients, no D1 euploid blastocysts were produced.

CONCLUSIONS: Retaining immature oocytes and performing Day 2 ICSI can yield good quality euploid blastocysts capable of supporting a pregnancy, although fertilization and embryo cleavage is reduced. Although the percentage of patients who may ultimately benefit from D2 ICSI is low, for poor prognosis patients these rescued immature oocytes may produce the only euploid blastocysts available for FET. Thus, incorporating D2 ICSI into the treatment protocol gives poor prognosis patients the best chance at ART success.

SUPPORT: None.
DO DIFFERENT SPERM SELECTION TECHNIQUES HAVE AN IMPACT ON EMBRYOLOGICAL FINDINGS AND CLINICAL OUTCOMES OF ABNORMAL SPERM DNA FRAGMENTATION PATIENTS COMPARED TO NORMAL ONES; A RETROSPECTIVE COHORT STUDY. Manar Mohamed Hozyen, MSC, Eman Mohamed Hassanen, BSc, Yasmine sayed Azzouz, BSc, Hanah Alkhadder, MBBCBH, Hosam Zaki, MBBCBH, MSC, FRCOG, Gannin Fertility Center, Cairo, Egypt.

OBJECTIVE: To determine the effect of sperm selection techniques for abnormal sperm DNA fragmentation (SDF) patients on the blastocyst grading, implantation and pregnancy rates compared to normal SDF.

DESIGN: Retrospective cohort study included 501 couples who underwent ICSI in Gannin Fertility Center from January 2017 to January 2019.

MATERIALS AND METHODS: Cases were assigned to normal SDF (125 couples) by ejaculated sperm processed by density gradient centrifugation (DGC) using Isolate and abnormal SDF group (376 couples) which subdivided to; 70 cases as ejaculated sperm processed by (DGC), 128 cases as physiological ICSI (PICSI) using ejaculated sperm selected by hyaluronan binding PICSI dishes, 107 cases as ejaculated sperm selected by magnetic activated cell sorting columns (MACS) using Annexin V microbead labeling followed by column separation and 71 cases using testicular sperm (TESTI). All included cases reached the blastocyst stage, female age was ≤ 37 years old and male with ≥ 5 millions of sperm count. SDF test was done by TUNEL assay and bench-top flow cytometer, Saudi J Biol Sci. 2016 Sep; 23(5): 598–606.

RESULTS: There were no significant differences in male age, female age, number of MII oocytes or number of embryos transferred between the groups. CONCLUSIONS: PICSI and MACS has superiority over TESTI as sperm selection techniques for patients with abnormal SDF and could improve the embryological and clinical parameters to the normal level. These findings should be confirmed by larger prospective randomized studies.


SUPPORT: None.

FERTILITY & STERILITY®

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IDENTIFICATION OF THE OPTIMAL PUNCTURE POSITION IN PIEZO-ICSI USING IMAGE ANALYSIS: A PILOT STUDY. Tomohiro Maekawa, M.MS.,* Shimpei Mizuta, M.HS.,* Yuya Kinishi, B.E.,* Chie Takahashi, MBBS.,* Hidehiko Matsubayashi, MD.,* Kotaro Kitaya, MD.,* Takumi Takeuchi, MD, PhD.,* Yutaka Hata, Ph.D.,* Tomomoto Ishikawa, MD.* Reproduction Clinic Tokyo, Tokyo, Japan; Reproduction Clinic Osaka, Osaka, Japan; Graduate School of Simulation Studies, Kobe, Japan.

OBJECTIVE: Oocyte degeneration may take place in Piezo-ICSI as a result of unintentional membrane rupture in the puncturing process. Identifying the appropriate puncturing position may decrease the likelihood of membrane rupture and thus degeneration. Therefore, it was evaluated using image analysis whether it was possible to identify the optimal puncture position.

DESIGN: Retrospective image analysis during ICSI procedure.

MATERIALS AND METHODS: Image feature analysis is generally used to represent the useful features such as color, brightness, and contour. Among capturing image features, Local Binary Patterns (LBP) can efficiently summarize the local structures of images, and it has been applied in texture analysis in various fields including face recognition and moving image analysis in real-time. We employed this methodology to analyze the moving images of 131 oocytes following ICSI. These oocytes were categorized as either unintentional rupture (UR; n = 101) or no rupture (NR; n = 30). An image of the oocyte before puncture and of the puncture position was acquired from the moving images, and LBP values were calculated in the analysis region centered around the puncture position. In order to select an effective pattern for evaluation of rupture from the 256 types of shape patterns acquired by LBP, median values for the UR and NR groups were calculated, and the patterns with little difference to the median were eliminated. Data was classified by hierarchical clustering method using the three effective patterns for evaluation. We employed the Ward’s hierarchical cluster analysis method, and calculated the Euclidean distance between the barycenter of the cluster and each data point in order to define an index indicating the implausibility of membrane rupture. A t-test was used for statistical analysis.

RESULTS: Two clusters, Cluster A and B, were classified from hierarchical clustering. Following ICSI, 2 out of 27 oocytes from Cluster A and 28 out of 104 from Cluster B happened to have UR. When Cluster A represented the NR group and Cluster B the UR group, the sensitivity was 0.93. A significant difference between the UR and the NR group was reported from the Euclidean distance calculations between the barycenter of Cluster A and each data point (P = 0.001), where data showed a longer distance from the barycenter amongst the UR group and a shorter distance in the NR group.

CONCLUSIONS: Through image feature analysis, the presence or absence of membrane rupture was evaluated from the shape feature of the oolemma. The distance from the barycenter of Cluster A was associated with the likeliness of unintentional rupture. From this, visualizing shape features of the oolemma in real-time can contribute to the decrease in ICSI degeneration rate. From now on, it will be necessary to analyze more sample images and establish a visualization technique.

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OBJECTIVE: To investigate the effectiveness of immobilized acid-solubilized zona pellucida in the selection of spermatozoa for intracytoplasmic sperm injection (ICSI).

DESIGN: A prospective sibling oocytes study.

MATERIALS AND METHODS: In this study were included 113 couples who fulfilled the inclusion criteria: 1) unexplained infertility factor; 2) good quality oocytes; 3) fertilization failure for 3-5 consecutive ICSI procedures; 4) at least one oocyte at germinal vesicle stage (GV) and 5) at least four metaphase II oocytes retrieved during follicular puncture. Zona pellucidae were isolated from the patient’s own GV. Zonae were acid solubilized and diluted in carbonate buffer (pH 9.6) for air dry immobilization on glass petri dishes. The partner’s semen was washed and placed in the dishes. The spermatozoa that adhered on the immobilized surface were used for ICSI in the half of the retrieved oocytes from each woman. The other half of the oocytes was fertilized by conventional ICSI. In total, 312 oocytes were injected with zona-selected spermatozoa (zona-selection group) and 366 oocytes were injected with conventionally-selected spermatozoa (control group). The resulted embryos from the zona-selection and the control group were used in 43 and 50 single embryo transfers, respectively. Main outcomes were fertilization rate, embryo quality, implantation rate and pregnancy rate. Statistical analysis was performed using SPSS Software ver.21.

RESULTS: Slightly higher fertilization rate was observed among the oocytes injected with zona-bound spermatozoa in comparison to the conventional ICSI group (75.6% vs. 72.3%, p = 0.38). Also no significant differences were observed in the embryo quality and in the implantation rates between the zona-selection and the control group (p = 0.24 and p = 0.59, respectively). However, the pregnancy rate was considerably higher in the zona-selection group when compared with the control group (34.8% vs. 16.4%, p = 0.02). Moreover the miscarriage rate also differed significantly (7% in zona-selection vs. 18% in control group, p = 0.03).

CONCLUSIONS: The use of patient’s zona pellucida immobilized proteins in selection of spermatozoa for ICSI increases pregnancy rates and reduces the risk of miscarriage in couples with unexplained infertility and good quality oocytes.

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**TABLE 1. Results**

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<tr>
<td>Age(years)</td>
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<td>37.8±4.2</td>
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<tr>
<td>MII oocytes(n)</td>
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<td>Fertilization(%)</td>
<td>62.2±27.1</td>
<td>64.9±32.0</td>
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<td>Fertilization failure (%)</td>
<td>13.2%</td>
<td>7.8%</td>
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<td>Embryos transferred(n)</td>
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<td>2.2±0.7</td>
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<tr>
<td>Implantation rate (%)</td>
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</tr>
<tr>
<td>Clinical pregnancy rate(%)</td>
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<td>42%</td>
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<td>Clinical pregnancy rate/transfer (%)</td>
<td>26%</td>
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**HIGHER PREGNANCY RATES AFTER ZONA PELLUCIDA SPERM SELECTION.** Rumiana Ganeva, MSc, Dimitar Parvov, PhD, Magdalena Vasileva, MSc, Kristina Nikolova, MSc, Georgi Stamov Stamenov, MD/PhD Nadezhdas Women’s Health Hospital, Sofia, Bulgaria.

OBJECTIVE: To investigate the effectiveness of immobilized acid-solubilized zona pellucida in the selection of spermatozoa for intracytoplasmic sperm injection (ICSI).

DESIGN: A prospective sibling oocytes study.

MATERIALS AND METHODS: In this study were included 113 couples who fulfilled the inclusion criteria: 1) unexplained infertility factor; 2) good quality oocytes; 3) fertilization failure for 3-5 consecutive ICSI procedures; 4) at least one oocyte at germinal vesicle stage (GV) and 5) at least four metaphase II oocytes retrieved during follicular puncture. Zona pellucidae were isolated from the patient’s own GV. Zonae were acid solubilized and diluted in carbonate buffer (pH 9.6) for air dry immobilization on glass petri dishes. The partner’s semen was washed and placed in the dishes. The spermatozoa that adhered on the immobilized surface were used for ICSI in the half of the retrieved oocytes from each woman. The other half of the oocytes was fertilized by conventional ICSI. In total, 312 oocytes were injected with zona-selected spermatozoa (zona-selection group) and 366 oocytes were injected with conventionally-selected spermatozoa (control group). The resulted embryos from the zona-selection and the control group were used in 43 and 50 single embryo transfers, respectively. Main outcomes were fertilization rate, embryo quality, implantation rate and pregnancy rate. Statistical analysis was performed using SPSS Software ver.21.

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CONCLUSIONS: The use of patient’s zona pellucida immobilized proteins in selection of spermatozoa for ICSI increases pregnancy rates and reduces the risk of miscarriage in couples with unexplained infertility and good quality oocytes.
WHAT IS THE BEST SPERM SOURCE AND METHOD OF SPERM SELECTION IN CASES WITH ABNORMAL SEMINAL OXIDATION-REDUCTION POTENTIAL (ORP) LEVELS ON THE DAY OF ICSI?

Emran Mohamed Hassanen, BSc, a Khaleed Mohamed Elquisi, BSc, a Yasmine sayed Azzouz, BSc, a Hanaa Ahmed Alkhader, MBChb, a Hosam Zaki, MBChb, Msc, FRCOG, b Ralf Henkel, PhD, b Ashok Agarwal, PhD, c "Ganin Fertility Center, Cairo, Egypt; dUniversity of the Western Cape, Bellville, South Africa; eCleveland Clinic, CLEVELAND, OH.

OBJECTIVE: To investigate whether PICSI or TESA is better for the selection of sperm in cases of abnormal seminal ORP levels for ICSI patients.

DESIGN: Prospective randomized trial, which included 74 patients undergoing ICSI at a busy Fertility Clinic, Cairo, Egypt, from January 2018 to January 2019. ClinicalTrials.gov ID: NCT03360526.

MATERIALS AND METHODS: A total of 74 patients with sperm counts of more than 5x10^6/mL and an ORP of more than 1.42 mV/10^6/mL were included in the study. Male partners were examined for infertility and seminal ORP was measured using the MiOXSYS analyzer. PICSI dishes (Origio, Knaardrupvej, Denmark) were prepared by hydrating the hyaluronan microdots with medium followed by incubation for sperm binding at 30°C. Sperm were checked for the hyaluronan binding capacity, immobilized and injected into mature oocytes. TESA was done by testicular tissue aspiration followed by sample processing and oocyte injection. Seminal ORP was tested in the same ejaculate that was used for ICSI and patients with abnormal ORP were randomized into two arms, PICSI (n=40) and TESA (n=34).

Embryological parameters included: fertilization, cleavage, blastulation and good quality blastocyst rates were recorded. Pregnancy was followed up after 15 days of embryo transfer and pregnancy rate calculated. All statistical calculations were done using SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) release 22 for Microsoft Windows.

RESULTS: There were no significant differences in the female age (30.1 ± 4.58 vs. 29.2 ± 4.16 yrs.) (P = 0.5369), male age (36.4 ± 5.87 vs. 34.6 ± 6.44 yrs.) (P = 0.2041), seminal ORP values (5.8 ± 6.22 vs. 5.8 ± 7.99 mV/10^6 sperm/ml) (P = 0.9808) and the number of mature injected oocytes (15.7 ± 7.8 vs. 16.8 ± 7.7) (P = 0.5631) between the PICSI and TESA groups, respectively. The blastulation rates between PICSI and TESA showed a significant difference (60.2% vs. 48.4%; P = 0.0114). In contrast no difference in ORP level was seen between PICSI and TESA, for fertilization (79.8% vs. 80.7%), cleavage (73.4% vs. 73.8%), high quality blastocyst (57.2% vs. 51.9%), pregnancy (67.8% vs. 50%), implantation (41.6% vs. 36.6%), and ongoing pregnancy rates (94.7% vs. 84.6%). There were also no correlations between ORP levels and fertilization (R = 0.1523, R² = 0.1792), blastulation (R = 0.1475, R² = 0.1724), cleavage (R = 0.1763, R² = 0.1623), and the percentage of high quality blastocyst formation (R = 0.0902, R² = 0.2055). The mean ORP level for the pregnant group was 6.36 ± 0.98 mV/10^6 sperm/ml as compared to 6.05 ± 3.81 mV/10^6 sperm/ml in the non-pregnant group (P = 0.9891).

CONCLUSIONS: The use of PICSI as a sperm selection method in patients with abnormal seminal ORP levels may result in better selection of sperm and improved blastulation rate. Thus, contrary to reports in the literature that TESA-retrieved sperm are unexposed to seminal reactive oxygen species, our study failed to show the advantage of TESA over PICSI dishes.
OBJECTIVE: Semen analysis (SA) fails to evaluate fertilizing ability and best identifies extreme infertility cases. Cap-Score™ functionally assesses sperm capacitation/male fertility and prospectively predicts pregnancy. Here, we examine the association of SA, Cap-Score, and Cap-Score’s relationship with the probability of generating pregnancy in 3 cycles (PGP; Schinfeld et al., 2018), in men having fertility exams vs fertile men.

DESIGN: Correlation study: Cap-Score, PGP and SA metrics were compared in 1610 men questioning fertility vs 76 fertile men (pregnant partner or recent father).

MATERIALS AND METHODS: Semen was collected from men having SA because of fertility concerns (9 clinics; 10/2016 to 3/2019). Volume, concentration and motility were assessed (WHO criteria; morphology omitted due to variable methods). Fixed samples were shipped to Androvia for Cap-Score and PGP determination. Fertile men were assessed previously (WIRB 20152233). Table 1 was designed with even PGP bins and evaluated by Chi-square.

RESULTS: 59% (948/1610) of men having SA were normospermic (volume, concentration, motility). Compared to fertile men (p<0.001), more men having fertility exams had Cap-Scores ≤ 31 (PGP bins of ≤ 19, 20-29 and 30-39). Fewer than expected had Cap-Scores ≥ 32 (PGP bins of 40-49, 50-59 and ≥ 60). This distribution revealed a high prevalence of reduced capacitation/fertilizing ability in men having fertility exams. Defects in sperm function were equally prevalent regardless of passing any single or multiple SA metrics, or those having > 10 million total motile cells (TMC; p=0.990).

CONCLUSIONS: Of normospermic men having fertility exams, 65% (616/948) had Cap-Scores ≤ 31 (PGP ≤ 39%); in contrast, only 25% of fertile men (19/76) scored in this range. Conversely, only 35% (332/948) of normospermic men questioned their fertility had Cap-Scores ≥ 32, in contrast to 75% of fertile men. These data support reports that reduced sperm function/fertilizing ability is common in men questioning their fertility and cannot be detected by traditional SA, contributing to the high percentage of men diagnosed with idiopathic infertility. In men having fertility exams, reduced Cap-Scores were detected equally in normospermic men vs all men examined. These data show that a test of sperm capacitation offers a powerful complement to traditional SA, capable of identifying normospermic men with reduced sperm fertilizing ability. Reference: Schinfeld et al.© Cap-Score™ prospectively predicts probability of pregnancy. Molecular Reproduction and Development. 2018; 85 (8-9), 654-664.

SUPPORT: Androvia LifeSciences LLC.

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PATERNAL CONTRIBUTION TO EARLY EMBRYOIC DEVELOPMENT IN SEVERE MALE FACTOR PATIENTS. Jenna Friedenthal, MD. a Dmitry Gouko, MA. a Joseph A. Lee, BA. a Christine Briton-Jones, PhD, HCLD. b Alan B. Copperman, MD. c Mert Yesiladali, MD. b Cem Neset Fıçıcıoğlu, MD. c

OBJECTIVE: Current evidence suggests that the maternal genome is primarily responsible for embryonic development until the cleavage stage, at which time, expression of paternal genes occurs along with activation of the embryonic genome [1]. Theoretically, sperm could influence early post-fertilization events, since defects in the sperm centrosome have the potential to compromise early cell division. Additionally, sperm DNA damage has been shown to adversely affect embryo quality as early as day 2 of development [2]. Evidence regarding the association between severe male factor infertility and embryonic development, embryonic aneuploidy, or clinical outcomes within in vitro fertilization (IVF) cycles utilizing intracytoplasmic sperm injection (ICSI) is contradictory [3]. Thus, we sought to assess the relationship between severe male factor infertility and early embryonic development in an IVF model that includes ICSI and preimplantation genetic testing for aneuploidy (PGT-A).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Our study included patients at a single academic center who underwent IVF-PTGA cycles from 2011 to 2019. ICSI was used in all study cases. Patients were divided into 2 cohorts: severe oligospermia (<5 million/mL), and normal semen analyses (SA) (≥5 million/mL). The primary outcome was cleavage rate (CR). Secondary outcomes were fertilization rate (FR), blastulation rate (BR), euploid rate (ER), ongoing pregnancy/live birth rate (OP/LBR), and clinical loss rate (CLR). Student’s t-test, chi-squares, and multivariate logistic regression analyses were used for statistical analysis, with p<0.05 considered significant.

RESULTS: A total of 3,029 patients underwent 3,488 IVF-PTGA cycles during the study period, leading to 4,716 single, euploid frozen embryo transfers. In our unadjusted analysis, the FR and CR were significantly lower in the severe oligospermia group compared to the normal SA group (FR 82.30% vs 77.78%, p<0.0001; CR 99.25% vs 98.23%, p = 0.007). There were no significant differences in BR, ER, or clinical pregnancy outcomes between the groups. After performing an adjusted analysis that controlled for confounding factors, a significant difference in CR between the oligospermia group and the normal SA group (β = 0.99, p = 0.03) remained.

CONCLUSIONS: In the largest study to date evaluating the association between the paternal genome and embryonic development, we demonstrated that oligospermic samples are associated with impaired early embryo development. Our results provide new insight into the role of the paternal genome in embryonic development prior to activation of the embryonic genome. Future studies should aim to examine more closely paternally-derived genomic actions, including epigenetic factors such as paternal centrosome function, chromatin packaging, or histone modification, which impact successful cell division and growth prior to the cleavage stage in severe male factor patients. Our findings may lead to a better understanding of the ways in which maternal-paternal genomic interactions drive early embryonic development.


SUPPORT: None.

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DOES THE USE OF MICROFLUIDIC SPERM SORTING FOR THE SPERM SELECTION IMPROVE IVF SUCCESS RATES IN MALE FACTOR INFERTILITY? Pinar Ozcan, MD, Assoc. Prof. a Taha Takanaz, MD. a Melis Gökçe Kocer Yazıcı, MD. a Oya Akin Alagoz, MD, Assoc. Prof. b Mert Yesiladali, MD. b Cem Neset Fıçıcıoğlu, MD. c

Vol. 112, No. 3, Supplement, September 2019
OBJECTIVE: IVF success rate may improve with the selection of viable, motile, and morphologically intact sperm.

DESIGN: This multicentric prospective RCT was designed to evaluate the clinical outcome of ART cycles in an male factor infertility, where the spermatozoa were selected using either a conventional gradient-density centrifugation technique or microfluidic sperm sorting.

MATERIALS AND METHODS: A total of 139 patients who underwent IVF because of male factor infertility at Bezmialem and Yeditepe University Hospital were included in this study. All patients were randomly divided into two groups according to the sperm selection method: group I (n=71): microfluidic sperm-sorting chip; group II (n=68): density-gradient centrifugation. Data collected included male and female age, type of infertility, duration of infertility, previous IVF attempts, total dosage of gonadotropins, maximum estradiol levels, duration of stimulations, endometrial thickness on hCG day, total number of oocytes retrieved, number of mature oocytes retrieved, number of PNs, sperm count, ejaculate volume, morphologically normal spermatozoa, total motile sperm count, and clinical PR.

RESULTS: There was a statistically significant improvement in clinical pregnancy rates in the microfluidic sperm-sorting chip when compared to other group (50.7% vs. 27.9%; p<0.01). In group I, sperm count, morphologically normal spermatozoa, total motile sperm count were significantly lower (Table 1; p<0.01, p<0.01 and p<0.05, respectively). The number of PNs was also higher in group I although it did not reach statistical significance (5.32±3.54 vs 4.38±3.37, p=0.06).

CONCLUSIONS: Microfluidic devices, “labs-on-a-chip”, are a disposable, easy to use, and inexpensive method for sperm sorting. Our results show that IVF success rates may improve with the use of a microfluidic sperm-sorting chip for sperm selection in male factor infertility.

TABLE 1. Sperm parameters and cycles characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I (n=71)</th>
<th>Group II (n=68)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sperm count (million/ml)</td>
<td>15.49±17.47</td>
<td>30.94±27.14</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Ejaculate volume (ml)</td>
<td>3.68±1.52</td>
<td>3.92±1.90</td>
<td>0.67</td>
</tr>
<tr>
<td>Morphologically normal spermatozoa (%)</td>
<td>1.08±1.16</td>
<td>2.04±1.65</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>TMSC</td>
<td>5.8±38.45</td>
<td>8.29±74.83</td>
<td>0.05*</td>
</tr>
<tr>
<td>Total dosage of gonadotropins (IU)</td>
<td>3145±1000</td>
<td>2852±920</td>
<td>0.06</td>
</tr>
<tr>
<td>Maximum estradiol levels (pg/mL)</td>
<td>2074±1154</td>
<td>1979±1375</td>
<td>0.35</td>
</tr>
<tr>
<td>Duration of stimulations (day)</td>
<td>9.5±1.48</td>
<td>9.27±1.61</td>
<td>0.18</td>
</tr>
<tr>
<td>Endometrial thickness on hCG day (mm)</td>
<td>9.8±1.9</td>
<td>10.2±2.8</td>
<td>0.79</td>
</tr>
<tr>
<td>Total number of oocytes retrieved</td>
<td>9.81±6.46</td>
<td>11.1±6.86</td>
<td>0.23</td>
</tr>
<tr>
<td>Number of mature oocytes retrieved</td>
<td>6.69±4.31</td>
<td>7.76±5.16</td>
<td>0.28</td>
</tr>
<tr>
<td>Number of PN</td>
<td>5.32±3.54</td>
<td>4.38±3.37</td>
<td>0.06</td>
</tr>
<tr>
<td>Pregnancy rate</td>
<td>50.7% (n=36)</td>
<td>27.9% (19)</td>
<td>&lt;0.01*</td>
</tr>
</tbody>
</table>

FERTILITY & STERILITY®

e283

MATERIALS AND METHODS: We analyzed outcomes of 148 patients with AZFc microdeletions undergoing 205 cycles with ejaculated and testicular sperm, 176 iNOA patients undergoing 265 cycles with ejaculated and testicular sperm and 177 azoospermic patients with AID sperm undergoing 284 cycles between September 2015 and September 2018. Experiment groups: group A, testicular sperms for ICSI in aPAZFcM; group B, ejaculated sperm for ICSI in patients with AZFc microdeletions; group C, testicular sperm for ICSI in iNOA patients; group D, ejaculated sperms for ICSI in iNOA patients. Control group (group E): AID sperm for ICSI in azoospermic patients. The parameters were fertilization rate (FR), 2PN cleavage rate (2PNCR), blastocyst formation rate (BFR), implantation rate (IR), cumulative pregnancy rate (CPR), cumulative live-birth rate (CLBR), cumulative miscarriage rate (CMR) and Cancelled Cycle Rate (CCR). Analysis of categorical variables was evaluated with χ2 or Fisher’s exact tests. A level of P<0.05 was considered statistically significant.

RESULTS: Comparing group A, group B has shown better ICSI outcome with statistically significant differences in FR, BFR, CPR, CLBR and CCR between the two groups (all p values were less than 0.02), while iNOA patients had similar ICSI outcomes either with testicular or ejaculated sperm. The group B, D and E had similar outcomes. The group E has exhibited much better ICSI outcome than group A with statistically significant differences in FR, BFR, IR, CPR, CLBR and CCR between the two groups (all p values were less than 0.005), while it was just little better than group C. The CCR is the highest in group A, and the FR is the highest in group E among all five groups.

CONCLUSIONS: Our results suggest that ICSI with ejaculated sperm is a better treatment for patients with AZFc microdeletions while iNOA patients didn’t like that. ICSI with AID sperm is a better treatment for azoospermic patients with AZFc microdeletion.

Support: No.

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WHICH IS THE BETTER CHOICE FOR THE AZOO-SPERMIC PATIENTS WITH AZFC MICRODELETIONS, TESTICULAR SPERM OR DONOR SEMEN (AID) SPERM? Li Zhang, Ph.D.,a Jaming Mao, MD,b Ping Liu, MD, Ph.D.,a Jie Qiao, MD, Ph.D.,a Ping Liu, MD, Ph.D.a Jie Qiao, MD, Ph.D.a

OBJECTIVE: We performed a retrospective study to investigate either testicular or AID sperm is the better choice for azoospermic patients with AZFc microdeletion.

DESIGN: Comparing the outcomes of aPAZFcM with patients with unexplained idiopathic non-obstructive azoospermia (iNOA) undergoing ICSI with testicular and ejaculated sperm versus azoospermic patients undergoing ICSI with AID sperm was conducted after excluding infertility caused by female factors and female older than 35.

CONCLUSIONS: Our results suggest that ICSI with ejaculated sperm is a more optimal treatment for patients with AZFc microdeletions while iNOA patients didn’t like that. ICSI with AID sperm is a better treatment for azoospermic patients with AZFc microdeletion.

Support: No.

P-439 Wednesday, October 16, 2019 6:30 AM

SPERM SELECTION WITH HYALURONIC ACID (PICSI) IMPROVES EFFICIENCY OF IVF CYCLES. Lucia Alegre, PhD,a Irene Hervas, PhD, student,a Lorena Bori Aral, PhD,a Alberto Tejera, Sr., PhD,b Thamara Viloria, PhD,a Jose Alejandro Remohi, MD, PhD,b Marcos Meseguer, PhD,a IVIRMA Global, Valencia, Spain. 

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Support: No.
ANEUPLOIDY. CHROMATIN MAY REDUCE EMBRYO P-440

Instituto de Salud Carlos III program. We believe that the use of PICSI technique could be a competitive advantage for patients undergoing oocyte donation. Higher pregnancy potential were found between PICSI and ICSI groups; nevertheless, the pregnancy rate was higher in PICSI group, (but non-significant) 74% vs. 88%, while in ICSI group was 71% (LogRank and Tarone-ware Test P-441). The implantation rate was comparable between PICSI and ICSI group.

DESIGN: This is the first reported study, up to now, where all transferred embryos were blastocyst stage and only couples undergoing oocyte donation were included, avoiding the oocyte factor bias. PICSI technique can identify mature spermatozoa from a sperm sample to select through HA (hyaluronic acid) receptors binding ability. Single centre analysis, prospective, randomized and triple-blinded trial were undertaken. In the project a total of 277 infertile couples were recruited, 142 in the PICSI group and 135 in the control.

MATERIALS AND METHODS: Spermatozoa were incubated in AH drops for selection before microinjection in PICSI samples. In both groups, zygotes were cultured in a time- lapse incubator (Geri, Genex or Embryoscope, Vitrolife). The study involved a total of 3104 mature injected oocytes, 2433 zygotes, 1144 viable embryos obtained (Transferred + Vitrified), 348 embryos were transferred while 235 were vitrified. The pregnancy rate was higher in PICSI group, (but non-significant) 74% vs. 70% PICSI group and Control, respectively. The implantation rate was comparable between PICSI and ICSI group. The pregnancy rate was higher in PICSI group, (but non-significant) 74% vs. 70% PICSI group and Control, respectively. No differences were found comparing PICSI-ICSI in fresh or vitrified transfer cycles. PICSI group showed a higher pregnancy rate (but non-significant) when patients presented lower sperm count. No differences were observed in ongoing pregnancy rate or live birth rates between PICSI-ICSI. However, after 4 cycles of embryo transfer the cumulative pregnancy rate in PICSI was significantly higher 88%, while in ICSI group was 71% (LogRank and Tarone-ware Test P-441). CONCLUSIONS: No differences between embryo quality and development potential were found between PICSI and ICSI groups; nevertheless, the global efficiency of PICSI cycles was higher. The use of the PICSI technique could be a competitive advantage for patients undergoing oocyte donation especially in those cases in which pregnancy is not successfully accomplished after first cycle.

SUPPORT: PI14/00523. Spanish Ministry of Economy and Competitiveness. Instituto de Salud Carlos III program.

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SELECTING SPERMATOZOA WITH INTACT CHROMATIN MAY REDUCE EMBRYO ANEUPLOIDY. Alessandra Parella, M.Sc., Zev Rosenwaks, M.D., Gianpietro D. Palermo, M.D., Ph.D., The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: We tested a novel approach for treating couples with complete and persistent embryo aneuploidy. Using a microfluidic device, we selected spermatozoa with the highest progressive motility and genomic integrity, capable of generating euploid embryos.

DESIGN: From October 2016 to April 2019, 13 consenting couples with male partners with high sperm chromatin fragmentation (SCF) in their ejaculate and a history of embryo aneuploidy and/or recurring implantation failure underwent a new PICSI cycle in which semen specimens were processed by microfluidics sperm selection (MFSS) and density gradient centrifugation (DGC).

MATERIALS AND METHODS: Consent men had their ejaculates screened by standard semen analysis according to WHO 2010 criteria. Specimens were processed by DGC and MFSS. SCF was measured by TUNEL utilizing a commercial kit (In Situ Cell Death Detection Kit, Roche). At least 500 spermatozoa were counted under fluorescent microscopy, with an established threshold of 15%. Fertilization and clinical pregnancy rates were assessed and compared between PICSI and conventional preparation methods.

RESULTS: A total of 13 men with an average age of 41.5±10 years had the following average semen parameters: concentration of 40.5±44 ×10⁶/ml, 26±19 motility, and 2.2±1.1 morphology. After DGC and MFSS, the sperm concentration was 27±41 and 4.4±7 ×10⁶/ml, with 47.7±43% and 97.1±4% motility, respectively. The average SCF decreased from 29% in the raw samples to following DGC (P=NS), and dropped to 2.2% after MFSS processing (P<0.0001). These couples (female partner, 39±6 years) underwent 15 ICSI cycles with DGC-selected spermatozoa and achieved a fertilization rate of 71.3% (97/136), which generated 64.5% (31/48) morphologically good-quality embryos; of these, 12.5% (6/48) were determined by PGT-A to be euploid. Two of these euploid embryos were transferred and did not yield a pregnancy. In a subsequent ICSI cycle with MFSS processing, a fertilization rate of 73.2% (104/142) resulted in 61.8% (34/55) good-quality embryos. Of these, 36.3% (20/55) were identified as euploid and were cryopreserved (P<0.05). Seven couples received a thawed single euploid blastocyst and all 7 became pregnant (P<0.0001), resulting in the delivery of two healthy babies, with 71.4% (5/7) still ongoing.

CONCLUSIONS: Dysfunction of the male genital tract increases both single-strand (ss) and double-strand (ds) DNA nicks and breaks, resulting in spermatozoa that impair embryonic development. Because dsDNA breaks in the male gamete can be responsible for embryo aneuploidy, the use of MFSS processing to select spermatozoa with the highest motility and genomic integrity may enhance the chances of obtaining a euploid conceptus for transfer.

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OBJECTIVE: To successfully achieve ICSI fertilization in couples with a history of complete fertilization failure due to a lack of sperm cytosolic activating factor.

DESIGN: In a prospective controlled manner, consenting couples (IRB 0712009553) with a history of ICSI fertilization failure were included. Various tests were carried out on the male partners’ ejaculates to confirm sperm-related activation deficiencies. Following the utilization of a proprietary gamete treatment method in a subsequent ICSI cycle, embryology and clinical outcomes were recorded and compared with same-patient history cycles.

MATERIALS AND METHODS: Spermatozoa were assessed by standard semen analysis. According to the initial morphological evaluation, subsequent tests were performed. These included an in-house PLC test assay to screen for the presence of sperm cytosolic activating factor, and aniline blue staining to assess protamine content. Transmission electron microscopy (TEM) and mouse oocyte activation test (MOAT) were also used to identify structural and functional deficiencies. A proprietary gamete treatment method was performed with ICSI to pre-treatment of spermatozoa and post-injection oocyte activating agents.

RESULTS: A total of 22 couples (maternal age, 35.8±5.5 yrs; paternal age, 40.1±6 yrs) were included. Prior to undergoing cycles with gamete treatment, these couples underwent a total of 29 ICSI cycles, resulting in a fertilization rate of 10.6% (23/216). However, no couples received a conceptus suitable for embryo aneuploidy and/or recurring implantation failure. Using a microfluidic device, we selected spermatozoa with the highest progressive motility and genomic integrity, capable of generating euploid embryos. These couples (female partner, 39±6 years) underwent a total of 15 ICSI cycles with DGC-selected spermatozoa and achieved a fertilization rate of 71.3% (97/136), which generated 64.5% (31/48) morphologically good-quality embryos; of these, 12.5% (6/48) were determined by PGT-A to be euploid. Two of these euploid embryos were transferred and did not yield a pregnancy. In a subsequent ICSI cycle with MFSS processing, a fertilization rate of 73.2% (104/142) resulted in 61.8% (34/55) good-quality embryos. Of these, 36.3% (20/55) were identified as euploid and were cryopreserved (P<0.05). Seven couples received a thawed single euploid blastocyst and all 7 became pregnant (P<0.0001), resulting in the delivery of two healthy babies, with 71.4% (5/7) still ongoing.

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and MOAT indicated a lack of sperm cytosolic activating factor and compromised fertilizing aptitude. The aniline blue assay also showed a sperm chromatin condensation deficiency, particularly in the globozoospermic patients, with a sperm chromatin fragmentation of 16.8%, corroborated by a 1.9% FISH aneuploidy.

All couples underwent a total of 37 ICSI cycles with gamete treatment, resulting in a 41.2% (120/291) fertilization rate and a 33.3% (8/24) clinical pregnancy rate (P<0.05). Of the 8 couples who achieved a clinical pregnancy, 4 delivered a healthy baby.

CONCLUSIONS: In couples with recurrent and complete fertilization failure, the application of a battery of bioassays can help to assess sperm activating factor dysfunction and compromised fertilizing ability. In these couples, gamete treatment in a subsequent cycle enhances the chances of fertilization and successful pregnancies. The achievement of healthy offspring indicates that gamete treatment to overcome fertilization failure appears safe.

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SECOND EJACULATION: A SIMPLE, COST FREE MECHANISM TO DEAL WITH HIGH SPERM DNA FRAGMENTATION. Michael H. Dahan, MD, a, Rabea Youcef Khoudja, MD, PhD, a, Abbie Gagnon, M.Sc., b, Grace Tan, D. Phil. b, Seang Lin Tan, MD, MBA. a, b Division of REI, McGill University and OrigenElle Fertility Clinic and Women’s Health Centre, Montreal, QC, Canada; b OriginElle Fertility Center, Montreal, QC, Canada.

OBJECTIVE: High sperm DNA fragmentation is a controversial subject. However, many physicians test for DNA fragmentation and feel it is important. If high, methods of dealing with DNA fragmentation include testicular sperm aspiration, Anexin sperm wash and ICSI. These procedures add cost, pain after surgery and are of undetermined value. Sperm DNA fragmentation is felt to occur in the epididymis while waiting to be expelled. This study was undertaken to determine if a second ejaculation 3-hours after the first could improve sperm DNA fragmentation, by limiting time in the epididymis.

DESIGN: A prospective cohort study where males were requested to wait 3-days without an ejaculation at which point a semen analysis and DNA fragmentation was performed and repeated 3-hours latter on a 2nd specimen.

MATERIALS AND METHODS: 112 subjects underwent the two semen analysis protocol as part of the fertility evaluation. All ejaculations were performed at the fertility center. DNA fragmentation was evaluated using the halo test. Data was compared by intra-subject t-test. Data is presented as % or mean±SD. Power analysis suggested ≥73 subjects were required for an 80% power and an alpha of 5% with a 2 unit mean difference with SD of 6 units. High DNA fragmentation is ≥35%.

RESULTS: Male age was 36±7 years (range 29-65). DNA fragmentation decreased from 34.6±19.4 to 23.7±16.0% (p=0.0001) in the 1st and 2nd specimens, respectively. Average percentage improvement 23%±30%. Among subjects with high fragmentation 22/49 (45%) failed to improve into the normal range. Regarding subjects with initial DNA fragmentation≥35%, comparison of 1st and second 2nd fragmentation were 52±16% & 36±17% (p=0.0001), respectively. Greatest improvement was 97%-28% DNA fragmentation. 7/112 had worse DNA fragmentation in the second specimen and of those only 2 fell above the normal range, both with a first specimen above the normal range as well. Among semen parameters volume went from 3.1±3.3ml to 1.9±0.8ml, p=0.001, concentration from 41±39 to 32±31 million/ml, p=0.001 & progressive motility increased from 57±21% to 60±21%, p=0.06. In none of the cases where the total motile sperm count was greater than 5 million did the quality of the second semen specimen convert the subject to ICSI. The first 10 subjects had both 1st and 2nd DNA fragmentation confirmed with the TUNEL assay and equivalent improvements were seen t=0.97 (p=0.35), this was not continued due to cost assumed by the clinic.

CONCLUSIONS: High DNA sperm fragmentation can often be managed with a second ejaculation 3 hours after the first. Changes in sperm quality are not clinically significant and none of the ICSI specimens from ejaculation 1 would have required ICSI based on the ejaculation 3 hours latter. 55% improve into the normal range. Therefore, a second ejaculation represents a safe, cost free mechanism to deal with this issue in many patients.

SUPPORT: None.

P-443 Wednesday, October 16, 2019 6:30 AM
SPERM-BORNE mRNAs AS A BIOMARKER FOR HUMAN SPERM QUALITY. Yunge Tang, Master degree, a, Ying Zhang, MD, PhD, b, Wenzhong Zhao, PhD, b, Xinzong Zhang, MD, PhD, b, Weiibing Qin, MD, PhD, b, Shunmei Deng, MD, b, Jiabao Wu, BSc, b, Mengyuan Zhang, PhD, b, Wei Yan, M.D., Ph.D. b, Family Planning Research Institute of Guangdong Province, Guangzhou, China; a Affiliation not provided; b University of Nevada, Reno School of Medicine, Reno, NV.

OBJECTIVE: Although the World Health Organization (WHO) criteria for semen quality are widely followed, a significant proportion of sperm samples provided by sperm banks around the world fail to lead to successful pregnancies, highlighting the need for better biomarkers that allow for identification of truly fertile sperm.

DESIGN: Laboratory study using human sperm samples.

MATERIALS AND METHODS: We profiled and compared mRNAs in sperm samples with higher (5 pregnancies out of <20 attempts, >25%; n=10) and lower (<1 pregnancy out of 30 attempts, <3.3%; n=10) pregnancy rates using RNA-Seq. Among numerous differentially expressed genes (DEGs) identified between sperm with high (HPR) and low (LPR) pregnancy rates.

RESULTS: We selected 23 spermatogenesis-related genes and 10 energy metabolic genes as potential biomarkers for sperm quality because these showed the greatest difference in abundance in the two groups. Further optimization by examining their expression levels in 30 HPR and 30 LPR sperm yielded a list of 9 genes that were selected as biomarkers because they could distinguish sperm samples with extremely high (>40%) or extremely low (<1%) pregnancy rates. We then re-tested all of the 60 samples in a blinded manner (i.e., no sample information provided to the examiner) and our results showed that these 9 genes can reliably distinguish the two extreme groups.

CONCLUSIONS: Our data suggest that sperm-borne mRNAs can be excellent biomarkers for predicting the fertility potential of sperm in addition to the current motility- and morphology-based methods. We are exploring other RNA species as well as epigenetic markers as potential biomarkers for human sperm quality.

SUPPORT: This work was granted by the Natural Science Foundation of Guangdong Province (2014A030313798, 2018A030313528) and the Science and Technology Foundation of Guangzhou (201510010188).

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DEEP LEARNING-ENABLING SMARTPHONE-BASED SYSTEM FOR AUTOMATED EMBRYO ASSESSMENTS AND EVALUATION. Manoj Kumar Kanakasabapathy, MS, Prudhi Thirumalaraju, BS; a, Charles L. Bornmann, PhD, b, Hemanth Kandula, BS, a, Sandeep Kota Sai Pavan, BS, a, Divyank Yarravarapu, BS, a, Hadi Shafiee, PhD, a, b Brigham and Women’s Hospital, Harvard Medical School, Boston, MA; a Massachusetts General Hospital, Harvard Medical School, Boston, MA.

OBJECTIVE: Traditionally, embryos are visually assessed by embryologists and the selection process has been shown to be highly subjective. Commercially available time-lapse imaging (TLI) systems have provided a standardized imaging platform and they provide automated and interrupted continuous imaging of embryos over the course of in-vitro embryo development. Recent reports of artificial intelligence (AI) systems make use of data obtained from such time-lapse systems. 1, 2. However, these systems are large and prohibitively expensive. Here, as proof-of-concept, we report for the first time, the development and evaluation of an inexpensive smartphone-based system that can perform embryo evaluations using deep convolutional neural networks (CNN) on- phone.

DESIGN: We have developed an inexpensive (<$5) smartphone imaging system that can be used to image embryos during in-vitro culture. The smartphone-based system automatically evaluates embryos based on their morphology using an AI algorithm. We used a depthwise convolutonal deep neural network and transfer-learned with retrospective embryo images captured at 113 hours post insemination (hpi) that was annotated by a total of 10 embryologists. We evaluated the system to differentiate 50 embryos based on their blastocyst status.

MATERIALS AND METHODS: Our device consisted of a 3D-printed housing that contained the objective lenses extracted from DVDs, a light
source, and batteries. A smartphone application was developed which performed the analysis locally. The AI utilized by the application was transferred, trained, and validated with 1790 embryo images. To test our system, 50 embryos donated by patients were imaged using the smartphone system. 33 hpi images were evaluated without a developed network without the need for any image processing. Performance metrics were calculated for the smartphone system and the overall performance of the smartphone system with the performance of deep-learning based approach that used Embryoscope data was compared.

RESULTS: The accuracy of such a system in classifying 50 embryos based on their blastocyst status was 96% (CI: 86.29% to 99.51%). Its sensitivity and specificity were 93.55% (CI: 78.58% to 99.21%) and 100% (CI: 82.35% to 100%), respectively, while its positive and negative predictive values were 100% and 90.48% (CI: 71.32% to 97.32%), respectively. A chi-squared analysis comparing the performance of an Embryoscope-based deep-learning approach with our smartphone system-based deep-learning approach revealed an insignificant difference of 5.03% (P=0.33, P=0.05).

CONCLUSIONS: The results reported here demonstrate that combined with the use of an AI-powered imaging system, automated embryo analysis is not limited to only expensive time-lapse hardware and inexpensive (<$100) systems can be developed for use at fertility centers without loss in performance. The overall impact of our AI-powered system is significant since it enables integration into clinical practices at resource-limited settings at very minimal costs.


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OBJECTIVE: To characterize the phenomenon of globozoospermia using various biomarkers and analyze reproductive outcomes in afflicted patients.

DESIGN: In 5 consenting men with globozoospermia, we assessed proteome content, sperm chromatin fragmentation (SCF), sperm aneuploidy, ultrastructural details by TEM, and epigenome. ICSI cycles with or without AOA were performed on 3 couples, and outcomes were compared.

MATERIALS AND METHODS: Semen analyses were performed on ejaculates of 5 consenting men. Proteome content was measured by Aniline blue assay on 200 spermatozoa, with a <20% normal threshold. SCF scored by TUNEL assay examined 500 spermatozoa, with a <15% normal threshold. Aneuploidy rate assessed by FISH was performed on 1000 spermatocytes, with a <1.6% normal threshold. Confirmatory TEM allowed observation of sperm ultrastructural details to confirm the extent of globozoospermia. The transcriptome of 1 man was profiled and compared to donor specimen with proven fertility. AOA was performed by exposing globozoospermia. The transcriptome of 1 man was profiled and compared to donor specimen with proven fertility. AOA was performed by exposing globozoospermia. The transcription of 1 man was profiled and compared to donor specimen with proven fertility. AOA was performed by exposing globozoospermia. The transcription of 1 man was profiled and compared to donor specimen with proven fertility. AOA was performed by exposing globozoospermia. The transcription of 1 man was profiled and compared to donor specimen with proven fertility. AOA was performed by exposing globozoospermia. The transcription of 1 man was profiled and compared to donor specimen with proven fertility. AOA was performed by exposing globozoospermia. The transcription of 1 man was profiled and compared to donor specimen with proven fertility. AOA was performed by exposing globozoospermia. The transcription of 1 man was profiled and compared to donor specimen with proven fertility.

RESULTS: Men (34.1 ± 4 years) had an average concentration of 39.6 ± 33 x10⁹/ml, motility of 31.8 ± 23%, and normal morphology of 0.1 ± 0.3%. Men were considered globozoospermic when standard morphology assessment showed that >70% of their spermatozoa had round heads. Concurrent testing revealed abnormal protamine content of 40.3 ± 8%, borderline normal ploidy of 14.4 ± 2%, and an aneuploidy rate of 4 ± 4%. Confirmatory TEM revealed 93 ± 12% occurrence of round heads. Complete globozoospermia was confirmed in 3 men. Epigenetic analysis of one man elucidated 2 under-expressed genes: MMP14 (P < 0.05) and AHNAK2 (P < 0.05). MMP14 encodes for matrix metalloproteinase involved in reproduction and embryo development, and AHNAK2 encodes nucleoprotein associated with calcium signaling and inferential oocyte activation. Three couples (male age, 35.1 ± 4 years; female age, 33.7 ± 2 years) underwent ICSI cycles (n=9). AOA cycles (n=4) resulted in a 59.2 ± 15% fertilization rate, 77.8% cleavage rate, 33.5 ± 17% embryo transfer (ET) rate, and 25% clinical pregnancy rate (CPR) and delivery rate. Cycles without AOA (n=5) yielded 11.6 ± 15% fertilization rate, 100% cleavage rate, 7.6 ± 9% ET rate, and 0% CPR. AOA cycles had higher fertilization rates (P<0.0005). In 2 couples with complete globozoospermia, all cycles without AOA resulted in fertilization failure, while AOA cycles resulted in fertilization rates of 59.2 ± 15%.

CONCLUSIONS: This study reported 2 novel genes related to globozoospermia, which can cause spermogenic abnormality and hinder oocyte activation. We also found that AOA can greatly enhance ICSI fertilization of globozoospermic men and is paramount in those with complete form.

P-445 Wednesday, October 16, 2019 6:30 AM

A NEW SPERM PREPARATION SOLUTION IMPROVES THE OUTCOME OF HUMAN CONVENTIONAL IN VITRO FERTILIZATION WITH HYPERACTIVATED SPERMATOZOA. Hiroyuki Tomari, Ph.D.,* Kou Honjo, M.D.,* Saki Gondo, M.D.,* Kensei Saito, M.D.,* Yumi Nagata, M.D., Ph.D.* "IVF Nagata Clinic, Fukuoka, Japan; *Affiliation not provided.

OBJECTIVE: Sperm preparation in human in vitro fertilization (IVF) requires not only good sperm motility but also sperm physiological function. We examined the effect of ORIGIO® Gradient (OG) Series™, a sperm preparation solution that mimics the physiological environment of the spermatozoa in vivo. The results showed that OG improved the fertilization and early embryonic development rates in conventional (c) IVF cycles (ASRM 2017). The purpose of this study was to clarify the effect of OG on pregnancy rate after embryo transfer (ET) in c-IVF cycles and to...
evaluate sperm motility function using a sperm motility analysis system (SMAS).

DESIGN: A prospective quasi-randomized controlled study was performed in a single IVF center between January 2016 and December 2017.

MATERIALS AND METHODS: Patients who undertook c-IVF were randomly allocated to two groups: for the control group, sperm preparation was performed using 80% Percoll solution (Sigma) with Sperm Washing Medium (Irvine Scientific); for the test group, sperm preparation was performed using 80% OG with ORIGIO® Sperm Wash (Origo). Sperm preparation was performed using density gradient centrifugation (25 min at 500 × g) with a subsequent swim-up (30 min). We examined 47 cycles of fresh ET and 99 cycles of vitrified-wormed ET. Clinical pregnancy and implantation rates after ET were compared between the two groups. We evaluated the sperm motility function after sperm preparation over time using SMAS (DITECT) between the two groups. We also evaluated the fractal dimension, which is one indicator of hyperactivated spermatozoa.

RESULTS: There were no significant differences in patient characteristics between the two groups. Among the 47 fresh ET cycles, 26 were in the control group and 21 were in the test group. Clinical pregnancy and implantation rates in the test group were higher than in the control group (24% vs. 15%, 18% vs. 12%, respectively). Among the 99 vitrified-wormed ET cycles, 44 were in the control group and 55 were in the test group. Clinical pregnancy and implantation rates in the test group were higher than in the control group (27% vs. 18%, 21% vs. 15%, respectively). There were no significant differences in sperm motility function (straight line velocity, curvilinear velocity, average path velocity, flagellar beat cross frequency, and amplitude of the lateral head) over time between the two groups. The fractal dimension of the test group was significantly higher (p < 0.05) than that of the control group after 5 hours (1.50 ± 0.05 vs. 1.36 ± 0.06, respectively).

CONCLUSIONS: Our results showed that the new sperm preparation solution improves clinical outcomes in human c-IVF programs, and suggest that the increase and maintenance of hyperactivated spermatozoa may contribute to the improvement of outcomes in c-IVF.

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YOUNGER FEMALE AGE MAY COMPENSATE THE HIGH SPERM DNA FRAGMENTATION IN THE ART PROGRAMS. Anastasia Kirillova, PhD,* Irina Vjačeschavlová Ushakova, PhD,† Maria Farmakovskaya, PhD,* Yulia Kiseleva, PhD., Olga Golubeva, PhD, Tatiana Volodzjaja, MSc,* Nona Mishieva, PhD,* Aydar Abubakirov, PhDd aEmbriologist, Moscow, Russian Federation; bReproductive endocrinology, Moscow, Russian Federation; cNona Mishieva, PhD,* Aydar Abubakirov, PhDd aEmbriologist, Moscow, Russian Federation.

OBJECTIVE: The impact of sperm DNA damage on the outcomes of IVF cycles remains controversial. The aim of our work is to determine if maternal age affects the outcomes of ART programs with high levels of partner’s DNA fragmentation.

DESIGN: This retrospective study included 287 couples, undergoing IVF treatment (n=86), ICSI (n=98), ICSI-PGT-A (n=103) with evaluation of functional semen parameters and sperm DNA fragmentation in 2 years (2016-2018). 287 women enrolled in the study were distributed according to their age as followed: under 30 y.o. (n=78); 31-34 y.o. (n=79); 35-40 y.o. (n=89); older than 40 (n=41).

MATERIALS AND METHODS: Sperm DNA fragmentation was evaluated using the TUNEL assay. Fertilization and embryo culture according to the manufacturers recommendations (COOK, Australia). Array CGH (Agilent, USA) was performed for 24-chromosome embryonic genome analysis. The fertilization rate, rates of blastocyst formation, and implantation rates were evaluated.

RESULTS: Our results showed that there are lower fertilization rates (72.3% vs. 84.3%; p < 0.05) and significantly lower rates of blastocyst formation (31.8% vs. 54.2%; p < 0.05) in the group with high values of sperm DNA fragmentation in comparison with the group with normal values of this parameter. Other results are presented in the table.

Our data demonstrates that for couples with a female partner under 30 there is no significant difference in the clinical pregnancies rates between the group with high values of sperm DNA fragmentation and the group with normal values of this parameter (39% vs 40% (IVF), 36% vs 34% (ICSI), 60% vs 59% (ICSI-PGT) respectively). On the contrary, for couples with female partners older than 31 the clinical pregnancies rates were higher for groups with normal values of sperm DNA fragmentation compared to the groups with high values of this parameter.

CONCLUSIONS: Our study shows that high values of sperm DNA fragmentation do not influence the outcomes of the ART programs only when a female partner is younger than 30 y.o. Thus, we can speculate that oocytes of younger women have the ability to compensate the spermatozoa damaged DNA.

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OBJECTIVE: To select spermatozoa with superior chromatin integrity, capable of increasing implantation and clinical pregnancy rates with ICSI.

DESIGN: From October 2016 to April 2019, semen specimens from consenting men (n=47) with prior ICSI failure due to high DNA fragmentation in their ejaculate were simultaneously processed by density gradient centrifugation (DGC) and microfluidic sperm selection (MFSS). TUNEL was carried out on the raw specimens and on the differently selected aliquots. In men treated by ICSI with their female partners, clinical outcomes were compared between the two sperm-selection methods.

MATERIALS AND METHODS: Fresh ejaculate specimens from consenting men were analyzed according to WHO 2010 criteria. DGC and MFSS were used to isolate spermatozoa based on cell motility and fluid dynamics. Sperm chromatin fragmentation (SCF) was assessed by TUNEL on at least 500 spermatozoa under a fluorescent microscope utilizing a threshold of ≥15%.

RESULTS: A total of 47 men with an average age of 40 ± 9 years had the following average semen parameters: concentration of 46.9 ± 38 x 10⁶/mL, 32.8 ± 14 motility, and 2.3 ± 1% morphology. After DGC or MFSS, the sperm concentration was 33.0 ± 27 and 11.6 ± 12 x10⁶/mL, with 62.0 ± 31% and 97.7 ± 2% motility, respectively (P < 0.0001). The morphology of the raw sperm sample improved from 2.3 ± 1% to 3.6 ± 1% after MFSS, while it remained at 2.4 ± 1% after DGC. The average SCF decreased from 24% in raw samples to 15% following DGC, and fell to 7.2% following MFSS (P < 0.0001).

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TABLE. Rates of clinical pregnancies, %

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<th>Age of women</th>
<th>IVF (&lt;30)</th>
<th>ICSI (&lt;30)</th>
<th>ICSI-PGT (&lt;30)</th>
<th>IVF (31-34)</th>
<th>ICSI (31-34)</th>
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<th>ICSI (&gt;40)</th>
<th>ICSI-PGT (&gt;40)</th>
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<td>Level of DNA fragmentation &lt;15%</td>
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<td>52%</td>
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<td>33%</td>
<td>11%</td>
<td>14%</td>
<td>13%</td>
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<tr>
<td>Level of DNA fragmentation &gt;15%</td>
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<td>59%</td>
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<td>41%</td>
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SUPPORT: None.

P-451 Wednesday, October 16, 2019 6:30 AM

SPERM RETRIEVAL RATES AND CLINICAL OUTCOMES WITH TESTICULAR SPERM EXTRACTION IN RELATION TO THE ETIOLOGY OF AZOOSPERMIA. Tomomoto Ishikawa, MD, a Shimpei Mizuta, M.HS., b Kohei Yamaguchi, MD, c Hidehiko Matsubayashi, MD, c Katori Kitaya, MD, c Takumi Takeuchi, MD, PhD. b Reproduction Clinic Osaka, Osaka, Japan; Reproduction Clinic Tokyo, Tokyo, Japan.

OBJECTIVE: Sperm retrieval rates (SRR) and clinical outcomes after in-tracytoplasmic sperm injection (ICSI) in testicular sperm extraction (TESE) cases in relation to the etiology of azoospernia have not well been investigated yet. Here we report our latest five-year experience in TESE.

DESIGN: Retrospective clinical analysis.

MATERIALS AND METHODS: This study investigated SRR of conventional TESE in obstructive azoospermia (OA) and microdissection TESE in cryptozoospernia and non-obstructive azoospermia (NOA) patients between September 2013 and December 2018 (1455 TESE attempts with 1222 patients). The etiologies of NOA were categorized as unexplained, Klinefelter’s syndrome (KS), post chemotherapy, post orchioxy, and microdeletion of azoospernia factor (AZF) on the Y chromosome. A total of 473 couples had 1128 TESE-ICSI cycles (136 couples and 337 couples and 716 cycles with NOA) were evaluated with respect to fertilization, embryonic development and clinical pregnancy rates (CPR).

RESULTS: SRR of patients with first TESE attempts (49.9%) was significantly higher than that of patients who previously failed sperm retrieval (32.5%) (P<0.001). In the first TESE cases, SRRs were 100% (152/152) in OA, 21.2% (102/482) in unexplained NOA, 50.5% (54/107) in KS, 47.8% (22/46) in post chemotherapy, 75.0% (33/44) in post orchioxy, and 87.1% (27/31) in AZF microdeletion. SRR of OA was significantly higher, while that of unexplained NOA was lower than any other groups. Normal fertilization rates in OA (62.0%) and post chemotherapy (63.4%) were significantly higher, but that of AZF microdeletion (39.7%) was significantly lower than any other groups. Blastocyst development rate and good-quality blastocyst rate in AZF microdeletion (27.4% and 9.3%) were significantly lower than any other groups and the rates in KS (40.5% and 15.1%) were lower than in OA (51.3% and 22.1%), post chemotherapy (50.6% and 23.6%), and post orchioxy (52.1% of blastulation). CPRs per embryo transfer were lower in unexplained NOA (29.7%), and AZF microdeletion (27.5%) than in OA (39.9%). We have had a total of 243 newborns so far with comparable congenital anomaly rate comparing to those with ejaculated sperm-ICSI.

CONCLUSIONS: The success of sperm recovery, fertilization and pre-implantation development was significantly influenced by the etiology of azoospernia. However, the offspring with testicular sperm was as healthy as that with ejaculated sperm at least in our experience.

Reference: None.

SUPPORT: None.

P-452 Wednesday, October 16, 2019 6:30 AM

FACTORS WHICH PREDICT IMPROVEMENT IN DNA FRAGMENTATION ON A SECOND SEEM SPECIMEN 3 HOURS AFTER THE FIRST. Michael H. Dahan, MD, a Rabea Youcef Khoudja, MD, PhD, b Abbie Gagnon, M.Sc., b Grace Tan, D. Phil, a Seang Lin Tan, MD, MBA, b "Division of REI, McGill University and OriginElle Fertility Clinic and Women’s Health Centre, Montreal, QC, Canada; "Originelle Fertility Center, Montreal, QC, Canada.

OBJECTIVE: High sperm DNA fragmentation is felt by many physicians to be important. Sperm DNA fragmentation occurs in the epididymus while waiting for ejaculation, so shortening the time since last ejaculation to 3 hours from 3 days improved DNA fragmentation results by an average of 23%. This study was undertaken to determine what factors predict at least a 30% improvement in sperm DNA fragmentation when comparing a first ejaculate after 3 days of abstinence and a second 3 hours after the first.

Reference: None.

SUPPORT: None.
DESIGN: A prospective cohort study was performed on semen analysis. Males waited 3 days without an ejaculation at which point a DNA fragmentation was performed and was repeated on a 2nd specimen 3 hours later.

MATERIALS AND METHODS: 112 subjects underwent the 2 semen analyses. All ejaculations were at the fertility center. Analysis were part of the initial work up. DNA fragmentation was evaluated with the halo test. Data was compared by intransubject t test. Data is presented as % or mean±SD. Power analysis suggested ≥ 73 subjects were required for an 80% power and an alpha of 5% with a 2 unit mean difference with SD of 6 units. Stepwise multivariate logistic regression was used to model predictors of ≥ 30% improvement in DNA fragmentation in the second specimen.

RESULTS: Male age was 36±7 years (range 29-65). DNA fragmentation decreased from 34.6±19.4 to 23.7±16.0% (p<0.0001) in the 1st and 2nd specimen respectively (23%±30%). 58/112 subjects demonstrated a > 30% improvement in sperm DNA fragmentation in the 2nd specimen compared to the 1st. 7/112 had worse DNA fragmentation in the 2nd specimen. Two factors predicted at least a 30% improvement in DNA fragmentation in the 2nd specimen: male age (95% CI 0.84-0.99, p=0.03) and use of a multivitamin (95% CI 1.25-19.8, p=0.02). 1st ejaculate volume (CI 0.84-2.65), 2nd volume (CI 0.23-1.39), 1st concentration (CI 0.98-1.005), 2nd concentration (CI 0.99-1.03), 1st motility (CI 0.97-1.03), 2nd motility (CI 0.98-1.04), smoking (CI 0.28-15.7), cannabis use (CI 0.10-2.45) and fathering previous pregnancies (0.19-2.9) failed to predict improvement. Initial DNA fragmentation trended towards being a predictor of improvement (CI 1.0-2.65, p=0.06).

CONCLUSIONS: High DNA sperm fragmentation can often be managed with a 2nd ejaculation 3 hours after the first. Younger men and those taking a sperm improvement vitamin supplement were more likely to have at least a 30% improvement in DNA fragmentation on the second specimen. All men should be proscribed such a vitamin who will undergo this protocol. Those male with extremely high DNA fragmentation may be less likely to show a 30% improvement, likely due to the greater change in absolute number needed.

SUPPORT: None.

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SPERM DNA FRAGMENTATION INDEX IS NOT ASSOCIATED WITH RECURRENT IVF/ICSI FAILURE. Jordan Best, B.S., Taylor P. Kohn, MD, MPhil, Raajith Ramasamy, M.D., University of Miami, Miami, FL; University of Miami Miller School of Medicine, Miami, FL; Johns Hopkins University School of Medicine, Baltimore, MD; Fertility & IVF Center of Miami, Miami, FL.

OBJECTIVE: To assess whether DNA Fragmentation Index (DFI) or High DNA Stallability (HDS) as measured by Spectrom Chramat Structure Assay (SCSA), was predictive of recurrent in vitro fertilisation (IVF) or intracytoplasmic sperm injection (ICSI) failure.

DESIGN: We performed a retrospective cohort study of couples undergoing IVF, ICSI and frozen embryo transfer (FET) cycles between 2009 – 2018 performed at a large volume fertility center. SCSA was performed for all males prior to IVF/ICSI cycles.

MATERIALS AND METHODS: All couples between 2009 to 2018 who underwent ≥ 2 IVF/ICSI cycles, with maternal age ≤ 40 were included in our analysis. Patients having undergone prior IVF/ICSI at outside centers were excluded. Recurrent IVF/ICSI failure was defined as ≥ 2 failed IVF/ICSI cycles in couples with maternal age ≤ 40. Success was defined as a cycle that led to live birth.

RESULTS: A total of 393 couples with 1215 cycles were included in the analysis with a pregnancy success of 36.9% and an average live birth of 20.6%. The average (±standard deviation) female age of 34.0 ± 3.6 and an average total motile sperm count of 68.1 ± 76.7 million sperm. DFI and HDS were not predictive for achieving a pregnancy (p=0.76 & p=0.96, respectively), nor was DFI predictive of spontaneous abortion (p=0.92). However, HDS was found to be predictive of spontaneous abortion, with higher rates of HDS seen in live births vs spontaneous abortion (12.4% vs 9.3%, p=0.003). DFI and HDS were not associated with recurrent IVF failure (p=0.43, p=0.14, respectively), nor were they predictive of IVF success, defined as live birth, in those with normal values of DFI and HDS when controlling for female age.

CONCLUSIONS: We found that neither DFI or HDS, as assessed by SCSA, were predictive of recurrent IVF failure in patients with high DFI or HDS when controlling for female age and total motile sperm count. This finding suggests that SCSA does not predict recurrent IVF failure.

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WITHDRAWN

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MULTI-SITE, BLIND PROSPECTIVE TRIAL ASSESSING WHETHER SEMEN OXIDATION REDUCTION POTENTIAL (SORP) ASSESSMENT CAN BE USED TO PREDICT LOW FERTILISATION WITH CONVENTIONAL IVF: INTERIM ANALYSIS. Georgie Pool, MSc,a Shaun Rogers, BSc,b Anastasia Maania, MSc,b Georgia Everett, MSc,b Alpesh Mahesh Doshi, M.Sc,a Sri Srikantarahajab, BYSc,a Hasmukh N. Joshi, BSc,b Martin Wilding, Ph.D., Samuel Bishop, MSc,b Lourdes Muriel, BSc,b Walid Maalouf, PhD,b Cristina Hickman, Ph.D. The City Fertility, London, United Kingdom; Kings Fertility, London, United Kingdom; IVF London, London, United Kingdom; Homerton NHS Hospital, London, United Kingdom; Homerton Hospital, London, United Kingdom; Create Fertility, London, United Kingdom; IWI, London, United Kingdom; Nottingham University, Nottingham, United Kingdom; Imperial College London, London, United Kingdom.

OBJECTIVE: To identify if static oxidation-reduction potential (sORP) can be used clinically at the time of insemination to predict low fertilisation.

DESIGN: Multi-site prospective control blind study involving 6 independent clinics. Interim analysis assessing data from the first 10 patients enrolled in the study. Primary outcome for the interim analysis: rate of low fertilisation (<25% 2PN/MII), normal fertilisation (2PN per MII). Secondary outcomes: overall fertilisation rate (2PN per MII), 1PN and 3PN rates per MII, daily embryo quality, morphokinetic parameters. Inclusion Criteria: patients undergoing IVF with at least 4 follicles ≥ 10mm, and 4 mature oocytes collected.

RESULTS: Out of the first ten patients (134 mature oocytes), nine had normal sORP (0.12-0.93, 121 oocytes, Control), and one patient had high sORP (1.69, 13 oocytes, Treatment). Interestingly, the only patient with a low fertilisation rate (2/13, 20%) was in the Treatment group, whilst normal fertilisation rates were all normal in the Control group (ranging from 50-100%, overall 88/121=73%). Compared to Control, Treatment group had a lower 2PN rate (Control vs Treatment: 88/121=73% vs 2/13=15%, p<0.01), higher polyploidy rate (5/121=4% vs 5/13=38%, p<0.001). Difference in overall fertilisation rate approached significance (93/121=77% vs 71/13=54%, p=0.07). 1PN rate (71/121=6% vs 0/13, NS), median number of cells on day 2 (4 vs 3, NS) and day 3 (7 vs 6.5, NS), did not differ between Treatment and Control. Cleavage embryos with more day 3 fragmentation (sORP 0.66– 0.37) or more unevenness (sORP 0.59–0.36, n=49) were associated with higher sORP than embryos with lower day 3 fragmentation (sORP 0.25±0.22 respectively, p<0.0001) or more evenness (sORP 0.38±0.4, n=25, p=0.03). However, good embryo quality rate on days 2 (45/88 vs ½, NS), and 3 (32/74 vs ½, NS) did not differ between Treatment and Control. Morphokinetics was not significantly affected by treatment.

CONCLUSIONS: Out of 10 patients undergoing IVF, sORP assessment correctly identified the 1 case where low fertilisation occurred. With 25% of normospermic samples leading to low fertilisation, new diagnostic tools are required to ascertain whether IVF is the correct treatment. This is the first multi-site prospective study assessing whether sORP can be used this way. Although preliminary, our results are encouraging and in line with other single-centre publications.
THE EVALUATION OF SEMINAL OXIDATION REDUCTION POTENTIAL CAN PREDICT NORMAL SPERM PARAMETERS. Mariem BEN, Khelifa, PhD,a Sonia Mnallah, Dr,a Mohamed Khouf, Dr,a Khaled Mahmoud, Dr,a M. E. D. Habib BEN Aribia, Dr,a Hanen Elsouri, Dr,a Fathi Zhioua, Dr,a Khaled Terras, Dr,a clinique la rose, centre FERTIL-LIA, Tunis, Tunisia; bclinique La Rose, Centre FERTILILLA, jardins du lac 2, Tunisia.

OBJECTIVE: The standard semen analysis is the most popular laboratory test in diagnosis of male fertility. However, it is well-known that normal results of semen analysis can not exclude men from the causes of couples infertility. One of the most important parameters of sperm, in its fertilizing potential is Sperm DNA integrity that has direct positive correlation with Assisted Reproductive Techniques (ART). The most common cause of sperm DNA damage is Oxidative Stress (OS). The evaluation of seminal oxidatives stress have a crucial role in the identification of patients who may benefit from treatments. The aim of our study was to use MiOXSYS System to evaluate OS and to correlate this evaluation sperm parameters, DNA fragmentation and chromatin decondensation.

DESIGN: This is a prospective comparative study that was performed between January 2018 and March 2019 includes patients with primary or secondary infertility (≥3 years). Human semen samples were obtained from 200 patients performing a complete exploration of semen parameters at a private ART clinic. Sperm parameters were evaluated according to World Health Organization 2010 guidelines. Exclusion criteria included azoospermia and samples with a concentration 1 × 10^6 sperm/mL.

MATERIALS AND METHODS: In each semen sample, in addition to conventional sperm parameters the following parameters were measured: (i) Spermatozoa with DNA strand breaks were assessed by TUNEL (cut-off value <30%), (ii) Abnormal chromatin condensation using Aniline Blue assays (cut-off value <20%), (iii) Oxidative stress was measured by MiOXSYS Analyzer. The study subjects were grouped into two groups referring to a cut-off value of 1.36 mV/10^6 sperm/mL of Seminal Oxidation reduction potential (sORP): group 1 with low level of sORP and group 2 with high level of sORP. We identified 2 subgroups in each group: groups (1A and 2A) had all normal criteria of sperm quality and groups (1B and 2B) failed to meet one or more criteria of sperm quality.

RESULTS: Comparing to patients of group 1, patients of group 2, had a significantly lower mean sperm count (14.73 vs 64.72 × 10^6 sperm/mL) progressive motility (24% vs 38%), and vitality (52% vs 68%). Conversely patients of this group had significantly higher levels of DNA fragmentation and chromatin decondensation. This results confirm that sORP, DNA fragmentation and chromatin decondensation were inversely associated with normal sperm parameters. When subgroups of patients were investigated according to normal or abnormal semen parameters we identified 2 subgroups in each group: a subgroup containing 25% of patients (n=29) of group 1B failed to meet one or more criteria of sperm quality and a second subgroup contain 93% (n=74) of group 2B. For these two subgroups we identified a negative correlation between sperm parameters and level of these two parameters: DNA fragmentation and chromatin hypocondensation (p<0.001).

CONCLUSIONS: The combination of conventional sperm parameters with the advanced sperm function test should be included in assessment of male infertility because they can have prognostic implications for couples undergoing ART.

USEFULNESS OF A NEW SPERM TRANSPORT CONTAINER “TRANSPORTER-S” FOR INFERTILITY TREATMENT. Toshiyuki Iwahata, MD, PhD,a Takashi Tanaka, BSc,a Akiyoshi Osaka, Bachelor of Medicine, a Atsushi Yamamoto, MD, PhD,a Yoshitomo Kobori, MD, PhD,a Kouhei Sugimoto, MD, PhD,a Hiroshi Okada, MD, PhD.a Dokkyo Medical University Saitama Medical Center, Koshigaya, Japan; bDokkyo Medical University Saitama Medical Center, Saitama-prefecture Koshigaya-city, Japan.

OBJECTIVE: The container for storage and transport of ejaculated semen is “clean and wide-bore glass or plastic container” in the guidelines in usual, and it is generally used that a cylindrical container with a height of about 8 cm is used. Since this container has a large volume relative to the amount of semen, which is 100 to 200 ml, it is difficult to completely remove it when collecting it for examination. The new container (Transporter-S: TS) is less likely to be exposed to air and has excellent liquid stability and is suitable for storage and transport of ejaculated semen compared with conventional products.

DESIGN: Prospective study.

MATERIALS AND METHODS: <Examination 1> TS is characterized in that stored samples are less susceptible to temperature changes than conventional containers, and the effects of storage environment on samples were compared between TS and conventional containers. As a substitute for semen in TS and conventional containers, put 5 ml of distilled water at 37 °C and leave each container in an environment at room temperature (25 °C) and the ambient temperature in winter (estimated at 10 °C) for 15 hours. It compared about the temperature change for every minute.

<Examination 2> Sperm tests were performed on each of the 14 healthy volunteers at the same abstinence period. At that time, with respect to sperm parameters and sperm DNA fragmentation index (DFI) in seminal fluid stored in a conventional container and transporter S, place them at room temperature 25 °C and change over time (0 hours 2 hours 4 hours 6 hours) Measurement survey.

<Examination 3> The volunteers who provided ejaculated semen were asked about the feeling of using TS and compared with the conventional container. The contents of the questionnaire were evaluated by comparing the conventional container and TS very good 5, good 4, normal 3, bad 2 very bad 1 of 5 stages.

RESULTS: Compared with conventional containers, TS has a slower change in sample temperature and is less susceptible to low ambient temperature and, it was more difficult to be affected when the outside temperature was low. In semen that was stored using TS, the decline in exercise rate and survival rate over time became slower than in conventional containers. (Motor rate changes are significantly different after 4 hours and 6 hours. Sperm survival rates are also significantly different after 6 hours.). The sequestration using TS became very good, 4 good, 5 normal, 1 bad, 1 bad. The average value of the questionnaire results was 3.07 ± 0.92. which was comparable to conventional containers. We think that TS use is effective in infertility treatment including the use that is not stable in the climatic area and the patient who takes time after preparation.

CONCLUSIONS: It is considered that TS is less likely to be exposed to air and has excellent liquid stability and is suitable for storage and transport of ejaculated semen, as compared with conventional containers. In the future, it is necessary to conduct further examinations by changing semen and storage temperature with relatively poor findings such as OAT cases.

Reference: None.

SUPPORT: None.
OBJECTIVE: To access the time-course and associated factors of oocyte maturation from GVBD to PBE in r-IVM.

DESIGN: Non-comparative; Prospective.

MATERIALS AND METHODS: Patients underwent intracytoplasmic sperm injection and had at least one GV oocyte after denudation were included. After denudation, GV oocytes were cultured in G-IVF® media and placed into a time-lapse incubator. Images were taken every 10 mins for 144 hours. The GVBD and PBE time were counted. Patient’s age, protocol, base and hCG day lateralizing hormone (LH), base follicle stimulation hormone (FSH), base and hCG day estradiol (E2), maturation rate, and big follicle acquisition rate (BFA) were recorded for univariable clustered Cox regression [1,2]. Variables (p < 0.10) were chosen for multivariable analysis. Hazard ratio (HR) with 95% confidence interval (95%CI) were reported.

RESULTS: There were 36 patients (79 GV oocytes) recruited. 12 GV oocytes did not mature. The overall time-course was 23.2h (95%CI 21.3-24.4h). The baseline and analysis results are shown in Table I. The BFA < 1 means GV oocytes were from big follicles. GV oocytes in group BFA < 1 showed shortened time-course in both univariable (HR 2.43, 95%CI 1.49-4.35, p < 0.001) and multivariable analysis (HR 2.38, 95%CI 1.32-4.35, p = 0.004). The adjusted chance of maturation in group base E2 concentration < 50 was revealed to be two times greater (HR 2.00 95%CI 1.06-3.81, p = 0.034).

CONCLUSIONS: We first demonstrate a precise time-course of GVBD to PBE in stimulated cycles, which can contribute significantly to catching the fertilization window in r-IVM as well as traditional IVM. We found that GV oocytes from big follicles or patient with higher base E2 have higher chance of maturation. These findings give clues for oocyte and follicle development, but further studies are needed to confirm. References: [1] Moore, D. F. (2016). Applied survival analysis using R, Springer.
CONCLUSIONS: The novel gripper-based technique is less traumatic to the blastocysts during a biopsy. It is also observed to be easier to perform a biopsy using a gripper than a holding micropipette where the aspiration has to be dynamically changed depending upon the pressure of aspirating the biopsy.

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DAY 2 LASER ASSISTED HATCHING (AH) SIGNIFICANTLY IMPROVES IMPLANTATION RATES IN FRESH BLASTOCYST TRANSFERS, Sarah H. Bjorkman, MD, Stephanie M. Nichols-Burns, PhD, Jonathan Lo, MSc, Nuri Kodaman, PhD, Finar Kodaman, MD/PhD, Dawn A. Kelk, Ph.D., HCLD, Yale School of Medicine, New Haven, CT.

OBJECTIVE: The efficacy of assisted hatching has been widely debated. The variable results reported for AH are confounded by the numerous methods of performing AH, including mechanical partial zona dissection, acid tyrode’s, and more recently by laser assistance. Assisted hatching has most commonly been performed on Day 3 embryos. This study assesses if Day 2 laser assisted hatching can improve implantation rates for fresh blastocyst transfers.

DESIGN: Prospective observational cohort.

MATERIALS AND METHODS: On the morning of Day 2 of culture, all embryos were sorted into groups (<4-cell, 4-cell and >4-cells). Those in the AH group underwent laser assisted hatching using an Octax laser (4.0ms) on the morning of Day 2 at the time of embryo check. All embryos were then cultured undisturbed until assessment on the morning of Day 5 when the highest quality embryo(s), based on morphology, were selected for embryo transfer. A total of 446 fresh Day 5 transfers between Jan 2016 - Mar 2019 were analyzed (244 transfers with AH and 202 transfers without AH). A total of 682 embryos were transferred in the 446 cycles (363 embryos in the AH group and 319 embryos in the non-AH group). Because 206 of the 446 transfers involved transfer of more than 1 embryo, a mixed model accounting for both fixed and random effects (i.e. repeated measurements) was used, with SAC modeled as a function of the fixed effects assisted hatching (AH), age, and body mass index (BMI).

RESULTS: Day 2 assisted hatching is associated with successful implantation (p = 0.036). As expected, age was negatively associated with implantation rate (p < 0.0001). BMI was not. The R-square for the model was 0.52, and the variance component of the random effects (owing to multiple embryo transfers) was 0.082 (95% CI [0.046-0.11]).

CONCLUSIONS: Large data sets such as the SART database do not allow for evaluation of the impact of specific AH techniques. Certainly, any embryo handling and exposure has the potential to be detrimental to blastocyst development and implantation rates. Here, we show that Day 2 laser AH can lead to a significant increase in implantation rates from 42.9% without AH to 53.4% with AH. Day 2 embryos generally have larger perivitelline space to a significant increase in implantation rates from 42.9% without AH to 53.4% with AH. Day 2 embryos generally have larger perivitelline space and 48.5% without AH. Day 2 embryos generally have larger perivitelline space to a significant increase in implantation rates from 42.9% without AH to 53.4% with AH. Day 2 embryos generally have larger perivitelline space

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AUTOMATED COMPUTER ANALYSIS OF HUMAN BLASTOCYST EXPANSION FROM EMBRYOSCOPE TIME-LAPSE IMAGE FILES, Thomas TF. Huang, PhD, Brienne C. Walker, MS, M. Y. Harun, BS, Aaron T. Ohta, PhD, M. A. Rahman, PhD, Joshua Mellinger, BS, Willy Chang, BS, aUniversity of Hawaii John A Burns School of Medicine, Honolulu, HI; bPacific In Vitro Fertilization Institute, Honolulu, HI; cDepartment of Electrical Engineering, University of Hawaii at Manoa, Honolulu, HI.

OBJECTIVE: To develop a rapid, quantitative, and automated analysis of human blastocyst expansion from Embryoscope time-lapse image files of zona-ablated embryos using artificial intelligence (AI).

DESIGN: A retrospective observational study comparing time-lapse image files of blastocyst expansion in zona-ablated embryos measured either manually using Embryoscope software tools versus automatically using a customized neural network to perform semantic segmentation (SemSeg) on exported Embryoscope image files.

MATERIALS AND METHODS: Manual expansion measurements of the trophoderm (TE) enclosed cavity was performed using the Embryoscope’s ellipsoidal measurement tool (ET) at 2.0-hr intervals for the first 10.0 hours of expansion after initial blastocyst formation in 46 laser-ablated human blastocysts. Manual measurements (μm²) were compared to values calculated using artificial intelligence (segmenting) to files of segmented images of 30 explosive time-lapse image/embryo over the same 10.0 hr period. All embryos had been laser-ablated to enable subsequent biopsy; thus, the total area of blastocyst expansion was defined as the sum of 1) the TE-enclosed area within the zona plus 2) the TE-enclosed area herniating irregularly from the ablative slit.

RESULTS: Compared to manual measurement using the Embryoscope’s ellipsoidal tool, the automated approach using SemSeg demonstrated many
advantages. Although the ET could accurately measure the TE within the uniformly elliptical zona pellucida, it less accurately demarcated the zona pellucida, it less accurately traced the irregular cellular outlines were more accurately demarcated by SemSeg with the neural network, which had an accuracy of > 99%, even in areas abutting embryo well boundaries. While the average discordance between the two approaches was 3.2-3.4% at both the beginning and end of the assay, some individual embryo measurements varied by more than 10% at 10.0 hours due to the limitations in the elliptical tool’s accuracy at embryo well edges and boundaries. The averaged median initial and final expansion areas were 12.69 ± 2μm² (using the ET) versus 13.05 ± 2.2 and 21439 ± 2 (using SemSeg). Using either approach, subsequent rank ordering of individual embryos within cohorts revealed an enrichment for euploidy among embryos most rapidly expanding. However, the greatest advantage of SemSeg is to enable an automated, objective analysis of large-scale data sets by machine learning platforms.

CONCLUSIONS: This is the first report of the successful application of automated image analysis to the dynamic process of trophoderm epithelium expansion in the human blastocyst from stock time lapse files in embryos that will undergo biopsy. This approach now enables the inclusion of this important morphokinetic information in machine learning applications aimed at the non-invasive identification of euploidy.

SUPPORT: This work was supported by the Division of Research of Department of Obstetrics and Gynecology and Women’s Health of the John A. Burns School of Medicine and an intramural grant from the Pacific IVF Institute.

ART OFFSPRING

P-463 Wednesday, October 16, 2019 6:30 AM

NEONATAL OUTCOMES OF SINGLETON LIVE BIRTHS WITH VANISHING TWIN SYNDROME FOLLOWING TRANSFER OF DOUBLE EMBRYOS IN ASSISTED REPRODUCTIVE TECHNOLOGY: A RETROSPECTIVE COHORT STUDY.

Junfang Yan, Master, The Third Affiliated Hospital of Zhengzhou University, Zhengzhou, China.

OBJECTIVE: To compare neonatal outcomes in singleton live births between groups with and without VTs following transfer of double embryos.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Anonymous data on all cycles performed in the China were obtained from the Reproductive medicine department of the Third Affiliated Hospital of Zhengzhou University, involving 6220 singleton live births (2772 fresh embryos transfer (ET) cycles and 3448 frozen embryos transfer (FET) cycles). We analyzed the obstetric outcomes of gestation age, PTB, SGA (small for gestation age), birthweight, LBW, congenital malformation, pediatric admission and NICU admission (aOR2.62, 95%CI: 2.14-3.21) and NICU admission (aOR 1.98, 95%CI 1.59-2.46) in cycles of fresh ET and FET. Logistic regression analysis was performed adjusting for confounders, including age of women, BMI, value of AMH, gestational age, PTB, SGA (small for gestation age), birthweight, LBW, congenital malformation, pediatric admission and NICU admission (aOR2.55, 95%CI 2.07-3.13) and NICU admission (aOR 2.45, 95%CI: 2.23-3.43) and LBW (aOR 2.67, 95%CI: 2.13-3.34) in the study group as compared to the control group. There was a significantly higher risk of PTB and NICU admission (aOR 2.62, 95%CI 2.14-3.21) and NICU admission (aOR 2.22, 95%CI: 1.43,3.46) in the study group as compared to the control group. There was a significantly higher risk of PTB and NICU admission (aOR 2.62, 95%CI 2.14-3.21) and NICU admission (aOR 2.22, 95%CI: 1.43,3.46) in the study group as compared to the control group.

CONCLUSIONS: There was a higher risk of LBW, LBW, congenital malformation was observed in singleton live births in both fresh and frozen ART cycles following transferring double embryos.

References: 1. Zander-Fox DL, Tremellen K, Lane M. Single blastocyst emb-}


SUPPORT: Not applicable.

P-464 Wednesday, October 16, 2019 6:30 AM

REPRODUCTIVE AND PERINATAL OUTCOMES USING CRYOPRESERVED OOCYTES: AN ANALYSIS OF NATIONAL DATABASE SPANNING OVER A DECADE USING THREE CLINICAL MODELS.

Mariano Mascarenhas, MS (OG), MRCOG, DNB (OG).

OBJECTIVE: To compare neonatal outcomes in singleton live births between groups with and without VTs following transfer of double embryos.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Anonymous data on all cycles performed in the China were obtained from the Reproductive medicine department of the Third Affiliated Hospital of Zhengzhou University, involving 6220 singleton live births (2772 fresh embryos transfer (ET) cycles and 3448 frozen embryos transfer (FET) cycles). We analyzed the obstetric outcomes of gestation age, PTB, SGA (small for gestation age), birthweight, LBW, congenital malformation, pediatric admission and NICU admission (aOR2.62, 95%CI: 2.14-3.21) and NICU admission (aOR 1.98, 95%CI 1.59-2.46) in cycles of fresh ET and FET. Logistic regression analysis was performed adjusting for confounders, including age of women, BMI, value of AMH, gestational age, PTB, SGA (small for gestation age), birthweight, LBW, congenital malformation, pediatric admission and NICU admission (aOR2.55, 95%CI 2.07-3.13) and NICU admission (aOR 2.45, 95%CI: 2.23-3.43) and LBW (aOR 2.67, 95%CI: 2.13-3.34) in the study group as compared to the control group. There was a significantly higher risk of PTB and NICU admission (aOR 2.62, 95%CI 2.14-3.21) and NICU admission (aOR 2.22, 95%CI: 1.43,3.46) in the study group as compared to the control group.

CONCLUSIONS: There was a higher risk of LBW, LBW, congenital malformation was observed in singleton live births in both fresh and frozen ART cycles following transferring double embryos.

References: 1. Zander-Fox DL, Tremellen K, Lane M. Single blastocyst em-}


SUPPORT: Not applicable.
**P-466 Wednesday, October 16, 2019 6:30 AM**

**DOES BODY MASS INDEX INFLUENCE THE ODDS OF A GOOD PERINATAL OUTCOME FOLLOWING FRESH AUTOLGOUOS IVF CYCLES AMONG PATIENTS WITH POLYCYSTIC Ovary SYNDROME? A NATIONAL STUDY.** Jenna S. Hynes, MD, a Jeremy M. Weber, MS, a Tracy Truong, MS, b Kelly S. Acharya, MD, b Jennifer L. Eaton, MD, MSC. c

**OBJECTIVE:** To examine the association between body mass index (BMI) and the odds of a term, normal-weight, singleton live birth among women with polycystic ovary syndrome (PCOS) undergoing in vitro fertilization (IVF).

**DESIGN:** Retrospective cohort study.

**MATERIALS AND METHODS:** We utilized the 2012-2015 Society for Assisted Reproductive Technologies Clinical Outcomes Reporting System (SART CORS) to identify fresh, autologous IVF cycles among women aged < 41 with ovulatory dysfunction. We included only women with anti-Mullerian hormone (AMH) >4.5 ng/mL to more accurately identify patients with PCOS. Patients were assigned to BMI categories based on the World Health Organization guidelines. The primary outcome was a good perinatal outcome, defined as singleton live birth at ≥ 37 weeks gestation with birth weight ≥ 2500g and ≤ 4000g. A multivariable GEE model was used to assess the association between BMI and a good perinatal outcome while accounting for the correlation between repeated IVF cycles and adjusting for age, race, parity, diagnosis, and smoking.

**RESULTS:** The analysis included 9,611 cycles from 8,431 women. Baseline characteristics were similar among groups. With increasing BMI, patients had fewer oocytes retrieved and embryos cryopreserved despite higher gonadotropin doses (Table). Pregnancy and live birth rates decreased with increasing BMI, while miscarriage rates increased. After adjusting for covariates, women with class III or super obesity were half as likely to have a good perinatal outcome as normal weight women (OR 0.50, 95% CI 0.37-0.68, p < 0.001). The frequency of multiple deliveries was 1.68% (48,425), including 13% from IVF. The frequency of small for gestational age (SGA) and malformations were the main neonatal data investigated after In Vitro Fertilization (IVF) and fresh transfer are at higher risk of low birthweight (LBW) for gestational age (GA), its frequency related to maternal characteristics, fetal sex, and single / multiple births.

**RESULTS:** Mean maternal age was 33.2 +/- 4.3 and 29.9 +/- 5.3 years in the IVF and non-IVF groups (p < 0.0001). The frequency of multiple deliveries was 1.68% (48,425), including 13% from IVF. The frequency of prematurity deliveries was higher in IVF vs non-IVF group, 19.3% vs 6.9% (p < 0.0001), as it was for single deliveries (9.0% vs 5.7%, p < 0.0001). The SGA rate was increased in IVF compared to non-IVF group, in all neonates, 21.6% vs 12.1%, (p < 0.0001); in singletons, 14.9% vs 11.4% (OR = 1.33 [1.30-1.37], p < 0.0001). Univariate analysis indicated that the risk was identical according to sex, higher in multiple births (OR = 4.8) and premature births (OR = 2.9), if maternal smoking (OR = 2.2), and other maternal morbidity (MM) events except diabetes, and congenital malformations (OR = 1.7). In multivariate analysis, the added risk of SGA in IVF group was 2.1 [2.07-2.016] after adjustment for age, smoking, maternal obesity; 1.37 [1.34-1.40] if adjusted in addition to multiple births; 1.34 [1.30-1.37] if adjusted in addition to MM; 1.33 [1.30-1.36] if further adjusted for prematurity.

**CONCLUSIONS:** Large observational studies identified that IVF pregnancies are associated with a significant risk of concerns for babies. SGA babies are known to be at increased risks of perinatal morbidity and mortality. The results of this large cohort, whose strength is the completeness of IVF treatment across cycles, may have implications for counseling women with PCOS undergoing IVF regarding weight management and timing of pregnancy.

**Cycle Characteristics and Outcomes**

<table>
<thead>
<tr>
<th>Cycle Characteristics</th>
<th>Underweight (N=233)</th>
<th>Normal (N=4181)</th>
<th>Overweight (N=2263)</th>
<th>Class I obesity (N=1576)</th>
<th>Class II obesity (N=947)</th>
<th>Class III obesity or Super obesity (N=411)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total FSH dose</td>
<td>1792.3 ± 835.6</td>
<td>1910.1 ± 910.3</td>
<td>2057.7 ± 925.0</td>
<td>2307.4 ± 1009.7</td>
<td>2639.9 ± 1197.7</td>
<td>2900.4 ± 1264.5</td>
</tr>
<tr>
<td># Oocytes retrieved</td>
<td>18 (13, 25)</td>
<td>19 (19, 26)</td>
<td>18 (12, 25)</td>
<td>18 (12, 25)</td>
<td>16 (10, 23)</td>
<td>15 (9, 22)</td>
</tr>
<tr>
<td># Embryos frozen</td>
<td>4 (1, 7)</td>
<td>3 (0, 7)</td>
<td>3 (0, 7)</td>
<td>2 (0, 6)</td>
<td>2 (0, 5)</td>
<td>2 (0, 5)</td>
</tr>
<tr>
<td>Clinical pregnancy</td>
<td>45.1%</td>
<td>44.2%</td>
<td>42.5%</td>
<td>42.2%</td>
<td>38.8%</td>
<td>33.8%</td>
</tr>
<tr>
<td>Miscarriage</td>
<td>10.5%</td>
<td>11.4%</td>
<td>15.4%</td>
<td>17.0%</td>
<td>18.5%</td>
<td>21.6%</td>
</tr>
<tr>
<td>Live birth</td>
<td>39.9%</td>
<td>38.4%</td>
<td>35.4%</td>
<td>33.9%</td>
<td>31.4%</td>
<td>26.3%</td>
</tr>
<tr>
<td>Multiple birth</td>
<td>24.7%</td>
<td>25.8%</td>
<td>30.0%</td>
<td>23.8%</td>
<td>27.6%</td>
<td>35.2%</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>23.7%</td>
<td>25.4%</td>
<td>30.4%</td>
<td>28.6%</td>
<td>33.0%</td>
<td>33.3%</td>
</tr>
<tr>
<td>Low birth weight</td>
<td>22.8%</td>
<td>24.5%</td>
<td>24.2%</td>
<td>23.8%</td>
<td>27.6%</td>
<td>28.0%</td>
</tr>
<tr>
<td>Good perinatal outcome</td>
<td>24.9%</td>
<td>22.7%</td>
<td>18.9%</td>
<td>18.5%</td>
<td>14.9%</td>
<td>12.4%</td>
</tr>
</tbody>
</table>

Values represent mean ± standard deviation, median (interquartile range), or number (%).

**EFFECT OF IN VITRO FERTILIZATION AND FRESH TRANSFER CONCEPTION ON BIRTHWEIGHT FOR GESTATIONAL AGE.** A. 2012-2016 FRENCH OBSERVATIONAL COHORT OF 49,224 NEONATES. Sylvie Epelboin, Sr. MD, a Morgane Valentin, Md. b Rachel Levy Sr. MD PhD, b Marianne Bergere Sr. Md. c Fabienne Pessione Sr. Dr. d "Hôpital Bichat-Claude Bernard, Assistance Publique Hôpitaux de Paris, Paris 7 Diderot University, Paris, France; "Hôpital bichat, Paris, France; "Hôpital Tenon Assistance Publique Hôpitaux de Paris Sorbonne University, Paris, France; "Agence de la Biomédecine, Saint-Des, France.

**OBJECTIVE:** The purpose of this study is to establish whether babies born after In Vitro Fertilization (IVF) and fresh transfer are at higher risk of low birthweight (LBW) for gestational age (GA).

**DESIGN:** This is an observational, exposed-unexposed national cohort study comparing pregnancies, births and neonatal data, focused on birth weight by gestational age, in births following IVF standard or using Intra Cytoplasmic injection (ICI) and fresh transfers versuses (vs) non-IVF controls data. The study included all 2,922,718 births from 2,832,578 deliveries registered between 2013 and 2016 in France, among which 1.7% (49,224) from IVF conception and immediate fresh transfer.

**MATERIALS AND METHODS:** Neonate’s data from births 2013-2016 in France were analyzed by extracting the Information Systems Medicalization Program (PMSI) French database. Premature birth < 37 gestational weeks (WG), SGA and malformations were the main neonatal data investigated for the 49,224 IVF and 2,873,474 non-IVF neonates. SGA is defined as birth weight less than the 10th percentile of gestational age (GA), its frequency related to maternal characteristics, fetal sex, and single / multiple births.

**RESULTS:** Mean maternal age was 33.2 +/- 4.3 and 29.9 +/- 5.3 years in the IVF and non-IVF groups (p < 0.0001). The frequency of multiple deliveries was 1.68% (48,425), including 13% from IVF. The frequency of prematurity deliveries was higher in IVF vs non-IVF group, 19.3% vs 6.9% (p < 0.0001), as it was for single deliveries (9.0% vs 5.7%, p < 0.0001). The SGA rate was increased in IVF compared to non-IVF group, in all neonates, 21.6% vs 12.1% (p < 0.0001); in singletons, 14.9% vs 11.4% (OR = 1.33 [1.30-1.37], p < 0.0001). Univariate analysis indicated that the risk was identical according to sex, higher in multiple births (OR = 4.8) and premature births (OR = 2.9), if maternal smoking (OR = 2.2), and other maternal morbidity (MM) events except diabetes, and congenital malformations (OR = 1.7). In multivariate analysis, the added risk of SGA in IVF group was 2.1 [2.07-2.016] after adjustment for age, smoking, maternal obesity; 1.37 [1.34-1.40] if adjusted in addition to multiple births; 1.34 [1.30-1.37] if adjusted in addition to MM; 1.33 [1.30-1.36] if further adjusted for prematurity.

**CONCLUSIONS:** Large observational studies identified that IVF pregnancies are associated with a significant risk of concerns for babies. SGA babies are known to be at increased risks of perinatal morbidity and mortality. The results of this large cohort, whose strength is the completeness of IVF treatment across cycles, may have implications for counseling women with PCOS undergoing IVF regarding weight management and timing of pregnancy.
and controls neonates data, provide evidence that the proportion of SGA birth post-IVF, including singletons, is increased compared to general population in multivariate analysis, after adjustment for age, smoking, maternal obesity, multiple births, maternal morbidity and prematurity. This is important to inform without worrying candidates for IVF, and understand possible concerns in IVF-children development. Further studies should allow to define more or less at-risk subgroups.

SUPPORT: None.

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OBSTETRIC, NEONATAL AND LONG-TERM OUTCOMES OF CHILDREN CONCEIVED FROM IN VITRO MATURED OOCYTES. Eun Jeong Yu, MD,1 Tae Ki Yoon, M.D, Ph.D,1 Woo Sik Lee, M.D. Ph.D,1 Hannah Kim, MD,1 Chanhong Park, M.D,2,3 Eun A. Park, MS,4 Jayeon Kim, MD, MPH,4 1CHA Seoul Fertility Center, OB&GY, Seoul, Korea, Republic of (South); 2CHA Seoul Fertility Center, Seoul, Korea, Republic of (South); 3Fertility Center of CHA Gangnam Medical Center, Seoul, Korea, Republic of (South); 4Fertility Center of CHA Gangnam Medical Center, SEOUL, Korea, Republic of (South).

OBJECTIVE: To investigate the obstetric, neonatal, and long-term outcomes of in vitro maturation (IVM) compared to conventional IVF in women with polycystic ovarian syndrome (PCOS).

DESIGN: Matched retrospective case-control study.

MATERIALS AND METHODS: One hundred eighty-four patients undergoing IVM were compared with 366 patients undergoing IVF. All had PCOS and matched for patients’ age, gestational age at birth, and the number of fetuses. Only women who had been conceived after fresh embryo transfer in the cycle of oocyte retrieval between January 1999 and December 2015 were included. Pregnancies using preimplantation genetic tests, testicular sperm extraction, or donor gametes were excluded. A questionnaire including pregnancy/neonatal outcomes and childhood medical problems/development was developed and distributed by reproductive specialists and administered via phone interview.

RESULTS: Women’s mean age at oocytes retrieval was 32.6±2.9 years. Children’s mean age was 7.5±2.3 years. There were no differences in the frequency of obstetric and neonatal outcomes between the two groups. No difference was found in birthweights between the two groups. The incidence of congenital anomalies was comparable between the groups (4.3% in IVM vs. 4.1% in IVF groups, p=0.65). No significant difference was observed between the two groups in the frequency and duration of hospitalization during childhood. Growth developmental status of both groups was within normal range.

CONCLUSIONS: In a matched setting between IVM and IVF babies born from women with PCOS, IVM is not associated with any additional risk compared to IVF after a mean follow-up of 7.5 years.

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COMPARISON OF BIRTHWEIGHT AND GESTATIONAL AGE AT DELIVERY IN SINGLE FROZEN EMBRYO TRANSFERS (FET) WITH AND WITHOUT PGT-A. Laura Perez Soriano, BA,1 Joshua Stewart, M.D.,2 Steven Spandorfer, M.D.,3 Zev Rosenwaks, M.D.3 1Weill Cornell Medical College, New York, NY; 2The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To compare perinatal outcomes and early hormonal trends between elective single blastocyst FET cycles with PGT-A and without PGT-A.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All patients undergoing an FET cycle of a single blastocyst between January 2015 and December 2017 were included. Cycles were divided into those with PGT-A and without. For PGT-A cycles, only euploid embryos were included. Inclusion criteria: delivery of a live singleton. Exclusion criteria: use of donor oocytes or multiple gestations. Primary outcomes were incidence of term or preterm delivery, low birth weight (LBW) and very low birth weight (VLBW). Secondary outcomes were early BhCG levels and trends. Groups were stratified by FET protocol, natural cycle, or medicated.

RESULTS: 876 cycles met inclusion criteria, 502 with PGT-A and 374 without. Main results summarized in table. There was no difference in mean gestational age (GA), birth weight, or incidence of preterm delivery, LBW, or VLBW between the groups. This equivalence persisted after controlling for maternal age and FET protocol type. In FET cycles with PGT-A, median initial and second BhCG levels were significantly lower in cycles resulting in a LBW or VLBW infant compared to NBW. This difference did not persist in cycles without PGT-A.

CONCLUSIONS: Reassuringly, there was no difference in mean GA, birth weight, or incidence of preterm delivery, LBW, or VLBW infants between FETs with PGT-A and without. Initial BhCG levels were significantly lower in pregnancies resulting in LBW or VLBW infants as compared to NBW.

<table>
<thead>
<tr>
<th>Demographics</th>
<th>PGT-A (n= 502)</th>
<th>Non PGT (n=374)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>36.4± 0.2</td>
<td>33.5± 0.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>BMI</td>
<td>23.4± 0.2</td>
<td>23.0± 0.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>AMH</td>
<td>3.8± 0.2</td>
<td>4.3± 0.3</td>
<td>0.01</td>
</tr>
<tr>
<td>Nulliparous</td>
<td>128 (25)</td>
<td>125 (33)</td>
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<tr>
<td>Multiparous</td>
<td>374 (75)</td>
<td>249 (67)</td>
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<tr>
<td>Perinatal Outcome</td>
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<tr>
<td>GA (Weeks)</td>
<td>39.2± 0.1</td>
<td>39.1± 0.1</td>
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<tr>
<td>Term</td>
<td>442 (93)</td>
<td>331 (92)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Preterm</td>
<td>37 (7)</td>
<td>28 (8)</td>
<td></td>
</tr>
<tr>
<td>Birth Weight (g)</td>
<td>3384±23</td>
<td>3356±30</td>
<td></td>
</tr>
<tr>
<td>NBW</td>
<td>455 (95)</td>
<td>335 (93.3)</td>
<td></td>
</tr>
<tr>
<td>LBW¹</td>
<td>24 (5)</td>
<td>22 (6.1)</td>
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</tr>
<tr>
<td>VLBW²</td>
<td>0 (0)</td>
<td>2 (0.6)</td>
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<table>
<thead>
<tr>
<th>BhCG level (mIU/ML), Median (IQR)</th>
<th>PGT-A (n=264)</th>
<th>Non PGT-A (n=200)</th>
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<tbody>
<tr>
<td>NBW (n=252)</td>
<td>LBW/LBW (n=12)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BhCG 1</td>
<td>280 (181 - 424)</td>
<td>180 (73 - 314)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>BhCG 2</td>
<td>783 (505 - 1996)</td>
<td>526 (316 - 1036)</td>
<td>0.01</td>
</tr>
<tr>
<td>BhCG 2 day % increase</td>
<td>242 (216 - 276)</td>
<td>280 (255 - 294)</td>
<td>0.01</td>
</tr>
<tr>
<td>NBW (n=189)</td>
<td>LBW/LBW (n=11)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BhCG 1</td>
<td>257 (156 - 383)</td>
<td>218 (112 - 424)</td>
<td>ns</td>
</tr>
<tr>
<td>BhCG 2</td>
<td>727 (417 - 1201)</td>
<td>733 (396 – 1219)</td>
<td>ns</td>
</tr>
<tr>
<td>BhCG 2 day % increase</td>
<td>235 (207 - 259)</td>
<td>245 (239 – 263)</td>
<td>ns</td>
</tr>
</tbody>
</table>

Student T-test for continuous, χ² for categorical, Wilcoxon rank sum for nonparametric variables.

a: Low Birth Weight, <2500 g at delivery
b: Very Low Birth Weight, <1500 g at delivery

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infants. This difference did not persist in cycles without PGT-A. Therefore, in pregnancies achieved by FET with PGT-A, early hCG trends may be a useful prognostic indicator for neonatal birth weight. Further studies will need to elucidate the mechanism behind this difference.

P-469 Wednesday, October 16, 2019 6:30 AM

ASSOCIATION BETWEEN EMBRYO QUALITY AND BIRTH WEIGHT AMONG SINGLETONS AND TWINS CONCEIVED THROUGH AUTOLOGOUS FRESH IVF CYCLES. Mengmeng Li, MSPH MBBS, Valerie L. Baker, MD, Johns Hopkins Bloomberg School of Public Health, Department of Population, Family and Reproductive Health, Baltimore, MD; Johns Hopkins University School of Medicine, Division of Reproductive Endocrinology and Infertility, Baltimore, MD.

 OBJECTIVE: To determine if embryo quality is associated with birth weight for infants conceived via autologous fresh IVF.

 DESIGN: Retrospective analysis of fresh autologous IVF cycles reported to SART CORS from 2008-2013.

 MATERIALS AND METHODS: All autologous fresh IVF cycles resulting in livebirth with outcome confirmed by review of medical record were eligible for inclusion in the analysis. Cycles were excluded if more than 2 embryos or embryos of different quality were transferred.

 The primary predictor was embryo quality (poor, fair, good). This grading system in SART CORS has been validated by Vernon et al (2011).1 Outcomes included continuous (in gram) and dichotomized birth weights (SGA: z-score < -1.28; LGA z-score ≥ 1.28). We adjusted for covariates (maternal age, BMI, race, smoking history, miscarriage, parity, infertility, gestational age, infant sex). Separate analyses were performed for singletons and twins, as well as for cleaved and blastocyst transfer. Depending on outcomes, multiple linear or logistic regression and Generalized Estimation Equation modeling were conducted.

 RESULTS: There were 5262 (67.86%) singleton births (cleaved: 2089, blastocyst: 3173) and 2492 twin births (cleaved: 950, blastocyst: 1542) included in the analysis.

 Among singletons conceived via cleaved embryo transfer, embryo quality was not predictive of birth weight. The difference in birth weight between fair vs. good quality was 33.6g (95% CI: -5.6, 72.8); poor vs. good: 123.7g (-30.1, 277.5). For singletons conceived via blastocyst transfer, fair quality was associated with decreased birth weight comparing with good quality (-38.0g (-74.1, -1.9)). No difference was seen for poor vs. good blastocysts (79.4g (-35.9, 212.7)). Among twins, quality for both cleaved embryos and blastocysts was not predictive of birth weight.

 Among singletons, embryo quality was not predictive of SGA (Table 1). Among twins, quality of cleaved embryos was not predictive of SGA. However, for blastocysts, fair quality was associated with reduced odds of SGA. Embryo quality was not predictive of LGA in any comparison.

 CONCLUSIONS: Embryo quality is generally not predictive of birth weight in infants conceived via autologous fresh IVF.

 Table 1

<table>
<thead>
<tr>
<th></th>
<th>SGA</th>
<th>LGA</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Good</td>
<td>Poor</td>
</tr>
<tr>
<td>Singleton (N=5262)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleaved Embryo (N=2089)</td>
<td>aOR (95% CI)</td>
<td>1</td>
</tr>
<tr>
<td>Blastocyst (N=3173)</td>
<td>aOR (95% CI)</td>
<td>1</td>
</tr>
<tr>
<td>Twin (N=2492)</td>
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<td></td>
</tr>
<tr>
<td>Cleaved Embryo (N=950)</td>
<td>aOR (95% CI)</td>
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<tr>
<td>Blastocyst (N=1542)</td>
<td>aOR (95% CI)</td>
<td>1</td>
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P-470 Wednesday, October 16, 2019 6:30 AM

IMPACT OF MODE OF CONCEPTION ON EARLY PREGNANCY HUMAN CHORIONIC GONDATROPIN RISE AND BIRTHWEIGHT. Hayley M. Richardson, MS; Charikleia Kalliora, MD; Monica Mainigi, MD; Christos Coutifaris, MD, PhD; Mary D. Sammel, ScD; Sunceta Senapati, MD, MSCE; University of Pennsylvania, Philadelphia, PA; University of Pennsylvania, Division of Reproductive Endocrinology and Infertility, Philadelphia, PA; University of Pennsylvania, Philadelphia, PA.

 OBJECTIVE: Altered hCG kinetics have been observed in conceptions after fresh vs. frozen/thawed embryo transfers and following blastomere biopsies in cleavage stage embryos. While preimplantation genetic testing has improved pregnancy rates in some populations, the impact of trophectoderm biopsy on hCG kinetics and subsequent birthweight is unknown. The aim of this study was to determine differences in first trimester hCG kinetics by mode of conception and subsequent risk of small and large for gestational age infants (SGA and LGA). Groups examined include unassisted natural conceptions, pregnancies after fresh embryo transfer (ET), frozen ET, and trophectoderm preimplantation genetic testing for aneuploidy (PGT-A).

 DESIGN: Retrospective cohort.

 MATERIALS AND METHODS: Serial serum hCG measurements were assessed for 598 singleton pregnancies between 10 and 28 days post-conception. All PGT-A subjects were also frozen embryo transfers. Chi-squared tests were used to test differences in the incidence of SGA and LGA by mode of conception. A joint random effects and logistic model was used to evaluate the effect of mode of conception on hCG slope (per day increase in log-transformed hCG) and incidence of SGA/LGA. Models were adjusted for maternal age, body mass index, and parity as appropriate. Odds ratios illustrate the change in risk associated with a one standard deviation increase in hCG slope.

 RESULTS: Fresh ET had the highest incidence of SGA (12%) and frozen ET had the highest incidence of LGA (16%). PGT-A had the lowest incidence of each event among the groups observed (4% SGA and 8% LGA). Estimated hCG rise per day by group was as follows: Unassisted (0.41), fresh ET (0.39), frozen ET (0.43), PGT-A (0.45). Significant differences in hCG slope were found for all five pairwise group comparisons tested: PGT-A/unassisted (p < 0.01), PGT-A/fresh ET (p < 0.01), PGT-A/frozen ET (p = 0.02), fresh ET/frozen ET (p < 0.01), fresh ET/unassisted (p = 0.03). Slower hCG rise is associated with SGA (OR = 0.64, p < 0.01) but not with LGA (OR = 1.16, p = 0.33).

 CONCLUSIONS: Slower hCG rise is associated with a higher risk of SGA; yet hCG rise does not impact LGA risk. There are differences in expected rate of hCG rise by mode of conception such that PGT-A has the fastest hCG rise, followed by frozen ET, unassisted, and fresh ET. Notably, PGT-A is not associated with abnormal fetal growth phenotypes, supporting the safety of this technology. These findings suggest the super-ovulated environment in fresh ET may predispose to abnormal trophoblast differentiation and early placentation resulting in altered hCG kinetics and fetal growth; yet the mechanisms of LGA in frozen embryo transfer may be mediated by other mechanisms beyond trophoblast function.


TABLE 1

<table>
<thead>
<tr>
<th></th>
<th>SGA</th>
<th>LGA</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Good</td>
<td>Poor</td>
</tr>
<tr>
<td>Singletons</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleaved Embryo (N=2089)</td>
<td>aOR (95% CI)</td>
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</tr>
<tr>
<td>Blastocyst (N=3173)</td>
<td>aOR (95% CI)</td>
<td>1</td>
</tr>
<tr>
<td>Twins</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleaved Embryo (N=950)</td>
<td>aOR (95% CI)</td>
<td>1</td>
</tr>
<tr>
<td>Blastocyst (N=1542)</td>
<td>aOR (95% CI)</td>
<td>1</td>
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</tbody>
</table>
FIRST TRIMESTER VAGINAL BLEEDING DOES NOT PREDICT SMALL FOR GESTATIONAL AGE NEWBORNS FOLLOWING SINGLE EUPLOID FROZEN EMBRYO TRANSFER. Sydney Chang, MD, a, Dmitry Gounko, MA, b Joseph A. Lee, BA, b Alan B. Copperman, MD, b

OBJECTIVE: Newborns that are small for gestational age (SGA) have birth weights below the 10th percentile. Uterine/placental factors associated with SGA neonates include decreased blood flow to the uterus and placenta, placental abruption, placenta previa, and uterine infection. A secondary analysis of data from the NICHD Fetal Growth Studies suggests that more than one day of vaginal bleeding (VB) in the first trimester is associated with lower infant birth weight. However, it is unclear whether this holds true in pregnancies achieved with the use of assisted reproductive technology treatment. The objective of this study was to determine in an infertile population undergoing ivf intervention (IVF) whether first-trimester VB is associated with the likelihood of having an SGA infant.

DESIGN: Retrospective, cohort study.

MATERIALS AND METHODS: The study included patients at an academic ART center who underwent a single euploid FET and experienced a first-trimester VB as associated with lower infant birth weight. However, it is unclear whether this holds true in pregnancies achieved with the use of assisted reproductive technology treatment. The objective of this study was to determine in an infertile population undergoing in vitro fertilization (IVF) whether first-trimester VB is associated with the likelihood of having an SGA infant.  

RESULTS: A total of 1611 FET cycles with a live birth outcome from 1528 patients were included in the study. The overall incidence of VB was 17.69% (n = 285). Pregnancies were divided into two groups: (1) pregnancies with VB prior to the 10th week of gestation and (2) pregnancies with no VB. Univariate analysis demonstrated significant differences in BMI, gravidity, and route of progesterone administration between groups. There was no difference in aspirin use, average birth weight, or gestational age at delivery between groups. There were a total of 18 (6.32%) SGA infants in the VB group, and 115 (8.67%) SGA infants in the no VB group. Controlling for BMI, gravidity, and route of progesterone administration, multivariate regression analysis did not demonstrate any significant association between VB and the incidence of SGA newborns (OR 0.53 [95% CI 0.24-1.20], p = 0.1-23).

CONCLUSIONS: In contrast to the study published by Bever et al., 1 patients who experienced first trimester VB did not demonstrate a higher incidence of SGA newborns. Use of natural language processing of electronic medical records enabled us to re-construct first trimester incidents not otherwise easily obtainable, limiting potential recall bias as a confounding variable. A limitation of our study design was the lack of a quantitative method to track quantity and duration of VB. Nevertheless, patients undergoing single euploid FET can be reassured that first trimester VB is not associated with a higher incidence of SGA infants.


SUPPORT: None.

P-472 Wednesday, October 16, 2019 6:30 AM

DELAYED BLASTULATION HAS NO IMPACT ON NEONATAL OUTCOMES IN FROZEN-TAWED SINGLE BLASTOCYST TRANSFER CYCLES. Aya Yamato, B.S., a Nanako Ishiki, M.S., a Yuka Miyazaki, M.S., a Hiroshi Matsutomo, M.S., a Satoshi Minzou, Ph.D., a Ryoko Minekawa, Dr., a Aisaku Fukuda, Dr., a Yoshinori Morimoto, MD, Ph.D b TVF Osaka Clinic, Osaka, Japan; Affiliation not provided; b TVF Osaka Clinic; b HORAC Grand Front Osaka clinic, Osaka, Japan.

OBJECTIVE: Blastocysts formed on day 6 (D6BL) are available in ART treatment although they are considered to be suboptimal for transfers due to delayed blastulation. As demonstrated in several reports, D6BLs have more abnormalities in mitotic apparatus, resulting in clinical outcomes in transfers as compared with blastocysts formed on day 5 (D5BL). However, impacts of delayed blastulation on prenatal outcomes after blastocyst transfers have not been fully investigated so far. The present study was designed to compare neonatal outcomes between singletons born after transfers of a frozen-thawed single blastocyst formed on Day 5 and Day 6.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A total of 1137 neonates born after transfers of a frozen-thawed single D5BL and 134 neonates after D6BL transfers performed between 2008 and 2016 were analyzed. Blastocysts that reached grade 3 by the Gardner’s score on day 5 or 6 were defined as D5BL and D6BL respectively. The following parameters were statistically analyzed using student’s t-test or chi-square test between singletons born after D5BLs and D6BLs transfers: birth weight, birth height, gestational age at birth, sex ratio and occurrence of congenital abnormalities. Multiple linear regression analysis was performed to investigate the influential parameters on fetal growth among gender, gestational age and day of blastulation.

RESULTS: Birth weight (g), birth height (cm), gestational age (weeks), sex ratio (m/f) and congenital abnormality rates (%) of babies born after transfers of D5BLs vs D6BLs were 3057.3 ± 477.7 vs 3041.2 ± 447.8 (ns), 48.7 ± 2.6 vs 48.7 ± 2.9 (ns), 38.7 ± 2.0 vs 38.5 ± 1.8 (ns), 1.04 vs 1.23 and 3.5 vs. 3.0 (ns), respectively. Multiple linear regression identified gender (p < 0.01) and gestational age (p < 0.01) as associated parameters with fetal growth. Delayed blastulation, on the other hand, was not related with either birth weight or height.

CONCLUSIONS: Our study showed that neonatal outcomes were not statistically different between babies born after transfers of D5BLs and D6BLs. Based on the results of both univariate and multivariate analyses, delayed blastulation has no influence on the neonatal outcomes, therefore transfer of D6BL is an optimal alternative for patients who miss blastocysts on day 5. Reference: None.

SUPPORT: None.

P-473 Wednesday, October 16, 2019 6:30 AM

IS LOW BIRTH WEIGHT RELATED TO HIGH OOCYTE YIELD DURING FRESH TRANSFER ART CYCLES? RETROSPECTIVE ANALYSIS FROM HOMOLLOGOUS CYCLES. Edelmino Garza-Padilla, M.D., a, Julio C. Rosales, M.D., a S. Alberto Dávila-Garza, M.D., b Karla A. Cantú, M.S.c Pasquale Patrizio, M.D., b Mario A. Patrón-Vázquez, M.D., b IECH, Monterrey, NL, Mexico; b Yale Fertility Center, New Haven, CT.

OBJECTIVE: To determine if the number of retrieved oocytes correlates with live birth rate (LBR) and incidence of low birth weight (LBW).

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: All cycles of fresh embryo transfer with the use of homologous oocytes (n = 2216) between 2006–2017 performed at a private fertility center were reviewed and included. Groups were established in relationship to the number of retrieved oocytes (group 1: ≤10, group 2: 11-15, group 3: ≥16) and women age (≤35 and ≥36). Non adjusted comparisons between groups were calculated using t-test and chi-squared distribution. Furthermore, one-way analysis of variance (ANOVA) and Tukey posthoc test, were used to assess mean comparisons among the three groups. Pregnancy rates (positive serum hCG) and live birth rates were calculated. Finally, after excluding multiple pregnancy newborns, using the Intergrowth® matrix, each newborn was classified according to its weight (percentiles and z-score) to examine its relationship with the number of retrieved oocytes.

RESULTS: The younger group (≤35yo, n = 1176, 53%) had a pregnancy rate of 41.5% and LBR of 29.7% per cycle. The other group (≥36yo, n = 1040, 47%) had a pregnancy rate of 28.2% and LBR of 16.7%. According to the number of retrieved oocytes, the group 2 and 3 had a statistically significant greater pregnancy rate (41.2% and 42%) than group 1 (29.8%) (p<0.001). However, there was no significant difference in the LBR between groups.

Comparative analysis between the number of retrieved oocytes, live birth rate and incidence of low birth weight (LBW) showed the following weight percentile or z-scores and number of retrieved oocytes for all patients and in the younger patients.

CONCLUSIONS: In homologous fresh embryo transfer with the use of homologous oocytes, there is no association between high number of retrieved oocytes and the incidence of live birth rate and LBW. Further studies are warranted to determine if a subgroup of women may be particularly vulnerable to certain maternal and fetal complications.
OBJECTIVE: Assisted reproduction (ART) has been associated with adverse perinatal outcomes, including extremes of birth weight (BW) and pre-term birth (PTB). We sought to explore the incidence of PTB, low birth weight (LBW), very low birth weight (VLBW), and macrosomia (MS) in GC pregnancies.

MATERIALS AND METHODS: Data from a large surrogate agency that consisted of matched GCs and intended parent (IP) couples for an index GC pregnancy were reviewed. The following was collected for each GC pregnancy: BW, number delivered, and gestational age (GA) at delivery. For each GC, history of PTB and history of multiple gestation were also collected. Definitions of LBW, VLBW, and MS were as defined by World Health Organization criteria. PTB was defined as gestation <37 weeks.

RESULTS: Of 836 GC pregnancies reviewed, BW data was available for 536 deliveries. Average BW of GC index pregnancies was 7.27 lbs (SD 1.53, minimum 1.62 lbs, maximum 15.8 lbs). Incidence BW extremes were: 58 (10.9%) LBW; 10 (1.9%) VLBW; 70 (13.1%) MS. GA data was available for 259 index GC pregnancies (Table 1). Overall PTB rate (15.1%) was higher and the majority were singleton gestations (76.7% in singletons vs 30% in multiples in patients with history of PTB, P < 0.001). Those with no history of PTB and who carried multiples had a lower rate of PTB; in fact, in this group, only 1 out of 35 patients had a PTB (<0.001). With no history of PTB and who carried multiples had a low rate of PTB; in fact, this group, only 1 out of 35 patients had a PTB with multiples.

CONCLUSIONS: Incidence of LBW and VLBW were similar to national averages. PTB rate was higher and the majority were singleton gestations in women with a history of PTB. In women with prior full term deliveries, carrying multiples did not impart a greater risk of PTB. A GC’s prior obstetric history appears to have the greatest impact on the GA at delivery in the GC pregnancy. These factors should be taken into account when identifying GC candidates and deciding on the number of embryos to transfer.

Reference: None.

SUPPORT: None.

TABLE 1. Differences between frozen embryo and fresh embryo births regarding birth percentile, gestational age and birth weight stratifications.

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<th>Percentile*</th>
<th>Gestational age*</th>
<th>Birthweight*</th>
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</thead>
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<td>&lt;10</td>
<td>&lt;34 wks</td>
<td>&lt;1500</td>
</tr>
<tr>
<td>10_90</td>
<td>34-37wks</td>
<td>1500-2499</td>
</tr>
<tr>
<td>&gt;90</td>
<td>&gt;37 wks</td>
<td>&gt;=2500</td>
</tr>
</tbody>
</table>

Fresh embryo (n=1443)(%) | 219 (15.2) 1117 (77.4) 107 (7.4) | 112 (7.8) 263 (18.2) 1067 (74.0) | 44 (3.0) 290 (20.1) 1109 (76.9) |
Frozen embryo (n=486)(%) | 36 (7.4) 376 (77.4) 74 (15.2) | 15 (3.1) 51 (10.5) 420 (86.4) | 4 (0.8) 34 (7.0) 448 (92.2) |
Total (n=1929) | 255 1493 181 | 127 (314) 1487 | 48 (324) 1557 |

*p<0.001.
RISK OF ADVERSE PERINATAL OUTCOMES AFTER OOCYTE DONATION: A SYSTEMATIC REVIEW AND META-ANALYSIS. Jose Antonio Moreno, MD,1 Checa Angel Miguel, MD, PhD,1 2Clinica de la Mujer - Medicina Reproductiva, vina del mar, Chile;3 FERTTY, Barcelona, Spain.

OBJECTIVE: To assess if in women with singleton pregnancies conceived after assisted reproductive technologies, do the in vitro fertilization with oocyte donation (IVF-OD) affects the perinatal and maternal outcomes compared to autologous in vitro fertilization (IVF-AO)?

DESIGN: Systematic review and meta-analysis of studies comparing perinatal and maternal outcomes in singleton pregnancies resulting from IVF-OD versus IVF-AO.

MATERIALS AND METHODS: An electronic literature search in PubMed, MEDLINE and Cochrane database was performed. The main outcome measures were preterm birth, early preterm birth, low birth weight, very low birth weight, hypertensive disorders in pregnancy, pregnancy induced hypertension, preeclampsia and severe preeclampsia.

RESULTS: 12 studies were included. IVF-OD is associated with a higher risk of preterm birth (RR 1.44; 1.20-1.74), early preterm birth (RR 1.68; 1.09-2.60), low birth weight (RR 1.26; 1.11-1.43), very low birth weight (RR 1.35; 1.21-1.50), hypertensive disorders in pregnancy (RR 2.66, 1.97-3.60), pregnancy induced hypertension (RR 1.69; 1.30-2.20), preeclampsia (RR 3.09; 2.60-3.68) and severe preeclampsia (RR 3.43; 2.34-5.04). There was no significant difference in the risk of small for gestational age.

CONCLUSIONS: IVF-OD patients must be considered an independent risk factor for some adverse perinatal outcomes, mainly hypertensive disorders in pregnancy, preeclampsia and severe preeclampsia, but also preterm birth and low birth weight. Immunological aspects may be involved in this results and further research focusing in the etiopathogenesis of these pathologies are needed.

ART PREGNANCY RISKS

OVERVIEW OF 2016 U.S. ASSISTED REPRODUCTIVE TECHNOLOGY (ART) TREATMENT OUTCOMES AND CONTRIBUTION OF ART TO MULTIPLE-BIRTH AND PRETERM INFANTS IN THE UNITED STATES. Saswati Sunderam, M.A PhD,1 Dmitry Kissin, MD, MPH,1 Yujia Zhang, PhD,1 Sheree Boulet, DrPH,1 Suzanne G. Folger, PhD,1 Lee Warner, PhD,1 Wanda D. Barfield, MD,1 Centers for Disease Control and Prevention, Chambly, GA; Centers for Disease Control and Prevention (CDC), Atlanta, GA; Centers for Disease Control and Prevention, Atlanta, GA; Centers for Disease Control and Prevention, Atlanta, GA.

OBJECTIVE: To assess national and state-specific ART utilization and outcomes and the contribution of ART to multiple births and prematurity.

DESIGN: Population-based cross-sectional analysis.

MATERIALS AND METHODS: Data for ART procedures and birth outcomes in 2016 were obtained from CDC’s National ART Surveillance System (years 2015 and 2016). Data for all infants born in the U.S. were obtained from 2016 National Vital Statistics System birth data. The number of ART procedures performed per million women 15-44 years of age (ART use), rates of elective single embryo transfers (eSET) among women <35 years, rates of ART preterm and multiple-birth infants, and proportions of ART-conceived infants among all infants, and all multiple-birth and preterm infants were calculated for each reporting area (50 States, District of Columbia, and Puerto Rico), by mother’s state of residence. The proportion of infants who were small for gestational age (SGA) (i.e., born at <10th percentile of birthweight for gestational age) was calculated for singleton births that occurred at <37 weeks (preterm), 37–41 weeks (term), and 22–44 weeks (overall births) for ART and all infants.

RESULTS: Among 3,974,132 infants born in the U.S., 1.8% (70,600) were conceived with ART (range: 0.3% in Puerto Rico to 4.7% in Massachusetts). ART use ranged from 385 (Puerto Rico) to 7,371 (District of Columbia) procedures per million women aged 15-44 years. The national eSET rate among women <35 years was 42.7% (range: 8.3% in North Dakota to 83.9% in Delaware). The rates of multiple-birth and preterm infants were 31.5% and 29.9% among ART infants versus 3.4% and 9.9% among all infants, respectively. Nationally, the proportion of ART-conceived infants among multiple-birth and preterm infants was 16.4% and 5.3%, respectively. The percentage of ART-conceived singletons that were SGA was 8.7% for preterm infants, 8.0% for term infants, and 8.1% overall; the corresponding percentages among all singletons were 9.3%, 10.5%, and 9.9%.

CONCLUSIONS: A higher proportion of ART infants are multiple and preterm in the U.S compared to all births. Wide variations were observed among reporting areas in the rates of ART utilization and eSET. Greater utilization of eSET, where appropriate, could reduce the contribution of ART to multiple-birth and preterm infants. Rates of SGA for singletons born preterm, term, and for all gestational ages were lower among ART-conceived infants compared with all infants, possibly indicating better health behaviors and care among ART patients.

SUPPORT: NONE.

IN VITRO FERTILIZATION AND GESTATIONAL HYPERTENSION/PREECLAMPSIA RISK: EFFECT OF DIAGNOSIS VERSUS TREATMENT PARAMETERS. Barbara Luke, ScD, MPH,1 Morton B. Brown, PhD,2 Michael L. Eisenberg, M.D.,3 Caitriona M. Callan, MBBCbir,4 Beverley Jayne Botting, PhD,1 Allian Pacey, BSc, PhD,1 Alastair G. Sutcliffe, MD, PhD,1 Valerie L. Baker, MD4 Michigan State University, East Lansing, MI;5 University of Michigan, Ann Arbor, MI;6 Stanford University, Stanford, CA;7 Affiliation not provided;8 University of Sheffield, Sheffield, United Kingdom;9 Johns Hopkins University School of Medicine, Division of Reproductive Endocrinology and Infertility, Lutherville, MD.

OBJECTIVE: To evaluate the risks of gestational hypertension by maternal fertility status and infertility diagnosis.

DESIGN: Women in 8 States (CA, CO, FL, MI, NY, OH, PA, TX) who underwent in vitro fertilization (IVF) cycles resulting in a live birth during 2004-2013 were linked to their infant’s birth certificates; a 10:1 sample of births from non-IVF deliveries were selected for comparison; those with an indication of infertility treatment on the birth certificate were categorized as subfertile, all others were categorized as fertile. The IVF pregnancies were additionally categorized by oocyte source (autologous vs donor) and embryo state (fresh vs thawed).

MATERIALS AND METHODS: Analyses within the IVF group were additionally categorized by infertility diagnosis. Gestational hypertension or preeclampsia (GH or PE) were identified from the birth certificate. GH and PE were considered as a composite primary outcome variable. GH/PE was modeled using logistic regression, and reported as adjusted odds ratios (AOR) and 95% confidence intervals (CI). For analyses of singleton fertile, subfertile, and IVF pregnancies, the reference group were fertile women. For analyses by oocyte source-embryo state within IVF pregnancies, the reference group was autologous-fresh for singletons.

RESULTS: The study population included 1,518,175 pregnancies (1,382,149 singleton/fertile, 7,815 singleton/subfertile, 86,907 singleton/IVF, and 41,304 twin/triplet/IVF). Compared to fertile women, subfertile women had increased risks for GH/PE [AOR 1.67, 95% CI 1.50, 1.87] compared to autologous-fresh cycles did not [AOR 1.02, 95% CI 0.97, 1.08]. Among IVF singleton births, the risk of GH/PE was increased for all non-autologous-fresh groups (autologous-thawed, 1.32 [1.22, 1.43]; donor-fresh, 1.97 [1.76, 2.22]; donor-thawed, 1.79 [1.53, 2.09]; and donor-thawed or fresh, 1.92 [1.72, 2.14]) relative to the autologous-fresh group. The results were similar in multiple births. In analyses by infertility diagnoses, with the autologous-fresh group as the reference, autologous-thawed cycles had significantly elevated risks for GH/PE in 7 of 10 infertility diagnoses, AORS of 1.29 to 1.54; donor-fresh cycles had elevated risks in 8 of 10 diagnoses, AORS of 1.66 to 4.51; donor-thawed cycles had elevated risks for 4 of 9 diagnoses, AORS of 1.67 to 2.03.

CONCLUSIONS: The risk of gestational hypertension/preeclampsia is increased in pregnancies for subfertile women, in pregnancies from oocyte donation and from frozen embryo transfer, but not with pregnancies from fresh autologous IVF cycles.

SUPPORT: NIH Grant R01 HD84377.

OBSERVATIONAL 4-YEARS STUDY OF OBSTETRIC COMPLICATIONS AFTER IN VITRO FERTILIZATION (IVF) AND FRESH EMBRYO TRANSFER IN A FRENCH NATIONAL COHORT OF 43,084 DELIVERIES. Sylvie Epelboin Sr., MD,1 Morgane Valentin, MD,2 Rachel Levy Sr., MD, PhD,3 Marianne Bergerre Sr., MD,4 Fabienne Pessione Sr., Dr.5 Hospital Bichat-Claude Bernard, Assistance
OBJECTIVE: The objective of this large cohort study is to identify by univariate and multivariate analysis whether there is an excess of maternal morbidity (MM) in ongoing pregnancies and deliveries after IVF and fresh transfer techniques, when compared to spontaneous conceptions (SC).

DESIGN: This is an observational, exposed-unexposed cohort study comparing pregnancies, deliveries and births following IVF, standard or using Intra Cytoplasmatic injection (ICSI), and fresh transfers to non-IVF controls. The study included all 2,832,578 national deliveries registered between 2013 and 2016 in France, among which 1.5% (43,084) resulted from IVF and immediate fresh transfer.

MATERIALS AND METHODS: Pregnancies and deliveries were analyzed by extracting the Information Systems Medicalization Program (PMSI) French database. The main identified maternal morbidity indicators for the 4,084 IVF and 2,789,494 non-IVF pregnancies were: venous and arterial thrombosis (VT, AT), gestational diabetes mellitus (GDM), pre-eclampsia (PE), Placenta Previa (PP), placenta abruption (PA) or hemorrhage at delivery (HD). The risks of MM in IVF were estimated in multivariate analysis after adjustment for maternal age, smoking and obesity, and multiple deliveries.

RESULTS: The mean maternal age was 33.3 and 29.9 years in the IVF and control groups (p<0.0001). The rate of multiple deliveries was 1.68%, of which 13% if IVF conception. Diabetes and hypertensive disorders during pregnancy were more common in the IVF vs non-IVF group: 10.1% vs 0.9% (p=0.01) and 1.04% vs 0.9% (p<0.001). Tobacco dependence and obesity were less common in the IVF vs non-IVF group (2.2% vs 4.5%, and 3.9% vs 4.3%, p<0.001). The frequency of premature deliveries was higher in IVF vs non-IVF (19.3% vs 6.9% (p<0.0001), persistent for single deliveries (9.0% vs 5.7%, p<0.001). The risk of MM (VT, GDM, PE, PP, PA, HD) was higher in IVF vs non-IVF (20.9% vs 14.3%, p<0.0001), even if single pregnancies (19.6% vs 14.1%, p<0.0001) except arterial thrombosis. The risk of MM increased significantly with age for all events except for PE. In multivariate analysis, IVF is a significant risk factor for all MM events except arterial thrombosis. The adjusted risk of the occurrence of at least one concern after IVF is 1.29 [1.26-1.32] at all and 1.32 [1.28-1.35] in single deliveries. This risk is stable over the four years.

CONCLUSIONS: Large observational studies identified that IVF pregnancies are associated with a significant risk of complications, initially attributed to multiple pregnancies, as compared with pregnancies after SC. The strength of this large national exposed-unexposed cohort study lies in the number and completeness of subjects studied. Our data provide in turn evidence for increased adjusted risk of premature delivery and maternal morbidity (VT, GDM, PE, PP, PA, and HD) after IVF, including in single pregnancies. The knowledge of the excess risk is an essential tool for informing without worrying couples candidate for IVF, and analyzing neonatal health of IVF-children. Future developments should allow to refine the knowledge of more or less at-risk subgroups.

SUPPORT: None.
approach that of the general population. This dramatic improvement was accomplished while simultaneously improving SIR such that delivery rates per transfer actually increased. It is now possible to perform SET in all patients without compromising delivery rates and drastically reducing the neonatal risks associated with LBW/VLBW endured by infertile couples and their progeny.

SUPPORT: None.

P-482 Wednesday, October 16, 2019 6:30 AM
TWIN PREGNANCY OUTCOMES OF WOMEN WITH A DIDELPHUS UTERUS AFTER IN VITRO FERTILIZATION-EMBRYO TRANSFER. Pei Cai, Master, a Xihong Li, MD./Ph.D, b Yan Ouyang, MD./Ph.D, b Qingqing Wu, Bachelor’s degree. b aCentral South University, Changsha, China; bReproductive and Genetic hospital of Citic-Xiangya, Changsha, China.

OBJECTIVE: To investigate the twin pregnancy outcomes of women with a congenital didelphus uterus after in vitro fertilization embryo-transfer (IVF-ET).

DESIGN: A retrospective matched case-control study.

MATERIALS AND METHODS: A retrospective 1:4 matched case-control study was conducted of 16 cases of twin pregnancy in women with a congenital didelphus uterus after IVF-ET from January 2004 to December 2017. For each case in the study group, 4 consecutive control twin pregnancies in women with a normal uterus were included. Women in both groups were matched for maternal age (MA), body mass index (BMI), cause of infertility, infertility type and insemination methods. Patients with the monochorionic twins and twins with spontaneous or selective reduction were excluded. The pregnancy and obstetric outcomes between these two groups were compared.

RESULTS: The didelphus group and the control group were statistically similar with respect to MA, BMI, cause of infertility, infertility type and insemination methods (P > 0.05).

Compared with the control group, the didelphus group had significantly higher rates of preterm delivery (75.0 vs. 42.2%; P = 0.019), very preterm birth (42.9 vs. 8.5%; P = 0.001), low birth weight (89.5 vs. 46.4%; P = 0.001) and perinatal mortality (32.1 vs. 5.1%; P < 0.001), and a significantly lower live birth rate (62.5 vs. 87.5%; P = 0.019); the gestational age at delivery (31.3 ± 5.7 vs. 35.6 ± 3.8 weeks; P = 0.017) and the live birth weight (1944 ± 387 vs. 2455 ± 475 g; P < 0.001) were significantly lower in the didelphus group than those in the control group. Additionally, the miscarriage rate (12.5 vs. 7.8%; P > 0.05) was higher in the didelphus group, but this difference was not significant.

CONCLUSIONS: Twin pregnancy was associated with increased rates of preterm delivery, low birth weight and perinatal mortality in women with a didelphus uterus after IVF-ET.

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PRECONCEPTION AND VERY EARLY PREGNANCY BLOOD PRESSURE AND DEVELOPMENT OF PRETERM PREECLAMPSIA, TERM PREECLAMPSIA AND GESTATIONAL HYPERTENSION. Carrie J. Nobles, PhD,a Pauline Mendola, PhD, b Sunni L. Mumford, PhD, c Robert M. Silver, MD, d Keewan Kim, PhD, a Victoria C. Andriessen, BS, a Lindsey A. Sjaarda, PhD, d Neil J. Perkins, PhD, d Enrique F. Schisterman, PhD, a NICHD, Bethesda, MD; dNational Institute of Child Health and Human Development, Bethesda, MD; eNational Institute of Child Health and Human Development, Bethesda, MD; eUniversity of Utah, Salt Lake City, UT; dEpidemiology Branch, DIPHR, NICHD, NIH, Bethesda, MD.

TABLE. The twin pregnancy outcomes between the didelphus group and the control group

<table>
<thead>
<tr>
<th>Pregnancy outcomes</th>
<th>The didelphus group(n=16)</th>
<th>The control group (n=64)</th>
<th>P-value</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Miscarriage %,(n)</td>
<td>12.5 (2/16)</td>
<td>7.8 (5/64)</td>
<td>NS</td>
<td>1.67 (0.30-9.61)</td>
</tr>
<tr>
<td>Preterm delivery %,(n)</td>
<td>75.0 (12/16)</td>
<td>42.2 (27/64)</td>
<td>0.019</td>
<td>4.11 (1.20-14.14)</td>
</tr>
<tr>
<td>Perinatal mortality %,(n)</td>
<td>32.1 (9/28)</td>
<td>5.1 (6/118)</td>
<td>&lt;0.001</td>
<td>8.84 (2.82-27.70)</td>
</tr>
<tr>
<td>Live birth rate %,(n)</td>
<td>62.5 (10/16)</td>
<td>87.5 (56/64)</td>
<td>0.019</td>
<td>0.240 (0.07-0.84)</td>
</tr>
<tr>
<td>The gestational age at delivery (weeks)</td>
<td>31.3 ± 5.7</td>
<td>35.6 ± 3.8</td>
<td>0.017</td>
<td>8.10 (1.10-32.85)</td>
</tr>
<tr>
<td>&lt; 32 gestational weeks %,(n)</td>
<td>42.9 (6/14)</td>
<td>8.5 (5/59)</td>
<td>0.001</td>
<td>9.81 (2.16-44.46)</td>
</tr>
<tr>
<td>The live birth weight (g)</td>
<td>1944 ± 387</td>
<td>2455 ± 475</td>
<td>&lt;0.001</td>
<td>8.10 (1.10-32.85)</td>
</tr>
<tr>
<td>&lt;2500 g %,(n)</td>
<td>89.5 (17/19)</td>
<td>46.4 (52/112)</td>
<td>0.001</td>
<td>9.81 (2.16-44.46)</td>
</tr>
</tbody>
</table>

FERTILITY & STERILITY® e301
OBJECTIVE: Although elevations in early- to mid-pregnancy blood pressure are related to risk of developing a hypertensive disorder of pregnancy, little is known regarding when this differentiation in blood pressure begins. We evaluated the relationship of preconception and very early pregnancy blood pressure with risk of developing preterm preeclampsia (PE), term PE, and gestational hypertension (GHTN).

DESIGN: Prospective cohort study set in the EAGeR trial, which enrolled 1228 couples attempting pregnancy who had a history of pregnancy loss. Women were randomized to receive 81 mg aspirin or placebo for up to 6 menstrual cycles attempting pregnancy and, if they became pregnant, up to 36 weeks’ gestation.

MATERIALS AND METHODS: Systolic and diastolic blood pressure were measured by trained staff at enrollment prior to conception and at gestational weeks 4, 8, 12, 16 and 20, and were used to derive mean arterial pressure. Hypertensive disorders of pregnancy, including preterm PE, term PE and gestational hypertension, were classified retrospectively from medical record abstraction. We excluded 9 participants with chronic hypertension (blood pressure over 140/90 mmHg and/or anti-hypertensive treatment during preconception or in early pregnancy). Log-binomial models assessed the relationship of blood pressure at preconception and in early- to mid-pregnancy with risk of developing a hypertensive disorder of pregnancy (preterm PE, term PE and GHTN), adjusting for maternal age, pre-pregnancy BMI, parity, and treatment assignment (low-dose aspirin or placebo). We additionally evaluated the interaction of blood pressure with assignment to aspirin due to its efficacy in preventing preeclampsia among high-risk women.

RESULTS: Of 588 women who had a live birth and no chronic hypertension, 10 developed preterm PE, 18 term PE and 24 GHTN. During preconception, systolic blood pressure levels were elevated to similar degrees for women who developed preterm PE, term PE and GHTN compared to women who did not develop hypertension in pregnancy. However, by 4 weeks gestation, those who developed preterm PE had relatively elevated blood pressure (124.8±3.6) compared to those with term PE (117.8±2.7) or GHTN (115.8±2.4), a trend that continued up to 20 weeks’ gestation. By as early as 4 weeks gestation, higher mean arterial pressure was associated with higher risk of preterm PE (relative risk [RR] 2.28, 95% confidence interval [CI] 1.01, 5.16 per 10 mmHg) and term PE (RR 1.57, 95% CI 1.02, 2.41 per 10 mmHg). No differences were observed by assignment to low-dose aspirin.

CONCLUSIONS: Although preconception blood pressure levels were similarly elevated for women who developed preterm PE, term PE and GHTN as compared to women who did not develop a hypertensive disorder of pregnancy, a differentiation in blood pressure for each condition was observed as early as 4 weeks gestation. This suggests that some of the physiologic changes associated with preterm PE may occur prior to 4 weeks’ gestation.

SUPPORT: Intramural Research Program, Division of Population Health Research, Eunice Kennedy Shriver National Institute of Child Health and Human Development.

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PERCEPTIONS OF MULTIFETAL GESTATION AMONGST PATIENTS BEING TREATED FOR INFERTILITY. Anne Hutchinson, M.D. Seth J. Barishansky, MS, Rafael Confino, BS, Angela K. Lawson, Ph.D., Mary Ellen Pavone, MD MSCI, Northwestern University, Chicago, IL.

OBJECTIVE: To assess the desire for multifetal gestation in our patient population and understand patient perceptions regarding maternal and fetal risks inherent in these pregnancies.

DESIGN: Cross-Sectional Study.

MATERIALS AND METHODS: We designed a 40-question digital survey based on a previously validated survey and approved by our IRB (Ryan et al, 2004). Between the months of February and April 2019, patients presenting with infertility were approached. After receiving verbal consent, patients were provided with a tablet, preloaded with our survey, which collected de-identified patient demographic information as well as treatment outcomes ranked in order of preference, specifically “no child”, “singleton pregnancy”, “twin pregnancy”, “triplet pregnancy”. Using a series of true/ false questions we also assessed knowledge of the complications of multiple births with questions regarding risks to the mother’s health during pregnancy and delivery, risks of cerebral palsy and long-term health problems in the infant and risk of death to the infant as well as knowledge of the financial and psychological risks of multifetal pregnancy.

These questions were then analyzed using chi-squared analysis to compare understanding of maternal and fetal risks of multifetal gestation between groups who identified singleton pregnancy as desired outcome to those who desired twin or triplet pregnancy.

RESULTS: 71 patients completed our survey. 68% reported singleton pregnancy as ideal treatment outcome, 30% reported twin pregnancy as ideal treatment outcome, 2% reported triplet pregnancy as ideal treatment outcome. A chi-squared analysis was used to compare the responses of patients desiring singleton pregnancy to those desiring twin or triplet pregnancy. Both groups showed similar understanding of increased risk of preterm birth in twin (88% vs. 100%) and triplet pregnancies (100% vs 92%). Similarly, both groups showed similar understanding of the increased risk of triplet pregnancies on maternal health (85% vs. 83%). Patients desiring twin and triplet pregnancies, however, showed less understanding of increased maternal risk in twin pregnancy (77% vs 52%, p<0.05), and increased risk of neonatal morbidity in twin pregnancy (17% vs 44%, p<0.05) and triplet pregnancy (26% vs 54%, p<0.05).

Both groups showed similar understanding of the increased risk of neonatal mortality in twin pregnancies (23% vs 22%) and triplet pregnancies (38% vs 30%).

CONCLUSIONS: A significant number of patients undergoing fertility treatment desire twin and triplet gestation. This desire seems to be associated with an incomplete understanding of maternal and neonatal risks associated with multifetal gestation. We believe that targeted patient education regarding these risks may decrease patient desire for multifetal gestation and help to bring patient and provider goals into better alignment.


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RISK OF ECTOPIC PREGNANCY AFTER DIFFERENT OVARIAN STIMULATION PROTOCOLS IN FRESH SINGLE EMBRYO TRANSFER: ANALYSIS OF 71,831 CYCLES FROM THE JAPANESE ART REGISTRY. Seung Chik Jwa, M.D., Ph.D., M.P.H.,a Sachie Seto, M.D., Ph.D.,b Masashi Takamura, M.D., Ph.D., Akira Kuwahara, M.D., Ph.D., Takeshi Kajihara, M.D., Ph.D.,a Osamu Ishihara, M.D., Ph.D. a Saitama Medical University, Saitama, Japan; bTokushima University, Tokushima, Japan.

OBJECTIVE: To investigate the risk of ectopic pregnancy following different ovarian stimulation protocols in fresh cycles.

DESIGN: Registry-based retrospective cohort study.

MATERIALS AND METHODS: This study included all autologous cycles that resulted in a clinical pregnancy after described ovarian stimulation protocols (natural, clomiphene (CC), CC+gonadotropin (GN), GnRH agonist and GnRH antagonist) in fresh single embryo transfers between 2007 and 2015 in Japan. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated using generalized estimating equations adjusted for potential maternal and treatment characteristics.

RESULTS: Among 71,831 clinical pregnancies, 1,049 (1.46%) ectopic pregnancies were reported. Ectopic pregnancy was more frequent for early cleavage stage embryo transfers than blastocyst transfers (1.54% vs. 1.29%, p = 0.008), and assisted hatching (AH) (1.75% in AH group vs. 1.36% in non-AH group, p = 0.003). The highest rate of ectopic pregnancy occurred with CC+gonadotropin (2.06%, 221/10,711), followed by CC alone (1.77%, 160/9,025), GnRH antagonist (1.49%, 216/14,490) and GnRH agonist protocols (1.40%, 415/29,585). The natural cycle had the lowest ectopic pregnancy rate of all ovarian stimulation protocols (0.46%, 37/8,201). Compared with the natural cycle, all other ovarian stimulation protocols were associated with a significantly increased risk of ectopic pregnancy. Ovarian stimulation using CC+gonadotropin had the highest increased risk for ectopic pregnancy (adjusted OR, 4.39, 95% CI, 2.55 to 7.54). In each stimulation protocol, there was no association between the risk of ectopic pregnancy and the number of oocytes retrieved, except with ovarian stimulation using CC.

CONCLUSIONS: Ovarian stimulation protocols were associated with a significantly increased risk for ectopic pregnancy in fresh cycles. These results suggest that ovarian stimulation agents may affect the tubal and intrauterine environment during fresh cycles.

SUPPORT: This study was supported by Health and Labour Sciences Research Grants.
OBSTETRIC AND NEONATAL RISKS IN TERM-SINGLETON ASSISTED REPRODUCTIVE TECHNOLOGY (ART) PREGNANCIES: A SINGLE-CENTER REPORT IN A PERIOD OF 9 YEARS. Satoshi Furuya, MD, Kiyoshi Kubonoya, MD, Ken Kubonoya, MD, Kubonoya Ob/Gyn Clinic, Kashiwai City Chiba Prefecture, Japan.

OBJECTIVE: It is well documented that a singleton pregnancy is safer and healthier than a multiple pregnancy and term (defined as a period from 37 to 41 weeks of gestation) is the optimal timing to give birth for humans. As the number of infertile couples requiring ART is increasing today, pregnancies obtained by ART have often been reported to be associated with a higher risk of poor pregnancy outcomes. This can be accounted for in part by the higher frequency of ART-conceived preterm or multiple births included, and study-design heterogeneity among researches. The aim of our study is to determine whether there is any increase in adverse obstetric and neonatal outcomes in ART pregnancies, compared with naturally conceived pregnancies, even when only term-singleton cases are selected as a base cohort.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We reviewed 14297 consecutive term-singleton labor and delivery cases managed in our facility from January 2010 to March 2019. All information was collected from medical records, including maternal age, parity, details of infertility treatment, pregnancy course and mode of delivery, complications during labor and puerperium, status of the infant at birth, etc. Infertile cases conceived by other than ART (n=676) were excluded from our study subjects in order to assess the effect of ART more precisely. The remaining study population (n=7501) were divided into two categories as follows: cases conceived through ART procedures (Group A: n=750), and cases conceived naturally (Group B: n=12871). We used multivariable logistic regression analysis (shown as odds ratio, 95% CI, and P value) to evaluate the impact of term-singleton ART pregnancy on obstetric and neonatal outcomes, while controlling for maternal age, parity, gestational weeks at birth, and neonatal sex.

RESULTS: Average maternal age in Group A and B was 35.8 ± 3.6 (y ± SD) and 32.9 ± 4.5, respectively. Group A constituted about 5.5% (750/13621) of all term-singleton births during the study period. Significant increased incidence of maternal medical complications (OR:1.42(1.10 - 1.81), P<0.001), HDP (hypertensive disorders of pregnancy; OR:1.64(1.18 - 2.25), P<0.001, forced delivery (i.e., emergency C-section or instrumental delivery: OR:1.52(1.28 - 1.80), P<0.001), abnormal postpartum hemorrhage (OR:2.29(1.77 - 2.94), P<0.001), placenta adhaerens/accrete (OR:3.33(1.81 - 5.82), P<0.001), vela-menous umbilical cord insertion (OR:7.85(5.03 - 12.11), P<0.001), and heavy-for-date newborn infant (OR:1.71(1.03 - 2.71), P=0.03) was observed in Group A. Difference in the incidence of placental abruption and other neonatal outcomes (Apgar scores, umbilical artery pH value, NICU admission, congenital anomaly) between Group A and B could not be confirmed.

CONCLUSIONS: Among term-singleton pregnancies, cases achieved by ART carry an increased risk for several adverse maternal and neonatal outcomes, compared with those conceived naturally. In order to secure the safety, obstetricians should recognize term-singleton ART pregnancies as high-risk ones and manage them more cautiously than ever before.

SUPPOT: None.
TABLE. Reproductive outcomes of SBET and DCET in women with a unicornuate uterus

<table>
<thead>
<tr>
<th>Reproductive outcomes</th>
<th>DCET</th>
<th>SBET</th>
<th>P</th>
<th>aOR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>383</td>
<td>156</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Embryos transferred (n)</td>
<td>766</td>
<td>156</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Implantation, % (n)</td>
<td>47.9 (367/766)</td>
<td>57.7 (90/156)</td>
<td>0.011</td>
<td>0.628 (0.439-0.899)</td>
</tr>
<tr>
<td>Clinical pregnancy, % (n)</td>
<td>68.1 (261/383)</td>
<td>57.7 (90/156)</td>
<td>0.039</td>
<td>1.522 (1.022-2.267)</td>
</tr>
<tr>
<td>Live birth % (n)</td>
<td>52.0 (199/383)</td>
<td>47.4 (74/156)</td>
<td>0.451</td>
<td></td>
</tr>
<tr>
<td>Multiple pregnancy, % (n)</td>
<td>41.4 (108/261)</td>
<td>3.3 (3/90)</td>
<td>&lt;0.001</td>
<td>20.046 (6.132-65.535)</td>
</tr>
<tr>
<td>Pregnancy (n)</td>
<td>200</td>
<td>86</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Miscarriage, % (n)</td>
<td>19.5 (39/200)</td>
<td>15.1 (13/86)</td>
<td>0.378</td>
<td></td>
</tr>
<tr>
<td>Preterm delivery, % (n)</td>
<td>24.5 (49/200)</td>
<td>12.8 (11/86)</td>
<td>0.028</td>
<td>2.213 (1.088-4.501)</td>
</tr>
<tr>
<td>Term delivery, % (n)</td>
<td>53.0 (106/200)</td>
<td>72.1 (62/86)</td>
<td>0.003</td>
<td>0.437 (0.253-0.754)</td>
</tr>
<tr>
<td>Babies born (n)</td>
<td>199</td>
<td>73</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Live births (n)</td>
<td>180</td>
<td>72</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perinatal mortality, % (n)</td>
<td>9.5 (19/199)</td>
<td>1.4 (1/73)</td>
<td>0.027</td>
<td>9.900 (1.294-75.734)</td>
</tr>
<tr>
<td>Low birth weight, % (n)</td>
<td>31.7 (57/180)</td>
<td>11.1 (8/72)</td>
<td>0.005</td>
<td>3.163 (1.416-7.062)</td>
</tr>
<tr>
<td>Live birth weight (g)</td>
<td>2750 ± 650</td>
<td>3050 ± 500</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Gestational age at delivery (weeks)</td>
<td>36.8±3.9</td>
<td>37.8±2.8</td>
<td>0.029</td>
<td></td>
</tr>
</tbody>
</table>

DESIGN: A retrospective cohort study.

MATERIALS AND METHODS: 539 infertile patients with a unicornuate uterus who underwent SBET or DCET from January 2012 to December 2017 were enrolled. SBET and DCET were performed in 156 and 383 patients, respectively. Only the first transfer cycle were considered. The reproductive outcomes were compared between these two groups. RESULTS: The two groups were statistically similar regarding age, body mass index and cause of infertility (p > 0.05), however, the infertility duration, infertility type and insemination methods were significantly different (p < 0.05).

Multivariate regression analysis showed a significantly lower implantation rate (47.9% vs. 57.7%), but markedly higher rates of clinical pregnancy (68.1% vs. 57.7%) and multiple pregnancy (41.4% vs. 3.3%) in the DCET group compared to the SBET group (p < 0.05). While the live birth rate was similar (52.0% vs. 47.4%, P = 0.451).

The DCET group was associated with statistically higher risks of preterm delivery (24.5% vs. 12.8%), low birth weight (31.7% vs. 11.1%), perinatal mortality (9.5% vs. 1.4%) and perinatal mortality at gestational age at delivery (36.8 ± 3.9 vs. 37.8 ± 2.8 weeks) compared to the SBET group (p < 0.05). While no significant difference was found in the miscarriage rate (19.5% vs. 15.1%, p = 0.378).

CONCLUSIONS: SBET could increase the implantation rate and decrease the risks of multiple pregnancy, preterm delivery and perinatal mortality, but with the same live birth rate as DCET. So SBET was recommended for women with a unicornuate uterus.

CONTRACEPTION/FAMILY PLANNING

P-490 Wednesday, October 16, 2019 6:30 AM

PREVALENCE, RISK FACTORS AND OBSTETRIC OUTCOMES OF ZYGOTIC SPLITTING AFTER SINGLE EMBRYO TRANSFER CYCLES. Romina Verdura, Physician, Maria Ayelen Demarco, Physician, Mercedes Papyannisd, BSc, Jimena Maidana, BSc, Mariana Gomez Peña, BSc, Claudio Bisioi, MSc, Guillermo Terrado Gil, MD, Fabio L. Sobral, Physician, Alejandro Oubiña, Physician, Laura J. Kopcow, Physician, Ignacio De Zuniga, Physician, Marcos Horton, Physician. Pregna Medicina Reproductiva, Buenos Aires, Argentina.

OBJECTIVE: To describe the prevalence, main determining factors and obstetric outcomes of multiple pregnancy due to zygotic splitting after single embryo transfer (sET).

DESIGN: We performed a retrospective observational study in 521 clinical pregnancies resulting from cleavage-stage or blastocyst single embryo transfer (sET) following IVF or ICSI cycles with autologous or donated eggs. Fresh and frozen-warmed sET from January 2015 to June 2017 were included, and analyzed for the occurrence of assisted hatching, embryo bi-opsy for PGT, or insemination type (IVF vs. ICSI). We also evaluated embryo grading, blastocyst expansion grade, and quality of embryo transfer.

MATERIALS AND METHODS: We retrospectively analysed all pregnancies achieved through single embryo transfers at our center. The population included IVF or ICSI cycles with autologous or donated eggs, and/or their subsequent frozen-thawed cycle. Monozygotic twinning was defined as 2 or more heart beats at 5-6 weeks ultrasound.

RESULTS: We analyzed 521 clinical pregnancies resulting from 1708 single embryo transfers in cleavage-stage (N=674) or blastocyst stage (N=1034). The overall MZT rate 2.87% (15/521), accounting for 0.87 % of cleavage stage derived pregnancies (1/115) and 3.45% of blastocyst stage derived pregnancies (14/406, p=0.01).

The incidence of MZT was higher with ICSI (14/368) compared to conventional IVF (1/153), although not statistically significant (P=0.08). In the blastocyst transfer group the incidence of MZT was not increased by Assisted Hatching (AH), Preimplantation Genetic Testing (PGT) nor was it affected by type of transfer, (either fresh or frozen) or quality/type of catheter used in the transfer.

Fifteen patients with MZT had 10 term deliveries with no neonatal complications, four of which had vanishing embryos, (one of them triple with a double vanishing embryo). One case had placenta accreta and underwent cesarean hysterectomy. Four patients miscarried, 2 in the first trimester and two in the second trimester (one due to cervical incompetence, and one voluntary interruption, due to a thoracopagus Siamese Twin pregnancy) Finally, one patient delivered at 30 weeks, with twin neonatal demise.

CONCLUSIONS: Although MZT is a rare event associated with ART it cannot be disregarded due to its potentially serious obstetric consequences, especially in a sET blastocyst transfer program. Monozygotic twinning is increased in blastocyst transfers, and special care should be taken to properly inform prospective parents when blastocyst are transferred.

P-491 Wednesday, October 16, 2019 6:30 AM

EFFECT OF SELF-ADMINISTERED LIDOCAINE IN-SITU GEL ON INTRAUTERINE DEVICE INSERTION PAIN: A RANDOMIZED CONTROLLED TRIAL. Ahmed M. Abbas, MD, a Shymaa Ali, MSc, b Noura H. Abd Ellah, PhD, a Omar M. Shaaban, MD, c Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; a Department of Obstetrics and Gynecology, Faculty of Medicine, Suez University, Suez, Egypt; c Department of Pharmacutics, Faculty of Pharmacy, Assiut University, Assiut, Egypt.

OBJECTIVE: Intrauterine contraceptive device (IUD) is a safe long-acting reversible contraceptive method. However, insertion-related pain presents a barrier to its widespread use in family planning. Our objective is to examine the analgesic effect of a novel self-administered lidocaine vaginal in-situ gel in alleviating pain during IUD insertion compared to placebo among parous women.

DESIGN: Randomized, double-blind, placebo-controlled trial (Clinical-trials.gov: NCT02943135).

MATERIALS AND METHODS: Reproductive-aged parous women requesting Copper-T 380 A IUD insertion for birth control were counseled to participate. Eligible women based on WHO guidelines were recruited and randomized (1:1) to lidocaine in-situ gel vs. placebo using a permuted

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block schedule. Ten minutes before IUD insertion, each participant self-injected the prefilled syringe with 5 ml lidocaine or placebo in-situ gel vaginally. Neither cervical ripening agents nor analgesics were used before the insertion. The main study outcomes were the participant’s self-rated pain perception utilizing a 10-cm Visual Analogue Scale (VAS) during cervical tenaculum placement, uterine sound and IUD insertion, then 15 minutes post-procedure. A 2 cm difference in VAS score between both arms was considered a clinically significant difference. The secondary outcomes included ease of insertion score, duration of insertion and need for additional analgesia. Mann Whitney and Fisher’s exact tests were utilized for analysis of these outcomes.

RESULTS: One hundred twenty women were enrolled and randomized to lidocaine in-situ gel arm (n = 60) or placebo (n = 58). Both arms were homogeneous regarding age, parity, BMI, and the prior mode of delivery. Lidocaine group reported significantly lower pain scores during tenaculum (median[IQR]: 2[1-2] vs 4[3-4], p < 0.001), uterine sound insertion (median[IQR]: 3[2-3] vs 5[4-6], p < 0.001), IUD insertion (median[IQR]: 2.3[2-3.75] vs 6[5.5-7], p < 0.001) and 15 minutes post-insertion (median[IQR]: 1[1-1.75] vs 2.5[2-3.75], p < 0.001). The ease score of IUD insertion was significantly higher in the lidocaine group (median[IQR]: 8[5-9] vs 7.5[6.25-8], p = 0.005). Additionally, the IUD insertion in the lidocaine group was associated with less time incomparable to the placebo group (mean±SD: 7.3±1.19 vs 8.75±1.11 minutes, p = 0.048). No difference regarding the need for additional analgesia.

CONCLUSIONS: self-administration of lidocaine in-situ gel 10 minutes before IUD insertion significantly reduces the induced pain with subsequent easier insertions.


SUPPORT: A fund No. (2016-11) received from The Institutional Grants' office.

P-492 Wednesday, October 16, 2019 6:30 AM

TREATMENT OF UNFAVORABLE BLEEDING PATTERNS IN CONTRACEPTIVE IMPLANT USERS. Katharine Simmons, MD, MPH, a Bliss Kaneshiro, MD, MPH, a Jennifer Hauschildt, CPH, a Kise Bond, BS, a PSM, a Jeffrey T. Jensen, MD, MPH, b Alison Edelman, MD, MPH, c The Permanente Medical Group, San Leandro, CA; aUniversity of Hawaii, Honolulu, HI; aOHSU, Portland, OR; aOregon Health & Science University, Portland, OR.

OBJECTIVE: Some users of the etonogestrel (ENG) subdermal contraceptive implant experience unfavorable vaginal bleeding patterns. We evaluated whether a 7-day treatment with oral tamoxifen could reduce the number of bleeding/spotting days in women using an ENG implant who have documented frequent and/or prolonged vaginal bleeding.

DESIGN: Randomized, placebo-controlled, double blind treatment study.

MATERIALS AND METHODS: Subjects started treatment if they experienced ≥ 5 days of consecutive bleeding/spotting (B/S) and could repeat treatment every 30 days if needed during the 90-day study interval. We collected a daily record of B/S using an interactive text messaging service. The primary outcome was the total number of B/S free days in the 30 days following first tamoxifen treatment; secondary outcomes included time to B/S cessation and restart with treatment and number of B/S free days over 90 days.

RESULTS: From January 2017 to November 2018, 112 women enrolled in the study, 107 completed at least 30 days, and 89 completed 90 days. The average subject was 23 years old, white, and had some college education. Women randomized to tamoxifen had more B/S free days in both the first 30 days [20 (SD 7) vs 15 (SD 7), p = 0.0001] and 90 days [57 (SD 17) vs 49 (SD 15), p = 0.026]. The tamoxifen group also had faster cessation of B/S with first treatment [6 (SD 4) vs 8 (SD 5), p = 0.037] and longer time before bleeding restarted [19 (SD 19) vs 8 (SD 8), p = 0.0001]. Study medications were well tolerated.

CONCLUSIONS: Treatment with oral tamoxifen reduces the duration of vaginal bleeding after one treatment as compared to placebo.

SUPPORT: Grant support for this research was from Merck Women’s Health Investigator Initiated Studies Program and the Oregon Clinical and Translational Research Institute (1 UL1 35RR024140 01) for access and use of REDCap electronic data capture system.

P-493 Wednesday, October 16, 2019 6:30 AM

A NOVEL IN VITRO FLUORESCENT REPORTER PLATFORM FOR IDENTIFYING MALE CONTRACEPTIVES. Krista Maye Symosko, B.S.; a Katherine A. Watkins, B.S.; a E. Rose Lawson, B.S.; a In Ki Cho, Ph.D., M.S.; b Anthony W. S. Chan, DVM, Ph.D.; b Charles A. Easley, IV, Ph.D., M.S.; aUniversity of Georgia, Athens, GA; bEmory School of Medicine, Atlanta, GA.

OBJECTIVE: Due to the challenges surrounding the development of male contraceptives, this study aimed to generate a high throughput testing platform to screen and identify potential male contraceptives.

DESIGN: To date, male forms of oral contraception have largely been ineffective. The current failures in developing male contraceptives stem from the lack of a robust, rapid, and unbiased human spermatogenesis platform. We previously developed a novel in vitro, human pluripotent stem cell model that mimics several aspects of human spermatogenesis.

MATERIALS AND METHODS: In order to address the challenges associated with male contraceptive development, we recently developed a novel in vitro fluorescent reporter platform, Testibow 1.0, that is coupled with our in vitro human spermatogenesis model. Testibow 1.0 is comprised of promoters for spermatogonia driving cyano fluorescent protein (cCFP) expression, promoters for primary spermatocytes driving green fluorescent protein (GFP) expression, and promoters for spermatids driving tdTomato expression. Since Testibow 1.0 utilizes fluorescence-based imaging, our model allows for the rapid identification of potential male contraceptives that successfully blocks spermatogenesis, but permits full restoration following treatment cessation.

RESULTS: Testibow 1.0 provides a unique, high content/high throughput imaging platform that can rapidly and efficiently identify novel compounds that could be used as male contraceptives regardless of genetic background. Currently, we are developing a polycistronic version of our fluorescent reporter system, Testibow 2.0, that will express all three of our fluorescent reporters simultaneously in order to begin identifying and characterizing chemical compounds that block spermatogonia differentiation or meiotic entry. Furthermore, our novel fluorescent reporter platform can be used to begin addressing the safety and efficacy challenges that are hindering male contraceptive development.

CONCLUSIONS: In conclusion, our fluorescent reporter system represents a suitable platform for evaluating the safety and effectiveness of potential male contraceptives prior to clinical trials.

SUPPORT: National Institutes of Health: K22ES025418 (Easley, Charles) and a Bill and Melinda Gates Grand Challenges Exploration Grant (Easley, Charles).

P-494 Wednesday, October 16, 2019 6:30 AM

POLIDOCANOL/DoxyCycline FOAM FOR NONSURGICAL PERMANENT FEMALE CONTRACEPTION: 6 MONTH DATA BABOON CONtraception STUDY. Jeffrey T. Jensen, MD, MPH, a Carol B. Hanna, Ph.D., a Shan Yao, M.D., b Emily Mishler, MS, a Daniel Chai, DVM, b Nicholas Mukaria Kiulia, MS, a Atunga Nyachieo, PhD, a D. Slayton, PhD aOregon Health & Science University, Portland, OR; aOregon National Primate Research Center, Beaverton, OR; aOregon National Primate Research Center, Beaverton, OR; aAffiliation not provided; aDepartment of Reproductive Health and Biology, Institute of Primate Research, Nairobi, Kenya; bProfessor, Portland, OR.

OBJECTIVE: Our goal is the development of a safe and low cost nonsurgical approach to permanent contraception for women with high efficacy following a single treatment. We previously reported that the addition of doxycycline to polidocanol foam increases the rate of tubal occlusion. Here, we sought to determine if a single transcervical administration of polidocanol/doxycycline foam (PDF) would prevent pregnancy in female baboons.

DESIGN: Controlled nonhuman primate cohort study.

MATERIALS AND METHODS: Healthy regularly cycling female baboons underwent laparoscopy with chromopertubation, for evaluation of
baseline tubal patency and pelvic adhesions, followed by transcervical infusion of either 20 mL of 5% PDF (each 5 mL of foam contains 25 mg doxycycline; n=12, 8 nulliparous, 4 parous), 20 mL of 1% control methylcellulose foam (MC; n= 6, 5 nulliparous, 1 parous), or no additional treatment (Control; n=6, all nulliparous). All of the females received an intramuscular injection of depomedroxyprogesterone acetate (DMPA, 2 mg/kg) after the treatment. After recovery, females were socially-housed with males (n=4) of proven fertility, and observed for resumption of menstrual cyclicity and evidence of mating. The primary outcomes was pregnancy within 6 months of resumption of menses. We plan to follow pregnancy and safety outcomes through 18 months in the PDF-treated animals, and evaluate histologic features of tubal occlusion.

RESULTS: The baseline laparoscopy demonstrated bilateral tubal patency in all of animals selected for the study. All females resumed normal menstrual cycles and mating activity within 3 months of treatment. After 6 months of regular cycles, 11/12 (92%) of control females became pregnant (6/6 MC control, 5/6 untreated control). Significantly fewer (2/12, 16%) pregnancies occurred in PDF-treated females (p < .001, Fisher’s exact test). All of the pregnancies were intrauterine. Both pregnancies in PDF-treated females occurred in nulliparous females - a group considered high-risk for failure. One progressed normally to term and one underwent spontaneous abortion.

CONCLUSIONS: A single transcervical treatment with PDF prevented pregnancy in most baboons. Pregnancy occurred in PDF-treated females considered at high risk of failure due to nulliparity.

SUPPORT: Bill and Melinda Gates Foundation OPP1025233, OPP1191953.

P-495 Wednesday, October 16, 2019 6:30 AM

PRE-REMOVAL PLASMA LEVONORGESTREL LEVEL AND RETURN OF FERTILITY AFTER LEVO-NORGESTREL 52 MG INTRAUTERINE SYSTEM DISCONTINUATION. Michael A. Thomas, MD, a
Gretchen S. Stuart, MD, MPH, b Carolyn L. Westhoff, MD, MSc, c
David L. Eisenberg, MD, MPH, b Andrea I. Olariu, MD, PhD, d
Mitchell D. Creinin, MD e University of Cincinnati, West Chester, OH; fAffiliation not provided; gColumbia University, New York, NY; hUniversity of California - Davis, Sacramento, CA.

OBJECTIVE: Evaluate return of fertility after levonorgestron (LNG) 52 mg intrauterine system (IUS) discontinuation according to pre-removal serum levonorgestrel levels.

DESIGN: Prospective clinical trial.

MATERIALS AND METHODS: Nulliparous and parous women 16-45 years old received the Liletta® LNG 52 mg IUS in an IRB-approved multicenter trial to evaluate efficacy and safety for up to 10 years. Participants in a pharmacokinetics sub-study had frequent plasma LNG evaluations over the first 3 years of the trial. All study subjects, beginning at 3 years of LNG IUS use, had plasma LNG evaluations every 6 months and at IUS removal (if no level had been obtained in the prior 3 months). Women who desired pregnancy were followed for up to 12 months for pregnancy occurrence. This analysis compares LNG concentrations at IUS discontinuation between women who did and did not conceive and evaluates time to conception, using Fisher’s exact and Mann Whitney U tests as indicated. We evaluated outcomes for women who conceived and did not conceive within 12 months of IUS removal. The majority of LNG levels among the 42 women who conceived within 3 months (124.5 pg/mL) after IUS discontinuation were similar to the 34 women who conceived at 4-12 months (103.5 pg/mL), p=0.23.

CONCLUSIONS: Plasma LNG levels were higher among women who conceived after LNG 52 mg IUS discontinuation compared to women who did not conceive. We found no evidence that higher LNG levels impact the ability to conceive or time to conceive following LNG 52 mg IUS removal.

SUPPORT: Medicines360.

P-496 Wednesday, October 16, 2019 6:30 AM

SELF-ADMINISTERED VAGINAL LIDOCAINE IN-SITU GEL PRIOR TO INTRAUTERINE DEVICE INSERTION IS AN EFFECTIVE ANALGESIC IN WOMEN WITH NO PREVIOUS VAGINAL DELIVERY. Ahmed M. Abbas, MD, a Noura H. Abd Ellah, PhD, b Meret Ayad, MSc, a Mohamed Abdellah, MD, b Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; cDepartment of Pharmacetics, Faculty of Pharmacy, Assiut University, Assiut, Egypt.

OBJECTIVE: Long-acting reversible contraception methods are highly effective for reduction of the unplanned pregnancy rate. The intrauterine device (IUD) can provide reliable, effective and long term contraception for many women. However, the insertion procedure can be associated with a troublesome degree of pain that prevent some women from choosing its use. Our objective is to assess the analgesic effect of self-administered vaginal lidocaine in-situ gel in pain relief during IUD insertion in women with no previous vaginal delivery.

DESIGN: Randomized, double-blind, placebo-controlled trial (Clinical-trials.gov: NCT03166111).

MATERIALS AND METHODS: Reproductive-aged women who previously delivered only by cesarean section (CS) requesting Multiload-375 Copper IUD insertion were counseled to participate. Eligible women category 1 or 2 based on WHO guidelines were recruited and randomized (1:1) to lidocaine in-situ gel vs. placebo using a permuted block schedule. Each woman was supplied by a syringe filled with 5 ml lidocaine or placebo in-situ gel to be self-administered vaginally 10 minutes prior to insertion. The primary outcome was the difference in pain scores during IUD insertion using a 10-cm Visual Analogue Scale (VAS). A 2 cm difference in VAS score between groups was considered clinically significant. The secondary outcomes included the difference in pain scores during cervical tenaculum placement, uterine sound insertion and 15 minutes post-procedure, ease of insertion score and need for additional analgesia. Mann Whitney and Fisher’s exact tests were used for the analysis of the outcomes.

RESULTS: The final analysis included 105 women randomized to lidocaine in-situ gel group (n=54) or placebo (n=51). Both arms were similar regarding age, parity, BMI, and a number of previous CS. Lidocaine in-situ gel group reported significantly lower pain scores during uterine sound insertion (median[IQR]: 3.5 [2-5] vs 6.5-8, p=0.001), IUD insertion (median[IQR]: 3.5[2-4.5] vs 5.5[4.75-7.5], p=0.002) and 15 minutes post-insertion (median[IQR]: 1.5[1-1.75] vs 4[2-4], p=0.03). No difference between scores during tenaculum placement (median[IQR]: 2.5[1.5-3] vs 3[2-4], p=0.07). The ease score of IUD insertion was significantly higher in the lidocaine group (median[IQR]: 8[7-9] vs 6.5[5.25-8], p=0.001). No difference regarding the need for additional analgesia.

CONCLUSIONS: Self-administered vaginal lidocaine in-situ gel 10 minutes prior to copper IUD insertion is effective in pain reduction in women with no previous vaginal delivery.

- SUPPORT: A fund No. (2016-1) received from The Institutional Grants’ office.
P-497 Wednesday, October 16, 2019 6:30 AM

WOMEN'S SATISFACTION WITH THE MULTIPURPOSE VAGINAL pH-REGULATOR (MVP-R; AMPHORA): RESULTS FROM THE PHASE 3 AMPower TRIAL. Michael A. Thomas, MD, a Kelly R. Culwell, MD, MPH, a Clint Dart, MS, b Brandi Howard, PhD, b University of Cincinnati, Cincinnati, OH; Evofem, Inc., San Diego, CA; Health Decisions, Durham, NC.

OBJECTIVE: As a multipurpose vaginal pH regulator, Amphora® is a novel, non-hormonal, woman-controlled, on-demand, contraceptive vaginal gel being investigated for prevention of pregnancy and sexually transmitted diseases. To better understand the treatment experience from the woman’s perspective, the Satisfaction Questionnaire was administered in the phase 3 AMPower trial (NCT03243305).

DESIGN: The phase 3 AMPower trial is a single-arm, open-label study designed to evaluate the efficacy and safety of and women’s satisfaction with Amphora over 7 cycles in sexually active women aged 18-35 years across 112 US sites. The primary efficacy endpoint was the cumulative 7-cycle pregnancy rate. Women’s satisfaction with Amphora was an exploratory endpoint.

MATERIALS AND METHODS: The Satisfaction Questionnaire was given at baseline and the subsequent study visits to assess women’s satisfaction in 4 categories: 1) satisfaction with most recent/study birth control method; and likelihood of 2) recommending this method to others considering a contraceptive vaginal gel, 3) recommending this method to others considering another birth control option, and 4) continuing this method after study termination.

RESULTS: 1330 women were included in the Satisfaction Questionnaire. At Visits 3 (Cycle 2) and 4 (Cycle 5 or 6), more women reported being “very satisfied” or “satisfied” with the study method (85.3% [954/1118] and 89.5% [734/820], respectively), compared with their previous birth control method before enrollment (46.5% [616/1325]). At Visits 3 and 4, 86.6% (968/1118) and 89.8% (736/820) of women, respectively, were “very likely” or “likely” to recommend the study drug as a contraceptive vaginal gel, and as an alternative birth control option (85.7% [958/1118] and 88.2% [723/820], respectively) to others. 82.1% (918/1118) and 81.0% (664/820) of women surveyed at Visits 3 and 4, respectively, were “very likely” or “likely” to continue with Amphora if it were to be available, compared with 2.2% (25/1118) and 3.2% (26/820) of women who were “unlikely” to continue.

CONCLUSIONS: Data from the phase 3 AMPower trial indicate a very high level of satisfaction in women on Amphora compared with their previous birth control method; ≥85% of women on Amphora would recommend the study drug to others, and ≥80% of women were in favor of continuing with Amphora after study termination. Amphora has the potential of fulfilling an unmet need in women’s sexual and reproductive health as a non-hormonal, woman-controlled, on-demand, contraceptive vaginal gel.

SUPPORT: Evofem Inc.

P-498 Wednesday, October 16, 2019 6:30 AM

REPRODUCTIVE AGED WOMEN ARE INTERESTED IN SELF-ADMINISTERED VAGINAL CONTRACEPTIVES THAT PREVENT SEXUALLY TRANSMITTED INFECTIONS. Emily G. Hurley, MD, a Giovanni Pauletti, PhD, a Michael A. Thomas, MD, b University of Cincinnati, West Chester, OH; University of Cincinnati, Cincinnati, OH.

OBJECTIVE: To develop a better understanding of women’s knowledge of and desire for pregnancy and sexually transmitted infection (STI) prevention. Women’s perspectives may help guide future development of new innovative products.

DESIGN: Questionnaire-based observational study.

MATERIALS AND METHODS: An IRB approved electronic survey investigating women’s opinions on contraceptive choice and STI prevention was distributed at women’s health clinics at the University of Cincinnati. Participation was voluntary and responses remained anonymous. The descriptive data were analyzed using percentages and medians.

RESULTS: One hundred and five surveys were completed. Participants ranged from 18-45 years of age (median 29, IQR 26, 33). The majority of participants were non-Hispanic white (82.9%) and sexually active (88.6%). Approximately 83.7% were sexually attracted to men, while 7.7% were attracted to females and 8.7% were attracted to both. A history of an unintended pregnancy was reported by 26.7% of all participants and 20.0% had previously been diagnosed with an STI. In participants who were sexually attracted to men or both genders, 94.8% had used some form of contraception, including a hormonal pill (83.5%), barrier method (68.1%) or an intrauterine device (30.8%). Approximately 35.1% reported consistently using a method to prevent STIs, of which, 100% used male condoms. When asked if one felt empowered to choose her desired contraceptive method, 8.2% said no and 7.2% said they were unsure. Approximately 13.4% of participants reported that they feel pressured by their partner to not use contraception and 21.6% feel pressured by their partner to not use protection against STIs. When participants were asked if they were interested in using a self-administered, discrete product that could both prevent pregnancy and STIs, 38.5% responded yes and 31.3% were unsure.

CONCLUSIONS: In women sexually attracted to men, nearly two-thirds do not routinely use STI prevention and some feel pressured by their partner not to use contraception/condoms. This makes women more vulnerable for unwanted infections and pregnancy. Because of this, there is a role for discretely self-administered female contraceptive products that also prevent STIs.

SUPPORT: University of Cincinnati Office of Research Strategic Collaborative Grants Program.

P-499 Wednesday, October 16, 2019 6:30 AM

THE EFFECT OF DIFFERENT PROGESTOSTERONE ONLY CONTRACEPTIVE METHODS ON FEMALE SEXUAL FUNCTION IN THE FIRST-TIME USERS: A CROSS SECTIONAL STUDY. Mohammed Khairy Ali, MD, Ahmed M. Abbas, MD, Ali Shouman, MB BCH, Ahmed M. Abdelmagied, MD, Alaa A. Makhlof, MSc, Mostafa Nazeer Ibrahim, MD, Ahmed Makhlof, MD Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt.

OBJECTIVE: The progesterin-only contraceptive (POC) methods are used frequently by women in the childbearing period. However; these methods are associated with female sexual dysfunction (FSD) especially injectables. There are potential predictors associated with FSD among POC users which should be put in the consideration during counseling for POC use. Our objective is to assess the female sexual function (FSF) in three POC methods among first-time users.

DESIGN: Cross-sectional study (Clinicaltrial.gov:NCT02579590).

MATERIALS AND METHODS: We included married women between 20-40 years with a heterosexually active relationship lasting for longer than four weeks. They were using one of the POC methods for at least six months for contraception only. Those women were first-time users with regular menstrual pattern, amenorrhea or even with minimal vaginal spotting not affecting the sexual life. The enrolled women were classified into four groups; non contraceptive users (group I), Depot Medroxyprogesterone Acetate 150 mg (DMPA) injection (group II), etonogestrel 68 mg subdermal implant (group III) and desogestrel 75 µg oral pills (group IV) users for the first time. All participants were asked to complete the Arabic form of the female sexual function index (ArFSFI). A total score of less than or equal to 28.1 points was determined as FSD. The main outcome of the study was to identify the prevalence of FSD among those users. The predictors associated with FSD among POC users were also explored. The data were analyzed using ANOVA, Chi-square test and the logistic regression model.

RESULTS: Four hundred forty-four women consented to participate and divided into two groups; 222 women were non contraceptive users, and 222 women were POC users (88 women were DMPA users, 87 women were etonogestrel implant users and 47 women were desogestrel containing pills users). All groups (non contraceptive users and POC users) were homogeneous in the baseline data. The mean ArFSFI score was significantly lower in POC users than non-contraceptive users (26.92±1.88 Vs. 27.42±2.02, p=0.006; respectively). The mean ArFSFI score was significantly lower in DMPA users in comparison to etonogestrel implant and desogestrel pills users (26.46±1.75, 27.13±1.89, 27.37±1.93, p=0.010; respectively). Furthermore; the number of women with FSD was significantly higher in DMPA users in comparison to other users (68 women; 77.2%, 44 women; 50.5%, 16 women; 34.0%; p=0.000; respectively). The baseline characteristics that were revealed from the regression model and significantly associated
with a higher likelihood of FSD with POC were circumcision (p = 0.001), parity > 3 times (p = 0.015) and duration of use > 12 months (p = 0.022). A ROC curve analysis in the predictive model demonstrated that circumcision yielded the highest sensitivity (82.84%) while the parity > 3 times had the lowest one (59.76%) and the duration of use > 12 months had a sensitivity of 60.36%.

CONCLUSIONS: There is a high prevalence of FSD in POC users especially DMPA users. The circumcision, parity > 3 times and > 12 months of use are potential significant predictors of FSD in POC users.

SUPPORT: None.

P-500 Wednesday, October 16, 2019 6:30 AM

CHINA FEMALE CONDOM (FCc) FUNCTIONALITY STUDY AGAINST AN EQUIVALENT MARKETED FEMALE CONDOM (FC2). Yimin Cheng Sr., M.D., National Research Institute for Family Planning, Beijing, China.

OBJECTIVE: To compare the differences of the rates of total clinical failure and four types of failures (Inagination, Misdirection, Slippage and Breakage) between two kinds of female condoms (FC) [China made FC (FCc) and USA made FC (FC2)] as well as to assess weather every failure of four rates is accord with the standard of WHO.

DESIGN: Prospective, double-blind randomized controlled.

MATERIALS AND METHODS: 300 participants were recruited. A computer-generated randomization sequence was used to assign the 300 participants to one of two groups (1:1). Group A used 5 FCcs first, followed by 5 FC2s. Group B used 5 FC2s first, followed by 5 FCcs. The FC is made from synthetic nitrile material and is manufactured by the Female Health Company (Chicago, IL, USA). The FCc is made of polyurethane and has a dumbbell shape. It is manufactured by Tianjin CondomBao Medical Polyurethane Tech. Co. (Tianjin, China).

RESULTS: The rate of loss to follow-up was 4.2% for FCc and 2.8% for FC2. The total clinical failure rate of FCc was 0.9% (95% confidence interval 0.5 – 1.3%) compared to 1.1% (95% confidence interval 0.7 – 1.5%) for FC2. The upper bound of the one-sided 95% confidence interval for FCc total clinical failure rate, minus the FC2 total clinical failure rate is equal to 0.2% (1.5% – 1.3% > 0.2%). The difference of the total clinical failure rates (1.1% vs 0.9%) between FCc and FC2 was statistically non-significant (P > 0.05). No breakage was found both in FCc users and in FC2 users. The failure rates of invagination, misdirection and slippage of FCc were 1.3%, 1.3% and 1.1% respectively. The failure rates of invagination, misdirection and slippage of FC2 were 1.8%, 0.1% and 2.5% respectively. The difference of slippage rates (2.5% vs 1.1%) was statistically non-significant (P > 0.05) between FC2 and FCc as well as the slippage rate of FCc was lower than the standard of WHO although the slippage rate of FC2 was slightly higher than that of FCc and slightly higher than the standard of WHO. The difference of invagination rates (1.8% vs. 1.3%) was also statistically non-significant (P > 0.05) between FC2 and FCc. Although the rate of misdirection for FCc was higher than that for FC2 (1.3% vs. 0.1%) and although the difference of the misdirection rates between two groups was statistically significant, but the rate of misdirection for FCc (1.3%) is lower than that of WHO standard (1.5%).

CONCLUSIONS: (1) The results indicated that the total clinical failure rate of FCc is non inferior to the total clinical failure rate of FC2; (2) The rates of four types of failure (Invagination, Misdirection, Slippage and Breakage) for FCc was that every failure rate is lower than the standard of WHO. (3) The upper bound of the one-sided 95% confidence interval for FCc total clinical failure rate, minus the FC2 total clinical failure rate is less than 3% (1.5% – 1.3% > 0.2%).

SUPPORT: National Research Institute for Family Planning provided financial support for this research.

P-502 Wednesday, October 16, 2019 6:30 AM

RETURN TO FERTILITY AFTER 1-YEAR USE OF A SEGESTERONE ACETATE/ETHINYL ESTRADIOL CONTRACEPTIVE VAGINAL SYSTEM USE. Ginger Constantine, MD,a Kurt T. Barnhart, MD, MSCE,b Anne E. Burke, MD, MPH,c Ruth B. Merkatz, PhD,d Shelli Graham, PhD,a Brian Bernick, MD,a Sebastian Mirkin, MD,e “Endo-Rheum Consultants, LLC, Malvern, PA; bUniversity of Pennsylvania, Perelman School Of Medicine, Philadelphia, PA; cJohns Hopkins School of Medicine, Baltimore, MD; dPopulation Council, New York, NY; eTherapeuticsMD, Boca Raton, FL.

OBJECTIVE: To assess the return to menstruation and/or fertility in a subset of women who used a contraceptive vaginal system (CVS; approved by the FDA in August 2018) releasing a daily mean of segesterone acetate (SA) 0.15 mg and ethinyl estradiol (EE) 0.013 mg for up to 13 cycles.

DESIGN: Two multicenter, single-arm, open-label, pivotal, phase 3 studies of the SA/EE CVS; one US-only study (15 US sites) and one international study (5 in the US; 3 in Europe; 3 in Latin America, 1 in Australia).

MATERIALS AND METHODS: Women used the same SA/EE CVS on a 21/7-day in/out regimen for up to 13 cycles. Those who wished to become pregnant after the completion of the 13 cycles could participate in a 6-month follow up for return to fertility. Women were instructed to perform a urine pregnancy test within 2-3 weeks following their last visit and then monthly if they experienced pregnancy symptoms and/or did not have a bleeding episode. Women were contacted every 2 months for pregnancy, menses, and contraceptive use information. Women who were pregnant returned to the clinic for pregnancy confirmation and a prenatal care referral. Bleeding <18 days after last CVS use was considered Poor compliance with providing a post vasectomy semen analysis (PVSA) has previously been reported in both the Family Medicine and Urologic literature, with rates ranging from 34-46%. Reasons for poor compliance with PVSA are not well described. Only one prior study was identified that examined the socioeconomic factors related to poor compliance. We sought to further characterize this population by examining the pre operative characteristics of patients of a large volume vasectomy surgeon that were predictive of failure to provide a PVSA.

DESIGN: A retrospective, single institution chart review

MATERIALS AND METHODS: Records were reviewed from April 2015 to April 2018, which identified 1137 patients who underwent vasectomy by a single surgeon. Patients who underwent vasectomy for non-fertility related reasons were excluded. Other exclusion criteria included requiring in vitro fertilization to conceive prior to the procedure. Patient characteristics analyzed include age, race, marital status, insurance type, and number of children. Univariate and multivariate logistic regression were performed to compare our two cohorts and to assess for factors predictive of post vasectomy compliaance.

RESULTS: 1,137 patients underwent vasectomy. The average age was 37.5 years. 89.5% and 88.7% of the patients were White/Caucasian and married, respectively. 27.5% of patients did not follow up for PVSA at any interval. Age was similar between patients who did and did not submit a PVSA (37.8 vs 37.3 years). However race, marital status, and insurance did differ, as patients in the no PVSA cohort were more likely to be African American (8.3% vs 3.7%), single (15.3% vs 9.7%) and have Title 19/Medicaid (2.9% vs 1.2% of insurance coverage). On multivariate analysis only relationship status was independently predictive of failing to present for post vasectomy semen analysis (RR 1.86, p = 0.02). Age (RR 1.02, p = 0.08) and increasing number of children (RR 1.11, p = 0.09) approached significance.

CONCLUSIONS: A significant percentage of patients do not provide a PVSA confirming sterility, with single relationship status being most predictive of noncompliance when controlling for all other preoperative variables. As with all vasectomy patients, counseling these patients that they are not sterile until proven with a PVSA is paramount.


SUPPORT: N/A.

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RISK FACTORS FOR NON-COMPLIANCE IN POST VASECTOMY FOLLOW UP. Johnathan Doolittle, MD, Peter N. Dietrich, MD, Pranav Dadhich, MD, Sarah M. Brink, BS, Daniel Roadman, BS, Kayvon Kiani, BA, G. Luke Machen, MD, Jay I. Sandlow, MD. Medical College of Wisconsin, Milwaukee, WI.

OBJECTIVE: Vasectomy is regarded as the most effective mode of birth control, with over half a million performed annually in the United States.
EARLY PREGNANCY

OBJECTIVE: It has been suggested that Non-invasive Prenatal Testing (NIPT) based on the analysis of cell-free placental DNA (cf-DNA) is less accurate in patients conceiving via assisted reproduction technologies (ART) than in those with natural conception (NC). In this study, we are investigating in a larger clinical sample whether this assumption is correct.

DESIGN: Cohort study.

MATERIALS AND METHODS: A total of 17,735 patients were included in this retrospective study. Patients were divided in two groups, natural conception (NC) (n=13,108) and ART (n=4,627). The ART group was divided in those using their own oocytes (OO)(n=3,107) or using oocyte donation (OD)(n=1,520). NIPT by massively parallel sequencing to assess chromosome aneuploidy for 13, 18, 21 and sex chromosomes was offered to the patients past 10 weeks of gestation, in addition to conventional prenatal screening. NIPT was performed by using the Illumina’s technology platform. Abnormal results rates, false positive rates, mean fetal fraction (FF) and rates to the patients past 10 weeks of gestation, in addition to conventional prenatal screening. NIPT was performed by using the Illumina’s technology platform. Abnormal results rates, false positive rates, mean fetal fraction (FF) and rates of samples with FF<4% as a parameter indicating the percentage of samples with non-informative results were compared among all groups. For quantitative data, pairwise comparison using t-test with non-pooled SD (P value adjustment method: Bonferroni) was applied. In order to compare qualitative data Chi-square test (with Yates correction) was performed.

RESULTS: Our study population consisted of 212 women (mean age 30.6). The majority of women were employed (89%), insured (94%), college educated (72%), and had no living children (79%). Only 16% of participants reported prior discussion with a provider about age-based fertility, and 44% reported this topic made them feel anxious. Following an educational intervention, 68% of all participants, and 79% of participants who desire more children, reported it would be helpful to discuss age-based fertility in office visits (Table 1). Women were significantly more likely to report learning from the intervention if they were <35 years old (OR 2.41; 95% CI 1.16, 5.00) or had public insurance (OR 2.29; 95% CI 1.04, 5.07).

CONCLUSIONS: A minority of women are discussing the role of age on fertility with providers. This study suggests a potential role for counseling in well-women visits to assist women with reproductive planning. Women under age 35 or enrolled in public insurance are most likely to benefit from education on age-based fertility.

### Table 1. Survey responses regarding age-based fertility prior to and following an educational intervention.

<table>
<thead>
<tr>
<th>Baseline data</th>
<th>Desires future children, % respondents</th>
<th>Childbearing complete, % respondents</th>
<th>Undecided, % respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age-based fertility: Have discussed this with a healthcare provider</td>
<td>16% (17/104)</td>
<td>15% (9/59)</td>
<td>17% (8/46)</td>
</tr>
<tr>
<td>Would like to discuss this*</td>
<td>41% (41/101)</td>
<td>5% (3/59)</td>
<td>32% (15/47)</td>
</tr>
<tr>
<td>Would like more information*</td>
<td>52% (54/103)</td>
<td>7% (4/59)</td>
<td>26% (12/46)</td>
</tr>
<tr>
<td>Following intervention Learned something new</td>
<td>71% (72/102)</td>
<td>65% (37/57)</td>
<td>66% (29/44)</td>
</tr>
<tr>
<td>Plan to discuss with partner/family*</td>
<td>46% (47/103)</td>
<td>7% (4/54)</td>
<td>27% (12/44)</td>
</tr>
<tr>
<td>Considering changing reproductive plans*</td>
<td>13% (13/102)</td>
<td>2% (1/55)</td>
<td>23% (10/44)</td>
</tr>
<tr>
<td>Feel it would be helpful to discuss at routine visits*</td>
<td>79% (81/102)</td>
<td>45% (25/56)</td>
<td>73% (32/44)</td>
</tr>
</tbody>
</table>

* = p<0.01
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IDENTIFICATION OF EARLY PLACENTAL HORMONE PRODUCTION IN PROGRAMMED EMBRYO TRANSFER CYCLES. Robert Seiton, MD, a Kelly McCarter, MD, a Lilli D. Zimmerman, MD, a Zev Rosenwaks, MD, a Steven Spandorfer, MD, a,b The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY; b Weill Cornell Medicine, New York, NY.

OBJECTIVE: There is a dearth of literature describing the onset of early placental steroidogenesis and the initiation of the luteal-placental shift. Patients undergoing programmed frozen-thawed embryo transfer (FET) or donor-egg recipient (DER) cycles offer a unique model to study this phenomenon, as these patients lack a corpus luteum. In this study we sought to identify the initiation of placental hormonal production as defined by the production of endogenous estradiol (E2) and progesterone (P4) in a cohort of patients undergoing programmed cycles with single embryo transfers resulting in liveborn singletons.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Patients undergoing programmed FET with autologous oocytes or DER cycles were screened for inclusion. Only patients who underwent a single embryo transfer, had a single gestational sac, and a resultant liveborn singleton were included. All patients were treated with E2 patches changed every other day and intramuscular progesterone injections daily. Main outcome measures were serial E2 and P4, with median values calculated for cycle days 28 (baseline) through 60. The baseline cycle day-28 median value was compared to each daily median cycle day value using the Wilcoxin Signed Rank test. P<0.05 was deemed statistically significant.

RESULTS: A total of 696 patients, 569 using autologous oocytes or DER cycles were screened for inclusion. Only patients who underwent a single embryo transfer with a resultant single sac and a resultant liveborn singleton were included. All patients were treated with E2 patches changed every other day and intramuscular progesterone injections daily. Main outcome measures were serial E2 and P4, with median values calculated for cycle days 28 (baseline) through 60. The baseline cycle day-28 median value was compared to each daily median cycle day value using the Wilcoxin Signed Rank test. P<0.05 was deemed statistically significant.

CONCLUSIONS: These results demonstrate that endogenous placental estradiol and progesterone production occur by cycle day 36 and cycle day 48 respectively, earlier than traditionally thought. These findings also suggest estradiol and progesterone production occur by cycle day 36 and cycle day 48 respectively, earlier than traditionally thought. These findings also suggest endogenous estradiol (E2) and progesterone (P4) in a cohort of patients undergoing programmed cycles with single embryo transfers resulting in liveborn singletons.

SUPPORT: None.

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CHALLENGING CURRENT VIEWS: A PROSPECTIVE SERIES OF ANGULAR PREGNANCIES MANAGED EXPECTANTLY. Kassie Jean Bollig, MD,a Danny I. Schust, MD, a Shvetha M. Zarek, MD,a Albert L. Hsu, MD,a Resident Physician, Columbia, MO; University of Missouri School of Medicine, Columbia, MO; Department of Reproductive Endocrinology and Infertility, Columbia, MO; Department of Reproductive Endocrinology and Infertility, University of Missouri, Columbia, MO.

OBJECTIVE: To describe the natural history and outcomes of the largest cohort of expectantly managed angular pregnancies diagnosed by specific ultrasound criteria.

DESIGN: Prospective case series.

MATERIALS AND METHODS: This was a prospective case series of women with prenatally diagnosed angular pregnancy at a single, academic, tertiary care center from March 2017 to February 2019. Participants were identified at a first-trimester ultrasound scan using specific ultrasound criteria.

RESULTS: A total of 4,071 patients with live singleton births were included. The median age, body mass index (BMI), E2 level and birth weight for the study cohort was 36 (33-39) years, 22.3 (20.4-25.0) kg/m², 1,554 (1,112.7-2,179) pg/mL, and 3,289 (2,920-3,628) grams respectively. Singletons in the 4th E2 quartile (8.56 mm) had a smaller CRL compared to all other E2 quartiles. The rate of LBW rose from 6.4% (E2 2,001-2,500 pg/mL) to 20.7% (E2 3,501-4,000 pg/mL), without a corresponding rise in the rate of PTB. The odds of term LBW with E2 >2,500 pg/mL were 6.1-7.9 times higher compared to the median E2. Peak E2 level was a weak predictor of LBW (AUC =0.64), but a strong predictor of LBW (AUC=0.86).

CONCLUSIONS: The results of the current study suggest that the hyperestrogenic milieu of ovarian stimulation can adversely impact early embryonic growth and ultimately perinatal outcomes. Our results emphasize the importance of minimizing the supraphysiologic elevations of E2 levels in fresh IVF-ET cycles to optimize the early peri-implantation environment and mitigate adverse perinatal outcomes.

SUPPORT: None.

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DOES THE HYPERESTROGENIC MILIEU IN FRESH IN VITRO FERTILIZATION CYCLES IMPACT EARLY EMBRYONIC GROWTH? Nigel Pereira, MD,a Nirali J. Shah, MD,a Isaac Kligman, M.D., a Zev Rosenwaks, M.D. a Ronald O. Perlman and Claudia Cohen Center for Reproductive Medicine, New York, NY; Weill Cornell Medicine, New York, NY; a The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, New York, NY.

OBJECTIVE: Recent studies have suggested that the hyperestrogenic milieu generated during ovarian stimulation may create a suboptimal peri-implantation environment, leading to adverse perinatal outcomes. In this study, we investigate whether supraphysiologic estradiol (E2) impacts early embryonic growth in vitro fertilization (IVF)-embryo transfer (ET) cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Normal responder patients, <40 years old, undergoing fresh IVF-ET cycles resulting in live singleton births were included. Patients with PCOS, multiple births, vanishing twins, or unknown perinatal outcomes were excluded. The primary outcome of interest was crown-rump length (CRL) at 7 to 8 weeks of gestational age. Secondary outcomes recorded were low birth weight (LBW, <2500 grams), pre-term birth (PTB, <37 weeks of gestation) and birth weight. Primary and secondary outcomes were assessed according to peak E2 quartiles. Receiver-operator-characteristic (ROC) curves were constructed for outcomes showing statistical significance.

RESULTS: A total of 4,071 patients with live singleton births were included. The median age, body mass index (BMI), E2 level and birth weight for the study cohort was 36 (33-39) years, 22.3 (20.4-25.0) kg/m², 1,554 (1,112.7-2,179) pg/mL, and 3,289 (2,920-3,628) grams respectively. Singletons in the 4th E2 quartile (8.56 mm) had a smaller CRL compared to all other E2 quartiles. The rate of LBW rose from 6.4% (E2 2,001-2,500 pg/mL) to 20.7% (E2 3,501-4,000 pg/mL), without a corresponding rise in the rate of PTB. The odds of term LBW with E2 >2,500 pg/mL were 6.1-7.9 times higher compared to the median E2. Peak E2 level was a weak predictor of LBW (AUC =0.64), but a strong predictor of LBW (AUC=0.86).

CONCLUSIONS: The results of the current study suggest that the hyperestrogenic milieu of ovarian stimulation can adversely impact early embryonic growth and ultimately perinatal outcomes. Our results emphasize the importance of minimizing the supraphysiologic elevations of E2 levels in fresh IVF-ET cycles to optimize the early peri-implantation environment and mitigate adverse perinatal outcomes.

SUPPORT: None.

### Table: Outcomes in the General Population

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Outcomes a (% Proportion)</th>
<th>Outcomes b (% Incidence)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Deliveries</td>
<td>21 (51.2)</td>
<td>-</td>
</tr>
<tr>
<td>Spontaneous Vaginal Deliveries</td>
<td>15 (71.4)</td>
<td>68.1</td>
</tr>
<tr>
<td>Low Transverse Cesarean Section</td>
<td>6 (28.6)</td>
<td>31.9</td>
</tr>
<tr>
<td>Term Delivery</td>
<td>17 (81.0)</td>
<td>88</td>
</tr>
<tr>
<td>Preterm Delivery</td>
<td>4 (19)</td>
<td>12</td>
</tr>
<tr>
<td>Miscarriage</td>
<td>7 (37.1)</td>
<td>10</td>
</tr>
<tr>
<td>Continuing Gestations</td>
<td>13 (31.7)</td>
<td>-</td>
</tr>
</tbody>
</table>
diagnostic criteria of an angular pregnancy and followed expectantly. Diagnostic criteria included 1) Nonanomalous uterus; 2) Implantation of the embryo in the lateral angle of the uterine cavity; 3) ≤1 cm of myometrial thickness surrounding the gestational sac; 4) Presence of completely circumferential endometrial circumference around the gestation; and 5) Lack of an “interstitial line sign.” Maternal and fetal data were gathered from the medical record.

RESULTS: Forty-two cases of angular pregnancy were identified at first-trimester ultrasound. At presentation, 33 patients (78.6%) were asymptomatic, eight (19.0%) had vaginal bleeding, and two (4.8%) had pain. The mean gestational age at diagnosis was 7.4 ± 1.0 weeks, and the mean myometrial thickness was 5.1 ± 1.6 mm (95% CI 4.6-5.6). At initial follow up, 23 cases (54.8%) had resolved, 13 cases (31.0%) persisted as angular pregnancies, and six cases (14.3%) resulted in miscarriage. Three cases (7.1% of total) that persisted had decreased myometrial thickness. At final follow up, 21 (51.2%) deliveries resulted in a live birth, seven (17.1%) in miscarriage, and 13 (31.7%) were continuing gestations. In cases of live birth, 15 (71.4%) were vaginal deliveries, six (28.6%) cesarean sections, 17 (81.0%) term deliveries, and four (19.0%) preterm deliveries. There were no cases of uterine rupture, maternal death, abnormal placentation, or hysterectomy.

CONCLUSIONS: In 42 cases of angular pregnancy diagnosed by first-trimester ultrasound, all but eight resolved with continued follow up. Outcomes were largely positive with a 51.2% live birth rate, 17.1% miscarriage rate, and 31.7% continuing pregnancy rate. Angular pregnancy may represent a clinical entity that more closely resembles a normal, non-ectopic intrauterine pregnancy rather than an ectopic pregnancy. Therefore, most cases can be safely observed, and efforts should be made to expectantly manage gestations while awaiting viability.

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INFLUENCE OF ASSISTED REPRODUCTIVE TECHNOLOGY (ART) ON EARLY FETAL GROWTH KINETICS. Audrey M. Mansidi, MD, a Caroline Violette, Bachelor of Science, b Victoria S. Jiang, MD, a Audrey J. Gaskins, ScD, a Jessica B. Spencer, MD, MSc, a Carolyn Drews-Botsch, Ph.D, MPH. a Emory University School of Medicine, Department of Gynecology and Obstetrics, Atlanta, GA; b Emory University School of Medicine, Atlanta, GA; c Emory University, Rollins School of Public Health, Atlanta, GA.

OBJECTIVE: The aim of this study was to evaluate variations in embryonic size early in pregnancy and to investigate if in vitro fertilization (IVF) is associated with significant differences in crown rump length (CRL) prior to 7 weeks gestation. This work may lay the foundation for understanding the way in which assisted reproductive technology (ART) might impact embryonic and fetal growth dynamics, as well as the implications for adverse pregnancy outcomes.

DESIGN: Retrospective cohort study of data from an academic IVF practice between January and December 2017.

MATERIALS AND METHODS: Our study population included 88 patients undergoing a transvaginal ultrasound at 6-7 weeks gestation following fertility treatment with intratubal insemination, timed intercourse with use of a trigger injection, or IVF (only when exact date of conception was known). Only women with singleton, intrauterine pregnancies with cardiac activity present were included. Patients with multiple gestations, spontaneous conception, or with first trimester miscarriage were excluded. At the time of the ultrasound, CRL, fetal heart rate, and average ultrasound age (AUA) were calculated. Fetal size was measured as CRL, and the difference between AUA and gestational age was calculated. The distribution of embryonic size was evaluated assuming a normal distribution of CRL. Differences in fetal size were evaluated using ANOVA to account for differences in age at scan. Deviations in AUA from expected gestational age were evaluated using student’s t-test.

RESULTS: Approximately half (58%) of women in our cohort were non-Hispanic White and 27% were African American. The majority of women became pregnant through IVF (66%) with the rest resulting from IUI (27%) or timed intercourse (7%). Even within this relatively limited age range, there was variation in CRL. Among 20 ultrasounds performed at 47 days, the mean ±standard deviation (SD) CRL was 0.73 (0.13) cm but the smallest embryo was 0.37 cm and the largest was 0.96 cm. After accounting for gestational age at ultrasound, pregnancies conceived through IVF were slightly smaller, on average, than other pregnancies (mean ±SD 0.56 ±0.22 versus 0.62 ±0.24), but this difference was not statistically significant (p=0.27). IVF pregnancies achieved using fresh embryos were slightly larger (0.08 ±0.05 cm) than those using frozen embryos, but this too was not statistically significant (p=0.13).

CONCLUSIONS: Early ultrasound is the gold standard for dating pregnancies despite known variation in these measures, even in early pregnancy. The degree to which this variation reflects variation in embryonic size, measurement error, and/or error in estimating date of conception is unknown. In this study, we confirmed that even after accounting for timing of conception, substantial variation in fetal size remains, even between 6-7 weeks gestation. Furthermore, the method of conception may be one factor associated with variation in early embryo growth. Further research is needed to determine if this variation in early embryo size is associated with later pregnancy outcomes such as preeclampsia and/or fetal growth.
RESULTS: Using quantitative RT-PCR, the mean fold increase in expression of CGB in endometrial samples of non-visualized IUP (n=5) compared to non-pregnant endometrium, was 20.2 (±2.0), which was significantly greater (p<0.01 by t-test) than the 8.0 (±2.8) fold-increased observed in EP.

CONCLUSIONS: The early trophoblast biomarker CGB is detectable in uterine aspirates of non-visualized presumed IUP at a large threshold difference compared to endometrium from EP. This is consistent with localized CGB expression by the invasive syncytiotrophoblast. This preliminary data suggests that molecular targets to specific early placental markers could be utilized for diagnosis of pregnancy location after direct endometrial sampling.

SUPPORT: This work has been supported by the Society of Family Planning Research Fund SFPRF11-J11 and by the NIH Women’s Reproductive Health Research Program (K12HD085809).

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PREDICTION OF PREGNANCY OUTCOME IN WOMEN WITH FIRST TRIMESTER BLEEDING BY THE DETECTION OF ALPHA-FETOPROTEIN (AFP) IN VAGINAL BLOOD. Amir Mor, MD PhD, a Karen Jubyanyk, MD, b Mursal Gardezi, BSc, b Stephanie M. Nichols-Burns, PhD. b Man Zhang, MD PhD. b Ecem Esenca, MD, M.A. b Burcin Simsek, Ph.D. b David B. Seifer, MD. b Hugh S. Taylor, M.D. d Yale School of Medicine, New Haven, CT. 1University of Pittsburgh, Pittsburgh, PA; 2Yale University, New Haven, CT; 3Yale University School of Medicine, New Haven, CT.

OBJECTIVE: We previously published that high concentration of alpha-fetoprotein (AFP) in vaginal blood confirms the presence of microscopic embryonic/fetal tissue. Here we attempted to detect the presence of AFP in dried blood collected on pads from women with first trimester bleeding.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: A sample of patients presenting to a fertility center or emergency department with positive pregnancy tests and vaginal bleeding were invited to participate in the study. After informed consent, a hygienic pad was collected from each participant. 1x1 cm2 pad patches with dried vaginal blood were placed into 1 ml saline. The dissolved AFP that originated from the vaginal blood (AFPVb) was quantified by an automatic chemiluminescence assay. Two outcomes were evaluated: 1) clinical and/or histopathologic evidence of passage of intrauterine embryonic/fetal tissue (a failed intrauterine pregnancy); 2) a threatened miscarriage with subsequent ongoing clinical pregnancy (heartbeat documented on ultrasound on the day of pad collection or at least once within the subsequent 5 weeks).

RESULTS: To date, 15 women with first trimester bleeding were enrolled. For these women, the median age, gravidity, and parity (with ranges in parentheses) were 32 (20-51) years, 3 (1-8), and 0 (0-3), respectively. Each woman provided a single pad with dried vaginal blood. Four women passed embryonic/fetal tissue and 11 had an ongoing pregnancy. AFPVb was detected in 5 women with a threatened miscarriage. Four women passed embryonic/fetal tissue and 1 woman had an ongoing pregnancy. AFPVb was not detected in the other 10 specimens, all from women with a threatened miscarriage and ongoing pregnancies. The detection of AFP in the vaginal blood was significantly associated with pregnancy loss while its absence was seen exclusively in successful pregnancies (P = 0.004 by Fisher exact test).

CONCLUSIONS: AFP can be extracted and detected in dried blood on pads collected from women with first trimester bleeding. When AFPVb is detected the likelihood of a failed intrauterine pregnancy is 80% whereas this likelihood drops dramatically when AFPVb is undetectable. Measurement of vaginal AFP may help to predict the fate of intrauterine pregnancy in the setting of first trimester bleeding.

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EARLY MULTIFETAL PREGNANCY REDUCTION OUTCOMES: NON-CHEMICAL-BASED METHOD YIELD IMPROVED PREGNANCY RATES AND MINIMIZE RISKS. Ivan Madrazo, MD, a Ginna Milena Ortiz, MD, a Karla Y. Santiago, MD, b Yolanda Piña, MD, b Milton D. Flores, MD, b Esther López-Bayghen, PhD b Ingenes México, Mexico City, DF, Mexico; bIngenes México, Mexico City, DF, Mexico; bAffiliation not provided; bCentro de Investigación y Estudios Avanzados IPN, México, EM, Mexico.

OBJECTIVE: Multifetal pregnancies increase maternal, and perinatal mortality, the presence of each additional fetus increases this risk; moreover, spontaneous loss of the entire pregnancy is 25% for quadruplets, 15% for triplets, and 8% for twins. Several studies showed that the reduction to a lower-order pregnancy (triplet or quadruplet to twin) reduces the risk of medical complications associated with maintaining multiple pregnancies. Multifetal pregnancy reduction is usually scheduled between 11 and 14 weeks of gestation, using chemical substances as adjuvants to help in the embryo reduction success rate. However, these chemical substances present alternative concerns and have been suggested to affect live birth rates. Therefore, we assessed a novel non-chemical-based procedure for fetal reduction performed during early gestation of high order pregnancies.

DESIGN: Single-arm prospective study conducted between December 2013 and September 2018.

MATERIALS AND METHODS: Multifetal pregnancy reduction was carried out between 6 and eight weeks of gestation. The patient was placed in a lithotomy position under general anesthesia. Using the same equipment used for transcervical ultrasound-guided oocyte recovery, the smallest embryo, located in a position with the easiest access route and preferably the one nearest the cervix, was selected for embryo reduction. An echo tipped needle (17 Cook medical ovum aspiration needle) was inserted through the posterior fornix and the posterior uterine wall to the intended gestational sac. Then the needle is inserted in the embryos cardiac area until the absence of fetal heartbeat was seen and confirmed by color and power Doppler. The needle is then extracted, and hemostasis is verified. We avoid aspiration and the use of any chemical substances. We verify the vitality of remaining embryos with color and power Doppler. Patients were followed until delivery, and the baby’s weight was a record as well as any complications.

RESULTS: For the proof of principle, only patient with three gestational sacs were analyzed (n=296). None of the women presented or indicated of any complication due to the surgery. Embryo reduction typically took place during the 7th week (range: 5--10.5 weeks). After the procedure, 3 patients lost their pregnancy (1.0%); however, 89.9% maintained the remaining 2 gestational sacs and 9.1% for 1 gestational sac. The live birth rates were 94.4% for the 2 gestational sacs (birth weight: 2111±625 grams) and 96.3% for 1 gestational sac (birth weight: 254±793 grams). There was no difference in the low birth weight rate (2 sacs: 14.5% v 1 sac: 11.5%). The most common for the 2 sacs group was requiring NICU intervention (4.5%), whereas, for the 1 sac group, was restriction of intrauterine growth (14.8%).

CONCLUSIONS: Here, we demonstrate that a non-chemical method can successfully reduce the number of embryos.

SUPPORT: Conacyt A250768.

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LUTEINIZING HORMONE (LH) SURGE SHOULD REPLACE LAST MENSTRUAL PERIOD (LMP) FOR IMPROVED ACCURACY OF PREGNANCY DATING. James J. Morong, MBBS, MPhil, a Dana B. McQueen, M.D., a M.A.S., b Mary D. Stephenson, M.D., M.Sc. c University of Illinois at Chicago, Chicago, IL; cNorthwestern University, Chicago, IL.

OBJECTIVE: To compare the accuracy of pregnancy dating by Luteinizing Hormone (LH) surge versus last menstrual period (LMP).

DESIGN: Observational cohort study of prospectively collected data in two academic RPL Programs from 2005-2018. Inclusion criteria included: women with a history of recurrent early pregnancy loss (REPL), defined as ≥ 2 pregnancy losses <10 weeks size; ≥ 1 subsequent pregnancy with a known LMP; documented LH surge, natural conception, and transvaginal ultrasound (TVUS) prior to 8 weeks from LMP, which resulted in a live birth.

MATERIALS AND METHODS: We compared the gestational age (GA) by LH surge (GA_LH) and LMP(GA_LMP) to the sonographic gestational age (GASRL), based on the first crown rump length (CRL) of ≤5 mm. Secondary analysis compared the accuracy of pregnancy dating with a measurable CRL <5 mm to the conventional CRL ≥ 5 mm. Scatter diagrams were created for the difference between GASRL-GA_LH and GASRL-GA_LMP, paired t-Tests were used for analysis. In addition, scatter diagrams were created for CRL vs. GA_LH and CRL vs. GA_LMP; correlation coefficients for each were compared using Fisher’s z-test. SAS 9.4 was used for statistical analysis, with significance P<0.05. Descriptive statistics were reported as mean, standard deviation and range.
RESULTS: A total of 115 women with a history of RPL, with 118 subsequent live births, met inclusion criteria. Subjects were 96% Caucasian and 6% Hispanic. Mean age at delivery was 35.6 years (3.4-26.3). Mean number of prior pregnancy losses <10 weeks was 3.6 (1.8-12) and mean number of prior live births was 1.78 (1.41-4.4).

Scatter diagrams of GA_CRL-GA_LH revealed tighter fit around zero vs. GA_CRL-GA_LMP. Paired t-test revealed a lower mean absolute difference between GA_CRL-GA_LH vs. GA_CRL-GA_LMP, 2.04 vs. 3.08 days, P=0.0001. Fisher’s z-test revealed a greater correlation between GA_CRL-GA_LH compared to GA_CRL-GA_LMP, r=0.77 vs. r=0.62, P=0.0018. This indicates a greater accuracy when using LH surge. Of 57 subjects who had at least one TVUS with a CRL of <5 mm, Scatter diagrams of GA_CRL-5mm-GA_LH revealed a trend towards a tighter fit around zero vs. GA_CRL-5mm-GA_LMP. Paired t-test revealed a trend towards a lower mean absolute difference between GA_CRL-5 mm-GA_LH vs. GA_CRL-5mm-GA_LMP, 1.86 vs. 2.25 days, although this did not reach statistical significance, P=0.33.

CONCLUSIONS: A highly accurate estimated date of delivery (EDD) improves antenatal surveillance and reduces iatrogenic prematurity. Pregnancy is optimally dated in the first trimester and becomes increasingly inaccurate with advancing GA. Numerous publications have concluded that LMP is unreliable for pregnancy dating. Based on the results in this study, LH surge should replace LMP for improved accuracy of dating of pregnancy. There was a trend towards improved accuracy with a CRL <5 mm.

The average GA at time of first ultrasound by all three methods (CRL, LH surge and LMP) was 7 weeks +/- 5 days. Therefore, we propose a new study, LH surge should replace LMP for improved accuracy of dating of pregnancy. Based on the results in this study, LMP is unreliable for pregnancy dating. Based on the results in this study, LH surge should replace LMP for improved accuracy of dating of pregnancy. There was a trend towards improved accuracy with a CRL <5 mm.

The average GA at time of first ultrasound by all three methods (CRL, LH surge and LMP) was 7 weeks +/- 5 days. Therefore, we propose a new threshold for very early pregnancy dating that supports redating the pregnancy by sonographic CRL if there is a discrepancy of more than 2 days from the LH surge or 3 days from LMP for gestations <14 weeks. P<0.008 and P<0.001 respectively. Age, BMI, infertility diagnosis, medical co-morbidities, and SCH size were not significantly different between these groups. Aspirin use in this population was common at 49.7%. SCH size was significantly lower in infertile patients taking aspirin, this study is the first to evaluate outcomes and suggest that there is no increased risk of miscarriage with aspirin use in pregnancies affected by early SCH. Future research should further evaluate the effect of aspirin on SCH prevalence and the impact of continuing aspirin in affected pregnancies.
OBJECTIVE: To identify the DNA cargo of extracellular vesicles (EVs) obtained from maternal endometrial fluid and determine whether cargo is incorporated into and thereby affects the embryo energetics regulation in terms of ATP modulation.

DESIGN: DNA cargo identification was performed by sequencing EVs [apoptotic bodies (ABs), microvesicles (MVs), and exosomes (EXOs)] isolated from human endometrial fluid (EF) samples from fertile donors (n=10). EVs populations originating from the same EF sample were evaluated in a paired design. The potential for EVs to transfer DNA to the embryo and to modify embryo energetics through ATP modulation was also investigated.

MATERIALS AND METHODS: EVs from human EF were treated with DNase to remove external DNA. Nextera XT DNA libraries were created and paired-end 300 cycles sequenced. EVs were labelled with 5-ethynyl-2’-deoxyuridine (specific DNA label) and incubated with hatching murine embryos (n=600) to investigate EVs DNA transfer into the embryo. Finally, hatching embryos (n=250) were cocultured with EVs, and embryonic ATP levels were quantified (FLASC kit, Sigma) and compared among embryos exposed to the different EV populations. Statistical comparisons were performed using ANOVA.

RESULTS: EVs were only the type in which specific DNA cargo was identified. NGS analysis revealed enrichment in mitochonadrial DNA comprising the 13 coding genes (11.12 ± 0.53-fold increase). Interestingly, transcription factor binding sites (TFBSs) were also enriched in these EVs population compared to ABs and EXOs (6.9 ± 1.5 and 11 ± 2.1-fold change, respectively), most of them mapping throughout the mitochondrial genome. Some of the associated transcription factors (SRF; GABP, E2F4, TR4, FOXA2, FOXA1, CTCF, GATA2, Pax5) are implicated in embryonic development, gametogenesis, and cell adhesion. Further, DNA-tagged EV populations were taken up by murine embryos and exhibited different patterns of DNA integration into the cytoplasm and nuclei of the trophectoderm. Interestingly, when embryos were cocultured in the presence of ABs, MVs, or EXOs, those in the presence of MVs maintained their ATP production when compared to EXOs (p < 0.001).

CONCLUSIONS: Our results suggest that EVs-derived EVs may act as modulators of embryo energetics. Specifically, EVs convey DNA cargo enriched in coding and modulatory mitochondrial DNA and support maintenance of embryonic ATP production. Finally, the ability of EVs to transfer DNA to the embryo suggests that this mode of maternal-embryonic communication may have implications on embryo energetics regulation.

CS & FV contributed equally.
RESULTS: 1301 RNA species were common to both the mouse and human DEGs. 318 of these genes were directly bound by FOXO1. Pathway analysis identified Wnt/b-catenin signaling (-log(p-value) 4.14, Z score -0.626), estrogen mediated proliferation (-log(p-value) 10, Z score -3.05), and IL-6 signaling (-log(p-value) 4.73, Z score 0.943) as significantly altered by both human cycle phase and murine FOXO1 deletion, strongly suggesting a role of FOXO1 in these critical pathways for normal endometrial function. ChiP-Seq demonstrated direct FOXO1 binding to multiple regulated genes involved in estrogen-mediated proliferation, IL-6 signaling, and Wnt/b-catenin signaling, supporting a direct action of FOXO1 on these essential signaling pathways. FOXO1 was also found to directly bind several upstream regulators critical to endometrial receptivity, including CEBPB and CCND1.

CONCLUSIONS: Epithelial FOXO1 directly regulates key pathways necessary for human uterine receptivity.


P-518 Wednesday, October 16, 2019 6:30 AM

PRESENCE OF p16-POSITIVE SENESCENT CELLS IN HUMAN ENDOMETRIUM DURING THE MID-LUTEAL PHASE OF THE MENSTRUAL CYCLE. Dimitar Parvanov, PhD,a Dragomira Nikolova, PhD,b Rumiana Geneva, MSc,c Nina Vidolova, MSc,c Georgi Stamenov Stamenov, MD/PhD,c Nadezhda Women’s Health Hospital, Sofia, Bulgaria; 3Department of Medical Genetics, Medical Faculty, Medical University – Sofia, Sofia, Bulgaria.

OBJECTIVE: Biomarkers for cellular senescence such as p16ink4a are commonly measured in order to explore the level of senescence in reproductive tissues. It is known that p16ink4a-positive senescent cells in the human endometrium are involved in its receptivity and participate in the acute cellular remodeling at the time of embryo implantation. The objective of the present study was to evaluate and compare the percentage of p16-positive cells in the stroma, glandular and luminal epithelial compartments of the human endometrium.

DESIGN: We measured the percentage of p16-ink4a-positive cells by immunohistochemistry in endometrial biopsy samples of 124 women.

MATERIALS AND METHODS: This is a prospective observational study of 124 fertile women who had an endometrial biopsy during the mid-luteal phase (7 days after LH surge) of the natural cycle. Patients older than 40 years, with BMI<18 kg/m2 or BMI>30 kg/m2, endometriosis, polycystic ovary syndrome (PCOS), endometrial polyps, abnormal uterine development and hydroalpinx were excluded from the study. Endometrial biopsies were obtained by pipelle suction and they were immediately fixed in 10% formalin. The endometrial tissue compartment was calculated after enumeration by two independent investigators in multiple endometrial sections. Values were expressed as mean ± SD. Paired t-test and Spearman correlation coefficient were used as appropriate. P<0.05 was considered statistically significant.

RESULTS: The percentage of p16-positive cells in the endometrial stroma during the mid-luteal phase of the cycle ranged between 0.03% and 8.38%, while it varied between 0.06% and 51.02% in the glands, and between 1.69% and 90.88% in the luminal epithelium. The presence of p16+ senescent cells was significantly higher in the endometrial luminal epithelial compared to glandular and stromal compartments (28.71%±23.73% vs. 6.72%±7.73% vs. 0.82%±1.29%, p<0.01, respectively). We also observed a significant correlation between the percentage of p16+ cells in glands and those in the luminal epithelium (R=0.61; p<0.01). In contrast, the stromal p16-positive cells were not significantly correlated neither with the glandular senescent cells, nor with the luminal epithelial p16+ cells (p>0.05).

CONCLUSIONS: The endometrial luminal epithelium during the mid-luteal phase of the cycle has the highest percentage of p16-positive senescent cells, followed by the glands and the stroma. Moreover, the p16+ cells rate in the luminal epithelium is strongly positively associated with the proportion of senescent cells in the glands.

P-519 Wednesday, October 16, 2019 6:30 AM

THE ENDOMETRIAL MICROBIOME OF CLINICAL MISCARRIAGE, ECTOPIC PREGNANCY AND DURING EARLY PREGNANCY IN A SUCCESSFUL LIVE-BIRTH. Iolanda Garcia Grau, MS,a Inmaculada Moreno, PhD,b David Perez-Villaroya, MS,b Davide Bau, PhD,c Marta Gonzalez-Monfort, BS,d Felipe Villela, PhD,e Carlos Simon, MD, PhD.e University of Valencia, Igenomix Foundation-INCLIVA, Valencia, Spain; 2Igenomix Foundation/INCLIVA, Paterna, Spain; 3Igenomix, Patera, Spain.

OBJECTIVE: Characterize taxonomically and functionally the endometrial microbiome in clinical miscarriage, ectopic pregnancy and successful live-birth.

DESIGN: The endometrial microbiome was analyzed in patients undergoing ART. We assessed the results of endometrial fluid samples analyzed prior to embryo transfer with euploid embryos resulting in 2 clinical miscarriages and 1 ectopic pregnancy (Patient 1), and a clinical miscarriage and a 4-week spontaneous successful pregnancy resulting in live birth (Patient 2).

MATERIALS AND METHODS: For taxonomic classification, 16S rRNA profiles were obtained using the Ion 16S metagenomics kit and sequenced on the Ion S5 XL system (ThermoFisher Scientific). Functional composition was assessed by Whole Metagenome Sequencing using the Nextera DNA Flex Library Preparation kit and sequenced on the NextSeq 500 system (Illumina).

RESULTS: The 16S rDNA sequencing of the endometrial fluid collected prior to clinical miscarriages and ectopic pregnancy showed the existence of a pathologic microbiota profile, whereas at 4-weeks of pregnancy had reversed to a normal Lactobacillus-dominated profile.

The functional metagenomics revealed different Lactobacillus species and associated functions between the clinical miscarriage and successful pregnancy. In clinical miscarriage, L. crispatus was detected with the indicated pathogens showing an unstable functional pattern with transposases and insertion elements. Whereas, in the same patient L. iners was the only bacteria present in the uterine cavity at the 4-week in the successful pregnancy, associated with defense mechanisms, energy production and cell division.

| Patient 1 | Patient 2 |
|---|---|---|---|
| **Ectopic (%)** | **Miscarriage (%)** | **Miscarriage (%)** | **Live birth (%)** |
| Lactobacillus | 12.1 | 0.8 | 48 | 17.6 |
| Gardnerella | 32.8 | 28.8 | 32.8 | 0.0 |
| Pseudodextrorosmonas | 14.2 | 16.8 | 0.0 | 16.3 |
| Bifidobacterium | 8.8 | 5.0 | 6.2 | 1.4 |
| Rhodanobacter | 5.6 | 13.0 | 0.0 | 0.0 |
| Atopobium | 0.4 | 13.4 | 5.4 | 0.0 |
| Streptococcus | 1.0 | 0.2 | 0.0 | 17.2 |
| Pseudomonas | 3.2 | 2.7 | 0.1 | 17.2 |
| Enterobacteriaceae | 1.5 | 0.0 | 0.0 | 3.7 |
| Staphylococcus | 0.5 | 0.0 | 0.0 | 2.9 |

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CONCLUSIONS: This is the first demonstration that the uterine microbiome in an early successful pregnancy is completely different from different clinical miscarriages and ectopic pregnancy, revealing the different uterine microbial environment encountered by the embryo at implantation in these clinical outcomes. The potential of these new findings remains to be proven in larger series.

ENDOMETRIOSIS

P-520 Wednesday, October 16, 2019 6:30 AM

CHANGES IN ANTI-MULLERIAN HORMONE AND AMOUNT OF ETHANOL USED DURING ULTRASOUND GUIDED ASPIRATION OF OVARIAN CYST. Lulu Huang, MD, a Ming-Yang Chang, MD, a Yu-Cheng Liu, MD b Chiang Gung Memorial Hospital Linkou Medical Center, Taipei, Taiwan; b 199 Tun-Hua North Road, 12F Taipei, Taiwan, Taiwan; a Affiliation not provided.

OBJECTIVE: To evaluate the effect of transvaginal ultrasound-guided aspiration and ethanol sclerotherapy on ovarian reserve and anti-mullerian hormone (AMH) in patients with ovarian endometriomas. Setting: Teaching hospital affiliated with Chiang Gung University, Taipei.

DESIGN: We retrospectively reviewed 124 patients with ovarian endometriomas who underwent trans-vaginal aspiration and sclerotherapy of endometrioma(s) in our hospital. Patients were grouped into minimal amount of ethanol retention, group 1, n=80, <5 mL of retention of ethanol, and group 2, n = 44, >5ml of retention.

RESULTS: The patients age, mean cyst size, bi/unilaterality in both groups were without significant differences. The mean pre-operative AMH levels for group 1 (≤ 5 mL of ethanol retention) and group 2 (>5ml of ethanol retention) were 3.80 and 3.06 respectively (p<0.05). The AMH at 6-month follow up for group 2 patients was significantly lower than for group 1 patients, with mean decrease of 0.72 (23.6%) and 0.10 (2.7%) respectively (p<0.05). No significant change in CA-125, recurrence rate or pain score was found within 1 year of aspiration.

CONCLUSIONS: Ultrasound-guided sclerotherapy with 95% ethanol is an effective therapy for ovarian endometriomas. The greater the amount of ethanol left in situ during sclerotherapy, the more AMH decreases post-operatively.

DESIGN: Multicenter retrospective assay of cohorts to compare the embryonic aneuploidy rate between patients with endometriosis (experimental group) and those without the disease (control group).

MATERIALS AND METHODS: Our study involved patients aged 18-42 years undergoing IVF with preimplantation genetic screening (PGS) in IVRMA Clinics between 2012 and 2017. To discard the impact of non-endometriosis disorders on embryo abnormalities, severe male factors and patients with altered karyotype or with chromosomal stabilization in previous embryos or pregnancies were excluded. The following PGS indications were included: Implantation failure (IF), Recurrent miscarriage (RM) and advanced maternal age (AMA). Both blastocyst and developing embryos analyzed for the complete chromosome set by comparative genomic hybridization (CGH) arrays or next generation sequencing (NGS) were only considered. Presence of endometriosis was evidenced at the time of abdominal surgery or after pelvic ultrasound or NMR findings. For the statistical analysis, chi-square test for categorical variables or Student’s-t-test for quantitative data were applied to compare baseline characteristics between groups. χ² test and Poisson regression model were used for comparing the proportion of aneuploid embryos in the different groups.

RESULTS: A total of 1622 embryos from 350 patients were biopsied in the endometriosis group while 17914 biopsied embryos from 4000 patients were included in the control group. Among these embryos, 1577 and 17566 were informative after PGS in the experimental and control group, respectively. One thousand seventy-two embryos from the endometriosis patients and 11997 from control patients were normal. No significant differences in the aneuploidy rate were observed when compared embryos from the experimental and the control group (68.0% versus 68.3%, respectively: p=0.794). Poisson regression analysis was performed, adjusting for baseline patient characteristics (age and body mass index), but the proportion of aneuploid embryos were still not significant.

CONCLUSIONS: Despite increased oocyte meiotic errors and chromosomal instabilities have been proposed as a potential cause for a lower IVF success in women with endometriosis, it does not seem to impact on their embryo aneuploidy risk. Further research is needed to determine if the embryo aneuploidy rate and blastocyst PGS analysis could help non-analyzed chromosomal anomalies. Anyway, disturbances during oocyte nuclear maturation, with subsequent less useful oocytes, could also explain the difficulties of these patients in becoming pregnant.

PREOPERATIVE SERUM ANTI-MULLERIAN HORMONE LEVELS IN WOMEN WITH OVARIAN ENDOMETRIOSIS COMPARED TO WOMEN WITH PERITONEAL ENDOMETRIOSIS, Serin I. Seckin, MD, a Tamer A. Seckin, MD, a Karli Provost Goldstein, DO, b Icahn School of Medicine at Mount Sinai West/St. Luke’s, New York, NY; b Lenox Hill Hospital/Northwell Health System, New York, NY.

OBJECTIVE: Anti-Mullerian hormone (AMH) is an important serum marker to gauge ovarian reserve and predicted response to number of oocytes retrieved after ovarian stimulation. Patients who have ovarian involvement of endometriosis have clinically demonstrated lower baseline AMH levels. Whether or not patients with peritoneal endometriosis only have lower baseline AMH levels has not been established. Our aim is to investigate preoperative baseline AMH levels in women who have ovarian endometriosis versus women who have peritoneal endometriosis without ovarian involvement.

DESIGN: Retrospective cross-sectional analysis.

MATERIALS AND METHODS: Pre-operative AMH levels were evaluated for 111 women aged 19-42 who underwent laparoscopic surgery from January 2017 and July 2018 for suspected endometriosis. Patients were identified for those who desired future fertility and had preoperative AMH levels drawn. Patients with a history of polycystic ovaries or history of prior endometriosis excision surgery and/or oocyte retrieval were excluded. AMH levels were analyzed according to where endometriosis was anatomically located and confirmed by pathology, comparing women who had peritoneal endometriosis (n=71) without any ovarian involvement versus women with ovarian involvement (n=40). Subanalysis of AMH values was also performed within three different age groups.

RESULTS: Preoperative serum AMH level was not significantly different in the ovarian endometriosis group compared to the peritoneal endometriosis group (3.22 ± 3.07 ng/mL vs 3.94 ± 2.90 ng/mL, P=0.113). Subgroup analysis by age demonstrated significantly lower AMH levels for women with ovarian endometriosis aged 27-35 (2.62 ± 2.28 ng/mL vs 3.85 ± 2.98 ng/dL, P=0.045). Patients with ovarian endometriosis were significantly more likely to have more endometriotic lesions confirmed on pathology (16.95 ± 8.75 lesions vs 8.97 ± 6.85 lesions, P <0.0001).

P-522 Wednesday, October 16, 2019 6:30 AM

DOES ENDOMETRIOSIS IMPACT ON THE EMBRYONIC ANEUPLOIDY RISK? Verónica Legidos, MD, a Purificación Hernández-Vargas, PhD, a Blanca Gadea, BS, a Victor Lozoya, BS, b Manuel Muñoza, MD, b IVIRMA ALICANTE, Alicante, Spain; b IVIRMA Foundation, Valencia, Spain.

OBJECTIVE: Endometriosis, a highly frequent gynecological disease, is often associated with female infertility and poor in vitro fertilization (IVF) outcomes. Many factors have been suggested to cause the fertility problems in these patients, including poor oocyte quality and alterations in meiotic spindle that could affect embryo aneuploidy rates. Our main objective is to ascertain if endometriosis increases embryonic aneuploidy risk.

DESIGN: Endometriosis is an inflammatory condition and research suggests that it could be associated with an increase in the production of oxidants and free radicals that could increase the risk of female infertility. The aim of this study was to evaluate the effect of endometriosis on the risk of aneuploidy. Therefore, we performed a case control study of 146 patients with endometriosis and 72 patients without endometriosis. Ovarian reserve was measured with anti-Mullerian hormone (AMH) and aneuploidy rate was measured with preimplantation genetic screening (PGS) after quantitative NGS analysis of blastomeres. Presence of endometriosis was assessed using a comparative genomic hybridization (CGH) array and/or next generation sequencing (NGS) tests. The AMH and aneuploidy rates were compared between patients with and without endometriosis using the Student's t-test.
CONCLUSIONS: Patients with ovarian endometriosis demonstrate lower serum AMH levels than baseline age-matched populations [1], thus reflecting ovarian function and potential success with oocyte retrieval. These findings indicate that some women with peritoneal endometriosis may be at a similar disadvantage in regards to ovarian reserve compared to women with endometriosis and could benefit from earlier intervention regarding active management of fertility preservation.


P-523 Wednesday, October 16, 2019 6:30 AM
DIENOGEST FOR PAIN AND INTESTINAL SYMPTOMS CAUSED BY RECTOSIGMOID ENDOMETRIOSIS: PROSPECTIVE COHORT STUDY. Simone Ferrero, MD, PhD, a Carolina Scala, MD, a Valerio Gaetano Vellone, MD, PhD, b Umberto Leone Roberti Maggiore, MD, PhD, b Ennio Biscaldi, MD, b Fabio Barra, MD, b DISOGMI, University of Genova, Genova, Italy; aIstituto G. Gaslini, Genova, Italy; aDISC, University of Genova, Genova, Italy; aDepartment of Gynecologic Oncology, IRCCS National Cancer Institute, Milan, Italy; aDepartment of Radiology, Galliera Hospital, Genova, Italy.

OBJECTIVE: The aim of this study was to evaluate the efficacy of dienogest (DNG) for treating pain and intestinal symptoms in patients with rectosigmoid endometriosis.

DESIGN: 24-month open-label prospective cohort study.

MATERIALS AND METHODS: This study included symptomatic women of reproductive age with rectosigmoid endometriosis. The diagnosis of rectosigmoid endometriosis was performed by transvaginal ultrasonography and confirmed by magnetic resonance imaging. Exclusion criteria for the study were: use of hormonal therapies for endometriosis in the 3 months before study entry (6 months for gonadotropin releasing hormone analogues), previous treatment with DNG, unwillingness to tolerate menstrual changes, undiagnosed vaginal bleeding, obstructive uropathy, complex adnexal cysts at imaging, estimated rectosigmoid stenosis >60%. Eligible women underwent hormonal treatment with DNG (2 mg/day) continuously for 24 months. Consultations were performed every 6 months. The primary endpoint of the study was patient satisfaction. Secondary endpoints were: changes in pain (assessed on a VAS scale) and intestinal symptoms (assessed by a 10-point symptom analogue scale and by the Gastrointestinal Quality of Life Index, GIQLI), changes in quality of life (assessed by the Endometriosis Heath Profile 30, EHP-30), changes in sexual function (assessed by the Female Sexual Function Index, FSFI), tolerability of the therapy, changes in the volume of the rectosigmoid nodules (estimated by using the virtual organ computer-aided analysis, VCOAL).

RESULTS: 132 women were enrolled in the study and 114 (86.4%) completed the 24-months treatment. The mean ±SD age of the study population was 34.8 ±4.1 years. 102 patients (77.3%) had already received previous hormonal treatment for treating endometriosis. 56 patients (42.4%) had previously undergone surgery for pelvic endometriosis. All pain symptoms (dysmenorrhea, non-menstrual pelvic pain, deep dyspareunia and painful defecation) significantly improved at 1-year of treatment compared with baseline. The severity of diarrhea, intestinal cramping and passage of mucus significantly improved at 6-, 12- and 24-month assessment compared with baseline. Abdominal bloating improved at 24-month assessment compared with baseline. The GIQLI, the EHP-30 and the FSFI were significantly improved at 24-month follow-up compared with baseline. There was a significant reduction in the volume of the bowel endometriotic nodules between baseline (4.3±0.8 cm³) and 12-month assessment (3.4±1.0 cm³; p<0.001) and between baseline and 24-month assessment (3.1±0.6 cm³, p<0.001). The volume of the nodules did not significantly change between the 12-month and the 24-month assessment. DNG was generally well tolerated, with no reported serious adverse events; the most common adverse effect was headache (8.3%).

CONCLUSIONS: A 2 year-therapy with DNG improves the symptoms caused by rectosigmoid endometriosis with a good safety-profile, proving also a slight reduction of the size of the bowel endometriotic nodules.

P-524 Wednesday, October 16, 2019 6:30 AM
FIBER AND GLUTEN INTAKE AND RISK OF LAPAROSCOPICALLY-CONFIRMED ENDOMETRIOSIS. Holly Harris, M.P.H., Sc.D., a Myriam C. Afiche, PhD, a Kathryn L. Terry, Sc.D., a Jorge E. Chavarro, MD, Sc.D., a Stacey A. Missmer, Sc.D. a Fred Hutchinson Cancer Research Center, Seattle, WA; bNestlé Research Center, Lausanne, Switzerland; bBrigham and Women’s Hospital and Harvard T.H. Chan School of Public Health, Boston, MA; bHarvard School of Public Health, Boston, MA; bMichigan State and Harvard T.H. Chan SPH, Grand Rapids, MI.

OBJECTIVE: We examined the association between intake of fiber (total fiber, legume, vegetable, cruciferous vegetable, fruit, and cereal fibers) and gluten and diagnosis of laparoscopically-confirmed endometriosis.

DESIGN: A prospective cohort study using data collected from 81,789 premenopausal women from 1991-2013 as part of the Nurses’ Health Study II (NHSII) cohort.

MATERIALS AND METHODS: Diet was assessed with a validated food frequency questionnaire every four years. Multivariable Cox proportional hazards models adjusted for race/ethnicity, menstrual cycle length, parity, age at menarche, body mass index, recent gynecologic/breast exam, and total calories, were used to calculate rate ratios (RR) and 95% confidence intervals (CI).

RESULTS: During 22 years of follow-up, 3793 incident cases of laparoscopically-confirmed endometriosis were reported. Higher intake of fruit fiber was associated with a lower risk of endometriosis diagnosis (RR for 5 thquantile vs 1 stquantile=0.89; 95% CI=0.80-0.98). A similar association was observed for cereal fiber (RR for 5 thquantile vs 1 stquantile=0.90; 95% CI=0.81-1.00). In contrast, vegetable fiber intake was associated with a higher risk of endometriosis diagnosis (RR for 5 thquantile vs 1 stquantile=1.12; 95% CI=1.02-1.24). This association appeared to be driven by the association with cruciferous vegetable fiber intake (RR for 5 thquantile vs 1 stquantile=1.17; 95% CI=1.06-1.30). No significant associations were observed with total fiber or legume fiber. Intake of gluten was associated with a lower risk of endometriosis diagnosis (RR for 5 thquantile vs 1 stquantile=0.82; 95% CI=0.72-0.93). This association was modified by fertility status. Specifically, the inverse association between gluten intake and endometriosis diagnosis was only apparent among women who had not reported infertility (RR for 5 thquantile vs 1 stquantile=0.82; 95% CI=0.71-0.95). The corresponding RR for those reporting infertility was 0.94 (95% CI=0.68-1.31).

CONCLUSIONS: Our findings suggest that different types of fiber intake are differentially associated with risk of endometriosis diagnosis. Further analyses are needed to identify whether these associations are driven by consumption of the foods that contribute to fiber intake or due to the fiber content itself. Our finding that gluten intake was associated with a lower risk of endometriosis diagnosis among women who had not reported infertility, and thus were more likely to present with pain symptoms, suggests that gluten intake is unlikely to contribute to heightened endometriosis risk among the general population or exacerbation of pain symptoms among women with endometriosis. The inverse association observed deserves further study in well-designed observational and intervention studies.

P-525 Wednesday, October 16, 2019 6:30 AM
IN UTERO AND EARLY LIFE EXPOSURES IN RELATION TO ODDS OF ENDOMETRIOSIS IN ADOLESCENTS AND YOUNG ADULTS. Naoko Sasamoto, M.D., M.P.H., a Lesli Y. Farland, Sc.D., a Allison F. Vitoonis, M.S., a Holly Harris, M.P.H., Sc.D., a Amy D. DiVasta, MD, MMSc, d Marc R. Laufer, M.D., a Kathryn L. Terry, Sc.D., a Stacey A. Missmer, Sc.D., a Brigham and Women’s Hospital, Boston, MA; aUniversity of Arizona, Tucson, AZ; aFred Hutchinson Cancer Research Center, Seattle, WA.
Objective: To investigate the relation between in utero life exposure and endometriosis diagnosis during adolescence and young adulthood.

Design: We conducted a nested case-control study among participants of The Women’s Health Study: From Adolescence to Adulthood (A2A), a longitudinal cohort of adolescents and young women enrolled from 2012-2018.

Materials and Methods: Participants (n=604; 295 laparoscopically-confirmed endometriosis cases, 309 population-based controls) in the A2A study (age < 25 yrs at enrollment) completed a modified WERF/EPheCT questionnaire at baseline. Information on in utero and early life factors were collected, including their mother’s age at delivery, birthweight, gestation length, parents’ smoking status during their pregnancy and/or during infancy and childhood, and if the participant was breastfed. We calculated odds ratios (OR) and 95% confidence intervals (CI) using logistic regression models, a priori adjusted for age at enrollment, race/ethnicity, maternal endometriosis diagnosis, and age at menarche. Analyses of birthweight were restricted to full term births.

Results: Median age at enrollment was 22 y (range 7-24) in controls and 17 y (range 12-24) in cases, with 68% and 83% non-Hispanic white, respectively. Median age at menarche was 12 y (range 8-15) for both groups. Among cases, 50% had mothers with endometriosis while only 9% of the controls did. The almost all cases (95%) were rASRM stage I or II at diagnostic surgery. Participants who were breastfed had lower odds of endometriosis diagnosis (OR: 0.40, 95% CI: 0.21-0.74). Young women whose mothers smoked during pregnancy (n=13) were four times more likely to be diagnosed with endometriosis < age 25 (OR: 3.93, 95% CI: 0.80-19.43), while those with mothers who smoked during infancy to childhood were 2.5 times more likely to be diagnosed (OR: 2.64, 95% CI: 1.10-6.32). Low birthweight (OR: 0.64, 95% CI: 0.08-4.87) and preterm birth (OR:1.30, 95% CI: 0.30-5.66) were not associated with endometriosis diagnosis < age 25.

Conclusions: Among adolescents and young adults, exposure to breastfeeding in early life was associated with lower odds of surgically diagnosed endometriosis. Exposure to maternal smoking during pregnancy and infancy/childhood was associated with greater odds of endometriosis, although the number exposed was small. Further exploration and replication are necessary to draw conclusions regarding risk among those diagnosed during adolescence compared to those diagnosed during adulthood. As these exposures are potentially modifiable, solidifying these associations will form the basis of informative public health messages to prevent endometriosis.

P-526 Wednesday, October 16, 2019 6:30 AM

Cumulative Clinical Pregnancy After Surgical Treatment of Infertile Women With Endometriosis. William Butler, MD, Arshia Rassi, DO, Kristina C. Hawkins, MD, Abdelmoneim Younis, DVM, PhD, Saint Louis University School of Medicine, St. Louis, MO; Miami Children’s Hospital, Miami, FL; Boston Children’s Hospital, Boston, MA; Boston Children’s Hospital and Boston Center for Endometriosis, Boston, MA; Brigham and Women’s Hospital and Harvard T.H. Chan School of Public Health, Boston, MA; Michigan State Univ and Harvard T.H. Chan SPH and Boston Ctr for Endometriosis, Grand Rapids, MI.

Objective: To determine the relation between in utero life exposure and endometriosis diagnosis during adolescence and young adulthood.

Design: We conducted a nested case-control study among participants of The Women’s Health Study: From Adolescence to Adulthood (A2A), a longitudinal cohort of adolescents and young women enrolled from 2012-2018.

Materials and Methods: Participants (n=604; 295 laparoscopically-confirmed endometriosis cases, 309 population-based controls) in the A2A study (age < 25 yrs at enrollment) completed a modified WERF/EPheCT questionnaire at baseline. Information on in utero and early life factors were collected, including their mother’s age at delivery, birthweight, gestation length, parents’ smoking status during their pregnancy and/or during infancy and childhood, and if the participant was breastfed. We calculated odds ratios (OR) and 95% confidence intervals (CI) using logistic regression models, a priori adjusted for age at enrollment, race/ethnicity, maternal endometriosis diagnosis, and age at menarche. Analyses of birthweight were restricted to full term births.

Results: Median age at enrollment was 22 y (range 7-24) in controls and 17 y (range 12-24) in cases, with 68% and 83% non-Hispanic white, respectively. Median age at menarche was 12 y (range 8-15) for both groups. Among cases, 50% had mothers with endometriosis while only 9% of the controls did. The almost all cases (95%) were rASRM stage I or II at diagnostic surgery. Participants who were breastfed had lower odds of endometriosis diagnosis (OR: 0.40, 95% CI: 0.21-0.74). Young women whose mothers smoked during pregnancy (n=13) were four times more likely to be diagnosed with endometriosis < age 25 (OR: 3.93, 95% CI: 0.80-19.43), while those with mothers who smoked during infancy to childhood were 2.5 times more likely to be diagnosed (OR: 2.64, 95% CI: 1.10-6.32). Low birthweight (OR: 0.64, 95% CI: 0.08-4.87) and preterm birth (OR:1.30, 95% CI: 0.30-5.66) were not associated with endometriosis diagnosis < age 25.

Conclusions: Among adolescents and young adults, exposure to breastfeeding in early life was associated with lower odds of surgically diagnosed endometriosis. Exposure to maternal smoking during pregnancy and infancy/childhood was associated with greater odds of endometriosis, although the number exposed was small. Further exploration and replication are necessary to draw conclusions regarding risk among those diagnosed during adolescence compared to those diagnosed during adulthood. As these exposures are potentially modifiable, solidifying these associations will form the basis of informative public health messages to prevent endometriosis.

P-527 Wednesday, October 16, 2019 6:30 AM

SERUM METABOLIC PROFILE AS A NON-INVASIVE ADJUNCT TOOL FOR THE DIAGNOSIS OF ENDOMETRIOSIS-RELATED INFERTILITY. Daniela Antunes Montiani, PhD, Daniela Paes de Almeida Ferreira Braga, PhD, Amanda Souza Setti, MSc, Assumpção Iaconelli, Jr., MD, Diogo Oliveira-Silva, PhD, Edson Borges Jr., PhD, UNIFESP, Diadema, Brazil; Fertility Medical Group / Sapientia Institute, Sao Paulo, Brazil.

Objective: Nonsurgical methods for the diagnosis of endometriosis could avoid unnecessary laparoscopies and improve quality of life. We aimed to develop an adjuvant tool for the diagnosis of endometriosis, based on mass spectrometry (MS)-metabolomics.

Design: Case-control study.

Materials and Methods: Serum samples from 100 patients undergoing intracytoplasmic sperm injection (ICSI), from January 2017 to December 2017, in a private university-affiliated in vitro fertilization center were collected. Samples were split into two groups according to the cause of infertility: the Endometriosis Group (n=50), consisting of samples derived from patients with grade III and IV endometriosis, classified according to the American Society for Reproductive Medicine (ASRM), and the Control Group (n=50), comprising samples derived from patients with isolated male factor infertility. Clinical diagnosis and classification of subjects in the endometriosis group were performed through laparoscopic surgery followed by histology to confirm the presence of endometriotic lesions. The metabolomic profile of each sample was obtained by mass spectrometry. Partial least square discriminant analysis (PLS-DA) was applied to the dataset in order to determine the discriminatory components based upon the combination of variable influence on projection (VIP) values. These values were used to build a single receiver operating characteristic (ROC) curve. To validate the model, 30 samples from infertile women without any evidence of endometriosis were tested.

Results: Except for the pregnancy rate, which was decreased in the Endometriosis Group (32.0% vs 72.0%, for Endometriosis and Control groups respectively, p=0.007), the patient and cycle characteristics were similar between groups. A total of 429 and 484 ions for the positive and negative ionization modes were analysed, respectively. Considering components one, two and three, the PLS-DA was able to clearly distinguish the Endometriosis-Group from the Control-Group for both positive and negative ionization modes. Ten potential biomarkers were selected based on their importance for model prediction, five in the positive and five in the negative ionization modes. These ions were used to build the ROC curve, which presented an area under the curve (AUC) of 0.904 (CI 95%: 0.796-0.985), indicating the accuracy of the biomarkers for sample classification in the Control.
OBJECTIVE: To appraise methodological quality of main endometriosis guidelines, including the 2018 Spanish Fertility Society Endometriosis Guideline, with four different evaluation methods: Agree II Instrument, the Right statement, the Australian ICAHE Checklist and the German MiCheck, to explore methodological quality differences among them and correlation between evaluation methods.

DESIGN: Apraisal of main Endometriosis Guidelines with different methodological quality assessment tools to establish differences among them and correlation between evaluation methods.

MATERIALS AND METHODS: Two reviewers (JAD, MCR) performed a systematic research at PubMed, EMBASE, and Web of Science from 2008 to 2019 for endometriosis guidelines, and consensus documents. Inclusion criteria: National or International Guidelines published in English, French or Spanish. The guidelines assessment was performed with the four appraisal tools described above.

Nine reviewers (GB, MCR, MCC, JAD, JMG, JLL, RM, EPB, CS) assessed the methodological quality of the guidelines to ensure each guideline was evaluated by at least four different reviewers with each of the four appraisal tools. Guidelines scoring system was calculated for each method and standardising the result of the assessment for comparison.

Guidelines were categorised as high quality when they score between 67-100%, moderate quality between 34-66% and low quality between 0-33% of the total score for each appraisal tool.

RESULTS: Ten guidelines along with the Spanish Fertility Society Endometriosis Clinical Guideline (SEF 2018) were included in the review (in chronological order): the Korean Society of Endometriosis Guideline (CNGOF 2018), the National Institute for Health and Care Excellence (NICE 2017), the German Guideline (S2K 2014), the European Society of Human Reproduction and Embryology Endometriosis Guideline (ESHRE 2013), the World Endometriosis Society Montpellier Consensus (WES 2013), the Spanish Health Ministry Guideline (2013), the Australasian Guideline (ACCEPT, 2012), American Society of Reproductive Medicine Endometriosis Committee Opinion (ASRM 2012), and Society of Obstetricians and Gynaecologists of Canada Endometriosis Guideline (SOGC 2010). All of them were assessed by all four methods. Considerable methodological variability was found.

NICE 2017 was the best rated, followed by SEF, 2018 and CNGOF, 2018. According to guideline classification in tertiles, with the Agree II instrument four guidelines reached the upper tertile (high quality) (>67%) NICE 2017, SEF 2018, CNGOF 2018 and ESHRE 2013. All the rest scored as moderate quality (34-66%). With the Right checklist, the classification remained the same. With iCAHE and MiChe appraisal, 4 guidelines moved into the high quality tertile: Canada 2010, ACCEPT 2012, WES 2013, and S2K 2014.

CONCLUSIONS: Endometriosis Guidelines have a high degree of methodological variability when appraised by different evaluation tools. Due to this fact, appraisal seems necessary prior to apply recommendations. Guidelines assessment has to be quick and easy so clinicians can perform it themselves in daily practice.
specimen. HHV-6 late antigens were located in endometrial epithelial cells and were not seen in stromal or hematopoietic derived cells.

CONCLUSIONS: The presence of reactivated HHV-6 in endometrial epithelial cells and the ability of the virus to up-regulate the expression of cytokines (IL-8, TNFa) and growth factors (VEGF) associated with proliferation, adhesion, and neoangiogenesis of endometrial cells, supports further study for a role of HHV-6 in the pathogenesis of endometriosis and associated infertility.


P-530 Wednesday, October 16, 2019 6:30 AM

EFFECTS OF DIENOGEST ON BREAST: MCF CELL LINE DATA. Hyun Jin Kim, M.D., Sung Hoon Kim, M.D., Ph.D. Young Sang Oh, M.S., DeYoung Kim, M.D., Sa Ra Lee, M.D. Ph.D., Hee Dong Chae, M.D., Ph.D., Byung Moon Kang, M.D. Ph.D. University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea, Republic of (South).

OBJECTIVE: Dienogest (DNG) is a widely used progestin which is safe and effective for long-term management of endometriosis. However, its association to breast cells remains to be elucidated. We perform this study to investigate whether in vitro treatment of DNG can cause any biologic changes on MCF cell line (human estrogen receptor (ER)-positive breast cancer cell line) experiments.

DESIGN: A laboratory study.

MATERIALS AND METHODS: Following in vitro culture of MCF cells, we treated those cells and compared cell viability and the expression of several markers have shown to be increased in breast cancer cells between with estradiol alone and estradiol with DNG. Cell viability was measured utilizing MTT(3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay and the expression of PCNA (proliferating cell nuclear antigen) and PAK4 (p21 activated kinase 4) was measured by western blot analyses. VEGF (vascular endothelial growth factor) and IL (interleukin)-32 were analyzed by ELISA, and MMP2 (matrix metalloproteinase 2) activity was assayed by zymography.

RESULTS: In vitro treatment of MCF7 cells led to an increased cell viability by estradiol alone and decreased by both estradiol and DNG after 24 and 48-hour culture. The expression of PCNA after 48 hours showed the same result. VEGF and IL-32 were also significantly increased with estradiol and decreased following DNG treatment. However, there was no significant changes in MMP2 activity and PAK4 expression.

CONCLUSIONS: These findings suggest that DNG may have inhibitory effects on carcinogenesis of breast cells by suppressing specific biologic changes treated by estradiol. However, further study is necessary using normal human breast cells.

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MAGNETIC RESONANCE WITH GEL ENEMA (MR-e) VERSUS COMPUTED TOMOGRAPHIC COLONOGRAPHY (CTC) FOR DIAGNOSING RECTOSIGMOID ENDOMETRIOSIS. Simone Ferrero, MD, PhD, Fabio Burra, MD, Carolina Scali, MD, Valerio Gaetano Vellone, MD, PhD, Ennio Biscaldi, MD, DI NOGMI, University of Genova, Genova, Italy; 2DISC, University of Genova, Genova, Italy; 3Department of Radiology, Galleria Hospital, Genova, Italy.

OBJECTIVE: An accurate diagnosis of the presence, location and extent of rectosigmoid endometriotic nodules is critical for the clinicians to perform the correct counseling on the potential surgical or medical treatments. This study aims to compare the accuracy of magnetic resonance with gel enema (MR-e) and computed tomography-based virtual colonoscopy (CTC) for diagnosing rectosigmoid endometriosis.

DESIGN: Retrospective analysis of a prospectively collected database.

MATERIALS AND METHODS: This study included patients with pain and/or intestinal symptoms lasting at least 6 months and clinical suspicion of rectosigmoid endometriosis. Exclusion criteria for the study were previous intestinal surgery (with the exception of appendectomy) or previous laparoscopic diagnosis of rectosigmoid endometriosis. Patients underwent both MR-e and CTC. Subsequently they underwent laparoscopy; rectosigmoid nodules were excised by segmental colorectal resection, nodulectomy or shave. The surgical specimens were sent to the pathologist in order to be evaluated by standardized criteria.

RESULTS: Out of 90 women included in the study, 44 (48.9%; 95% CI, 38.2%-59.7%) had rectosigmoid nodules. Seven patients underwent shaving of the colorectal nodules; 28 patients underwent segmental colorectal resection, in these patients the mean (+ SD) length of the resected bowel specimen was 12.0 ± 2.1 cm. At histology, endometriosis infiltrated only the muscularis propria in 33 patients, the submucosa in 8 patients and the mucosa in 3 patients. There was no significant difference in the accuracy of both radiologic exams for diagnosing the presence of rectosigmoid endometriosis (p = 0.344); in particular, for MR-e, sensitivity was 93.2% (95% CI, 81.3-98.6%), specificity 97.8% (95% CI, 88.5%-99.9%), positive predictive value (PPV) 97.6% (95% CI, 85.5%-99.7%) and negative predictive value (NPV) 93.8% (95% CI, 83.4%-97.9%). For CTC, sensitivity was 88.64% (95% CI, 75.4%-96.21%), specificity 93.48% (95% CI, 82.10%-98.63%), PPV 92.9% (95% CI, 81.2%-97.5%) and NPV 89.6% (95% CI, 80.0%-95.2%). The mean ± (SD) largest diameter of the main endometriotic nodule at histology was 26.8 ± (9.7) mm. The nodule was preoperatively identified by both MR-e and CTC in 37 patients. MR-e was more accurate than CTC in estimating the largest diameter of the main rectosigmoid nodule (p < 0.001). The mean difference in the estimated length of the nodule was 3.1 mm (95% CI, 2.4 to 3.7); limits of agreement, -0.7 to 6.8 mm) at CTC and 1.6 at MR-e (95% CI, -1.0 to 2.1; limits of agreement, -1.8 to 4.9 mm) when compared with histology. MR-e was more precise than CTC in identifying multifocal disease. Patients complained more discomfort during CTC than during MR-e (p < 0.001).

CONCLUSIONS: This study showed that MR-e and CTC have similar diagnostic accuracy in diagnosing rectosigmoid endometriosis. However, MR-e is more accurate in estimating the largest diameter of the main rectosigmoid nodule, in diagnosing multifocal disease and it is better tolerated than CTC. Moreover, MR-e does not require to administer ionizing radiations.

P-532 Wednesday, October 16, 2019 6:30 AM

MARKERS OF LOCAL AND SYSTEMIC ESTROGEN METABOLISM IN ENDOMETRIOSIS. Velja Mijatovic, M.D., Ph.D.1, Essam R. Othman, MD,2 Maha Y. Khashbha, MSc,3 Ibraheem I. Abdelaal, MD,1,2 Ahmad Abu Markeb, PhD,4 Ahmed N. Feith, MD,4 C. B. Lambalk, MD Ph.D.4 Amsterdam University Medical Center, location VU, Amsterdam, Netherlands; 2Associate professor, OB-GYN department, Assiut, Egypt; 3Women’s Health Hospital, Assiut, Egypt; 4Associated professor, OB-GYN department, Assiut, Egypt; 5Professor, Department of Obstetrics, Assiut University, Assiut, Egypt; 6Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; 7Department of Obstetrics and Gynecology, Women’s Health Hospital, Amsterdam, Netherlands.

OBJECTIVE: Endometriosis is an estrogen dependent disease. Estrogen metabolites can work independently of their parent hormones. Therefore, we hypothesize that in endometriosis patients estrogen is metabolized along hormonally active pathways to keep a highly estrogenic milieu.

DESIGN: Cross sectional study in which paired urine, eutopic and ectopic endometrial samples were taken from patients with endometriosis and control women and analyzed for estrogen metabolites.

MATERIALS AND METHODS: We recruited 62 Endometriosis cases (disease proven laparoscopically and histologically) and 52 control women (in whom laparoscopy was normal) among patients undergoing laparoscopy for pelvic pain and/or infertility during proliferative phase of cycle. Urine samples were collected preoperatively. At surgery we collected eutopic endometrial samples from endometriosis cases and control women and analyzed for estrogen metabolites.

RESULTS: Endometriosis cases and control women had similar baseline characteristics.

CONCLUSIONS: These findings suggest that DNG may have inhibitory effects on carcinogenesis of breast cells by suppressing specific biologic changes treated by estradiol. However, further study is necessary using normal human breast cells.

endometriosis patients or ectopic endometrium in levels of 16α-OHE1, 20HE1, and 20HE1/16α-OHE1 ratio. Eutopic endometrium of endometriosis patients, compared to control endometrium, had significantly higher 40HE1 [30 (30-260)] versus 30 (30-30) ng/g tissue, respectively, P = 0.017], 40HE2 [341 (150-960)] versus 100 (100-100) ng/g tissue respectively, P = 0.0001], and 40HE2 [225 (200-1290.7)] versus 200 (200-200) ng/g tissue respectively, P = 0.0001]. Levels of 40HE2 were significantly elevated in eutopic endometrium of endometriosis patients than in ectopic endometrium [225 (200-1290.7)] versus 200 (200-200) ng/g tissue respectively. P is 0.0001]. Urinary estrogen metabolites: Endometriosis patients; compared to control women, had significantly higher urinary levels of 16α-OHE1 [14.6 (3.4-34.6) versus 4.9 (3-12.8) ng/mg creatinine respectively. P is 0.024] and 20HE1 [10.7 (3.9-15.5) versus 4.8 (1.4-13.7) ng/mg creatinine, respectively. P is 0.018]. All other metabolites did not differ significantly between cases and controls.

CONCLUSIONS: Eutopic endometrium of endometriosis patients metabolizes estrogen preferentially to estradiolically active (20HE2), and potentially genotoxic (40HE1, 40HE2) metabolites. This adds explanation on endometriosis etiology, provides a link between endometriosis and cancer, and may help in identifying potential endometriosis biomarker of the disease. In urine, a similar pattern could not be identified as ratio of antiproliferative 20OHE1 to proliferative 16α-OHE1.

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P-533 Wednesday, October 16, 2019 6:30 AM

IMPACT OF GONADOTROPIN-RELEASING HORMONE AGONIST POST-OPERATIVE TREATMENT ON OVARIAN RESERVE CHANGES AFTER LAPARO-SCOPIC SURGERY OF OVARIAN ENDOMETRIOMA.

Yoo jin Shim, MD., Jung Ryeol Lee, MD. PhD., Seoul National University Bundang Hospital, Seongnam, Korea, Republic of (South).

OBJECTIVE: Hormonal treatment including gonadotropin-releasing hormone agonist, dienogest and oral contraceptive (OC) has been found to be effective in post-operative recurrence prevention. However, evidence is very limited regarding the change of ovarian reserve following these hormonal treatments. The objective of this study was to compare the impact of dienogest or OC alone versus gonadotropin-releasing hormone agonist (GnRHa) plus dienogest or OC on ovarian reserve.

DESIGN: Retrospective study at university hospital.

MATERIALS AND METHODS: A total of 81 patients undergoing laparoscopic ovarian cystectomy for ovarian endometriosis and subsequent treatment of at least 2 times of GnRHa plus dienogest/OC (group A, n=46) or dienogest/OC alone (group B, n=35) between October 2012 and April 2018 were retrospectively analyzed. Main outcome measures included AMH reduction ratio (preoperative – postoperative AMH / preoperative AMH x 100), and 12 months after operation, CA 125 reduction ratio (preoperative – postoperative CA-125 / preoperative CA-125 x 100) and 12 month recurrence of the 2 groups.

RESULTS: Prior to operation, there were no significant differences between the group A and B in terms of age (33.4 ± 0.6 vs 32.1 ± 5.6, P=0.375), body mass index (21.5 ± 3.3 kg/m² vs 20.9 ± 2.8 kg/m², P=0.365), ASRM score (63.6 ± 36.5 vs 69.4 ± 43.2, P=0.520), bilaterality of endometrioma (54.3 % in both groups, P=0.996), and pre-operative CA-125 levels (94.6 ± 72.3 U/mL and 91.0 ± 43.1 U/mL, P=0.163).

Pre-operative AMH levels were significantly different in the two groups (3.9 ± 3.3 ng/mL vs 3.6 ± 1.6 ng/mL, respectively, P=0.820). At 3 and 6 months of treatment, AMH level was more reduced in Group A than Group B, but this difference was not statistically significant. (1.1 ± 0.9 ng/mL vs 1.9 ± 1.8 ng/mL, P=0.311 at 3 months, 1.5 ± 1.8 ng/mL vs 1.7 ± 1.7 ng/mL, P=0.610 at 6 months).

The AMH reduction ratio was non-significantly higher in Group A (46 ± 23 % vs 51 ± 25 %, P=0.330 at 3 months, 63 ± 20 % vs 55 ± 30 %, P=0.358 at 6 months). At 12 month follow up, these trends were reversed and the AMH level was higher in group A, but this difference was also statistically not significant. (1.95 ng/mL vs 1.64 ng/mL, P=0.615). CA 125 level and reduction ratio at 12 months were not statistically different between the 2 groups. There was no recurrence at 12 months in both groups.

CONCLUSIONS: These results show that, use of GnRHa reduces immediate post-op AMH level more at 3 and 6 months. However, after 12 months this effect is reversed. Long-term effects of GnRHa treatment in ovarian reserve and recurrence could be elucidated with further study with longer follow-up.

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A LONGITUDINAL ASSESSMENT OF THE IMPACT OF ENDOMETRIOSIS ON PATIENTS’ SALARIES.

Stephanie J. Estes, MD,a Ahmed M. Soliman, MS, PhD,b Hongbo Yang, PhD,c Jessie Wang, ScD,a Penn State Milton S. Hershey Medical Center, Hershey, PA;AbbVie, North Chicago, IL;Affiliation not provided.

OBJECTIVE: To evaluate the longitudinal indirect burden of endometriosis (EM) by assessing the impact of disease on salary and salary growth over a 5-year period.

DESIGN: A retrospective cohort study using data from the OptumHealth Reporting and Insights claims database.

MATERIALS AND METHODS: Women aged 18-49 years with ≥1 EM diagnosis (International Classification of Diseases codes 617.x or N80.x) were matched 1:1 to women without EM control by birth year, index year, employer industry, and geographic region. For EM patients, index dates were their first EM diagnosis date; for controls, index dates were random dates during the period where patients had continuous eligibility. Continuous eligibility in a health plan for ≥1 year pre- and post-index and active employment during the 1-year baseline period were required. Women with menopause or cancer diagnosis during baseline were excluded. Baseline characteristics were compared between EM and control cohorts with descriptive analyses. Average annual salaries for EM patients and controls were compared at each of the 5 post-index years using generalized estimating equations that accounted for matching. A multivariate longitudinal model was also used to estimate and compare the 5-year salary changes from baseline between the two cohorts. The model adjusted for baseline characteristics and correlations between observations. Salaries were inflated to 2018 USD using the Consumer Price Index.

RESULTS: Among the 6,851 matched pairs, the mean age at index date was 38.7 years. During baseline, EM patients, compared to matched controls, had significantly higher modified Charlson Comorbidity Index (CCI: 0.16 vs. 0.12, p<0.01) and lower average annual salary ($60,080 vs. $64,081, p<0.01). While oral contraceptive use was comparable between the two cohorts (20.1% vs. 20.2%, p=0.86), more EM patients used NSAIDs (32.4% vs. 20.1% vs. p<0.01) and opioids (44.6% vs. 26.0%, p<0.01) during baseline than controls. In the first year after the index date, EM patients had an observed average annual salary of $61,322 compared to $64,720 for controls (p<0.01). In each of the subsequent four years, the observed average salary for EM patients was less than that of controls by $3,697, $5,099, $6,286, and $6,600 (all p<0.01) among matched pairs that both had observed data. In comparing the salary changes from baseline over the 5-year study period, EM patients consistently had smaller salary growth than controls (p=0.02 for the difference in rate of salary growth between cohorts). In the first year after index date, EM patients had an estimated salary increase of $438, while it was $1,058 for controls. The salary changes from baseline for EM patients vs. controls were $1,555 vs. $2,562, $2,672 vs. $4,066, $3,789 vs. $5,570, and $4,906 vs. $7,074 for each of the subsequent four years respectively.

CONCLUSIONS: Patients with EM had a lower salary at baseline and a smaller increase in salary over time compared to their matched controls.

SUPPORT: Financial support for conducting the study was provided by AbbVie.

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ELEVATED SERUM INTERLEUKIN-32 LEVELS IN PATIENTS WITH ENDOMETRIOSIS: A PROSPECTIVE CASE-CONTROL STUDY.

Sung Hoon KIM, M.D., Ph.D., Si Hyeon Cho, M.D., Ph.D.,a Young-Sik Choi, M.D., Ph.D.a Young Sik Choi, M.D., Ph.D.a University of Ulsan College of Medicine, Asan Medical Center, Seoul, Korea, Republic of (South);bYonsei University College of Medicine, Gangnam Severance Hospital, Seoul, Korea, Republic of (South);cSeverance Hospital, Seoul, Korea, Republic of (South).

OBJECTIVE: Recently, interleukin (IL)-32 has been suggested to be involved in the pathogenesis of endometriosis. The aim of this study is to investigate whether serum IL-32 level might be used as a biomarker for diagnosis of endometriosis.

DESIGN: Prospective case-control study.

MATERIALS AND METHODS: We recruited the serum samples of 50 patients with histologically confirmed endometriosis and 35 controls. Enzyme-linked immunosorbent assay was used to analyze the serum IL-
32, IL-6, IL-10, tumor necrosis factor (TNF)-α, IL-1β, and CA-125 levels in patients with and without the disease and the diagnostic potentials of the cytokines were assessed using the area under the ROC curve (AUC).

RESULTS: Among evaluated cytokines, only serum IL-32 levels showed significant differences between patients with and without endometriosis (1111.24±149.59 vs. 6311.10±120.23; P<0.018, respectively). When the diagnostic power of serum IL-2 was evaluated, the area under the curve (AUC) was 0.638 (95% confidence interval (CI) 0.521-0.766, P<0.031). When serum IL-32 levels were combined with serum CA-125 levels, the AUC was increased to 0.749 (95% CI 0.640-0.858, P<0.001) with sensitivity and specificity of 60.0% and 82.9% at cut-off value of 0.640, which led to detect 25 more cases of endometriosis than the use of serum CA 125 with the cut-off value of 35 IU/ml (36/50 vs. 11/50, P<0.001) without sacrificing the specificity of the marker.

CONCLUSIONS: Serum IL-32 levels are elevated in patients with endometriosis and with combination of serum CA-125 levels, it may serve as a potential biomarker for endometriosis.

SUPPORT: This research was supported by a grant of the Korea Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health & Welfare, Republic of Korea (grant number: HI16C1682).

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ULTRALONG-TERM CYCLIC USE OF LOW-DOSE MONOPHASIC COMBINED ORAL CONTRACEPTIVE PILLS FOR THE MANAGEMENT OF RECURRENT SEVERE ENDOMETRIOSIS AFTER SECOND-LINE SURGERY. Chung-Hoon Kim, M.D., Ph.D., Ji-Won Moon, M.D., Shin Yong Moon, M.D., Ph.D., Fertility Center, Seoul, Korea, Republic of (South).

OBJECTIVE: We performed this study to evaluate the efficacy of ultralong-term cyclic administration of low-dose monophasic combined oral contraceptive pills (OCP) for more than 60 months in the resolution of pain and regression of recurrent endometrioma and pseudocyst after second-line surgery for recurrent severe endometriosis.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Twenty-two patients who were prescribed low-dose monophasic combined OCP to be taken with follow-up ultrasonogram (USG) for more than 60 months after January 2001 for the treatment of recurrent severe pain and endometrioma and pseudocyst after second-line surgery were included. All patients included in the present study received cyclic therapy (daily 21 to 35 days followed by 7 day interval) with low-dose monophasic combined OCP (ethinyl estradiol 0.02 mg and desogestrel 0.15 mg daily or ethinyl estradiol 0.02 mg and drospirenone 3 mg daily). Pain and endometrioma and pseudocyst on ultrasonogram (USG) were evaluated. For the evaluation of pain improvement, visual analogue scale (VAS) was used.

RESULTS: In 22 patients included in this study, 6 patients had a unilateral endometrioma while 16 patients had bilateral endometriomas. Sixteen patients and pseudocyst while 6 patients had no visible pseudocyst. Duration of treatment ranged from 64 months to 150 months. Nine patients completed the treatment after complete resolution of dysmenorrhea and complete regression of endometriomas and pseudocysts but 13 patients are currently getting treatment. Pain score by visual analogue scale (VAS) was significantly lower from 12th month of treatment compared with baseline assessment (P<0.001), and all patients reported complete resolution of dysmenorrhea at 36th month of treatment. Endometrioma size measured at 12th month of treatment significantly decreased compared with baseline size (P<0.001) and consistently decreased and endometriomas assessed by USG were completely regressed in 20 patients (90.9%) at 60th month of treatment. Pseudocyst size measured by USG was significantly smaller from 12th month of treatment (P=0.003) and pseudocysts were completely regressed in all patients at 36th month of treatment. Eight patients (36.4%) of 22 patients reported breakthrough vaginal bleeding but bleeding was small and transient and did not cause discontinuations. Except vaginal bleeding, no patients reported any other adverse effects attributed to the ultralong-term use of low-dose monophasic combined OCP.

CONCLUSIONS: Ultralong-term treatment with low-dose monophasic combined OCP is effective without any serious adverse effect in eliminating pain and regressing recurrent endometriomas and pseudocysts in patients with pelvic pain and endometriometric after second-line surgery. Therefore this long-term treatment using low-dose monophasic combined OCP can be an effective strategy in patients with pseudocysts as well as severe pain and recurrent endometriomas despite the second-line surgery. SUPPORT: None.

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THE USE OF DEXTROAMPHETAMINE SULFATE TO ALLEVIATE PELVIC PAIN DOES NOT INFLUENCE DELIVERED PREGNANCY RATES FOLLOWING IN VITRO FERTILIZATION-EMBRYO TRANSFER (IVF-ET) IN YOUNGER WOMEN. Jerome H. Check, M.D., Ph.D.a Diane L. Check, BS, MT,b Rachael Cohen, D.O.c Eric Chang, D.O.c Carrie K. Wilson, B.A.d Cooper Medical School of Rowan University, Camden, NJ; Cooper Institute for Reproductive Hormonal Disorders, PC, Mt. Laurel, NJ.

OBJECTIVE: Standard medical therapy with oral contraceptives, progesterins, gonadotropin releasing hormone (GnRH) agonists or antagonists for pelvic pain syndromes preclude pregnancy while taking the medication, and there is no evidence that such treatment improves subsequent fecundity. Surgical treatment is frequently not effective in relieving pain and can sometimes cause oocyte depletion. Furthermore, it is not clear if surgical removal of endometriosis improves subsequent fecundity, or may have a negative effect related to diminishing oocyte reserve. One of the most effective treatments for pelvic pain is dextroamphetamine which would allow the patient to try to conceive while gaining pain relief. The objective of the present pilot study was to determine if the use of this sympathomimetic amine has any negative effects on pregnancy rates or adverse fetal outcomes.

DESIGN: Prospective randomized controlled intervention study.

MATERIALS AND METHODS: Women with moderate to severe dysmenorrhea, who also wanted or needed IVF to become pregnant, were treated with dextroamphetamine sulfate. They were advised that in pharmacologic dosages the drug does not appear to be a teratogen, but its effect on pregnancy rates is not known. Patients were required to be aged ≤35 with normal oocyte reserve (serum anti-mullerian hormone (AMH) level over 1.06 ng/ml). If all embryos were created but none was selected for transfer, the cycle was not counted. The dosage of dextroamphetamine sulfate varied from 9.4mg to 37.6mg. The clinical and live delivered pregnancy rates were compared to historical controls who did not necessarily have pelvic pain.

RESULTS: There were 23 women treated with dextroamphetamine sulfate who had day 3 embryo transfers. All stated their pelvic pain was moderately to markedly improved. There were 197 historical controls having day 3 transfers. The clinical pregnancy rate was 56.5% (13/23) vs. 47.2% (93/197) the live delivered pregnancy rate was 45.3% (10/23) vs. 37.6% (74/197) (p=NS, Chi-square analysis). The implantation rates were 39.5% vs. 32.5%. The average number of embryos transferred was 1.9 for both groups. All babies in the amphetamine treated group were normal.

CONCLUSIONS: Though the study group was small, there does not seem to be any negative effect of using dextroamphetamine sulfate for pelvic pain on pregnancy rates following IVF-ET. Since some believe that endometriosis may have a negative effect on IVF outcome, if there was a bias, it would be against the study group. If anything, there may have been a trend for higher pregnancy rates in the amphetamine treated group. Based on these data a randomized controlled study is planned comparing pregnancy outcome in women with pelvic pain taking amphetamine vs. no amphetamine who are undergoing IVF-ET to achieve a pregnancy.

P-538 Wednesday, October 16, 2019 6:30 AM
ANALYSIS OF METABOLIC PATHWAYS AS A NOVEL CLINICAL BIOMARKERS OF ENDOMETRIOSIS. Ya-Ching Chou, Ph D.a Chii-Ruey Tzeng, MD, MPH.b "National Chiao Tung University, Hsinchu, Taiwan; "Taipei Medical University Hospital, Taipei, Taiwan.

OBJECTIVE: Endometriosis is a common gynecological disease and causes infertility. The discovery of biomarkers has been demonstrated to play an important role in medicine and diagnosing the patient. Metabolomics and metabolic profiling have become popular in many research projects and discovery novel biomarkers. Till now, little is known about the association of metabolic pathways and endometriosis. We investigate the seven metabolic pathways in endometriosis, including alpha-1 antitrypsin (AAT), alpha-1 acid glycoprotein (AGP-1), Hemopexin, Retinol-binding protein 4 (RBP4), Transferrin, Transhyretin and Vitamin D-binding protein (VDBP).

P-539 Wednesday, October 16, 2019 6:30 AM
LONG TERM TREATMENT OF ENDOMETRIOSIS ASSOCIATED PAIN (EAP) WITH LINZAGOLIX: EFFICACY AND SAFETY AFTER 12 MONTHS OF TREATMENT. Robert N. Taylor, MD PhD, Elke Bestel, MD, Jean-Pierre Gotteland, PhD, Veronique Lecomte, Pharm D, Rachel Dubouloz, MSc, Paul Terrill, PhD, Andrew Humberstone, PhD, Ernest Loumaye, MD, PhD. University of Utah Health, Salt Lake City, UT, ObsEva SA, Plan-les-Ouates, Switzerland; Cytel Inc, London, United Kingdom.

OBJECTIVE: To assess safety and maintenance of efficacy of linzagolix with low-dose add-back hormonal therapy.

MATERIALS AND METHODS: Participants were women with surgically confirmed endometriosis and moderate to severe EAP. Efficacy was assessed using a daily eDiary as the % of responders (≥ 30% reduction in mean 28-day scores) in overall pelvic pain (OPP), dysmenorrhea (DYS) and non-menstrual pelvic pain (NMPP). Dyspareunia and dyschezia scores were also assessed. Bone mineral density (BMD) of the femur, hip and spine were assessed by dual-energy X-ray absorptiometry (DXA).

RESULTS: At 12 w, there was a significant increase in the % of responders for OPP, DYS and NMPP for doses of 75 mg and above compared to PBO. These effects were generally maintained or increased at 24 and 52 w. At 12 w, there were significant improvements in dyspareunia (200 mg only) and dyschezia scores which were maintained or increased at 24 and 52 weeks. Mean BMD losses (spine) at 24 weeks were <1% at doses of 50 and 75 mg and increased with increasing dose up to 2.6% for 200 mg. A similar pattern was observed at 52 w: BMD changes in femur and hip were similar but generally smaller.

CONCLUSIONS: Linzagolix at daily doses of 75 mg and above significantly improved EAP symptoms at 12 w and these effects were maintained or increased at 24 and 52 w. These data support Phase 3 trials in women with EAP using linzagolix 75 mg once daily alone and 200 mg once daily with low-dose add-back hormonal therapy.

SUPPORT: The study was funded by ObsEva SA.

P-540 Wednesday, October 16, 2019 6:30 AM

DECREASED CLINICAL PREGNANCY AND LIVE BIRTH RATES IN WOMEN WITH ENDOMETRIOSIS, IN THE “EIVF” DATABASE. Kassie Jean Bollig, MD, Henok G. Woldu, PhD, Judy E. Stern, PhD, Albert L. Hsu, MD, Resident Physician, Columbia, MO; Biostatistics and Research Design Unit; University of Missouri, Columbia, MO; Dartmouth-Hitchcock, Lebanon, OR; Department of Reproductive Endocrinology and Infertility; University of Missouri, Columbia, MO.

OBJECTIVE: To determine whether surgically-confirmed endometriosis is associated with decreased implantation, pregnancy, or live birth rates compared with male factor infertility in women undergoing in vitro fertilization (IVF).

DESIGN: Retrospective multivariable analysis of 34,278 fresh IVF cycles in Massachusetts between 2003-2006, from the “eIVF” database.

MATERIALS AND METHODS: IVF cycles in women with surgically-confirmed endometriosis were compared with those in couples with male

TABLE 1

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<tr>
<th>N</th>
<th>12 w</th>
<th>24 w</th>
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<tr>
<td>50 mg</td>
<td>49</td>
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<td>36</td>
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<tr>
<td>75 mg</td>
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<td>-2.3 (1.8)</td>
<td>-2.1 (2.9)</td>
<td>-2.9 (3.1)</td>
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</table>

| BMD spine Mean (95% CI) % CFB | 24 w | 52 w |
|---|---|
| 0.14 (-0.83, 1.11) | 0.14 (-1.04, 1.31) |
| -0.80 (-1.57, -0.03) | -1.14 (-2.21, -0.07) |
| -1.37 (-2.14, -0.59) | -1.40 (-3.35, 0.55) |
| -2.60 (-3.56, -1.65) | -2.19 (-3.59, -0.78) |

1PBO only to 12 w; Subjects randomized to 200 mg received 100 mg from 24 to 52 w; *p < 0.05 compared to PBO.
factor infertility; only fresh IVF cycles that resulted in an embryo transfer were analyzed. Couples with both endometriosis and male factor infertility, and women with "suspected endometriosis" (not surgically confirmed), were excluded from analysis. Implantation rates were calculated in two ways: (1) gestational sacs (GS) per embryos transferred (ET), and (2) heartbeats (HB) per ET. Clinical pregnancy and live birth rates per cycle were also calculated. Means were compared using two-sample t-tests; medians were compared with Mann-Whitney U test; pregnancy and live birth rates were compared using Chi-square tests; and multivariable analyses were performed using logistic regression. SAS version 9.4 (SAS Institute, Cary, NC) was used for all analyses.

RESULTS: 350 fresh IVF cycles in women with surgically-confirmed endometriosis were compared with 2,824 cycles in couples with male factor infertility only. Women with endometriosis were significantly younger and leaner, with lower max E2 levels. On univariable analysis, fewer women with endometriosis had implantation rates >= 50%, while no differences were found in pregnancy or live birth rates (Table). When adjusting for age and BMI in multivariable analysis, the odds of a clinical pregnancy was 35.5% higher in pregnant women with endometriosis (OR 1.36, 95% CI [1.07-1.71]), and the odds of a live birth was 33.9% higher in male factor infertility (OR 1.34, 95% CI [1.02-1.76]), compared to women with surgically-confirmed endometriosis.

CONCLUSIONS: Compared with male factor infertility, surgically-confirmed endometriosis is associated with lower odds of implantation, clinical pregnancy and live birth in couples undergoing IVF.

P-541 Wednesday, October 16, 2019 6:30 AM
CIRCULATING PLACENTAL GROWTH FACTOR (PLGF) CONCENTRATION IN PREGNANT WOMEN WITH ENDOMETRIOSIS: A CASE-CONTROL STUDY. Simone Ferrero, MD, PhD,a Fabio Barra, MD,a Valerio Gaetano Vellone, MD, PhD,a Umberto Leone Roberti Maggiore, MD, PhD,b Carolina Scala, MD,a,b DINOGMI, University of Genova, Genova, Italy; DISC, University of Genova, Genoa, Italy; Department of Gynecologic Oncology, IRCCS National Cancer Institute, Milan, Italy; ISTITUTO G. Gaslini, Genova, Italy.

OBJECTIVE: It is widely accepted that angiogenesis is pivotal to the establishment of endometriotic lesions and it is fundamental in the regulation of placentation development starting from the early stages of pregnancy. Circulating vascular endothelial growth factor and placental growth factor (PLGF) levels have been reported to be increased in women with endometriosis when compared with controls, conversely decreased levels of PLFG have been reported in pregnant women developing preeclampsia. For this reason, the presence of endometriosis might be a protective factor for the development of early onset preeclampsia during pregnancy, since the increased level of PLGF in these patients might promote placentation development. The objective of this study was to assess the first trimester serum concentrations of circulating PLGF in pregnant women with endometriosis compared to those without endometriosis.

DESIGN: Case-control study based on the retrospective analysis of a prospectively collected database.

MATERIALS AND METHODS: This study included 40 pregnant women who had histological diagnosis of endometriosis (E) and 40 pregnant women without endometriosis (C). Women included in the control group had no evidence of endometriosis at laparoscopy. Exclusion criteria were previous uterine surgery or uterine malformations, major fetal malformities, diabetes, alcohol and/or drug abuse, chronic hypertension disease, known autoimmune diseases, fetal aneuploidy or multiple gestations.

RESULTS: Compared to C women, those with E had no statistically significant difference regarding maternal demographic characteristics (age, BMI, parity, smoking, mode of conception). No statistically significant difference was observed in the first trimester PAPP-A levels, first trimester and mid-pregnancy mean UIA Doppler PI, neonatal birth weight (BW) centiles, SGA fetuses and early onset preeclampsia (<37 weeks of gestation) prevalence. However, women with E had statistically significant higher first trimester concentration of PLGF compared to those without endometriosis (C) (group E: PLGF MoM 1.40; group C: PLGF MoM 1.19; p<0.05).

CONCLUSIONS: First trimester serum concentrations of PLGF are significantly higher in pregnant women with endometriosis compared to those without the disease. The major limitations of this study were that it was retrospective and it had a relatively small sample size. The small number of pregnant women with endometriosis did not allow performing a further subanalysis according to the different forms of endometriosis (peritoneal endometriosis, deep endometriosis, ovarian endometriosis).

P-542 Wednesday, October 16, 2019 6:30 AM
PELVIC FLOOR MUSCLE SPASM, COMORBID PAIN AND MENTAL HEALTH CONDITIONS IN WOMEN WITH ENDOMETRIOSIS-ASSOCIATED CHRONIC PELVIC PAIN. Pamela Stratton, MD,a Hannah K. Tandon, BA,b Vy Phan, BS,b Ninet Sinaii, PhD, MPH,c Jay Shah, MD,b Margaret Behns, PhD, RN,d Barbara I. Karp, MD,a Office of the Clinical Director, Intramural Research Program, National Institute of Neurological Disorders and Stroke, NIH, Bethesda, MD; Rehabilitation Medicine Department, Intramural Research Program, National Institute of Neurological Disorders and Stroke, NIH, Bethesda, MD; Biostatistics & Clinical Epidemiology Service, Intramural Research Program, National Institute of Neurological Disorders and Stroke, NIH, Bethesda, MD; Department of Gynecologic Oncology, IRCCS National Cancer Institute, Milan, Italy; Institute of G. Gaslini, Genova, Italy.

OBJECTIVE: Describe pelvic pain pattern, and pain and mental health comorbidities in women with endometriosis-associated chronic pelvic pain (endo-CPP).

DESIGN: Baseline, cross-sectional data from a prospective, double-masked, placebo-controlled study of botulinum toxin injection for persistent endo-CPP despite optimal pain, surgical and hormonal treatment.

MATERIALS AND METHODS: Subjects described headache (including migraine) history and completed standardized questionnaires: Pelvic Pain Questionnaire; Patient-Reported Outcomes Measurement Information System (PROMIS) scales for anxiety, depression, fatigue, and sleep disturbances; Rome Criteria I/II/III; irritable bowel syndrome (IBS); hypervigilance syndrome (PBS); Oswestry Disability Index. Patients underwent pelvic exam to confirm pelvic floor spasm and determine pelvic pain pattern. Allodynia and hyperalgesia were assessed paraspinally to determine the extent of pelvic (T9-S2) and widespread (C2-S2) spinal segmental sensitization. Ordinal data were analyzed for trends using the Jonckheere-Terpstra Test. Unordered dichotomous variables were compared using Fisher’s exact test.

RESULTS: Women (n=30, age 18-50yr) with endo-CPP (median duration 10.5yr; range 2-20) were evaluated, 22/23 women using hormonal methods (progestin IUD/combinendoral contraception/depot medroxyprogesterone) had menses suppression; 7 others avoided hormones due to side effects. At pelvic exam, 30/30 had pelvic floor spasm that each identified as a primary focus of endo-CPP. Non-menstrual pelvic pain was reported by 29, dysmenorrhea at their last menses by 27, and dyspareunia by 14/15 who had sex in the last month; 7 others avoided sex because of pelvic pain. Women had widespread 18 had pelvic spinal segmental sensitization. Most women reported anxiety (18), depression (14), fatigue (23) and sleep disturbances (18). 16 women met criteria for IBS, 22 for PBS, and 17 reported migraine. Moderate disability was reported by 14 women and severe disability by 3. Having either IBS or PBS was associated with depression (p=0.031), anxiety (p=0.003), and fatigue (p=0.029) but not sleep disturbances or disability. Moderate pain was associated with pelvic and widespread sensitization (p=0.025 and p=0.009, respectively), but not PROMIS outcomes.

CONCLUSIONS: Not surprisingly, women with endometriosis-associated chronic pelvic pain persisting despite treatment report non-menstrual pain, dysmenorrhea and dyspareunia. Importantly, they experience significant
comorbid pain and mental health conditions. Pelvic muscle spasm and associated sensitization may be a key manifestation of their endometriosis-associated chronic pelvic pain. Comorbid pain conditions and mental health may factor into endo-CPP. These women merit comprehensive assessment and management of their pain patterns.

Clinicaltrials.gov: NCT01553201

SUPPORT: Funded by Intramural Research Program of NINDS, NICHD and the Clinical Center, NIH.

**P-543** Wednesday, October 16, 2019 6:30 AM

**EFFECT OF ENDOMETRIOSIS ACTIVITY ON PREGNANCY OUTCOME IN PATIENTS WITH REPEATED IMPLANTATION FAILURE.** Chenyi Zhong, Master,a Liusjije Gao, Master,a Jingsjin Mao, Master,a Yundong Mao, professor aFirst Affiliated Hospital of Nanjing Medical University, Nanjing, China; bAffiliation not provided; cOB/GYN, Nanjing, China.

OBJECTIVE: Patients face a problem in IVF/ICSI treatment. repeated implantation failure. In order to explore whether endometriosis affects the implantation of embryo when IVF/ICSL.fhis study compared the pregnancy outcomes of patients with endometriosis who failed to implant repeatedly. So as to explore the appropriate treatment plan for such patients.

DESIGN: Endometriosis patients with repeated implantation failure were grouped according to the timing of treatment and whether down-regulated or not.

MATERIALS AND METHODS: patients who asked for IVF/ICSI treatments in our Reproductive Center.A retrospective cohort study was performed on endometriosis patients with repeated implantation failure. The differences in pregnancy outcomes were compared. The comparison between quantitative data was tested by analysis of variance. The differences between the classification data were analyzed by chi-square test.

RESULTS: 1) According to treatment timings, the cumulative delivery rate(according to the numbers of people) was significantly lower than that of the early treatment group(28.17% vs 43.30%, P<0.05) and the late treatment group(28.17% vs 47.06%, P<0.01). The available embryo rate(93.56%) and high quality embryo rate(81.84%) in the early treatment group were significantly higher than those in the untreated group(85.20% and 62.93%) and the late treatment group(88.20% and 69.61%), P<0.01. The high quality embryo rate in the late treatment group(69.61%) was also significantly higher than that in the untreated group(62.93%), P<0.05. 2) Kaplan-Meier curve analysis showed that the time required to get a pregnancy(live birth) for late treatment group was the longest(21.54±0.49, 22.27±0.45), P<0.001. 3) Down-regulation increased the clinical pregnancy rate of the untreated group and the late treatment group (41.18% vs 26.32% vs 50.00% vs 24.62%, P<0.05), and the live birth rate of the treatment group(38.78% vs 17.97% and 41.67% vs 17.69%, P<0.01). Down-regulation can increase the overall cumulative live birth rate (cycle) (27.78% vs 13.51% vs 24.24% vs 12.99% and 46.30% vs 13.69%, P<0.05).multivariate logistic regression analysis adjusted the basic line, the live birth rate of the down-regulated group was 2.249 times higher than that of the non-down-regulated group (P<0.05). 4) According to the EMs activity, the clinical pregnancy rate(38.84%) and live birth rate(29.75%) of the EMs-controlled patients were increased compared to the control group (26.25% and 18.13%, P<0.05).

CONCLUSIONS: 1) The treatment of endometriosis will improve the cumulative pregnancy rate and live birth rate of repeated implantation failure; 2) The down-regulation cycle can also improve the pregnancy outcome of endometriosis patients with repeated implantation failure; 3) The control of endometriosis activity can lead to better clinical outcomes in patients with repeated implant failures; 4) It is necessary to control the activity of endometriosis in patients with repeated implantation failures in IVF/ICSI treatment.

**P-544** Wednesday, October 16, 2019 6:30 AM

**SYMPTOMIMETIC AMINE THERAPY MAY IMPROVE LIVE DELIVERED PREGNANCY RATES (PRs) FOLLOWING IN VITRO FERTILIZATION-EMBRYO TRANSFER (IVF-ET) IN WOMEN OF ADVANCED REPRODUCTIVE AGE – A PILOT STUDY.** Jerome H. Check, M.D., Ph.D.,a Rachael Cohen, D.O.,a Diane L. Check, B.S., M.T.,b Eric Chang, D.O.,b,2 Cooper Medical School of Rowan University, Camden, NJ; 2Cooper Institute for Reproductive Hormonal Disorders, P.C., Mt. Laurel, NJ.

OBJECTIVE: A very effective medical therapies for various types of pelvic pain is the use of dextroamphetamine sulfate. The probable mechanism for pain relief seems to be by releasing more dopamine from sympathetic nerve fibers which diminishes cellular permeability. Increased cellular permeability may be the cause of pelvic pain related to increased absorption or irritating chemicals into pelvic tissues leading to excessive inflammation. Increased inflammatory cells, especially natural killer cells, could be a cause of infertility or miscarriage. There have been anecdotal reports of successful pregnancies in patients with repeated failures to successfully conceive despite multiple embryo transfers with this treatment. The objective of the present study was to perform a pilot study to determine if treatment with dextroamphetamine sulfate could improve the chance of a successful pregnancy following IVF-ET, in a poor prognosis group, i.e., women of advanced reproductive age.

DESIGN: Prospective patient option controlled study.

MATERIALS AND METHODS: Women age 40–42 with normal oocyte reserve as evidenced by a day 3 serum FSH ≤ 11 mIU/mL and a serum anti-mullerian hormone (AMH) level > 1.06 ng/mL with a history of moderate to severe dysmenorrhea, dyspareunia, mittelschmerz, or chronic pelvic pain who requested or required IVF-ET were given the option of being treated with dextroamphetamine sulfate during the IVF cycle and the first trimester of pregnancy. They were advised of the theoretical benefit, but the lack of hard data, just anecdotal reports. The IVF would not be started until the dosage that best corrected the pain with acceptable side effects was achieved. The starting dosage was 9.4mg extended release capsules. The maximum dosage was 37.6 mg. All embryo transfers were performed on day 3.

RESULTS: There were 12 couples recruited (grp A) and 11 made it to ET. These results were compared to 77 historical controls (grp B). The historical control group did not have to have a history of pelvic pain. The average number of embryos transferred were 2 vs. 2.1 for grp A and B. The clinical PR per transfer was 27.3% (3/11) vs. 18.2% (17/77). The live delivered PR was 27.3% vs. 11.7% (9/77). The implantation rates were 18.2% and 11.8%. All 11 grp A women had marked improvement of their pelvic pain. The 3 babies born in grp A were all term and healthy. The small pilot study group precluded meaningful statistical evaluation.

CONCLUSIONS: This pilot study showed sufficient benefit to improving fecundity in this poor prognosis group that we plan to submit a proposal to the IRB for a larger randomized control trial. Many of these grp A women may have had endometriosis. The advantage of dextroamphetamine sulfate over other medical therapies for pelvic pain is that it allows the patient to conceive while receiving pain relief.

ENDOMETRIOSIS - BASIC

**P-545** Wednesday, October 16, 2019 6:30 AM

**OVEREXPRESSION OF CD44v6 IS INVOLVED IN THE DEVELOPMENT OF THE EARLY ENDOMETRIOTIC LESION IN A XENOGRAFT MODEL.** Jennifer Knudtson, MD,a Jessica E. McLaughlin, MD,a Marlen Tellez Santos, BS, MS,b Robert Schenken, MD.a aUniversity of Texas Health Science Center San Antonio, San Antonio, TX; bUniversity of Incarnate Word, San Antonio, TX.

OBJECTIVE: We previously showed decreased development of endometriotic lesions in CD44 knockout mice compared to control.4 CD44 has 10 different variants and a standard form. Menstrual endometrial cells (MECs) from women with endometriosis have increased adhesion and also other medical therapies for pelvic pain is the use of dextroamphetamine sulfate. The probable mechanism for pain relief seems to be by releasing more dopamine from sympathetic nerve fibers which diminishes cellular permeability. Increased cellular permeability may be the cause of pelvic pain related to increased absorption or irritating chemicals into pelvic tissues leading to excessive inflammation. Increased inflammatory cells, especially natural killer cells, could be a cause of infertility or miscarriage. There have been anecdotal reports of successful pregnancies in patients with repeated failures to successfully conceive despite multiple embryo transfers with this treatment. The objective of the present study was to perform a pilot study to determine if treatment with dextroamphetamine sulfate could improve the chance of a successful pregnancy following IVF-ET, in a poor prognosis group, i.e., women of advanced reproductive age.

DESIGN: Prospective patient option controlled study.

MATERIALS AND METHODS: Women age 40–42 with normal oocyte reserve as evidenced by a day 3 serum FSH ≤ 11 mIU/mL and a serum anti-mullerian hormone (AMH) level > 1.06 ng/mL with a history of moderate to severe dysmenorrhea, dyspareunia, mittelschmerz, or chronic pelvic pain who requested or required IVF-ET were given the option of being treated with dextroamphetamine sulfate during the IVF cycle and the first trimester of pregnancy. They were advised of the theoretical benefit, but the lack of hard data, just anecdotal reports. The IVF would not be started until the dosage that best corrected the pain with acceptable side effects was achieved. The starting dosage was 9.4mg extended release capsules. The maximum dosage was 37.6 mg. All embryo transfers were performed on day 3.

RESULTS: There were 12 couples recruited (grp A) and 11 made it to ET. These results were compared to 77 historical controls (grp B). The historical control group did not have to have a history of pelvic pain. The average number of embryos transferred were 2 vs. 2.1 for grp A and B. The clinical PR per transfer was 27.3% (3/11) vs. 18.2% (17/77). The live delivered PR was 27.3% vs. 11.7% (9/77). The implantation rates were 18.2% and 11.8%. All 11 grp A women had marked improvement of their pelvic pain. The 3 babies born in grp A were all term and healthy. The small pilot study group precluded meaningful statistical evaluation.

CONCLUSIONS: This pilot study showed sufficient benefit to improving fecundity in this poor prognosis group that we plan to submit a proposal to the IRB for a larger randomized control trial. Many of these grp A women may have had endometriosis. The advantage of dextroamphetamine sulfate over other medical therapies for pelvic pain is that it allows the patient to conceive while receiving pain relief.
RESULTS: Expression of mRNA and protein confirmed appropriate OE of CD44s, CD44v3 and CD44v6 in the different cell types. CD44v6 OE did slightly induce CD44v6 expression. At necropsy, the majority of cells attached to the peritoneum. CD44v6 OE increased attachment of hESCs compared to control (p<0.01). CD44v6 OE did not change attachment of iEECs. There was no difference in attachment in iEECs or hESCs with OE of CD44s or CD44v3.

CONCLUSIONS: Overexpression of CD44v6 increases attachment of ESCs to PMCs in an in vivo xenograft model. Mesenchymal endometrial cell type and CD44 variants play a complex role in the development of the early endometriotic lesion.


SUPPORT: KL2 TR001118 (JK), American Society of Reproductive Medicine (JK).

P-546 Wednesday, October 16, 2019 6:30 AM

ABERRANT EXPRESSIONS OF CHLORIDE CO-TRANSPORTERS IN ENDOMETRIOSIS. Inha Lee, M.D.a Young Bin Won, M.D.a Heeyoung Kim, M.D.a Jae Hoon Lee, M.D.a Bo Hyun Yoon, M.D.a Seok Kyo Seo, M.D.a Young Sik Choi, M.D., Ph.D.a Byung Seok Lee, M.D., Ph.D.a SiHyun Cho, M.D., Ph.D.a Yonsei University College of Medicine, Severance hospital, Seoul, Korea, Republic of (South); Yonsei University College of Medicine, Gangnam Severance Hospital, Seoul, Korea, Republic of (South).

OBJECTIVE: Recent studies have shown that cell membrane ion channels play an important role in cell migration, also shown in the context of cancer development and metastasis. Although endometriosis is a benign gynecological disease, endometriosis shows a behavior similar to cancer in terms of migration and invasion of nearby tissues and organs. However, there are only few studies on cell membrane ion channels and their association with endometriosis. The aim of this study was to investigate the effect of these ion channels on endometriosis.

DESIGN: Experimental study using human endometrial tissue and human endometrial stromal cell.

MATERIALS AND METHODS: In the endometriosis group(n=21), eutopic endometrial tissue and ectopic endometrial tissue were obtained from the patients who had undergone laparoscopic ovarian cyst enucleation due to endometriosis. In the control group(n=18), eutopic endometrium was obtained from patients who had undergone laparoscopic cyst excision for benign ovarian causes other than endometriosis. Quantitative real time PCR (qRT-PCR) and western blot were performed to quantify ion channel-related NKCC1, NKCC2 and CLC3 mRNA expressions and protein concentrations in endometrial tissue. Furthermore, to test the influence of ion channels on endometrial migration of endometrial stromal cells, siRNA transfection and migration assay of eutopic endometrial cell of endometriosis patients.

RESULTS: mRNA expression of NKCC1, NKCC2 and CLC3 in ectopic endometrial tissue from endometriosis patients was significantly higher than in eutopic endometrium for both endometriosis and control group (p<0.05). The mRNA expression of eutopic endometrium from endometriosis patients was higher than the control group, but the difference was not statistically significant. Western blot showed an increased expression of NKCC1, NKCC2 and CLC3 in both the eutopic and ectopic endometrium of endometriosis group, compared to the expression in eutopic endometrium of control group (p<0.05). After siRNA transfection, qRT-PCR showed a decreased expression of MMP2 and MMP9. Migration assay further suggested a decreased migratory potential of the eutopic endometrial cells. Additional analysis showed that the magnitude of expression of NKCC1, CLC3 and the size of endometriotic ovarian cyst were positively correlated.

CONCLUSIONS: The expression of NKCC1, NKCC2 and CLC3 associated with plasma membrane ion channels is increased in endometriosis patients, which may be implicated in the increased cell migration potential in endometriosis.

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PROPRANOLOL INHIBITS CATECHEOLOSTROGEN-INDUCED HUMAN ENDOMETRIAL STROMAL CELL SURVIVAL MEDiated BY p38 MAPK SIGNALING. Rachel Grimes Sprague, MD, Jong Woul Kim, PhD, Asli Ozmen, PhD, Xiaofang Guo, MD, Anthony N. Imudia, MD, Charles J. Lockwood, MD, MHCM, Ronald R. Magness, PhD, Umit A. Kayisli, PhD. Department of Obstetrics and Gynecology, Morsani College of Medicine, University of South Florida, Tampa, FL.

OBJECTIVE: Catecholesterogens (CCes), 2-Hydroxyestradiol (OHE2) and 4-OHE2, are biologically active metabolites of 17β-estradiol (E2). Studies indicate that local increases in E2 production as well as aberrant expression of E2 metabolizing enzymes enhance local generation of CCes in women with endometriosis. CCes have low binding affinity to estrogen receptors whereas CCes display high binding affinity to β2-adrenergic receptor (AR), which induce uterine endothelial cell proliferation during gestation. Our recent data demonstrated β2-AR expression in eutopic and ectopic endometrial tissue. In addition, binding of CCes to β-AR enhances huma endometrial stromal cell (HESC) viability, suggesting contribution of CCes to the pathogenesis of endometriosis. Thus, we tested the hypothesis that the mechanism of CCE-enhanced HESC viability involves alterations in either proliferation or apoptosis mediated by β-AR-induced common intracellular signaling pathways, i.e. AKT, MAPK and/or NFκB.

DESIGN: BrdU, Apoptotic Cell Detection ELISA, q-PCR, Western blot and XTT analyses were performed on cultured HESCs derived from endometrial biopsies.

MATERIALS AND METHODS: Cultured HESCs treated with 10^-8 M E2 or 10^-7 M OHE2 or 10^-7 M 4-OHE2, were measured by BrdU proliferation and ELISA for apoptosis (n=3 with quadruplicate). Total RNA from control HESCs was isolated and pro-apoptotic, anti-apoptotic, and proliferation markers were evaluated by q-PCR (n=5 with duplicate). Total and phosphorylated AKT, p38 and ERK1/2 MAPKs, and NFκB levels were detected in lysates of cultured HESCs (n=3 with triplicate) treated for 10 min with vehicle (control) or 10^-7 M E2 or 2-OHE2 or 4-OHE2 ± 2x10^-5 M non-specific β-antagonist (propranolol). Subsequently, XTT assays were conducted with p38 MAPK inhibitor to assess the effect of p38 MAPK on CCE-induced enhanced HESC viability (n=4 with triplicate). Results were analyzed by One-way ANOVA and post hoc Tukey test.

RESULTS: An increased HESC proliferation index by E2 and OHE2 (P<0.05 and P<0.05, respectively) and decreased apoptosis were detected in HESCs treated with 2-OHE2 and 4-OHE2 vs. control (P<0.01 and P<0.01, respectively). Analysis of apoptotic markers by q-PCR revealed a significant decrease in Bax mRNA expression in response to 2-OHE2 treatment vs. control (P<0.01). Among the several intracellular signaling cascades analyzed, only phosphorylation levels of p38 MAPK were increased by either treatment with 2-OHE2 or 4-OHE2 (P<0.05 and P<0.05 vs. control, respectively), but not with E2. β-AR antagonism with propranolol mitigated this increased phosphorylation in p38 MAPK levels (P<0.05 and P<0.01, respectively) and inhibition of p38 MAPK by SB203580 blocked CCE-induced HESC survival (P<0.05 and P<0.01, respectively).

CONCLUSIONS: These data indicate that induction of endometrial stromal cell viability by CCE-β-AR interactions results from an imbalance in both proliferation and anti-apoptotic mechanisms and is specifically mediated by the activation of p38 MAPK signaling. These data also suggest that inhibition of β-ARs with propranolol may be a novel treatment option in endometriosis.

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ENDOMETRIOSIS INCREASED ATHEROSCLEROSIS IN A MURINE MODEL. Ramaniaah Mamillapalli, PhD,a Nikoletta Toffoloni, BA,b Joshua Huttler, BA,b Yan Zhang, MD,a Peng Chen, MD, PhD,a Nina Stachenfeld, PhD,a,b Hugh S. Taylor, M.D.a,Yale University School of Medicine, New Haven, CT; bThe John B. Pierce Laboratory.

OBJECTIVE: Epidemiologic studies have identified an association between endometriosis and subsequent development of cardiovascular disease. Here we used an animal model to determine if endometriosis caused atherosclerosis. Further, identifying the molecular mechanisms responsible for atherosclerosis in women with endometriosis is necessary to develop targeted treatment strategies to reduce cardiovascular risk in women with endometriosis. This study aims to determine if endometriosis increases aortic plaque formation in a murine model and explores the conditions that are mechanistically responsible for the observed changes.

DESIGN: Experimental endometriosis was induced in mice to identify changes related to atherosclerosis and cardiovascular disease. Oil Red O (ORO) staining, biochemical assays and qRT-PCR were performed to measure the degree of atherosclerotic plaque development, lipid levels, and the differential gene expression of inflammation mediators.

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MATERIALS AND METHODS: Endometriosis was induced in 9-week-old female ApoE<sup>-/-</sup> C57BL/6 mice by suturing donor uterine tissue to the walls of the peritoneal cavity. A sham control group was also created using no uterine tissue. After 23 weeks post-surgery, mice were euthanized and serum was collected from the blood. Biochemical assays were carried out for lipid profile at the Yale Core Center. Total RNA was extracted from the serum using Trizol reagent and used for qRT-PCR to analyze the gene expression of inflammatory mediators. Whole aortas were dissected and stored in DPBS at 4°C until being subjected to ORO staining. The degree of staining was quantified using ImageJ software. The total area of each longitudinally-opened aorta was measured and the percent of red stain was then calculated using the same red threshold for all samples.

RESULTS: The mice in the endometriosis group showed noticeable bilateral atherosclerotic lesions, while no lesions were found in the corresponding location in the control mice. ORO staining of the aorta indicated minimal plaque formation in the control mice and a significant increase in plaque development in the endometriosis group. The difference in average percent stain between the groups was 4.75% indicating that the endometriosis group showed significantly more staining than the control group: control, 3.13 ± 0.95, n=5; endometriosis, 7.89 ± 1.56, n=5, (mean ± SEM; P<0.03, unpaired t test). Biochemical assays from serum showed no significant difference between the control and the endometriosis groups with respect to total cholesterol, HDL, LDL, TG, and glucose levels. However, serum inflammation markers associated with cardiovascular disease such as TNF-α, C-Reactive Protein, and IL-6 were altered by endometriosis in the mouse model. 

OBJECTIVE: Endometriosis is a leading cause of pelvic pain and infertility. Prostaglandin E2 (PGE2) is widely regarded to be central to its pathogenesis. We tested the hypothesis that endometriotic tissue expresses PGE2 and that this expression plays a role in regulating the propagation of endometriosis. Future studies into different CCEs and β-ARs may identify points of fragility for future translational therapies.


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α1D-ADRENERGIC RECEPTOR EXPRESSION IN HUMAN ENDOMETRIAL STROMAL CELLS CONTRIBUTES TO CATECHOLESTRADIOL-INDUCED CELL SURVIVAL: IMPLICATIONS FOR ENDOMETRIOSIS.

Objective: Catecholestrogens (CCEs), 2-Hydroxyestradiol (OHE<sub>2</sub>) and 4-OHE<sub>2</sub>, are biologically active metabolites of 17β-estradiol (E<sub>2</sub>). Local increases in E<sub>2</sub> production as well as aberrant E<sub>2</sub> metabolism can facilitate generation of CCEs in women with endometriosis. During gestation, CCEs bind to adrenergic receptors (ARs) to mediate uterine endometrial cell proliferation. Our recent data demonstrated that compared to the basals of the endometrium, the functionalis layer displayed increased β2-AR expression in women with endometriosis. Moreover, binding of CCEs to β-ARs enhanced human endometrial stromal cell (HESC) viability in culture, suggesting a modulatory role for CCE-β-AR binding in retrograde menstruation that contributes to endometriosis development. It is unknown if, in addition to β-ARs, α-ARs also have a role in this process. We, therefore, tested the hypothesis that ectopic endometrial tissue expresses α1D-AR and that 2-OHE<sub>2</sub> and 4-OHE<sub>2</sub> will potentiate HESC viability via α-ARs.

Design: Immunohistochemistry was performed on paired eutopic/ectopic endometrial tissue and XTT analysis was conducted on cultured CCE-treated HESCs derived from endometrial biopsies.

Materials and Methods: Paired eutopic/ectopic endometrial sections from women with endometriosis in the proliferative (n=5) or secretory (n=4) phases were immunostained using α1D-AR antibody and evaluated semi-quantitatively by HSCORE. Confluent HESCs derived from endometrial biopsies at time of surgery for benign reasons were cultured in 96-well plates (5x10<sup>3</sup> cells/well) and treated with vehicle (control) or with 10<sup>-8</sup> M E<sub>2</sub> or 2-OHE<sub>2</sub> or 4-OHE<sub>2</sub> ± non-specific α-AR inhibitor (phentolamine) for 48h. XTT assays measured cell viability. Experiments (n=4) were performed in duplicate and data were analyzed by One-way ANOVA with post hoc Tukey.

Results: Immunohistochemistry analysis revealed overall weak to moderate α1D-AR staining in endometrial epithelial cells and weak staining in endometrial stromal cells with no significant difference between eutopic and ectopic endometrial tissues in either phase. Compared to the basals layer, both stromal and epithelial cells in the functionalis layer of eutopic endometrium displayed stronger α1D-AR staining. In vitro XTT analyses revealed that phentolamine partially inhibited (P<0.05 and P=0.001, respectively) 2-OHE<sub>2</sub> and 4-OHE<sub>2</sub>-enhanced HESC survival versus control (P<0.05 and P<0.05, respectively). This inhibitory effect of phentolamine was specific to CCEs since E<sub>2</sub>-enhanced HESC survival was not inhibited by phentolamine.

Conclusions: Immunostaining with α1D-AR showed similar expression patterns as β2-AR in that there was increased staining to the functionalis layer of the endometrium; albeit, α1D-AR staining was overall weaker in both eutopic and ectopic tissue. Our in vivo and in vitro results indicate that induction of HESC viability by CCE-α1D-AR binding may contribute to the propagation of endometriosis. Future studies into different α-AR isofoms expressions in endometriotic lesions are warranted.

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NFX2 Expression in Endometriosis Is Regulated by miRNA Let-7b.

Valerie A. Flores, MD, Peng Chen, MD, PhD, Joshua Hutter, BA, Yuping Zhou, BA, Tran Dang, BS, Ramanaiah Mamillapalli, PhD, Hugh S. Taylor, M.D., Yale University School of Medicine, New Haven, CT.

FERTILITY & STERILITY® e327
OBJECTIVE: Endometriosis is a debilitating gynecologic disease characterized by aberrant inflammation. We have previously demonstrated differential expression of several microRNAs (miRNAs) in endometriosis, and dysregulated expression of several inflammatory cytokines. Altered miRNA expression may modulate the inflammatory response, ultimately increasing severity of disease. Nuclear factor-kappaB (NFkB) is a transcription factor involved in the immune response. It is activated initially by inflammatory cytokines and chronically activated in endometriosis, thus capable of promoting a chronic inflammatory state and altered progesterone response. We hypothesize that miRNAs (Let-7b, 3613-5p, and 125b) alter expression of NFkB1, NFkB2, and progesterone receptor gene (PGR) in women with endometriosis.

DESIGN: In vitro human primary cell culture.

MATERIALS AND METHODS: Primary eutopic endometrial cells from 6 subjects were cultured in six-well plates (1x10^5 cells). Once cells reached 70% confluence they were transfected with miRNA Let-7b, 3613-5p, or 125b miRNA mimic or respective miRNA inhibitor. Each transfection was carried out with respective controls and in duplicate. Total RNA was extracted 48 hours post-transfection. Quantitative RT-PCR was performed for genes of interest (NFkB1, NFkB2 and PGR). Relative expression was calculated using the 2^-ΔΔC(T) method. Student's t-test was used for statistical analysis.

RESULTS: Cells transfected with miRNA Let-7b Mimic demonstrated a 2.25-fold decrease in NFkB2 expression (p = 0.04); there was no significant change in NFkB2 expression in cells treated with Let-7b inhibitor. There was no difference in NFkB2 expression in cells transfected with miRNAs 3613-5p or 125-5p mimic or inhibitor. There was no significant effect on expression of NFkB1 or PGR when cells were transfected with miRNAs Let-7b, 3613-5p, or 125-5p (mimic or inhibitor).

CONCLUSIONS: Endometriosis sequela are in large part due to the inflammatory nature of the disease. As NFkB2 is a key mediator in the inflammatory response, aberrant miRNA levels can mediate inflammation and aggressiveness of disease through regulation of NFkB2 expression. Here we demonstrate that low Let-7b levels that we have previously reported in endometriosis lead to increased NFkB2 expression and increased inflammation. Let-7b regulation in endometriosis is a key endogenous regulator of inflammation. MiRNA Let-7b and NFkB2 represent novel, non-hormonal targets for treating endometriosis.

R01 HD076422

SUPPORT: NIH U54 HD052668.

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INCREASED EXPRESSION OF YAP (YES-ASSOCIATED PROTEIN) IS ASSOCIATED WITH THE DECREASED CELL AUTOPHAGY IN THE EUTOPIC ENDOMETRIAL STEM CELLS OF WOMEN WITH ENDOMETRIOSIS. Wei Huang, Ph.D., M.D.; Tianjiao Pei, M.D., Xin Huang, M. M. Candidate; Yujing Li, M.D.; West China Second University Hospital of Sichuan University, Chengdu, China; Department of Obstetrics and Gynecology, West China Second University Hospital of Sichuan University, Chengdu, China; Affiliation not provided.

OBJECTIVE: To explore the role of Yes-associated protein (YAP) in the regulation of cell autophagy in the eutopic endometrial stromal cells (ESCs) from a subset of women with endometriosis.

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DESIGN: Experimental study using primary cell culture, quantitative real-time PCR (qRT-PCR), Western blotting, drug interference, and transfection in isolated ESCs.

MATERIALS AND METHODS: Endometrial samples were collected during hysterectomy, including eight patients diagnosed with endometriosis by laparoscopy and six women laparoscopically diagnosed endometriosis-free as controls. The expressions of YAP pathway and cell autophagy markers (mTOR, LC-3) in ESCs of women with or without endometriosis were validated by qRT-PCR and Western blotting. The protein levels of autophagy markers were detected in the eutopic ESCs after verteporfin and rapamycin treatments and the transfection with YAP-knockdown vector in ESCs, respectively. Student’s t test was used for comparisons between two groups after assessing the normality and homogeneity of variance.

RESULTS: The mRNA levels of YAP, TEAD, mTOR were all increased in the eutopic ECs of women with endometriosis compared with controls, but no statistically difference (P > 0.05). The protein levels of YAP (P < 0.05) and mTOR (P < 0.05) were significantly increased in the eutopic ECs of women with endometriosis compared with controls, whereas the ratio of the autophagy marker protein LC3-II/LC3-I (P < 0.05) was significantly decreased in the eutopic ECs of women with endometriosis compared with controls. Moreover, verteporfin treatment interfered the YAP function and led to an increase trend of cell autophagy level, but it had no effect on mTOR expression; rapamycin treatment and YAP knockdown in the eutopic ESCs both inhibited the expression of YAP and increased the level of cell autophagy significantly with an increased ratio of LC3-II/LC3-I (P < 0.05).

CONCLUSIONS: Our study demonstrates that the decreased cell autophagy level is associated with the increased expression of YAP and YAP may participate in the mTOR-autophagy pathway in the eutopic ESCs of endometriosis.

SUPPORT: This research was supported by the Grant from the Science and Technology Bureau of Sichuan (2018SZ0124) (to Wei Huang).

OBJECTIVE: To confirm the theory of endometriosis (EMT) stem cell origin and to investigate the role of estrogen on the process of bone marrow mesenchymal stem cell (BMSC) chemotactic migration and differentiation.

DESIGN: To illustrate this hypothesis, we employed 17β estradiol for the co-culture of BMSC and endometrial stromal cells (ESC) in vitro and established BMSC+ESC+17β estradiol treatment group. After 5 days of culture, the chemotaxis of 17β-estradiol was observed through Transwell experiments, and the chip technique was used to analyze the expression of chemokines in the culture medium. Mouse EMT model was established and HE staining was performed. BMSCs were injected through the tail vein into the EMT mice. The mice were divided into two groups according to BMSC 17β-estradiol pretreated or not. The immunofluorescence was used to detect the expression of protein B-cell lymphoma-2 (BCL-2), proliferating Cell Nuclear Antigen (PCNA), Matrix metalloproteinase (MMP-1) in ESC after one month.

RESULTS: We showed that the migration of BMSC promoted by ESC, and the migration ability of BMSC was enhanced after the treatment of 17β-estradiol. Through gene chip detection, 17β-estradiol may accelerate the secretion of chemokines by ESC, which can promote the expression of 25 chemokines, especially for stromal cell derived factor-1α as the main target. Furthermore, the immunofluorescence results in animal experiments showed that the expression of BCL-2, PCNA, MMP-1 in 17β-estradiol pre-treated group was higher than control group. It confirmed that 17β-estradiol might promote the differentiation, proliferation and apoptosis of ESC in ectopic lesions through the migration, differentiation and proliferation of BMSCs, thereby increasing the degree of lesions in ectopic lesions.

CONCLUSIONS: Estrogen promoted the chemotactic migration of BMSC to a proper microenvironment and differentiation into endometrial cells forming endometriosis.

SUPPORT: The National Natural Science Foundation of China (Grant number: 81501234).

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CD4 AND CD8 BUT NOT DN MUCOSA-ASSOCIATED INVARIANT T CELLS FOSTER THE DEVELOPMENT OF ENDOMETRIOSIS: A PILOT STUDY. Huanhuan Jiang, Doctor, Kaihuan Bi, Bachelor’s, Zhimin Lu, Bachelor’s, Caihua Li, Doctor, Peipei Guo, Graduate, Yunxia Cao, Doctor, The First Affiliated Hospital of Anhui Medical University, Hefei, China.

OBJECTIVE: Our study aims to demonstrate the relationship between Mucosa-associated invariant T (MAIT) cells and endometriosis.

DESIGN: Case-control study.

MATERIALS AND METHODS: The study group comprised 32 patients with a diagnosis of endometriosis. 18 women with only ovarian benign cysts or uterine leiomyoma who underwent laparoscopy were recruited as control group (CG). MAIT cells were characterized as CD3+CD161+Vβ(+) (PB) was obtained shortly before the surgery. We investigated MAIT cells and ectopic lesions through the migration, differentiation and proliferation of MAIT cells forming endometriosis.

RESULTS: The proteins of MAIT cells forming endometriosis were validated by qRT-PCR and Western blotting. The protein levels of autophagy marker protein LC3-II/LC3-I was significantly decreased in the eutopic ECs of women with endometriosis compared with controls. Moreover, verteporfin treatment interfered the YAP function and led to an increase trend of cell autophagy level, but it had no effect on mTOR expression; rapamycin treatment and YAP knockdown in the eutopic ESCs both inhibited the expression of YAP and increased the level of cell autophagy significantly with an increased ratio of LC3-II/LC3-I (P < 0.05).

CONCLUSIONS: Our study demonstrates that the decreased cell autophagy level is associated with the increased expression of YAP and YAP may participate in the mTOR-autophagy pathway in the eutopic ESCs of endometriosis.

SUPPORT: This research was supported by the Grant from the Science and Technology Bureau of Sichuan (2018SZ0124) (to Wei Huang).

OBJECTIVE: To discover genes that may interact with the endometriosis risk allele in the WNT Family Member 4 (WNT4) gene.

DESIGN: Endometriosis is a common gynecological condition with complex etiology defined by the presence of endometrial glands and stroma in ectopic locations outside of the uterus. Twin and family studies have shown increased relative risk in families. Multiple genome-wide association studies (GWAS) show that several polymorphisms in the region harboring WNT4 and Cell Division Cycle 42 (CDC42) are associated with endometriosis across multiple ethnicities. In this study, we explored whole exome sequencing (WES) data in women carrying the risk allele T (rs2235529) in the WNT4 gene to see if the risk allele interacts with rare protein altering variants in other genes.

MATERIALS AND METHODS: WES was conducted on 1731 women with a confirmed diagnosis of endometriosis and 774 population controls of Northern European Ancestry. Whole exome sequencing (WES) was performed using Ion Proton Instrument with the AmpliSeq Exome Capture Kit. All missense and truncating mutations including stop gain, stop loss, splicing, and frameshifts were considered for downstream analysis. Population frequency of these variants are provided if present in the gnomAD database (n=1,000).

RESULTS: The risk allele T in WNT4 (rs2235529) is present in either homozygous or heterozygous form in 787 subjects (554 endometriosis cases and 233 controls). Eight endometriosis patients and none of the controls had histone deacetylase 2 (HDAC2) protein altering mutations identified. The T risk allele was associated with HDAC2 altering mutation burden [p=1.7E-03, OR=15.4 (95% confidence limits 1.9-125.5)].

CONCLUSIONS: In this study, we found that women with mutation in HDAC2 gene in the background of WNT4 risk allele T are more likely to
be susceptible to endometriosis. It has been reported that the levels of HDAC1 and HDAC2 are deregulated in endometriotic stromal cells. HDAC1 and HDAC2 are key regulators of WNT and p38 pathways. During nucleosome remodeling, the deacetylase complex physically interacts with the WNT4 chromatin in an HDAC-dependent manner, leading to suppression of the WNT4 gene and WNT4-dependent morphogenesis. Analyses of the ten other human HDAC genes are underway.

SUPPORT: Juneau Biosciences, LLC.

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WITHDRAWN

ENDOMETRIUM

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CELL-SPECIFIC EFFECTS OF CLOMID AND E2 ON ENDOMETRIUM: INSIGHTS INTO WNT SIGNALING AND STROMAL-EPITHELIAL INTERACTIONS. Melanie Evans, MS, MD, a
Lucy Xi Chen, MD, b Ann Word, MD, b John Wu, MD, b Patrick Keller, BS, b Bruce Carr, MD, b Orhan Bukulmez, MD, b 4 Parkland/UTSW Resident, Dallas, TX, UT Southwestern, Dallas, TX; 4 UT Southwestern Medical Center, Dallas, TX.

OBJECTIVE: Hormonal effects on epithelial cells of endometrium are often mediated through stromal cell receptors. Endometrium from women undergoing IVF using minimal stimulation (MS-IVF) with clomiphene citrate (CC) is characterized by marked atrophy of endometrial glands accompanied by relative increases in stromal cells, despite supraphysiologic levels of E2. Previously, we discovered dramatic stromal cell-specific upregulation of Wnt antagonists (secreted frizzled related proteins 1,4, SFRP) in endometrium from MS-IVF. Although SFRPs inhibit Wnta signaling during endometrial decidualization and gland formation in endometrial cancer, physiologic regulation of Wnt signaling in endometrium is not well understood. Our objective was to test the hypothesis that SFRPs are secreted constitutively by stroma cells but regulated in vivo by stromal-epithelial interactions.

DESIGN: Epithelial cells (Epi, Ishikawa) and primary human endometrial stromal cells were used alone or in co-culture with transwell cell culture inserts. Stromal cells were pretreated for 48 h in serum free media prior to treatment with vehicle or estradiol (E2, 3.6 nM) ± CC (20 nM).

MATERIALS AND METHODS: Gene expression was quantified by qPCR and normalized to two housekeeping genes, GAPDH and b-actin. Endometrial tissue extracts from spontaneously ovulating women (24 h after LH surge, n = 4) were studied. ANOVA and Student’s t test were used for statistical analyses as appropriate.

RESULTS: E2 treatment of stromal cells increased PR-B (from 1 ± 0.1 to 6.7 ± 0.4 RU; p < 0.01) and total PR (from 1.0 ± 0.11 to 5.4 ± 0.23 RU, p < 0.01). CC was not an ER antagonist in stromal cells also increasing PR gene expression. In contrast to in vivo results, CC did not alter expression of sFRP4 or sFRP4 in stromal cell cultures. In co-culture, Epi did not alter E2-induced upregulation of PRs in stroma. However, co-culture with Epi downregulated stromal cell sFRP4 (83 ± 3%). The magnitude of sFRP4 suppression was dose-dependent with increasing number of Epi cells (from 10² to 10⁷/cm²). Epi co-culture also decreased stromal sFRP7 to 34 ± 11% and expression of stromal growth factors (FGF9 and TGF-α) significantly. To investigate physiologic relevance, treatment of tissue explants from ovulatory women with E2 for 72 h (to induce epi growth) resulted in suppression of sFRP4 (from 1.44 ± 0.3 to 0.55 ± 0.08 mRNA, p < 0.02).

CONCLUSIONS: Although CC did not have direct effects on sFRP in stroma, secretions from glandular epithelial cells suppressed Wnt antagonists sFRP4 and sFRP7 in stroma. These results support the hypothesis that CC-induced inhibition of epithelial cell growth results in immature, atrophic glands that are insufficient to suppress Wnt inhibitors in stroma thereby accentuating loss of epithelial differentiation and growth. In the absence of CC, E2 induces epithelial cell growth and suppression of stromal sFRPs culminating in full maturation of the endometrium. Although it is believed that CC exhibits its effects simply as an ER antagonist, these studies indicate that the effects of CC are more complex and involve inhibition of Wnt signaling in cell-specific compartments.


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DOES UNIVERSAL SCREENING FOR CHRONIC ENDOMETRITIS IMPROVE PREGNANCY RATES? Holly Mehr, MD MSEd, a Mousa Shamonki, MD, b Chunnin Wang, PhD, b Richard Buyalos, MD, b Gary Hubert, MD, b Molly M. Quinn, MD, b University of California, Los Angeles, Los Angeles, CA; c Fertility and Surgical Associates of California, Thousand Oaks, CA.

OBJECTIVE: A growing body of evidence suggests a link between chronic endometritis (CE) and infertility. We investigated whether the implementation of universal screening for CE at the time of oocyte retrieval was correlated with a change in pregnancy rates after initial single thawed euploid embryo transfer (STEET).

DESIGN: Retrospective cohort analysis at a high volume private fertility center.

MATERIALS AND METHODS: The analysis included the initial STEET of all patients undergoing autologous IVF/PGT-A with endometrial biopsy screening (EMB) on day of oocyte retrieval from January 2017 to December 2018 and historic controls without universal EMB from September 2015 to August 2016. Cycles performed in the six-month window surrounding the policy implementation were excluded. The pathologic diagnosis of CE was established via CD138 staining of endometrial specimens. Patients found to have CE after biopsy were treated with doxycycline and metronidazole and re-biopsied. If persistent CE was demonstrated, a protocol designated second and third-line treatment algorithms prior to embryo transfer. Patients using a gestational carrier, oocyte or embryo donation, and those who had previous embryo transfer were excluded from the analysis. The CE rate, implantation rates (IR) and ongoing pregnancy rates (OPR) were calculated. Statistical analysis was done with t test, Mann-Whitney U, Chi squared tests, and logistic regression where appropriate.

RESULTS: A total of 375 initial STEETs were analyzed. The average age of the EMB screened and non-screened population differed (35.7 ± 3.9 vs 36.7 ± 4.1, p = 0.0157). In analyses controlled for age, there was no difference in IR (AOR 1.12, 95% CI 0.77-1.80) or OPR (AOR 1.06, 95% CI 0.69 - 1.63) between screened and non-screened cohorts. The rate of CE found on day of oocyte retrieval was 14.0% (n=31). The median number of CD138 cells per 10 high powered fields was 11 (IQR 8-15) in the CE positive group and 0 (IQR 0-1) in the CE negative group (p < 0.0001). No difference was seen in the IP (76.3% vs 67.7%, p = 0.31) or OPR (60.5% vs 58.1%, p = 0.80) between the treated, CE positive and CE negative groups in their first embryo transfer. CE cure rate was 81% (n=21). Nineteen percent of CE positive patients (n=6) were not cured after 3 cycles of antibiotics. The non-cured group had an 83% OPR.

CONCLUSIONS: A universal screening strategy detected a lower baseline CE rate than has been previously reported. No association was demonstrated between universal CE screening and IR or OPR. A larger sample size is needed to confirm these findings.

P-560 Wednesday, October 16, 2019 6:30 AM

GATA BINDING PROTEIN 2 EXPRESSION AT IMPLANTATION WINDOW DIMINISHES IN WOMEN WITH ADENOMYOSIS: IMPLICATIONS FOR IMPAIRED ENDOMETRIAL RECEPTIVITY. Joung Woul Kim, PhD, a Chih-Feng Yen, MD, PhD, b Rachel Grimes Sprague, MD, a Asli Ozmen, PhD, a Nihan Semerci, MSc, a Charles J. Lockwood, MD, MHCM, a Anthony N. Imudia, MD, a Umit Kayisli, PhD, a Department of Obstetrics and Gynecology, Morsani College of Medicine, University of South Florida, Tampa, FL; a Department of Obstetrics and Gynecology, Chang Gung Memorial Hospital at Linkou, Chang Gung University College of Medicine, Kwei–Shan, Taoyuan, Taiwan.

OBJECTIVE: Adenomyosis in reproductive age women has negative impacts on embryo implantation. Impaired progesterone (P4) responsiveness causes female infertility associated with endometrial receptivity. Mice deficient in the transcription factor, GATA binding protein 2 (GATA2), are infertile due to embryo implantation failures associated with defective decidua formation and endometrial receptivity. Uterine tissues of GATA2 deficient mice display decreased progesterone-receptor (PR) levels and diminished P4 responsiveness. We hypothesized that reduced endometrial GATA2 expression during the window of implantation may contribute to implantation failure seen in women with adenomyosis.

DESIGN: Thus, we evaluated the endometrial expression of GATA2 in patients with adenomyosis.

SUPPORT: This work was supported by the tissue core laboratory of NIH HD087150.
MATERIALS AND METHODS: Uterine specimens were obtained during the window of implantation (cycle days 18-23) from patients with adenomyosis (n=5, age <45 years) who underwent hysterectomy and from age-matched controls who had no endometriosis or adenomyosis (n=5). The GATA2 expression was detected by immunohistochemistry, quantified by a histologic scoring system (iHSCORE) and statistically compared using a t-test.

RESULTS: During the window of implantation, both endometrial and myometrial cells displayed predominantly nuclear immunoreactivity for GATA2 expression. Compared to those in the control group, patients with adenomyosis showed significantly reduced GATA2 expression in endometrial luminal epithelium (Mean ± SEM 103.9 ± 15.5 vs. 55.4 ± 14.1, p= 0.049), stromal cells (128.6 ± 20.7 vs. 53.3 ± 10.6, p= 0.012) and myometrial cells (133.7 ± 12.3 vs. 72.6 ± 15.9, p=0.016). On the other hand, glandular epithelial cells were weakly GATA2 immunoreactive with no difference between women with or without adenomyosis (85.0 ± 9.9 vs. 55.6 ± 26.3; p=0.325).

CONCLUSIONS: The significant reduction in human uterine GATA2 expression may impair endometrial receptivity by diminishing P4 responsiveness in patients with adenomyosis, which may impair endometrial receptivity by diminishing P4 responsiveness in patients with adenomyosis.

P-561 Wednesday, October 16, 2019 6:30 AM
DEFINING CHRONIC ENDOMETRITIS: ARE PLASMA CELLS SUFFICIENT? Dana B. McQueen, M.D., M.A.S., Kruti P. Maniar, M.D., Anne Hutchinson, M.D., Rafael Confino, BS, Jared C. Robins, MD, Lila A. Bernardi, MD, Mary Ellen Pavone, MD, MSCI, Northwestern University, Chicago, IL.

OBJECTIVE: There is considerable variability in the diagnostic criteria used for chronic endometritis: including number of plasma cells, immunohistochemistry and inclusion of stromal changes. The objective of this study was to compare the prevalence of chronic endometritis in women with unexplained recurrent pregnancy loss (RPL) using different diagnostic criteria.

DESIGN: Cohort Study.

MATERIALS AND METHODS: IRB approval was obtained. The cohort included women with two or more pregnancy losses, endometrial biopsy (EMB) between 1/2016 and 12/2018, TSH values < 4 mU/L, negative antiphospholipid antibodies and normal uterine anatomy. H&E and CD138 immunohistochemical staining were performed. A single pathologist blinded to patient history recorded the number of plasma cells per 10 HPF and the presence or absence of endometrial stromal changes (spindling, edema, foci of breakdown, inflammatory cells, and pigment deposition).

RESULTS: 50 women were included, with a mean age of 35.2 (SD 4.1) years, BMI of 27.1 (SD 6.3) kg/m² and 3.1 (SD 0.9) prior pregnancy losses. Stromal and myometrial plasma cells were required, the prevalence was 16% (8/50) with ≥ 1 plasma cell, 24% (12/50) with ≥ 2 plasma cells and 4% (2/50) with ≥ 5 plasma cells. When stromal changes and plasma cells by CD138 were required, the prevalence was 30% (15/50) with ≥ 1 plasma cells, 28% (14/50) with ≥ 2 plasma cells and 16% (8/50) with ≥ 5 plasma cells.

CONCLUSIONS: Establishing specific diagnostic criteria for chronic endometritis is necessary for both research and evidence based treatment guidelines. The definition of chronic endometritis significantly alters its prevalence. Recruitment of a control cohort is currently ongoing to establish the most appropriate diagnostic criteria for chronic endometritis.

SUPPORT: Friends of Prentice Grant.

P-562 Wednesday, October 16, 2019 6:30 AM
IMPROVEMENT OF ENDOMETRIAL RECEPTIVITY THROUGH THE USE OF AUTOLOGOUS PLATELET-DERIVED MICROPARTICLES. Enriqueta Garjo Lopez, OBGYN; Laura Garcia Bernardo, OBGYN; Federico Galera Fernandez, OBGYN; Instituto Madrileño de Fertilidad, Madrid, Spain; Instituto Madrileño de Fertilidad, Madrid, Spain.

OBJECTIVE: The goal of the present trial is to evaluate the effectiveness of the application of platelet-rich plasma (PRP) derived from the patient’s autologous plasma in the basal layer of the endometrium for the treatment of patients with suboptimal endometrium.

DESIGN: This is a single arm trial carried out at the Fertility Institute of Madrid. The trial included eighteen patients which presented a suboptimal endometrium, refractory to estrogen therapy between June 2014 and November 2017.

MATERIALS AND METHODS: The trial included thirteen patients that presented a suboptimal endometrium (< 7 mm) and five presented implantation failures (in more than three embryo transfers with high quality embryos). Blood was extracted the same day of the application. The blood was centrifuged at 600g for ten minutes to separate red blood cells from plasma. The plasma was centrifuged at 600g for ten minutes to separate red blood cells from plasma. After each centrifugation, the plasma was removed and platelet-rich plasma (PRP) was reconstituted with the patient’s autologous plasma.

RESULTS: 50 patients were included, with a mean age of 35.2 (SD 4.1) years, BMI of 27.1 (SD 6.3) kg/m² and 3.1 (SD 0.9) prior pregnancy losses. Stromal changes and plasma cells by CD138 were required, the prevalence was 30% (15/50) with ≥ 1 plasma cells, 28% (14/50) with ≥ 2 plasma cells and 16% (8/50) with ≥ 5 plasma cells.

CONCLUSIONS: Establishing specific diagnostic criteria for chronic endometritis is necessary for both research and evidence based treatment guidelines. The definition of chronic endometritis significantly alters its prevalence. Recruitment of a control cohort is currently ongoing to establish the most appropriate diagnostic criteria for chronic endometritis.

SUPPORT: Friends of Prentice Grant.

Patient Age IVF/OVO Endometrium before/after Pregnancy
1 41 OVO 7/8,5mm yes
2 36 OVO 6,7mm no
3 45 OVO 7/8,1mm no
4 50 OVO 8/10,6mm yes
5 35 FIV 6,2/8mm yes (miscarriage)
6 48 OVO 5/6mm no
7 42 FIV 6,7/8mm yes
8 43 OVO 7/8,3mm yes
9 39 OVO 6,6/7,6mm yes (biochemical pregnancy)
10 41 OVO 6,7/8mm yes
11 41 OVO 7/8,5mm no
12 46 OVO 8/10mm yes
13 46 OVO 6,6/7mm no
14 48 OVO 10/12mm yes
15 38 FIV 6,7/8mm no
16 38 OVO 6,7/8mm no
17 40 OVO 6,6/7,2mm yes

Defining Chronic Endometritis (n=50):

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Stromal Changes Not Required</th>
<th>Stromal Changes Required</th>
</tr>
</thead>
<tbody>
<tr>
<td>H&amp;E: 1 or more plasma cells/10 HPF</td>
<td>24% (12/50)</td>
<td>14% (7/50)</td>
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<tr>
<td>H&amp;E: 2 or more plasma cells/10 HPF</td>
<td>16% (8/50)</td>
<td>12% (6/50)</td>
</tr>
<tr>
<td>H&amp;E: 5 or more plasma cells/10 HPF</td>
<td>4% (2/50)</td>
<td>4% (2/50)</td>
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<tr>
<td>CD 138: 1 or more plasma cells/10 HPF</td>
<td>56% (28/50)</td>
<td>30% (15/50)</td>
</tr>
<tr>
<td>CD 138: 2 or more plasma cells/10 HPF</td>
<td>44% (22/50)</td>
<td>28% (14/50)</td>
</tr>
<tr>
<td>CD 138: 5 or more plasma cells/10 HPF</td>
<td>26% (13/50)</td>
<td>16% (8/50)</td>
</tr>
</tbody>
</table>
supernatant was separated into three fractions, from low to rich factor concentration. Calcium Chloride were added in order to activate the platelets. A hysteroscopy was carried out using saline solution as a distention medium and a puncture needle of 17G and 300mm was introduced through the hysteroscope work guide during menstrual period. Several subendometrial injections were administered using the needle, in the uterine lining, until the entire plasma (15 ml) was injected. After the hysteroscopy, the patients started the replacement treatment with oestradiol valerate with a dosage of 6mg per day. Once the endometrium had a thickness of more than 7mm, 200 mg of progesterone was applied 3 times a day, and the embryo transfer was scheduled.

RESULTS: The thickness of the endometrium increased in all 18 patients. All except for one achieved the minimum 7mm required for the transfer. On average, the endometrium thickness increased by 1.52mm. Ten patients showed positive BHCGr thirteen days after the transfer (55%). Two of these ten patients miscarried on the first trimester (20%). The rest of the pregnancies concluded with the birth of a healthy child. No adverse effects have been reported.

CONCLUSIONS: PRP can stimulate the proliferation and regeneration of tissues with a great amount of growth factors and cytokines. This is the first study where PRP are applied via a hysteroscopy and subendometrial injections instead of through intrauterine perfusions with a cannula. It is suggested that PRP increase the chances of pregnancy in patients with suboptimal endometrium and recurrent implantation failures. It is necessary to carry out randomised and controlled clinical trials to confirm these results.

P-563 Wednesday, October 16, 2019 6:30 AM
REDUNDANT ENDOMETRIUM AND ENDOMETRIAL POLYPS: IS THERE A LINK? Irene Peregrin Alvarez, MD, Robert Roman, MD, Mary Emily Christiansen, MD, Ghassan Saed, MD, Laura Detti, MD, University of Tennessee Health Science Center, Memphis, TN; Wayne State University School of Medicine, Detroit, MI.

OBJECTIVE: Endometrial polyps (EP) and redundant endometrium (RE) are often detected incidentally during routine transvaginal ultrasoundography. Several studies on the expression of hormone receptors, oncogenes and anti-mitotic proteins have been conducted to elucidate the molecular mechanisms underlying EP, however, no studies have been reported on the biology of RE. We explored whether the expression of different endometrial markers could vary in patients with EP and RE and what is their role in etiology and pathogenesis of endometrial pathology.

DESIGN: Pilot experimental study.

MATERIALS AND METHODS: We examined the expression of estrogen receptor (ER), progesterone receptor (PR), androgen receptor (AR), insulin-like growth factor receptor 1 (IGFR-1), B-cell lymphoma 2 (bcl-2), Ki67, HOXA10 and thyroid receptor beta 1 (TR beta 1) in EP and RE. We obtained endometrial specimens from 16 patients aged 20-45 years, that presented to our center between September 2017 and May 2018 who were undergoing hysteroscopy for benign gynecologic pathology (EP, RE or submucosal fibroids). Fragments of the endometrial samples were processed for real-time RT-PCR for evaluation and for the expression of the above-mentioned markers. The main outcome measure was tissue expression of these markers and comparison between EP and RE. We performed ANOVA for analysis among the 3 groups. Our results were summarised as median and quartiles (Q1, Q3) and we used SPSS v25 for Windows (SPSS, Chicago, IL); p<0.05 defined significance.

RESULTS: 8 patients had RE, 5 had EP, 1 RE plus EP, 2 had normal endometrium. Compared to EP, RE showed increased bcl2 and Insulin-R but similar Ki67,IGF-R1 and HOXA10 expression. Compared to normal endometrium, RE showed increased bcl2, IGF-R1 and Insulin-R expression, while Ki67 was decreased and HOXA10 unchanged.

CONCLUSIONS: RE showed biochemical characteristics similar to endometrial polyps, both stemming from environmental factors. Cell differentiation seemed more advanced than replication. Similarly to EP, RE could be detrimental for embryo implantation, especially when extensive.

This should be considered in women undergoing fertility treatments.

References: (1) Peregrin Alvarez I, Roman RA, Christiansen ME, Detti A. Endometrial abnormalities: correlation between different diagnostic modalities. Presented at the American Institute of Ultrasound in Medicine (AIUM) Annual Convention, April 6-9, 2019, Orlando, FL.


P-564 Wednesday, October 16, 2019 6:30 AM
PREVALENCE OF CHRONIC ENDOMETRITIS IN PATIENTS WITH ENDOMETRIAL POLYPS AND UNEXPLAINED INFERTILITY. Alexander Volodarsky-Perel, M.D., Ahmad Badeghiesh, M.D., MPH, Guy Shrem, M.D., Naama Steiner, M.D., Togas Tulandi, M.D. McGill University Health Centre, Montreal, QC, Canada.

OBJECTIVE: To assess the prevalence of chronic endometritis (CE) in patients with endometrial polyps and unexplained infertility compared to patients without history of infertility.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: We evaluated patients underwent hysteroscopy and polypectomy in the period of 2015 to 2018. The inclusion criteria were age 25-42 and histologically confirmed endometrial polyps. Patients with cycle day 3-5 FSH > 10 mIU/mL with intrauterine devices, history of repeated implantation failure and recurrent pregnancy loss, autoimmune diseases, suspected placental residua, endometrial cancer, atypical hyperplasia, previous diagnosis of CE, and received any antibiotic treatment in the period of 3 months before hysteroscopy were excluded. Study group included patients with unexplained infertility. The control group included those with no previous history of infertility, not taking hormone treatment in the past 3 months before hysteroscopy or having spontaneous pregnancy in the previous 3 years before the procedure. The diagnosis of CE was established after hematoxylin and eosin and CD 138 staining and was based on the presence of one or more plasma cells per 10 high-power fields. The primary outcome was the prevalence of CE compared between fertile and fertile patients. The secondary outcomes included clinical pregnancy rate (CPR), live birth rate (LBR) and miscarriage rate (MR) of infertile patients after CE treatment (Doxycycline 100 mg twice daily for 14 days) compared to infertile patients without CE. To determine factors significantly associated with CE we used multivariate logistical regression. A sample size of 100 in each group has 80% power of showing a 15% difference in primary outcome with an alpha of 0.05.

RESULTS: A total of 237 patients were included in the analysis. Demography, hysteroscopy cycle day, polyp location and diameter were similar between the groups. The prevalence of CE in group of patients with unexplained infertility (n=137) was significantly higher compared to the control group (n=100) [22.6% vs. 8.6%; P = 0.001]. Cumulative CPR, LBR and MR were similar between women with treated CE (n=31) and patients without CE (n=106). Multivariate logistical model showed that infertility diagnosis was significantly associated with the diagnosis of CE (OR 3.16; 95% CI 1.53 – 6.49).

CONCLUSIONS: In women with endometrial polyps the prevalence of CE is higher in patients with unexplained infertility compared to patients without infertility history. The pregnancy outcome of infertile patients with CE treated with one course of Doxycycline was similar to those without CE.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Redundant Endometrium Median (Q1, Q3)</th>
<th>Polyp Median (Q1, Q3)</th>
<th>Normal Median (Q1, Q3)</th>
<th>p-value RE vs Polyp</th>
<th>p-value RE vs normal</th>
</tr>
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<tbody>
<tr>
<td>BCL2 (fg/ug RNA)</td>
<td>0.263 (0.16, 0.32)</td>
<td>0.082 (0.07, 0.09)</td>
<td>0.066 (0.06, 0.07)</td>
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<td>HOXA-10 (fg/ug RNA)</td>
<td>35.05 (28.8, 43.7)</td>
<td>35.33 (29.2, 48.9)</td>
<td>ns</td>
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<td>Ki67 (fg/ug RNA)</td>
<td>1.45 (1.1, 2.3)</td>
<td>2.51 (2.5, 7.3)</td>
<td>5.72 (4.5, 5.9)</td>
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<tr>
<td>IGF1-R (fg/ug RNA)</td>
<td>6.25 (4.5, 7.0)</td>
<td>4.42 (3.9, 5.8)</td>
<td>2.61 (2.6, 2.8)</td>
<td>ns</td>
<td>0.0184</td>
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<tr>
<td>Insulin-R (fg/ug RNA)</td>
<td>53.33 (47.6, 58.6)</td>
<td>39.69 (26.8, 44.4)</td>
<td>15.6 (15.4, 16.0)</td>
<td>0.0318</td>
<td>0.0002</td>
</tr>
</tbody>
</table>
WHAT IS THE MOST EFFECTIVE TREATMENT FOR ENDOMETRITIS IN WOMEN UNDERGOING ASSISTED REPRODUCTIVE TECHNOLOGY?

Sweta A. Canumalla, MBBS, a Jennifer K. Blakemore, MD, b James A. Grifo, MD, PhD, c David L. Keeffe, M.D. a ’ NYU School of Medicine, New York, NY; 3 NYU Langone School of Medicine, New York, NY; 4 NYU Langone Fertility Center, New York, NY; 5 New York University School of Medicine, Department of Obstetrics and Gynecology, New York, NY.

OBJECTIVE: Treatment of chronic endometritis (CE) improves implantation rates in patients undergoing assisted reproductive technology (ART), but causative organisms are difficult to identify and the most effective treatment regimen remains undefined. Our objective was to identify the optimal duration and choice of antimicrobial(s) on clearance of CE.

DESIGN: Retrospective cohort study of patients between 1/2017 and 12/2018 at a single academic center with an endometrial biopsy (EMB) showing CE.

MATERIALS AND METHODS: All patients diagnosed with CE (defined as ≥1 plasma cell/HPF; stained for CD138) on EMB followed by test of cure biopsy (TOC) were included. Antimicrobial agents prescribed and length of course were recorded. Revisions were classified as 14 days or less versus 15 days or more (up to 21 days), and by spectra of coverage: Gram positive, Gram negative, Anaerobe, Atypical and Anti-fungal. Primary outcome was presence or absence of CE on TOC. If a patient remained positive on TOC, subsequent treatment(s) were included as separate course(s) for analysis. Statistical analysis included chi square test of independence and a stepwise multiple logistic regression, with p < 0.05 significant.

RESULTS: 144 women with an initial EMB positive for CE received a total of 225 treatment courses. 11 TOC results were unavailable, leaving 214 courses of treatment with known TOC outcomes. The most common indication for EMB was failed frozen embryo transfer(s) (FET) (MEAN 0.98±1.0, range 0-7), euploid pregnancy loss or recurrent pregnancy loss. The mean age of women in the cohort was 36.90±3.93 years (range 27-47). Mean number of courses required for clearance was 1.55±0.86 (range 0-6). All courses included antimicrobials providing gram positive and negative coverage. 62.6% (134/214) included anaerobic coverage and 66.3% (142/214) included atypical agent(s). 2 courses included anti-fungals. Including anaerobic coverage did not affect outcome (58.2% with vs 61.3% without, p = 0.67), nor did use of an atypical agent (59.2% with vs 59.67% without, p = 1.00). Antibiotic regimens lasting 14 days or less (n=155) had lower rates of CE clearance when compared to those lasting 15 days or more (54.8% vs 71.2%, p < 0.027, Omnibus test for variance p < 0.001, Hosmer-Lemeshow test for fit p = 0.99).

CONCLUSIONS: CE is a treatable but poorly defined inflammatory process, which may affect ART success. Ideally, CE is cleared with the first treatment. Our results show that longer courses (15-21 days) are more effective, regardless of antimicrobial choice. This suggests that patients do not need to take less tolerable agents to achieve high clearance rates, and highlights the need for further, prospective analyses.


SUPPORT: None.

NEW RELATION BETWEEN DYSBIOSIS OF THE VAGINAL AND ENDOMETRIAL MICROBIOTA AND RIF FOUND. Takahiko Ichiyama, M.D., Ph.D. a ’ Yoko Nagai, Ph.D. a ’ Daichi Urushiyama, M.D., Ph.D. a ’ Motoharu Ohno, M.D., Ph.D. a ’ Takashi Yamaguchi, M.D., Ph.D. a ’ Motoi Nagayoshi, M.D., Ph.D. a ’ Yoshihisa Sakurai, Ph.D. a ’ Fumio Yamasaki, M.D., Ph.D. a ’ Keiji Kuroda, M.D., Ph.D. a ’ Kenichiro Hata, M.D., Ph.D. a ’ Shingo Miyamoto, M.D., Ph.D. a ’ Atsushi Tanaka, M.D., Ph.D. a ’ Atsuo Itakura, M.D., Ph.D. a ’ Satoru Takeda, M.D, Ph.D. a ’ Saint Mother Hospital, Kitakyushu, Japan; 3 Saga Central Hospital, Saga, Japan; 4 Sugiyama Clinic Shirinjuku, Tokyo, Japan; 5 National Research Institute for Child Health and Development, Tokyo, Japan; 6 Juntendo University School of Medicine, Tokyo, Japan.

OBJECTIVE: Repeated implantation failure (RIF) is estimated to occur in 15%-20% of infertile women undergoing in vitro fertilization-embryo transfer (IVF-ET). Molecular identification recently confirmed that the uterine microbiota may have implications for reproductive and obstetrical outcomes. We evaluated dysbiosis of the vaginal and endometrial microbiota in patients with RIF to comprehensively analyze their microbiota using 16S rRNA gene sequencing and compared the microbiota profiles in the RIF patients and healthy women.

DESIGN: This study was conducted from October 2017 to June 2018. It was performed retrospectively for 166 women who consented to participate. It was approved by the Saint Mother Clinic’s ethical committee.

MATERIALS AND METHODS: 145 women who had been diagnosed with RIF were enrolled in the study. 21 healthy women were also enrolled as controls. We investigated their vaginal and endometrial microbiotas using 16S rRNA gene sequencing and compared the microbiota profiles in the RIF patients and controls.

RESULTS: The endometrial microbiotas had a higher alpha diversity than did the vaginal microbiotas (controls p = 2.41e-07, RIF patients p = 2.2e-16). To compare the compositional dissimilarity between the endometrial and vaginal microbiotas, the beta diversity was analyzed. By the principal coordinates analyses (PCoA) based on weighted UniFrac distance, significant associations were observed between microbiotas (p = 0.001).

Assessing the alpha diversity revealed no significant differences between the control and RIF groups in either the uterus or vagina. Beta diversity of the endometrial microbiota showed no significant associations between the controls and RIF patients (p = 0.301). Beta diversity of the vaginal microbiota did not differ significantly between the controls and RIF patients (p = 0.052), but a weak difference in bacterial composition was noted.

In the endometrial microbiotas, 20 bacterial genera (Delftia, Schlege- lella, Burkholderia, Gardnerella, Prevotella, Megaplasma, Cloacibacterium, Dietzia, Rothia, Enterococcus, Atopobium, Micrococcus, Staphylococcus, Exiguobacterium, Hydrogeno- phaga, Sediminibacterium, Limnobacillus, and Vagococcus) exhibited significantly different levels between the controls and RIF patients (all p < 0.05). In the vaginal microbiota, 7 bacterial genera (Corynebacterium, Atopobium, Megaplasma, Varibaculum, Gardnerella, Peptoniphilus, and Prevotella) showed significantly higher levels in the RIF patients (p < 0.05). In contrast to previous reports, we discovered no significant differences in the endometrial Lactobacillus, with average levels of 51.6 ± 38.33% in the controls and 51.15 ± 37.48% in the RIF patients (p = 0.961). However, the average vaginal Lactobacillus levels differed significantly at 91.8 ± 22.73% in the controls and 76.38 ± 38.85% in the RIF group (p = 0.015).

CONCLUSIONS: Analysis of the vaginal and endometrial microbiota using 16S rRNA gene sequencing may be a new biomarker of RIF and may help treat RIF and consequentially help raise the implantation success rate for RIF patients.


FERTILITY & STERILITY® e333
COMPARISON OF THE ENDOMETRIAL RECEPTIVITY ARRAY TO ENDOMETRIAL THICKNESS, ESTRADIOL AND PROGESTERONE LEVELS AS A MARKER FOR ENDOMETRIAL RECEPTIVITY PRIOR TO FROZEN EMBRYO TRANSFER. Shannon T. Alexa, DO, Inspira Health Network, Vineland, NJ.

OBJECTIVE: Endometrial thickness (ET), estradiol (E2) and progesterone (P4) levels have been traditionally used as a marker for endometrial receptivity when preparing for frozen embryo transfer (FET) with patients undergoing in vitro fertilization (IVF). We propose that using these known receptivity markers in conjunction with Endometrial Receptivity Array (ERA) results will increase the sensitivity of detecting optimal endometrial receptivity for embryo transfer and implantation.

METHODS AND MATERIALS: A retrospective chart review of 143 patients who had undergone testing for the ERA at the Reproductive Science Center of New Jersey, Eatontown NJ, between 2016-2019 was done. All of the 143 patients underwent a mock cycle with endometrial biopsy and a subsequent ERA modified cycle with FET. The patients then underwent medical management and evaluation with laboratory testing of their E2 and P4 levels and ultrasounds to evaluate ET and uterine blood flow. Data on the patient’s age, body mass index (BMI), ERA Results, ET, E2 levels, P4 levels, Pulsatility Index (PI), Resistance index (RI) and modified cycle pregnancy outcome were collected. Exclusion criteria included chronic endometritis, congenital uterine abnormalities, endometriosis, and patients who underwent biopsy but whose cycle was not managed by the primary site leaving 91 total patients.

RESULTS: Utilizing SAS, pairwise comparisons were made for the 4 ERA results and a T-test was done using a pooled standard error. The 4 ERA results were compared to E2, P4, number of hours of P4 given prior to biopsy/transfer, ET and uterine artery PI and RI. Of these variables only the hours of P4 given during a modified ERA cycle was significant (p < 0.0001). In addition, E2 and number of hours of P4 during the modified cycle were highest for patients with a pre-receptive result (mean 457.1 and 140.3) and BMI was highest in patients with post-receptive results. There were minimal differences in means independent of the ERA result for P4 levels, hours of P4 given prior to biopsy, ET, PI and RI. Despite identification of higher results for some of the variables none of the differences were statistically significant. In addition there was no significant difference in pregnancy outcome of modified cycles for previously receptive vs. non receptive ERA results.

CONCLUSIONS: In conclusion only the number of hours of P4 given during a patients modified cycle had a significant effect on the ERA result. Given this, it would appear that no linear relationship between these variables including the ERA result exists and that there is no significant relationship between any ERA result and pregnancy outcome exists suggesting a more multifaceted relationship that warrants further exploration. Further understanding of a cumulative effect allows for higher rates of implantation reducing the total number of transfers needed, total cost and emotional burden to the patient.

P-567 Wednesday, October 16, 2019 6:30 AM

IDENTIFICATION OF NEW BIOMARKERS OF HUMAN ENDOMETRIAL RECEPTIVITY AND MATERNAL-FETAL DIALOGUE. Imane EL. Kasmi, Ph.D.a Soumaya Messaoudi, Ph.D.a, Cédille Lesaint, Ph.D.a, François Bissonnette, MD.a Isaac-Jacques Kadoch, MD.a,b Research Associate, Montreal, QC, Canada; aResearch associate, Clinique Ovo, Montreal, QC, Canada; aScientific Director, Clinique Ovo, Montreal, QC, Canada; aClinique ovo, Montréal, QC, Canada.

OBJECTIVE: The endometrial receptivity is a key process for the success in assisted reproductive technology. Despite careful embryo selection, two of every three in vitro fertilization (IVF) cycles fail to result in pregnancy, making reproduction in humans an inefficient process. The key to successful implantation is synchronization. The embryo must not only evolve to the blastocyst stage, but the endometrium must also achieve a specific receptive status and cross-talk between the embryo and endometrium must occur during the window of implantation (WOI). Therefore, it appears essential to identify inadequate endometrial conditions to offer personalized care management. Molecular diagnostic tools currently available to characterize this process are very limited. In this study, we describe the development of a new personalized molecular test based on endometrial receptivity and maternal-fetal dialogue.

DESIGN: As a result of a single site study at ovo clinic from December 2016 to March 2019, the development and clinical validation of a new test, Adhesio Pro® (APF), we decided to analyze the biopsies of which 50 endometrial biopsy samples and 35 autologous endometrial co-culture samples were analyzed by using microarray technology and 130 biopsies from IVF-patients with a known pregnancy outcome were used for clinical validation.

MATERIALS AND METHODS: Microarray data from 50 endometrial biopsies obtained during the optimal theoretical implantation window LH+7 to LH+11 in natural cycle (35 with successful clinical pregnancy 15 with implantation failure). Similarly, a total of 215 biopsies were performed on autologous-endometrial co-culture (14 endometrial cells cultured in absence of embryo, 5 in presence of good-quality embryo successfully transferred, 10 with good quality embryo but with implantation failures). Microarray data were analyzed and selected biomarkers were assessed using RT-qPCR.

RESULTS: 10 genes have been identified for the first time by using a new approach that incorporates two specific transcriptomic signatures obtained by next generation genomics and statistical technologies applied to microarray analyses:

1. A specific transcriptomic signature of 1717 genes specifically modulated associated to biopsies from patients with successful clinical pregnancy versus biopsies from patients with implantation failure. Gene ontology analyses revealed that cell division, cellular proliferation, cell adhesion and mitotic cycle are the most over-represented biological terms in this group of genes.

2. A second specific signature of 60 genes associated to endometrial co-culture successfully transferred was obtained using class prediction approach.

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IDENTIFICATION OF NEW BIOMARKERS OF HUMAN ENDOMETRIAL RECEPTIVITY AND MATERNAL-FETAL DIALOGUE. Imane EL. Kasmi, Ph.D.a Soumaya Messaoudi, Ph.D.a, Cédille Lesaint, Ph.D.a, François Bissonnette, MD.a Isaac-Jacques Kadoch, MD.a,b Research Associate, Montreal, QC, Canada; aResearch associate, Clinique Ovo, Montreal, QC, Canada; aScientific Director, Clinique Ovo, Montreal, QC, Canada; aClinique ovo, Montréal, QC, Canada.

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Gene expression was validated by RT-qPCR. Clinical validation was performed on 130 biopsies from IVF-patients with a known pregnancy outcome.

CONCLUSIONS: Evaluation of receptivity and embryo implantation with new molecular signature can predict IVF success and may help in the management of endometrial preparation for embryo transfer and optimizes chances of successful pregnancy for many couples.

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PROGESTERONE AND ESTRADIOL CONCENTRATIONS IN HUMAN ENDOMETRIUM DURING THE MID-LUTEAL PHASE OF THE MENSTRUAL CYCLE. Dimitar Parvanov, PhD, Rumiana Ganeva, MSc, Nina Vidolova, MSc, Polya Penkova, MD, Teodora Tlhomirova, MD, Georgi Stamenov Stamenov, MD/PhD, Nadezhda Women’s Health Hospital, Sofia, Bulgaria.

OBJECTIVE: The aim of this study was to estimate the local progesterone and estradiol concentrations in the endometrial tissue, to compare them with their serum concentrations and to investigate possible associations between the two.

DESIGN: Observational study.

MATERIALS AND METHODS: The concentration of (P4) and estradiol (E2) were investigated in serum and endometrial biopsy samples from 58 women aged between 26 and 41 years during mid-luteal phase (7 days after LH surge). The endometrial samples were weighed and homogenized in a glass homogenizer with a Teflon pestle in a PBS buffer followed by centrifugation at 12,000 g for 10 minutes at 4°C. The obtained supernatant was used for P4 and E2 measurement by electrochemiluminescence immunoassay (ECLIA) on the Cobas e411 analyzer (Roche Diagnostics, Mannheim, Deutschland). Statistical analysis was performed using SPSS v.21 (IBM Corp., Armonk, NY, USA).

Descriptive parameters and patient characteristics were reported as mean ± SD and median. P < 0.05 was considered statistically significant.

RESULTS: The observed endometrial P4 levels ranged from 0.001 to 270.54 ng/mg tissue, with a mean of 23.41 ± 57.63 ng/mg tissue and a median of 0.80 ng/mg tissue. The endometrial E2 concentrations ranged between 0.01 ng/mg and 0.32 ng/mg tissue with a mean of 0.1 ± 0.06 ng/mg tissue and a median of 0.08 ng/mg tissue. The determined mean P4 concentration in the endometrial tissue was 17.9 times higher than the P4 found in the serum samples, while the mean tissue E2 concentration was 1510 times lower in comparison with the E2 serum levels. As a result, the mean P4/E2 ratio (P4 [ng/mg] /E2 [ng/mg]) in the tissue was 57.63 ng/mg tissue, with a mean of 0.86 ng/mg tissue, and a median of 0.35; p = 0.01. A similar relation was observed between the E2 levels in the endometrial tissue and in the serum (P = 0.35; p = 0.02). Again, modest but significant relation was present between the P4 and E2 tissue levels (R = 0.35; p = 0.02).

CONCLUSIONS: We conclude that the mid-luteal endometrium contains relatively high levels of P4 and significantly low levels of E2 compared to their serum levels. Endometrial P4 and E2 concentrations are positively but slightly associated between each other and with their respective levels in serum.

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LIPID PROFILING OF PERI-IMPLANTATION ENDOMETRIUM IN PATIENTS WITH PREMATURITY PROGESTERONE RISE IN LATE FOLLICULAR PHASE. Jingjie Li, M.D, Pan Chen, PhD, Xiaoyan Liang, M.D, the Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; the First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China.

OBJECTIVE: To investigate alterations of lipid profile at the window of implantation in patients with premature progesterone rise.

DESIGN: Lipidomics variation of endometrium was evaluated by ultra-high performance liquid chromatography coupled with electrospray ionization high-resolution mass spectrometry (UHPLC-ESI-HRMS).

MATERIALS AND METHODS: 43 patients undergoing IVF/ICSI by the reason of tubal factor or male factor were included in this study. The patients were divided into high progesterone group (P > 1.5ng/ml, 15 patients) and control group (P < 1.5ng/ml, 28 patients) on the day of hCG administration. The endometrium tissues were obtained by pipelle biopsy 7 days after hCG trigger.

RESULTS: A total of 1026 ions were identified and 25 lipids were showed significantly up-regulated. The endometrium lipid profile was characterized by significant increase in concentration of phosphatidylcholine (PC), phosphatidylethanolamine (PE), lysophosphatidylcholine (LPC), diacylglycerol (DG), ceramide (Cer), phosphatidylinositol (PI), phosphatidylserine (PS) in patients with premature progesterone rise at the end of the follicular phase. The correlation analysis between progesterone concentration level with the lipids showed stronger negative correlation between PE and PS with progesterone level.

CONCLUSIONS: Premature progesterone elevation disturbs lipid homeostasis of endometrium in the peri-implantation period. The altered lipids may impair endometrial receptivity and early embryo implantation.

SUPPORT: This study was financially supported by the National Natural Science Foundation of China (No. 81601347, 81503156), Natural Science Foundation of Guangdong Province (No. 2014A030310096) and Public Welfare Research and Capacity Building Fund of Guangdong (No. 2016A020218006).

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EFFECT OF ESTRACE ON PREGNANCY RATES FOR WOMEN WITH THIN ENDOMETRIAL LINING UNDERGOING INTRAUTERINE INSEMINATION. Jasymn K. Johal, MD, MSc, Sara J. Vaughn, MD, Lusine Aghajanova, MD/PhD, Stanford University School of Medicine, Stanford, CA.

OBJECTIVE: To evaluate the effect of exogenous estradiol on pregnancy rates for women with thin endometrial lining undergoing intrauterine insemination (IUI) as compared to women who did not receive estradiol for endometrial support; we hypothesize that there was no difference in pregnancy rates between the two groups.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: All IUI cycles completed at Stanford University Clinic for Reproductive Medicine from March–December 2017 were reviewed. All monitored IUI cycles were included. Cycles with the addition of exogenous estradiol given vaginally or orally were compared to those without exogenous estradiol. Differences in endometrial parameters, pregnancy rates, miscarriage rates and live birth rates were compared between both groups.

RESULTS: A total of 885 IUI cycles were included. In 85 cycles, exogenous estradiol was initiated for thin endometrium. Baseline characteristics including maternal age, body mass index, ethnicity, number of IUI cycles per patient, type of IUI cycle, and total motile sperm count were similar between the two groups. Mean baseline endometrial lining was thicker in the non-estradiol group, and the non-estradiol group was more likely to have a diagnosis of unexplained infertility whereas the estradiol group was more likely to have a diagnosis of diminished ovarian reserve. Despite initiation of estradiol, the mean endometrial thickness at trigger scan remained significantly thinner in estradiol group as compared to the non-estradiol group (6.4 ± 1.3 cm vs. 8.4 ± 1.9 cm, respectively, p < 0.001), although the change in thickness in the estradiol group from baseline to trigger scan did increase on average by 2.2 cm. Pregnancy, miscarriage and live birth rates were similar between the estradiol and non-estradiol groups (see Table 1).

CONCLUSIONS: Although there is limited data supporting the use of exogenous estradiol to improve outcomes during IUI cycles, this low risk intervention is often employed in the setting of a thin endometrial lining in the late follicular phase. In women undergoing IUI with exogenous estradiol supplementation due to thin endometrial lining, pregnancy, miscarriage and live birth rates were similar to women undergoing IUI without exogenous estradiol use.

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Estradiol (n=85)</th>
<th>No Estradiol (n=800)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endometrial Lining thickness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(cm)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>4.2 ± 1.3</td>
<td>4.9 ± 1.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Estradiol initiation</td>
<td>4.9 ± 0.8</td>
<td>6.4 ± 1.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Trigger</td>
<td>6.4 ± 1.3</td>
<td>8.4 ± 1.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pregnancy Rate, n (%)</td>
<td>14 (20%)</td>
<td>81 (10%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Spontaneous</td>
<td>8 (10%)</td>
<td>30 (4%)</td>
<td>0.08</td>
</tr>
<tr>
<td>Abortions, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Live births to date, n (%)</td>
<td>5 (10%)</td>
<td>42 (10%)</td>
<td>0.78</td>
</tr>
</tbody>
</table>
OBJECTIVE: To evaluate if genistein and daidzein (soy-derived phytoestrogens) levels in urine and follicular fluid (FF) could have an impact on the number of antral follicles, MII oocytes, fertilization, embryo quality on day 3, and aneuploidy rates.

DESIGN: Prospective, observational study including preimplantation genetic testing for aneuploidy (PGT-A) cycles in which urine and FF was collected the day of ovum pick (December 2013 - July 2018).

MATERIALS AND METHODS: A total of 36 PGT-A cycles in women <38 years were analyzed by Next Generation Sequencing (NGS). Indications for PGT-A were recurrent miscarriage or repetitive implantation failure. Genistein and daidzein were measured using Ultra-Performance Liquid Chromatography/Electrospray Mass Spectrometry (UPLC/ESI-MS) and normalized according to creatinine levels. In urine samples genistein and daidzein levels were classified in three categories: <10ng; 10-50ng and >50ng. The number of informative urine samples with levels above the limit of detection was 26 for genistein and 36 for daidzein. In FF, lower levels were detected and were classified as follows: <2ng; 2-5ng and >5ng. The number of informative FF samples with levels above the limit of detection was 13 for genistein and 9 for daidzein. The statistical comparisons among groups were carried out using the Graphpad InStat v. 2.05a package (Graphpad Software, San Diego, CA, USA).

RESULTS: For genistein levels in urine, a significant increase in the mean number of antral follicles was observed in the group with higher concentration (14.9±5.3; 18.2±5.3 and 24.5±9.6; p<0.05). A similar trend was observed for the mean number of MII oocytes and 2PN, but without significant differences. Day 3 embryos showed a significant increase in mean blastocyst number (6.6±2.0; 5.9±1.8 and 7.2±1.0; p<0.05), and a decrease in fragmentation degree (8.1±6.9; 8.6±6.5 and 5.0±4.1; p<0.05) in the group with higher urine genistein concentration. Genistein levels in FF were correlated with the levels in urine and significant differences were found for the same variables: mean number of antral follicles (11.2±3.7; 19.5±3.3 and 25±4.8; p<0.05); mean blastomere number (6.7±3.3; 6.0±1.9 and 7.5±0.7; p<0.05) and fragmentation degree (6.7±5.8; 11.0±8.2 and 2.5±3.5; p<0.05). Aneuploidy rates were significantly decreased in urine genistein levels >50ng (60.8% vs. 42.3%; p<0.05), and a similar trend was observed for FF >5ng, but without reaching statistical significance (69.7% vs. 47.1%). For daidzein levels in urine and FF, no clear correlation was observed with ovarian response and embryo quality.

CONCLUSIONS: In PGT-A couples, genistein, a soy-derived phytoestrogen, enhances ovarian response, embryo quality and euploidy rates. A protective effect of a soy-diet has been previously described in a mouse model (Mulhausner et al., 2009). In ART patients, soy isoflavones intake has been positively related to livebirths (Vanegas et al., 2015). Therefore, a soy-enriched diet could be beneficial for women undergoing ART, and more specifically in PGT-A cycles.


SUPPORT: Merck research grant 2015-2018.

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THE ASSOCIATION BETWEEN SEASON AT CYCLE START AND CLINICAL PREGNANCY FOLLOWING FRESH EMBRYO TRANSFER. Leslie V. Farland, Sc.D., Katherine Corrhea, PhD, Stacey A. Missmer, Sc.D., Catherine Racowsky, PhD, "University of Arizona, Tucson, AZ; "Amherst College, Amherst, MA; "Michigan State and Harvard T.H. Chan SPH, Grand Rapids, MI; "Brigham & Women’s Hospital, Boston, MA.

OBJECTIVE: Improvements in laboratory techniques and clinical protocols have led to increasing livebirth rates from in vitro fertilization (IVF). Despite this impact, the reproductive potential of patients remains a primary determinant of success. It is therefore of interest to investigate any environmental factors that may influence this potential. As delivery rates from spontaneous conception vary according to season, outcomes from IVF may also be season-dependent. The present study was designed to test the hypothesis that there is an association between season at IVF cycle start and clinical pregnancy.

DESIGN: Retrospective cohort of 5,878 fresh embryo transfers.

MATERIALS AND METHODS: Start dates for all autologous cycles resulting in fresh cleavage or blastocyst stage transfers performed in our IVF program between January 2012-December 2017 were categorized by season

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EFFECT OF GENISTEIN AND DAIDZEIN LEVELS ON OVARIAN RESPONSE AND EMBRYO QUALITY IN PGT-A CYCLES. Lucia Marin, MSc, Inmaculada Campos-Galindo, PhD, Francisco Dominguez, Ph.D., Ma José de los Santos, PhD, Carmen Vidal, M.D, Ph.D., Amparo Mercader, Ph.D, Carlos Simon, MD, PhD, Carmen Rubio, PhD, Igenomix Foundation - ISSLaFe Biomedical Research Institute, Valencia, Spain; IVIRMA Valencia, Valencia, Spain; University of Valencia; Igenomix Foundation-INCLIVA, Valencia, Spain; Igenomix, Valencia, Paterna (Valencia), Spain.

OBJECTIVE: To test the hypothesis that genistein and daidzein (soy-derived phytoestrogens) levels in urine and follicular fluid (FF) could have an impact on the number of antral follicles, MII oocytes, fertilization, embryo quality on day 3, and aneuploidy rates.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Data regarding AQI were obtained directly from the Environmental Protection Agency. A LifeAire System is used for air purification in UCSF’s IVF laboratory. During the fires, there were <10ppb volatile organic compounds and <1 ug/m3 of particles (0.1-10 µm) measurable in the laboratory. Clinical outcome data were collected from exposed patients with oocyte retrievals within a month following the Camp Fire (from November 8th to December 8th, 2018). Data on fertilization, blastocyst, and euploid rate were compared to a control population of patients who had oocyte retrievals at UCSF within the year prior to the Camp Fire. Student’s t-test was used to analyze differences in mean rates for each clinical outcome. Chi squared test was used to compare cycle cancellation rate between groups. Regression analyses with cluster analysis for pairwise comparison were performed on exposed patients with prior unexposed cycles, to assess for differences in clinical outcomes within a patient.

RESULTS: Median AQI in the year prior to the Camp Fire was 37 (IQR 31-52), in comparison to a median AQI of 164 (IQR 151-173) during the two weeks of the Camp Fire (p=0.001). One hundred and twelve patients were exposed during the fire, and 45% of them completed preimplantation genetic screening for aneuploidy (PGT-A). There were 969 patients in the control population, with 45% completing PGT-A. No significant differences were noted in age, body mass index, race, infertility diagnosis, or stimulation protocol. When comparing all non-exposed to exposed patients who had oocyte retrievals within a month following the Camp Fire, there were no differences noted in fertilization (73% vs 79%, p=0.44), blastocyst (51% vs 57%, p=0.16), or euploid (40% vs 47%, p=0.14) rates. There were also no differences in cycle cancellation rate. Forty-six exposed patients had non-exposed cycles with the same or different stimulation protocol. When comparing all non-exposed to exposed cycles within a patient, there were no differences noted in fertilization (73% vs 76%, p=0.67), blastocyst (48% vs 41%, p=0.22), or euploid (31% vs 41%, p=0.24) rate.

CONCLUSIONS: Unhealthy AQI during the 2018 Camp Fire was not associated with statistically significant differences in clinical outcomes of patients undergoing IVF treatment in a code compliant laboratory. These findings suggest that acute exposure to unhealthy air does not impact egg or sperm function, however, further studies are needed to assess for impact of long-term exposure on outcomes.

SUPPORT: None.
and Co might have significant inverse effects on AHM, which also showed between infertile women living in the Eastern China and Southern China. Fe (follicle stimulating hormone (FSH), luteinizing hormone (LH), estrat tween AMH levels were adjusted by age, BMI and reproductive hormones AMH levels are tested. The places of residence were collected from the elec by the included patients, FF samples during the oocyte retrieval were

- Regional differences of metal levels in follicular fluid and serum AMH level between infertile women from Eastern China and Southern China. Jinyin Xu, MD; Yanyun Ying, B.S.Med; Jianpeng Chen, MD; Dan Li, MD; Dan Zhang, MD, PhD; Key Laboratory of Reproductive Genetics (Ministry of Education) and Department of Reproductive Endocrinology, Hangzhou, Zhejiang, China; Women’s Hospital, Zhejiang University School of Medicine, Hangzhou, China; Key Laboratory of Reproductive Genetics (Ministry of Education) and Department of Reproductive Endocrinology, Hangzhou, China.

OBJECTIVE: The metal exposure can result in different bioaccumulation in the reproductive tissues as well as diverse disturbance of the reproductive outcomes in different regions, which requires additional research on regional effects on environmental exposure and reproductive toxicity. Therefore, the study aims to assess the regional difference of metal levels in follicular fluids and serum Anti-mullerian test tube hormone (AMH) of infertile women from Eastern China and Southern China.

DESIGN: A cross sectional study was approved by the Institutional Review Board Committee, and was conducted between September 2017 and December 2017 in infertility ward in Women’s Hospital, Zhejiang University School of Medicine. 648 female patients diagnosed with unexplained infertility from Eastern China and Southern China were included.

MATERIALS AND METHODS: After informed written consent signed by the included patients, FF samples during the oocyte retrieval were collected. Nineteen elements (vanadium, chromium, manganese, iron, cobalt, nickel, copper, zinc, arsenic, selenium, strontium, molybdenum, silver, cadmium, tin, antimony, bario, titanium, and mercury) were analyzed in FFs by inductively coupled plasma mass spectrometry (ICP-MS), and serum AMH levels are tested. The places of residence were collected from the electronic medical record of the hospital. The associations of metal levels between AMH levels were adjusted by age, BMI and reproductive hormones (follicle stimulating hormone (FSH), luteinizing hormone (LH), estradiol(E2), progesterone(P), testosterone(T) and prolactin(PRL)).

RESULTS: We observed that iron(Fe) levels and Cobalt(Co) levels in FFs were both inversely related to serum AMH level (P < 0.05, respectively). Infertile women living in the Eastern China have a significant higher level of Fe and Co in FFs (P < 0.05, respectively) with a significant lower AMH level (P < 0.05, respectively) compared to infertile women from Southern China.

CONCLUSIONS: Bioaccumulations of Fe and Co were quite different between infertile women living in the Eastern China and Southern China. Fe and Co might have significant inverse effects on AHM, which also showed significant regional differences between Eastern China and Southern China. There might be some difference of Fe and Co exposure pathways between two areas, while additional prospective research is needed to corroborate these findings in the general population.

SUPPORT: This work was supported by the National Key Research and Development Program of China (2017YFC1000103), the National Natural Science Foundation of China (No. 817171535), the Natural Science Foundation of Zhejiang Province (No. LZ18H040001), and the Zhejiang Provincial Key Medical Technology Program (WKJ-ZJ-1826).

CIGARETTE SMOKE-INDUCED OXIDATIVE STRESS ALTERS DNA METHYLATION PATTERNS IN SPERM AND NEUROLOGICAL GENE EXPRESSION PATTERNS IN OFFSPRING. Patrick J. Murphy, PhD; Jingtao Guo, PhD; Timothy G. Jenkins, PhD; John R. Hoidal, MD; Thomas Huecksteadt, BS; James Hotaling, MD; Douglas T. Carrell, PhD; Bradley R. Cairns, PhD; Kenneth I. Aston, PhD; University of Rochester Medical Center, Department of Biomedical Genetics, Rochester, NY; University of Utah School of Medicine, Andrology and IVF Laboratories, Salt Lake City, UT; University of Utah School of Medicine, Department of Internal Medicine, Salt Lake City, UT; Howard Hughes Medical Institute, Department of Oncological Sciences and Huntsman Cancer Institute, University of Utah School of Medicine, Salt Lake City, UT.

OBJECTIVE: We investigated the impact of pre-conception paternal cigarette smoke exposure on sperm DNA methylation and gene expression in the offspring as well as the mechanism underlying smoke-induced changes. In addition, we evaluated the capacity for sperm DNA methylation patterns to correct following removal of smoke exposure for 1-5 spermatogenic cycles (28-171 days).

DESIGN: Mouse model-based intervention versus non-intervention study.

MATERIALS AND METHODS: Male mice were exposed to tobacco smoke at the body mass-adjusted equivalent of 10 to 20 cigarettes per day for 60 days. Following the exposure period, some exposed and unexposed mice were bred to unexposed female mice, while additional exposed and control mice (recovery group) were maintained for 28-171 days following removal of smoke exposure. Sperm were collected from the sires and recovery animals, and reduced representation bisulfite sequencing (RRBS) was performed to analyze genome-wide sperm DNA methylation patterns associated with cigarette smoke exposure and recovery. Exposure of sperm and control mice were euthanized at 14-17 weeks of age, and DNA methylation and gene expression patterns in the frontal cortex were evaluated to determine whether paternal smoking status impacted offspring neurological profiles. The Bismark RRBS pipeline and the USeq program DefinedRegionDifferentialSeq were utilized for measuring changes in DNA methylation and gene expression respectively. Statistical analysis was performed using R.

RESULTS: We identified significant differences in sperm DNA methylation patterns associated with smoking status. Remarkably, the changes in sperm DNA methylation were largely recapitulated in Nrf-/− mice independent of smoke exposure. The assessment of heritable effects revealed changes in DNA methylation patterns as well as gene expression in the offspring of mice exposed to cigarette smoke, and strikingly the epigenetic and transcriptional changes identified in the offspring of smoke-exposed mice were also observed in Nrf-/− offspring irrespective of paternal smoking status. Recovery experiments indicated that about half of differentially methylated regions returned to normal within 28 days of removal from smoke, however additional recovery following a longer recovery period was not observed, indicating potential long-term effects following smoking cessation.

CONCLUSIONS: The current study provides abundant evidence that cigarette smoke exposure induces epigenetic changes in sperm. Further, studies in offspring suggest that pre-conception paternal smoking status impacts neurological epigenetic and gene expression status in a consistent manner. Parallel studies performed in Nrf-/− mice provide strong evidence for oxidative stress as the predominant underlying mechanism for smoke-induced epigenetic changes to sperm as well as the offspring of smoke-exposed sires. Lastly, recovery experiments indicate that while many epigenetic changes are corrected following removal of smoke exposure, a residual effect persists at a significant number of regions even after five spermatogenic cycles.

SUPPORT: This work was supported by a grant from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, USA (R01HD082062).
AMBIENT TEMPERATURE IN THE WEEK PRIOR TO DELIVERY AND RISK FOR STILLBIRTH.
Pauline Mendola, PhD, a Jenna Kanner, BS, b Andrew D. Williams, PhD, b Sandie Ha, PhD, c Carrie J. Nobles, PhD, d Marion Ouidir, PhD, d "NICHD, Bethesda, MD; bNational Institutes of Child Health and Human Development, Bethesda, MD; cUniversity of California Merced, Merced, CA.

OBJECTIVE: To assess the impact of higher ambient temperature on the risk of stillbirth during the warm season. Extreme ambient temperature events are becoming more prevalent and changes in ambient temperature represent an understudied but potentially modifiable stillbirth risk factor.

DESIGN: Retrospective cohort study based on hospital delivery admission electronic records from 19 hospitals for all deliveries 20 weeks gestation or later.

MATERIALS AND METHODS: We identified the first stillbirth case per mother (n=498) among singleton deliveries in the NICHD Consecutive Pregnancy Studies (Utah, 2002-2010). Ambient temperature was derived from the Weather Research and Forecasting model and air pollution data were based on modified Community Multiscale Air Quality models. We conducted a case-crossover analysis to estimate the hazard ratio (HR) and 95% confidence interval (95% CI) for the risk of stillbirth for each increase of 1° Celsius during the warm season (May – September). Risk periods included day of delivery and each of the 7 days prior to delivery as well as the average temperature for the week prior to delivery. Two control periods were selected: two weeks prior to delivery and two weeks after delivery. Women serve as their own controls in this analysis and all non-time-varying factors are controlled by design. Models were adjusted for time-varying relative humidity, ozone, and particulate matter <2.5 microns.

RESULTS: During the week prior to delivery, daily risk of stillbirth significantly increased between 5-11% for each 1° Celsius increase in temperature beginning 2 days prior to delivery (HR=1.05; 95% CI: 1.00-1.10) with the highest risk observed at 7 days prior (HR=1.11; 95% CI: 1.06-1.17). Point estimates for the day of delivery, the day immediately preceding delivery and average temperature in the week prior to delivery were elevated but not significantly associated with stillbirth.

CONCLUSIONS: Our findings suggest temperature may be a modifiable risk factor for stillbirth. Notably, the risks we observe beginning 2 days prior to delivery appear consistent with the fact that most stillbirths occur 48-72 hours prior to delivery. High temperature can induce physiologic stress including increased heart rate and inflammatory processes, but the specific underlying biologic mechanisms related to stillbirth remain to be explored. Stillbirth risk associated with ambient temperature merits attention given the under studied but potentially modifiable stillbirth risk factor.
was calculated for each participant. We used generalized linear regression models to estimate fecundability ratios (FR). We also used a logistic regression to estimate the odds ratios (OR) for early pregnancy loss.

RESULTS: In our primary analysis, fecundability was higher for couples living near a major road, but the confidence interval included the null (FR < 0.78, 95% CI: 0.74, 0.82) (Table). For clinical pregnancies, proximity was not associated with fecundability (Table). Odds of early pregnancy loss was higher in women who lived <200 meters from a major road (OR: 2.08, 95% CI: 0.85, 5.09) or who lived 200 - <500 meters away from a major road (OR: 1.82, 95% CI: 0.78, 4.24), but numbers were small (47 losses).

CONCLUSIONS: Living near a major roadway was not associated with reduced fecundability. Proximity to major roads may be associated with early pregnancy loss, but this should be investigated in a cohort with a larger number of early losses. Planned analyses of existing data in this cohort include implantation timing and characteristics of early loss in relation to proximity.

TABLE. Fecundability Ratios for roadway proximity.

<table>
<thead>
<tr>
<th>Roadway proximity (m)</th>
<th>FR</th>
<th>95%CI</th>
<th>n</th>
<th>FR</th>
<th>95%CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Per 100m increase</td>
<td></td>
<td></td>
<td>608</td>
<td>0.99</td>
<td>(0.98, 1.01)</td>
</tr>
<tr>
<td>&lt;200</td>
<td>1.42</td>
<td>(0.94, 2.14)</td>
<td>79</td>
<td>0.94</td>
<td>(0.77, 1.20)</td>
</tr>
<tr>
<td>200 - &lt;500</td>
<td>1.11</td>
<td>(0.83, 1.67)</td>
<td>157</td>
<td>1.10</td>
<td>(0.76, 1.59)</td>
</tr>
<tr>
<td>500 - &lt;1000</td>
<td>1.18</td>
<td>(0.83, 1.67)</td>
<td>137</td>
<td>1.10</td>
<td>(0.76, 1.59)</td>
</tr>
<tr>
<td>&gt;1000</td>
<td></td>
<td></td>
<td>235</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

3. Adjusted for: female age, male age, education, income, occupation.

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P-581 Wednesday, October 16, 2019 6:30 AM

WOMEN’S KNOWLEDGE ABOUT THE IMPACT OF FEMALE AND MALE AGE, WEIGHT, AND SMOKING ON FERTILITY: RESULTS FROM A NATIONAL SURVEY. Amber K. Worthington, PhD,a Erin E. Burke, PhD,b Carly Leahy, BA,b Penn State University, University Park, PA; bModern Fertility, San Francisco, CA.

OBJECTIVE: Women’s misconceptions about the impact of female and male age, weight, and smoking on a couple’s fertility likely lead to uninformed decisions regarding reproductive health and family planning; however, little research has examined women’s fertility knowledge. The goal of this study was to provide a large-scale assessment of women’s knowledge about the impact of risk factors on female and male fertility.

DESIGN: A national, cross-sectional survey.

MATERIALS AND METHODS: 327 women were recruited through an e-newsletter in March 2019; no incentive was provided. Eligible participants were aged 18 to 59, identified as women, lived in the USA and provided informed consent. Participants completed an online survey that assessed their knowledge about the impact of female and male age, weight, and smoking on fertility. The data were analyzed using descriptive statistics and dependent sample t-tests; the power was excellent (.99).

RESULTS: Participants ranged in age from 18 to 59 (M = 34.11, SD = 6.64) and the majority identified as heterosexual (95%) and had a partner (81%).
3 items assessed knowledge about the impact of age on female fertility, and 3 items assessed knowledge about the impact of age on male fertility (e.g., “female fertility significantly declines between the ages of 35 and 39” (T); “male fertility significantly declines between the ages of 45 and 49” (T)). Participant responses on all 6 items were coded as correct or incorrect. 87% answered both items about female weight and smoking correctly; 49% answered both about males correctly. A dependent samples t-test revealed that women were less knowledgeable about the impact of male age on smoking and fertility (M = 1.41, SD = 0.64, range = 0 - 2) than female weight and smoking on fertility (M = 1.86, SD = 0.38, range = 0 - 2); t(26) = 13.13, p < .001.

CONCLUSIONS: These results suggest that women are relatively informed about the impact of their own age, weight, and smoking on fertility but less informed about the impact of male age, weight, and smoking on fertility. These misconceptions may disproportionately assign responsibility for preconception health to women. Providers should be aware of these misconceptions in order to educate patients on the role of male fertility risk factors. Correcting these misconceptions may be a critical step towards decreasing infertility by changing unhealthy behaviors and alleviating the emotional load on opposite-sex couples.

SUPPORT: This research was funded by Modern Health, Inc.

P-582 Wednesday, October 16, 2019 6:30 AM

THE DEGRADATION OF VITAMIN D ACROSS TIME: AN ISSUE LEADING TO UNRELIABLE RESULTS IN REPRODUCTIVE RESEARCH. Evelin E. Lara-Molina, MD,a Jason M. Franasiak, MD,b Almudena Devesa-Peiro, MSc,c Marina Lopez-Nogueroles, PhD,d Mireia Florensa, MSc,d Marta Martín, MSc,e Agustín Ballestros, PhD,f Antonio Pellicer, MD, PhD,g Patricia Diaz-Gimeno, PhD,h IVI RMA Barcelona, Barcelona, Spain; hIVI-RMA New Jersey, Basking Ridge, NJ; iIVI Foundation IVIRMA Global, Biomedical Research Institute La Fe, Valencia, Spain; iIVIRMA ROMA, Roma, Italy.

OBJECTIVE: Vitamin D deficiency is widely reported with significant impact on many health processes, including reproduction. However, many studies evaluate the impact of vitamin D utilizing banked samples, and the stability of vitamin D after a prolonged storage is often not taken into account. We aimed to determine if 25-hydroxyvitamin D (25(OH)D3) and its main catabolite 24,25-dihydroxyvitamin D (24,25(OH)2D3) in serum and follicular fluid, are stable across time in frozen samples.

DESIGN: Prospective, non-interventional study.

MATERIALS AND METHODS: Controlled ovarian stimulation was performed in thirty-five egg donors using an antagonist protocol and standard doses of subcutaneous FSH. After 36 hours of a GnRH agonist bolus, the oocytes retrieval was performed. Serum samples and pooled follicular fluid from mature follicles were collected during pick-up for 24.25(OH)2D3 and 25(OH)2D3 measurements via LC-MS/MS using a UPLC-TQ-S Xevo Waters system with a Waters Acquity BEH C18 (1.7µm, 2.1x100 mm) column. A baseline Vitamin D analysis and a second one after seven months of storage at -80°C were performed. After testing the normal distribution of metabolites concentration with Shapiro-Wilktest, a t-test (when normal distribution) or a Wilcoxon test (for non-normal distribution) was performed in order to contrast mean differences before and after storage.

RESULTS: A significant decrease in 25(OH)D3 concentrations after 7 months of storage was found in serum (from 91.56 ± 39.01 nM to 62.235 ± 24.09 nM, p-value =2.68e-11) and follicular fluid (from 58.13 ±19.55 to
OBJECTIVE: To investigate the associations between laboratory TVOC levels measured during in vitro manipulation of human oocytes/embryos and subsequent implantation.

DESIGN: Retrospective cohort study in a private IVF center.

MATERIALS AND METHODS: Consecutive IVF cycles (n=103; female age 35.9±4.5 yr) performed at Reproductive Medicine Center, Tianjin United Family Hospital, between August 2018 and April 2019 were included. Impaired implantation (ICSI) cycles were excluded due to the confounding effect of extra exposure of oocytes during sperm injection. Ambient TVOC readings were continuously logged at 6-minute intervals by a specialized designed device (HuChuang, China) at a fixed position in the embryology laboratory. The readings were retrieved at the closest time point to 4 procedures where embryos were exposed to the ambient environment, namely egg collection, insemination, fertilization check, and D3 embryo check. Embryos were cultured in MINC incubators (Cook) at 37°C perfused with clean cylinder gas (6% CO2, 5% O2, and balance N2) post in-line VOC removal. One or two embryos ranked the highest from the cohort were transferred on either D3 or D5, depending on the prognosis of individual patients. Implantation detected by rising hCG was evaluated via multiple variable logistic regression against cycle characteristics, embryology parameters and TVOC levels, expressed by odds ratio (OR) and 95% confidence interval (CI). Proportional embryology parameters were compared using the χ² analysis.

RESULTS: TVOC readings ranged from 0.15 to 1.98 ppm despite extensive filtration of laboratory air (in-situ HEPA filters, stand-alone IQAir and Coda Tower), reflecting the influence of outside atmospheric conditions. Multiple variable logistic regression showed statistically significant associations between implantation and female age (OR=0.817[0.723-0.924], P=0.001), D3 embryo transfer (OR=12.078[1.105-132.062], P=0.041), and the TVOC levels at egg collection (OR=0.171[0.035-0.835], P=0.029).

No effect was seen on the number of previous attempts (1.240[0.725-2.120], P=0.432), stimulation protocol (1.269[0.486-3.316], P=0.627), number of eggs collected (0.954[0.828-1.098], P=0.509), number of embryos transferred (8.954[0.871-92.021, P=0.065), TVOC levels at insemination (1.782[0.162-19.664], P=0.637), at fertilization check (1.013[0.277-3.704], P=0.984) and at D3 embryo check (1.401[0.563-3.489], P=0.468). Using a cut-off at the median TVOC reading (0.64 ppm) at egg collection, there were no significant differences in the fertilization rates (64.1% vs 65.0%, P=0.776), D3 good quality embryo rates (65.5% vs 65.1%, P=1) and embryo utilization rates (50.5% vs 50.6%, P=1). However, a significantly reduced implantation rate (57.7% vs 37.3%, P=0.038) was seen when comparing low to high TVOC groups.

CONCLUSIONS: High levels of TVOC at egg collection, rather than at insemination or fertilization check or D3 embryo check, were associated with a reduced chance of implantation following IVF. However, conventional embryology parameters were not adversely affected.

P-584 Wednesday, October 16, 2019 6:30 AM

SEASONAL ENVIRONMENTAL CONTAMINANTS APPEAR TO INFLUENCE GAMETE PRODUCTION AND PREGNANCY OUTCOME FOLLOWING ART. Lindsay L. Perenose, PhD, a Christopher B. Ellen, B.S., a Frances K. Hanson, M.S., a Khaliq Ahmad, PhD, a Jau-Chen Huang, MD, a Samuel D. Prien, PhD a Texas Tech University Health Sciences Center, Lubbock, TX; bTexas Tech University, Lubbock, TX; cTexas Tech University Health Science Center - Lubbock, Lubbock, TX.

OBJECTIVE: It is well known that environmental contaminants can affect many aspects of human health including fertility. While most research has focused on compounds like bisphenol A (BPA), there are other compounds, such as 2,4-dichlorophenoxyacetic acid (2,4-D) and Paraquat, that could be of concern in areas with intensive agriculture. Due to their chemical structures, common herbicides and pesticides could potentially interrupt reproductive function. The objective of this study is to correlate environmental exposure differences between urban and rural populations with fertility treatment success and to better understand patient responsiveness to assisted reproductive technologies (ART) as a result of these environmental exposure differences.

DESIGN: Chart review study evaluating the relationship between patient environment and ART outcomes.

MATERIALS AND METHODS: Patients were assessed based off of ART procedure reports from 2014-2017 (N = 267) and were categorized into urban and rural populations. For male patients, sperm concentration, semen volume, and percent motility were evaluated pre- and post-wash. For female patients, the number of oocytes retrieved, normal versus abnormal fertilization, embryo development, and pregnancy outcome were analyzed. Further, pregnancy outcomes were evaluated based on month of retrieval to examine seasonality. Differences related to rural agricultural practices of the region. Statistical significance was determined using statistical package for social sciences (SPSS) to run two-way ANOVA, Tukey, and one-way statistics.

RESULTS: Men who lived in rural environments had significantly lower pre-wash sperm concentrations (p=0.05) than men who lived in urban environments; however there was no difference in pre-wash semen volume (p=0.05) or women who lived in rural environments had lower numbers of embryos retrieved (p<0.05), lower numbers of healthy embryos (p=0.05) and lower numbers of healthy embryos (p=0.05) compared to women from urban environments. However, fertilization rates, embryo development, and pregnancy outcome did not differ (p=0.45). While not statistically significant due to not reaching power, pregnancy outcomes based on season appear to correlate with decreased success in months with intensive agricultural activity with success rates ranging from 8.3%-34.8% in March, April, September, and October while in months that are relatively the growing season and post-harvest, ART success rates range from 41.7%-69.2%.

CONCLUSIONS: Semen parameters vary between urban and rural populations, as demonstrated in previous research. Pre-fertilization parameters are different between women from urban and rural environments. However, embryo development and pregnancy outcomes are not different. Pregnancy outcomes from assisted reproductive technologies may be affected by season and corresponding environmental factors. There appears to be a change in success of ART procedures during various times of year that could be caused by agricultural activity, but further research is needed to determine if and how environmental factors affect gamete production and ART outcomes.

SUPPORT: None.

P-585 Wednesday, October 16, 2019 6:30 AM

THE USE OF PRESCRIPTION DRUGS AMONGST MEN AND WOMEN UNDERGOING ASSISTED REPRODUCTIVE TECHNOLOGY (ART) PROCEDURES. Edmond W. M. Rostand, Medical Student, a Suhaire Ibrahim, MMBS MRCOG, a Abigail Sharpe, MMBS, MRes. a Mariano Mascarones, MS (OG), MRCOG, DNB (OG), Post-doctoral fellow in reproductive medicine, b Harish M. Bhandari, MMBS MD MRCOG, b School of Medicine, University of Leeds, Leeds, United Kingdom; cLeeds Fertility, Seacroft Hospital, Leeds, United Kingdom.

OBJECTIVE: A pilot study aiming to determine the trends of prescription medication amongst men and women undergoing ART and the associated live birth rates.

DESIGN: This was a retrospective cohort study of heterosexual couples undergoing ART between October 2016 and November 2017 in a tertiary reproductive medicine unit. This pilot study was conducted as an undergraduate medical student project.

MATERIALS AND METHODS: A predefined proforma was used to extract data manually from each patient record for couples who had undergone ART in the defined time period. Information obtained included the drug history of both partners as well as smoking status and units of alcohol consumed each week. The outcome of the ART cycle was recorded. This data was then entered electronically into a spreadsheet and prevalence and
trends of prescription medication use were analysed. Since the sample size was insufficient for reliable statistical analysis, a descriptive report of the prescription drug utilisation patterns was created.

RESULTS: • MATERNAL MEDICATION
Out of 400, there were 90 (22.5%) women taking prescription medications and 44 (11%) on no medications. There were 266 (66.5%) women on folic acid and/or vitamin D alone. The live birth rate of the women on prescription medications was 32.2% (n = 29). The live birth rate of the 44 women on no medications was 29.5% (n = 13). The live birth rate of the women on folic acid and/or vitamin D was 33.5% (n = 89).

There were a total of 60 different medications at an average of 1.4 per patient.

The most common medications were asthma medications (n = 22), levothyroxine (n = 12), selective serotonin re-uptake inhibitors (SSRIs) (n = 10), ferrous sulphate (n = 8), and diabetic medications (n = 7).


• PATERNAL MEDICATION
Out of 400, 88 male partners were on prescription medication (22%). The live birth rate for those on medication was 30.7% (n = 27) compared to those not on medication 33.0% (n = 103).

• SMOKING
Female: out of 376, 19 smoked (5.1%) averaging 6.1 per day (Standard Deviation (SD) 4.47). Live birth rate in the smokers was 21.1% (n = 4) compared to non-smokers, 30.5% (n = 109).

Male: Out of 316 male patients, 44 smoked (13.9%) averaging 8.3 per day (SD 6.9). The live birth rate in smokers was 27.3% (n = 12) compared to 32.0% (n = 101).

• ALCOHOL
Female: out of 275, 178 drank alcohol (47.5%), averaging 5.8 units per week (SD 5.6). The live birth rate in drinkers was 28.1% (n = 50) compared to 36.5% (n = 72).

Male: out of 375, 240 drank alcohol (64%), averaging 9.1 units per week (SD 8.2). The live birth rate in drinkers was 33.8% (n = 81) compared to 30.4% (n = 41).

CONCLUSIONS: The study found that a large number of women are prescribed C, D or X drugs when attempting ART. The effect these drugs have on the success of ART is unclear. More information is required in order to expand these results and help counsel couples on prescription drug use, smoking and alcohol consumption.

SUPPORT: None.

P-586 Wednesday, October 16, 2019 6:30 AM
DIETARY CADMIUM INTAKE AND FECUNDABILITY IN A NORTH AMERICAN PRECONCEPTION COHORT STUDY. Tommyo Filippini, M.D., a, b Sydney K. Willis, M.P.H., a Amelia K. Wesselink, Ph.D., a Elizabeth E. Hatch, Ph.D., a Kenneth J. Rothman, Dr.P.H., a Marco Vinceti, M.D., Ph.D., a Lauren A. Wise, Sc.D. a, b Department of Biomedical, Metabolic and Neural Sciences, University of Modena and Reggio Emilia, Modena, Italy; bBoston University School of Public Health, Boston, MA; bBoston, MA.

OBJECTIVE: To evaluate the association between dietary cadmium intake (D-Cd) and fecundability. Diet is one of the main sources of cadmium, and D-Cd is often used as indicator of cadmium exposure, particularly in non-smoking populations. In a previous preconception cohort study of 501 couples,1

MATERIALS AND METHODS: Pregnancy Online Study (PRESTO) is a North American prospective preconception cohort of pregnancy planners. At baseline, female participants aged 21-45 years completed a web-based questionnaire on demographic, lifestyle, medical and reproductive factors. Ten days after enrollment, participants completed the National Cancer Institute Dietary History Questionnaire II, a validated food frequency questionnaire (FFQ) of average intake during the previous year. D-Cd (µg/day) was estimated after computing FFQ responses with US Food and Drug Administration food data on food cadmium content. Participants were then followed for up to 12 months or until reported pregnancy, whichever came first. The analysis included 4,768 women attempting to conceive for ≤ 6 cycles at study entry and not using fertility treatment. We used a proportional probabilities regression model to estimate fecundability ratios (FR) and 95% confidence intervals (CI), adjusted for age, body mass index (BMI), smoking history, parity, physical activity, last method of contraception, daily use of multivitamins, alcohol, caffeine, education, income, geographic region, and the 2010 healthy eating index score. We used the nutrient residual approach to adjust for energy intake.

RESULTS: Median D-Cd was 8.0 µg/day (interquartile range: 7.0-9.1 µg/day). The top 5 contributors to D-Cd were nuts and seeds; fried potatoes; dark green lettuce; cooked greens; and white potatoes. Compared with an average D-Cd of ≤ 6.8 µg/day, FRs for D-Cd quintiles of 6.8-7.6, 7.7-8.4, 8.5-9.5, and ≥ 9.6 µg/day were 1.03 (CI: 0.92-1.14), 1.07 (CI: 0.96-1.18), 1.07 (CI: 0.96-1.19), and 1.08 (0.97-1.20), respectively. Results were not appreciably different among never smokers with no current passive smoke exposure, for whom cadmium exposure from other sources (e.g., cigarettes) would be lower (respectively FRs: 1.02, 1.05, 1.06 and 1.02). Results did not differ materially by age (< 30 vs. ≥ 30 years), BMI (< 30 vs. ≥ 30 kg/m²), total fiber intake (< 25 vs. ≥ 25 g/day), geographic region of residence (West, Midwest, Northeast, South, Canada), or attempt time at study entry (< 3 vs. ≥ 3 cycles).

CONCLUSIONS: Dietary intake of cadmium was not appreciably associated with fecundability, though exposure misclassification and confounding could explain the null results.

SUPPORT: None.


P-587 Wednesday, October 16, 2019 6:30 AM
ACCUACY OF SELF-REPORTED MENSTRUAL CYCLE CHARACTERISTICS AND INFERTILITY IN A COHORT HIGHLY EXPOSED TO ENDOCRINE-DISRUPTING COMPOUNDS (EDCs). Victoria S. Jiang, MD,a Sarah W. Curtis, BS,a Sabrina A. Gerkowitz, MD,a Jessica B. Spencer, MD, MSc,b Mettreca L. Terrell, MSPH,a Michael F. Neblett, II, MD,a Michele Marcus, PhD,a Alicia K. Smith, PhD,a Emory University School of Medicine, Department of Gynecology and Obstetrics, Atlanta, GA; bLaney Graduate School, Genetics and Molecular Biology Program, Atlanta, GA; cRollins School of Public Health, Department of Epidemiology, Atlanta, GA.

OBJECTIVE: To determine whether reproductive health outcomes are associated with changes in menstrual function among women within the Michigan Polybrominated Biphenyl (PBB) Registry.

MATERIALS AND METHODS: Cross-sectional survey of women in the Michigan PBB Registry. Women were identified as PBB exposed if they were born between January 1, 1964 and June 30, 1967, and lived in the Michigan counties of Bay, Saginaw, Midland, or Genesee, or were adopted from those counties. Women were classified as exposed if they resided in the 'hotspots' of Bay County or the 'marginal hotspots' in the counties of Saginaw, Midland, or Genesee. Exposed women were interviewed and completed a reproductive health survey. Women were classified as controls if they were born in January 1, 1964 and June 30, 1967, and lived in the same counties, but were not born in the 'hotspots' of Bay County or the 'marginal hotspots' in the counties of Saginaw, Midland, or Genesee. Controls were matched by year of birth and county of residence with exposed women. A total of 176 women completed a reproductive health survey, obtained daily morning urine samples throughout 4 menstrual cycles, and completed 6 months of daily menstrual cycle diaries. The morning urine samples were analyzed for Estrone-3-glucuronide (E13G), Pregnanediol-3-glucuronide (PD3G), mid-cycle creatinine, and day of luteal transition (DLT). We used a nested mixed linear model to quantify the accuracy of menstrual cycle data and to test for association between endometriosis, infertility, and urinary hormone metabolites.

RESULTS: Women’s self-reported cycle and bleed length correlated accurately with their actual cycle length (p = 0.002) and bleed length (p = 2.31E-13) from urine metabolite data. Women with self-reported endometriosis were noted to have higher preovulatory E13G (p = 0.001), mid-luteal E13G (p = 0.0006), and overall luteal phase E13G (p = 0.033) levels. Women with self-reported infertility were noted to have higher mid-luteal E13G (p = 0.045) and overall luteal phase E13G (p = 0.008) levels.

CONCLUSIONS: Women with self-reported diagnoses of endometriosis and infertility showed statistically significant changes in their menstrual function urinary metabolites. Additionally, this study found that the self-
reported cycle characteristics were positively associated with actual cycle characteristics. Further analyses are required to determine the clinical implications of these menstrual function metabolite changes within this population of women highly exposed to endocrine disrupting compounds.

P-588 Wednesday, October 16, 2019 6:30 AM
IMPACT OF NANOPARTICLES ON MOTILITY OF HUMAN SPERMATOZOA. Hyoeun Kang, MS,a Hyojeong Kwon, MS,b Boyoung Jeon, Bs EunJi Lee, MS,b TaiEun Shin, MS,a Jung-Jae Ko, Ph.D.,b Dae Keun Kim, M.D., Ph.D.,c Wojciech Chrzanowski, Ph.D.,d Jae Ho Lee, PhD,e CHA Fertility Center in Seoul, Seoul, Korea, Republic of (South); Department of Biomedical Science, CHA University, Seoul, Korea, Republic of (South); CHA Fertility Center Seoul Station, Urology, Seoul, Korea, Republic of (South); Sydney Nano Institute, Sydney Pharmacy School, The University of Sydney, Sydney, NSW, Australia; CHA University Biomedical Science, Seoul, Korea, Republic of (South).

OBJECTIVE: Nanomaterials, including a large array of nanoparticles are integral components of daily-used products including food, sunscreens, cosmetics and pharmaceutics. Human and environmental exposure to nanomaterials is commonly occurring, and as the use of nano-enabled products become more widespread, so too will concerns around their safety and impact on human and environmental health. Nanoparticles are reported to be amongst major factors that influence development of various medical conditions including reproductive disorders. But until now, the impact of nanoparticles on sperm motility has not been established. Here we investigate for the first time how nanoparticles affect human sperm motility.

DESIGN: Experimental study with human normal sperm.

MATERIALS AND METHODS: We treated human normal sperm with titanium dioxide (E171) and nanodiamond. Then we performed human sperm motility assay after incubation with titanium dioxide and nanodiamond particles. Human spermatozoa were incubated with 1 ng, 10 ng, 100 ng and 1000ng of each of the nanoparticle class. Sperm motility profiling was done using computer-aided sperm analysis (CASA) system every 30 min until overnight. We analysis whether nanoparticles were attracted to regions of spermatozoa by electrical microscope. Furthermore, we imaged the surface with electrical microscopy.

RESULTS: Both nanoparticles have shown significantly decreased in sperm motility. Titanium dioxide has been shown 20–30% decrease motility compared with control group. Nanodiamond also reduced 10–20% motility of sperm. In the CASA study, both nanoparticles showed significantly reduction in straight movement pattern compare with control sperm. However, both nanoparticles did not show any significant cytotoxicity to the human sperm up to 1000 ng/ml concentration.

CONCLUSIONS: In this study, we showed that nanograin concentration of nanoparticles decreases motility of human sperm. There is no literature evidence regarding the exposure of human testis and sperm to nanoparticles that become more widespread, so too will concerns around their safety and impact on human and environmental health. Nanoparticles are reported to be amongst major factors that influence development of various medical conditions including reproductive disorders. But until now, the impact of nanoparticles on sperm motility has not been established. Here we investigate for the first time how nanoparticles affect human sperm motility.

P-590 Wednesday, October 16, 2019 6:30 AM
BISPHENOL A INDUCES INSULIN RESISTANCE IN SKELETAL MUSCLE BY DOWN-REGULATING THE EXPRESSION OF IRS1 THROUGH ESTROGEN RECEPTOR, Zhanghong Ke, Doctor,a Binzheng Zheng bachelor,b Fujian Provincial Maternity and Children’s Hospital, Affiliated Hospital of Fujian Medical University, Fuzhou, China; Fujian Provincial Maternity and Children’s Hospital, Fuzhou, China.

OBJECTIVE: To investigate the effect of human relevant doses of bisphenol A (BPA), an endocrine disruptor, on insulin resistance and the underlying mechanisms.

MATERIALS AND METHODS: Mice were administered with water containing BPA of human relevant doses. C2C12 myocytes were treated with BPA and selective estrogen/androgen receptor down-regulator. Bioinformatic analysis was applied to search for estrogen receptor response element (ERE) in Irs1.

RESULTS: Mice were administered with water containing BPA of human relevant doses. C2C12 myocytes were treated with BPA and selective estrogen/androgen receptor down-regulator. Bioinformatic analysis was applied to search for estrogen receptor response element (ERE) in Irs1.

CONCLUSIONS: Our study showed lower semen parameters in infertile males and lower embryology and pregnancy outcomes in infertile females who were either current or former smokers, alcohol consumers, or drug users.
OBJECTIVE: To determine whether the menstrual pictogram super absorbent polymer containing version 3 (MP SAP-c v3) and uterine fibroid daily bleeding diary (UF-DBD) demonstrate reliability, validity, and sensitivity to change and can replace the Alkaline Hematin (AH) method for assessment of efficacy in UF clinical trials.

DESIGN: Post-hoc analysis of vilaprisan phase 2 (ASTEROID 1 and 2) clinical study data in terms of psychometric properties, missing data, and comparability of methods.

MATERIALS AND METHODS: ASTEROID 1 (N=623) study data collected by MP SAP-c v3, UF-DBD, and the AH method were used to assess psychometric properties of the MP SAP-c v3 and UF-DBD, and degree of comparability and extent of missing data with the AH method. Daily scores aggregated over 28 days (monthly) and during bleeding episodes at randomization (RND) and end of treatment (EoT) were analyzed. ASTEROID 2 (N=228) study data were used to confirm ASTEROID 1 findings as appropriate.

RESULTS: ASTEROID 1 data analysis showed that the response distributions of MP SAP-c v3 and UF-DBD appropriately reflected the natural cycle of menstrual bleeding and treatment-related changes. The full range of responses were used to assess bleeding severity. Based on bleeding severity defined by the AH method and overall patient global impression of severity, differences in MP SAP-c v3 and UF-DBD scores between low- and high-severity groups were large and significant (p<0.001). Strong Spearman’s rank correlations were observed between MP SAP-c v3 monthly sum scores and those of both AH (τ_s=0.72 and 0.97) and UF-DBD (τ_s=0.56 and 0.89) at RND and EoT, respectively. Moderate to strong correlations were also observed between UF-DBD and AH monthly sum scores at RND (τ_s=0.44) and EoT (τ_s=0.84). Test-retest reliability and sensitivity to changes were also demonstrated. Analyses of ASTEROID 2 data largely confirmed findings from ASTEROID 1.

In ASTEROID 1, details of more sanitary protection items were provided using the MP SAP-c v3 than with the AH method. Fewer days with missing data were observed with the MP SAP-c v3 and UF-DBD than with AH; over the course of the study the mean absolute (relative) number of days with missing values per patient was 16.1 (11.8%) for MP SAP-c v3, 15.5 (11.6%) for UF-DBD and 18.1 (15.9%) for AH.

Both instruments showed good agreement with the AH method in assessments of study eligibility (MP SAP-c v3) and treatment response (MP SAP-c v3 and UF-DBD). The positive predictive value (PPV) of MP SAP-c v3 to distinguish women with heavy menstrual bleeding at baseline vs. the AH method (reference standard) was 75.8%. The PPVs of MP SAP-c v3 and UF-DBD for reaching amenorrhea were 100.0% and 99.3%, respectively.

CONCLUSIONS: The MP SAP-c v3 and UF-DBD are valid, reliable, and sensitive measures of menstrual bleeding severity in the UF population. Use of both instruments is more convenient, less burdensome, and associated with greater compliance than the AH method. Coupled with positive results from cognitive interviews and Bland-Altman analyses, these results support the use of MP SAP-c v3 and UF-DBD in UF clinical studies instead of the AH method.

SUPPORT: This study was funded by Bayer AG. Medical writing support provided by Huntsworth Health was funded by Bayer.

P-593 Wednesday, October 16, 2019 6:30 AM

PHENOME-WIDE ASSOCIATION STUDY OF UTERINE FIBROIDS USING A LARGE MULTI-RACIAL CLINICAL POPULATION OF WOMEN

Digna R. Velez Edwards, M.S., Ph.D., Vanderbilt University Medical Center, Nashville, TN.

OBJECTIVE: Uterine fibroids affect up to 70% of women by menopause. Prior studies have identified several clinical factors associated with fibroid risk by evaluating candidate risk factors from observational epidemiology. We identified novel clinical characteristics of women associated with fibroids, gaining insight on causal mechanisms by broadly evaluating the clinical phenomenon.

DESIGN: A phenome-wide association study (PheWAS) tests disease diagnoses across a patient’s clinical record for association with a specific outcome. We conducted a PheWAS of uterine fibroids utilizing diagnoses from electronic health records (EHRs) of patients at Vanderbilt University Medical Center (VUMC) in Nashville, TN.

MATERIALS AND METHODS: Fibroid cases and controls were identified using a previously validated phenotyping algorithm. We conducted PheWAS analyses with logistic regression models adjusted for body mass index.

FERTILITY & STERILITY®
PATIENT-REPORTED OUTCOMES OF A PHASE 1 CLINICAL TRIAL OF INJECTABLE COLLAGENASE CLOSTRIDIUM HISTOLYTICUM (EN3835) FOR TREATMENT OF UTERINE FIBROIDS. Bhuchitra Singh, M.D., MPH, MS,* Irene Trueheart, RN, BSN, MA,* Holly Sims, RN, BSN,* Jean-Marie Soma, MS,* Rosina Dixon, M.D.,* Phyllis Leppert, M.D., PhD,* Gayane Yenokyan, PhD,* James Segars, MD.* Johns Hopkins School of Medicine, Baltimore, MD; †BioSpecifics Technologies Corporation, Lynbrook, NY; ‡Duke Medicine, Durham, NC; §Biosciences Center, Johns Hopkins School of Public Health, Baltimore, MD; *Johns Hopkins University, School of Medicine, Baltimore, MD.

OBJECTIVE: Uterine fibroids may cause a significant reduction in quality of life for affected women. Since fibroids contain an excessive extracellular matrix, we injected fibroids with purified collagenase Clostridium histolyticum (EN3835) under transvaginal ultrasound guidance in women scheduled for fibroid removal. Here we report the impact of the treatment on the fibroid-related symptoms following injection with study drug and before fibroid removal.

DESIGN: Phase 1 clinical trial.

MATERIALS AND METHODS: Changes in subject’s quality of life and fibroid-related symptoms were assessed at baseline and following injection of study drug. Standardized-validated questionnaires were used to assess the patient-reported outcomes of quality of life and fibroid-associated symptoms. The McGill Pain questionnaire, the Uterine Fibroid Symptom Health-Related Quality of Life (UFS-QoL), and the Visual Analogue Scale (VAS) for pain were utilized. Study subjects were divided into 2 groups. Group 1 had injection followed by surgery at 2-3 days, and subjects in Group 2 had injection followed by surgical removal of fibroids 60-90 days later. Therefore, Group 1 subjects (n = 3) completed the post intervention questionnaire at 24-48 hours post-study drug injection. Group 2 subjects (n = 9) completed the post intervention questionnaires at 4-8 days and 60-90 days post study drug injection. To compare the changes in patient-reported outcomes, generalized linear mixed effects models with random intercepts for person and paired t-tests were used; p < 0.05 was considered significant.

RESULTS: No clinically significant adverse events related to the study drug were reported. Of note, all subjects reported a decrease in fibroid-related pain on the McGill Pain Questionnaire following study drug injection. Specifically, for Group 1 there was a trend (p = 0.195) and for Group 2, 4-8 days post injection (p = 0.056) and 60-90 days post injection (p = 0.079). Similar trends were observed on the Visual Analogue Scale for pain. No Group 1 subject reported an increase in pain post study drug injection. In Group 2, no subject reported an increase in pain 4-8 days post study drug injection (p = 0.854) and only 3 out of 9 reported a mild increase in pain 60-90 days post study injection (p = 0.6982). UFS-QOL Part-1: the symptom severity score for Group 1 showed a mild increase in symptoms in 2 out of 3 subjects, for Group 2, the general trend was a decrease in symptom severity both at 4-8 days and 60-90 days post injection. UFS QOL Part 2: all 3 subjects in Group 1 reported an improvement in health-related quality of life, for Group 2, 7 out of 9 subjects reported an improvement in health-related quality of life 4-8 days post injection, and 5 of these subjects sustained the increasing trend at 60-90 days post study drug injection.

CONCLUSIONS: Injection of Collagenase Clostridium histolyticum into fibroids was well tolerated by all study participants. Interestingly, fibroid-related pain was reduced and there was a trend of decreasing fibroid-related symptoms and improving quality of life. (ClinicalTrials.gov number: NCT02889484).

SUPPORT: BioSpecifics Technologies Corporation.

P-595 Wednesday, October 16, 2019 6:30 AM

MEASURING PATIENT-REPORTED OUTCOMES IN WOMEN WITH HEAVY MENSTRUAL BLEEDING ASSOCIATED WITH UTERINE FIBROIDS: THE BLEEDING AND PELVIC DISCOMFORT SCALE. Juliet Li, PhD,* Jennifer B. Kang, MS, MPH, Elke Hunsche, PhD,* Stacie Hudgens, MA, *Myovant Sciences, Inc., Brisbane, CA; †Myovant Sciences GmBH, Basel, Switzerland; *Clinical Outcomes Solutions, Tucson, AZ.

OBJECTIVE: The Uterine Fibroid Symptom and Quality of Life (UFS-QoL) instrument consists of 6 scales and has been used frequently in clinical trials; the symptom severity scale has 8 items covering different types of symptoms and is multi-factorial. The objectives were to a) determine from the UFS-QoL symptom severity scale a factor consisting of items relevant to most women with heavy menstrual bleeding (HMB) associated with uterine fibroids (UF), b) assess the psychometric properties of the new subscale (factor), and c) determine a threshold based on which responders to treatment can be identified.

DESIGN: Analyses were based on pooled, blinded data from the first one-third of patients with HMB enrolled in 2 Phase 3 studies of relugolix in UF (N = 254), who completed the Patient Global Assessment (PGA) of symptom severity and the UFS-QoL at Baseline and at Week 24.

MATERIALS AND METHODS: To assess the factor structure of the UFS-QoL symptom severity scale, factor analyses were performed. The subscale (factor) consisting of symptoms experienced by the majority of postmenopausal patients was chosen for further analysis; psychometric properties were evaluated, including item performance (floor and ceiling effect, item-total correlation, item discrimination index), internal consistency reliability, known-groups validity, and ability to detect change. The meaningful change threshold, which is the smallest improvement on the new subscale that is considered meaningful by patients, was derived by applying anchor-based methods with change in PGA of symptom severity as an anchor. Within and between anchor group changes from Baseline to Week 24 on the subscale were evaluated using the pair t-test analysis of variance. Cumulative distribution function and probability density function curves of change from Baseline by anchor categories were used as supportive information in determining the threshold.

RESULTS: Factor analyses revealed that the UFS-QoL symptom severity scale consisted of 3 factors with 3, 2, and 2 items, respectively. Factor 1 had 3 items representing symptoms of HMB in UF that are associated with a high burden experienced by most patients: heavy bleeding during period, passing blood clots during period, and feeling tightness or pressure in pelvis. Hence, this factor, named the Bleeding and Pelvic Discomfort (BPD) scale, was further assessed psychometrically. The BPD scale had no ceiling effects, and all response options were used by patients. The items of the BPD scale were found to work cohesively to inform the total score and to adequately distinguish between patients of different severities. Descriptive statistics supported the construct validity and responsiveness of the BPD scale. A 20-point change on the BPD scale score (range from 0-100) was recommended as the minimum meaningful change threshold for defining a responder. This threshold estimation was based on the ‘1 category improvement’ PGA group as the anchor.

CONCLUSIONS: The BPD scale is a short, patient-reported outcome measure relevant to patients with HMB due to UF that can be used to assess their symptom burden.

SUPPORT: Myovant Sciences, Inc. provided financial support for the MVT-601-3001 and MVT-601-3002 clinical trials that data are from in this abstract.

P-594 Wednesday, October 16, 2019 6:30 AM

BLEEDING AND PELVIC DISCOMFORT ASSOCIATED WITH UTERINE FIBROIDS: THE MEASURING PATIENT-REPORTED OUTCOMES IN WOMEN WITH HEAVY MENSTRUAL BLEEDING. Bhuchitra Singh, M.D., MPH, MS,* Irene Trueheart, RN, BSN, MA,* Holly Sims, RN, BSN,* Jean-Marie Soma, MS,* Rosina Dixon, M.D.,* Phyllis Leppert, M.D., PhD,* Gayane Yenokyan, PhD,* James Segars, MD.* Johns Hopkins School of Medicine, Baltimore, MD; †BioSpecifics Technologies Corporation, Lynbrook, NY; ‡Duke Medicine, Durham, NC; §Biosciences Center, Johns Hopkins School of Public Health, Baltimore, MD; *Johns Hopkins University, School of Medicine, Baltimore, MD.

OBJECTIVE: Uterine fibroids may cause a significant reduction in quality of life for affected women. Since fibroids contain an excessive extracellular matrix, we injected fibroids with purified collagenase Clostridium histolyticum (EN3835) under transvaginal ultrasound guidance in women scheduled for fibroid removal. Here we report the impact of the treatment on the fibroid-related symptoms following injection with study drug and before fibroid removal.

DESIGN: Phase 1 clinical trial.

MATERIALS AND METHODS: Changes in subject’s quality of life and fibroid-related symptoms were assessed at baseline and following injection of study drug. Standardized-validated questionnaires were used to assess the patient-reported outcomes of quality of life and fibroid-associated symptoms. The McGill Pain questionnaire, the Uterine Fibroid Symptom Health-Related Quality of Life (UFS QoL), and the Visual Analogue Scale (VAS) for pain were utilized. Study subjects were divided into 2 groups. Group 1 had injection followed by surgery at 2-3 days, and subjects in Group 2 had injection followed by surgical removal of fibroids 60-90 days later. Therefore, Group 1 subjects (n = 3) completed the post intervention questionnaire at 24-48 hours post-study drug injection. Group 2 subjects (n = 9) completed the post intervention questionnaires at 4-8 days and 60-90 days post study drug injection. To compare the changes in patient-reported outcomes, generalized linear mixed effects models with random intercepts for person and paired t-tests were used; p < 0.05 was considered significant.

RESULTS: No clinically significant adverse events related to the study drug were reported. Of note, all subjects reported a decrease in fibroid-related pain on the McGill Pain Questionnaire following study drug injection. Specifically, for Group 1 there was a trend (p = 0.195) and for Group 2, 4-8 days post injection (p = 0.056) and 60-90 days post injection (p = 0.079). Similar trends were observed on the Visual Analogue Scale for pain. No Group 1 subject reported an increase in pain post study drug injection. In Group 2, no subject reported an increase in pain 4-8 days post study drug injection (p = 0.854) and only 3 out of 9 reported a mild increase in pain 60-90 days post study injection (p = 0.6982). UFS-QOL Part-1: the symptom severity score for Group 1 showed a mild increase in symptoms in 2 out of 3 subjects, for Group 2, the general trend was a decrease in symptom severity both at 4-8 days and 60-90 days post injection. UFS QOL Part 2: all 3 subjects in Group 1 reported an improvement in health-related quality of life 4-8 days post injection, and 5 of these subjects sustained the increasing trend at 60-90 days post study drug injection.

CONCLUSIONS: Injection of Collagenase Clostridium histolyticum into fibroids was well tolerated by all study participants. Interestingly, fibroid-related pain was reduced and there was a trend of decreasing fibroid-related symptoms and improving quality of life. (ClinicalTrials.gov number: NCT02889484).

SUPPORT: BioSpecifics Technologies Corporation.
OBJECTIVE: To study the effect of ulipristal acetate (UPA) treatment in infertile patients with single type 2-3 FIGO myomas undergoing IVF.

DESIGN: Prospective study.

MATERIALS AND METHODS: This study included infertile women of reproductive age who had single type 2 or 3 FIGO myoma and had to undergo IVF due to in vitro fertilization and oocyte retrieval were performed before treating the uterine myomas. All patients underwent transvaginal ultrasonography and hysteroscopy before and after 3-month treatment with UPA (5 mg/day). The largest diameter and volume of uterine myomas (estimated by virtual organ computer-aided analysis, VOCAL) were recorded before and after UPA treatment. Hysteroscopy was performed after UPA treatment to assess if the myoma distorted the uterine cavity. Patients with myomas that were not distorting the uterine cavity underwent embryo transfer; the other patients underwent hysteroscopic or laparoscopic myomectomy. Pregnancy rate was defined as fetal heart beat observed by transvaginal ultrasonography.

RESULTS: 46 women were included in the study. The mean age (±SD) of the study population was 35.6 (±3.8) years. 25 patients had type 2 FIGO myomas and 21 had type 3 FIGO myomas. The mean (±3.8) diameter of the myomas before treatment was completed by 3-month UPA treatment was significantly higher in patients with type 3 myomas (n = 9; 42.9%; 95% CI, 21.8%-66.0%) than in those with type 2 myomas (n = 3; 12%; 95% CI, 2.5%-31.2%); p = 0.018. These patients underwent frozen-thawed embryo transfer. All patients with myomas distorting the uterine cavity after UPA treatment underwent myomectomy. There was no significant difference in the pregnancy rate per embryo transfer in patients who underwent myomectomy (12/46; 33.3%; 95% CI, 9.9%-65.1%) and those who did not undergo surgery (4/12; 35.3%; 95% CI, 19.7%-53.5%; p = 0.902). The patients underwent a median of two embryo transfer (range, 1-4). There was no significant difference in the pregnancy rate per patient in women who underwent myomectomy (18/34; 52.9%; 95% CI, 35.1%-70.2%) and in those that did not undergo surgery (7/12; 58.3%; 95% CI, 27.7%-84.8%; p = 0.104).

CONCLUSIONS: In patients with FIGO type 3 myomas, 3-month treatment with UPA may allow to avoid myomectomy and to immediately perform embryo transfer.

THE IMPACT OF ISOLATED NON-CAVITY DISTORTING INTRAMURAL FIBROIDS ON PREGNANCY OUTCOMES IN IN VITRO FERTILIZATION CYCLES: A SYSTEMATIC REVIEW AND META-ANALYSIS. Kiran Rikraj, MD,* Justin Tan, MD, MPH,* Omar Taskin, MD,* Aline Laire, PhD,* Paul Yong, M.D.,* Mohamed Ali Bedaiwi, M.D., Ph.D.* 1University of British Columbia, Vancouver, BC, Canada; 2Women’s Health Research Institute, Vancouver, BC, Canada; 3UBC, Vancouver, BC, Canada; 4University of British Columbia, Department of Obstetrics and Gynaecology, Vancouver, BC, Canada.

OBJECTIVE: To investigate the impact of non-cavity distorting intramural fibroids on pregnancy outcomes in women undergoing IVF.

DESIGN: An exhaustive literature search using EMBASE, MEDLINE, Google Scholar, Cochrane Library, and PUBMED was performed from inception to May 2018. Relevant search terms included: “intramural fibroid,” “intramural leiomyoma,” “intramural myoma” and “IVF” or “in vitro fertilization.” We also searched Biomed Central, ClinicalTrials.gov, WHO International Clinical Trials Registry Platform (ICTRP) and Thomson CenterWatch for unpublished works and ongoing clinical trials.

MATERIALS AND METHODS: We included studies with women undergoing IVF treatment who had at least one non-cavity distorting intramural fibroid. The studies had to report one of: Live birth rate (primary outcome), implantation rate, clinical pregnancy rate and miscarriage rate (secondary outcomes). We excluded studies where women also had submucosal fibroids or had undergone myomectomy. Two authors independently selected studies and extracted data. Methodological quality was assessed using PRISMA guidelines.

RESULTS: Among all 15 observational studies that were included (10 retrospective and 5 prospective), patients with non-cavity distorting intramural fibroids had 32% lower odds of clinical pregnancy (estimated average OR = 0.68, 95% CI = 0.56-0.83, p = 0.0002) and 44% lower odds of live birth than patients without fibroids undergoing IVF (OR = 0.56, 95% CI = 0.46-0.69, p < 0.0001). While there was a trend toward lower implantation rate (estimated average OR = 0.76, 95% CI = 0.58 to 1.12, p = 0.06) and increased miscarriage rate (estimated average OR = 1.38, 95% CI = 0.98 to 1.95, p = 0.07) in patients with these fibroids, the results did not reach statistical significance.

Among studies that explicitly excluded patients with concurrent subserosal fibroids, patients with isolated intramural fibroids showed consistently lower odds of clinical pregnancy and live birth (OR = 0.70, 95% CI = 0.50-0.97 and OR = 0.62, 95% CI = 0.45-0.84, respectively). Similarly, this trend was consistent among studies that reported pregnancy rate per IVF cycle (0.70, 95% CI = 0.53-0.92) as well as those that reported cumulative pregnancy rates (0.72, 95% CI = 0.55-0.94).

CONCLUSIONS: This meta-analysis demonstrates that non-cavity distorting intramural fibroids are associated with decreased live birth rates and clinical pregnancy rates in women undergoing IVF. However, RCTs and prospective studies that standardize their patient selection criteria and IVF methods are needed in order to better address this question.

RISK FACTORS FOR COEXISTENT LEIOMYOMA AND ADENOMYOSIS COMPARED TO COEXISTENT LEIOMYOMA AND ENDOMETRIOSIS IN PATIENTS WITH SYMPTOMATIC LEIOMYOMA REQUIRING MYOMECTOMY. Mamta Mamik, MD,* Faraj Touchan, MD,* Nilofar Kazi, BS, Vanessa Sarfoh, MD MPH,* Leah Haworth, BS, Louise Van Der Does, PhD,* Natalya Danilyants, MD,* Paul Mackoul, MD,* Center for Modern Surgery, Montclair, NJ; 3Center for Innovative GYN Care, Rockville, MD; 4Center for Innovative GYN Care, Rockville, MD.

OBJECTIVE: To investigate the risk factors for coexistent leiomyoma with endometriosis and leiomyoma with adenomyosis in a population of women who elect for myomectomy due to symptomatic leiomyoma.

DESIGN: Retrospective study.

MATERIALS AND METHODS: This was a single-center case control study to compare patients with leiomyoma only, to those that had either coexistent leiomyoma and endometriosis or leiomyoma and adenomyosis. Multinomial logistic regression models were used to compute relative-risk ratios (RRR) for the association between patients with endometriosis or adenomyosis and coexistence of leiomyoma and endometriosis or leiomyoma and adenomyosis in a population of women who undergo IVF. The analysis was first performed for each independent variable alone and subsequently, a best-subset selection method was used to construct a parsimonious model by selecting the model with lowest Akaike information criteria (AIC). The analysis was then performed in order to better address this question.

TABLE 1. Relative-risk ratios (RRR) from most parsimonious* multinomial logistic regression model

<table>
<thead>
<tr>
<th>Fibroids only (base outcome)</th>
<th>RRR</th>
<th>95% C.I.</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.960</td>
<td>0.912, 1.010</td>
<td>0.107</td>
</tr>
<tr>
<td>Parity</td>
<td>0.308</td>
<td>0.109, 0.875</td>
<td>0.027</td>
</tr>
<tr>
<td>Uterine length</td>
<td>0.931</td>
<td>0.864, 1.002</td>
<td>0.058</td>
</tr>
<tr>
<td>Constant</td>
<td>1.368</td>
<td>2.046, 1.163</td>
<td>0.747</td>
</tr>
</tbody>
</table>

Note: Constant estimates baseline relative risk for each outcome.

* Based on model with lowest Akaicke information criteria (AIC)
2013 and 2018 at a free-standing ambulatory surgical setting. The LE group was significantly younger (35.2 ±5 years) (RR 0.95 95% C.I. 0.911-0.986) compared to the LA group (39.4 ±5.7 years) (RR 1.08 95% C. I. 1.035-1.129) (p<0.001). LE group (RR 0.23 95% C.I. 0.80 – 0.661) (p<0.006) had higher nulliparity rate compared to LA group (RR 1.6 95% C.I. 1.193-2.148) (p <0.002). The uterine length was significantly shorter in the LA group compared to the LE group. (L – 12.3 +3.7 cm, LE 11.7 +3.7, LA 10.4 +3.1 cm (p<0.001)).

CONCLUSIONS: Age is an important predictor of developing adenomyosis but not endometriosis. The risk of developing adenomyosis in patients with leiomyoma increases by almost 9% for every year of age compared to those but not endometriosis. The risk of developing adenomyosis in patients undergoing fertility treatment. We sought to determine if the presence of non-cavity distorting intramural myomas has an impact on pregnancy outcomes in an ideal study group of patients: patients undergoing either frozen embryo transfer cycles & donor egg recipient (DER) cycles were included in this prospective study which began enrollment in September 2018. Patients were stratified based on whether they had myomas or not.

OBJECTIVE: A recent ASRM guideline highlights that there is insufficient evidence to determine whether non-cavity distorting intramural myomas is associated with a decreased likelihood of achieving pregnancy in patients undergoing fertility treatment. We sought to determine if the presence of non-cavity distorting intramural myomas has an impact on pregnancy outcomes in an ideal study group of patients: patients undergoing either frozen-thawed embryo transfer (FET) of normal euploid embryos or elective single embryo transfer of donor oocytes.

DESIGN: Prospective cohort study, interval analysis.

MATERIALS AND METHODS: Patients who underwent cycles with either autologous FET after preimplantation genetic testing for aneuploidy (PGT-A) or donor egg recipient (DER) cycles were included in this prospective study which began enrollment in September 2018. Patients were stratified based on whether myomas were detected (group A) or no myomas were detected (group B) on pelvic ultrasonography at the time of study enrollment during the patient’s treatment cycle. The FIGO classification system was used and the distance from the endometrial lining to the closest myoma was recorded. The primary outcome was positive pregnancy rate. The secondary outcomes were ongoing pregnancy rate and miscarriage rate. Statistical analysis included Mann-Whitney U test and chi-square test. P<0.05 was deemed statistically significant.

RESULTS: Currently, 53 patients enrolled in the study have completed their ART cycles. 15/53 (28.3%) had a non-cavity distorting intramural myoma. The patients who had myomas were older and had a higher BMI. The peak endometrial thickness was similar between the two groups. Of the patients who had myomas 11/15 conceived, and of the patients without myomas 30/38 conceived. There was no difference in the primary outcome of positive pregnancy rate. There was also no difference for the secondary outcomes of ongoing pregnancy rates and miscarriage rates between the two groups.

CONCLUSIONS: An interval analysis of our ongoing prospective study suggests that non-cavity distorting myomas do not affect positive pregnancy rates, ongoing pregnancy rates, or miscarriage rates in a good-prognosis population with patients undergoing either autologous FET with PGT-A or donor egg recipient cycles. However, this study is ongoing and will continue to evaluate this further.


SUPPORT: None.

FIBROIDS - BASIC

P-600 Wednesday, October 16, 2019 6:30 AM

EFFECT OF SIMVASTATIN ON INTEGRIN-β1 AND ITS DOWNSTREAM MEDIATORS IN HUMAN LEIOMYOMA CELLS. Sadia Afrin, PhD, Md, Soriful Islam, PhD, Szu-Chi Su, MS, Mostafa A. Borahay, MD, PhD. Johns Hopkins University, School of Medicine, Baltimore, MD.

OBJECTIVE: Integrins, extracellular matrix (ECM) receptors, are key mediators of out-in and in-out signaling between a cell and its ECM environment and neighboring cells. Leiomyoma cells were shown to overexpress integrin-β1, which on activation, induces FAK auto-phosphorylation of and activates its downstream signaling including ERK, p38 MAPK, PI3K and cyclin D1. In addition, phosphorylated FAK leads to activation of AKAP13 and RhoA which further recruits ROCK and MLCK activation. Activation of this cascade promotes leiomyoma development by increasing proliferation, cell spreading and ECM deposition. Therefore, integrin-β1 signaling may serve as a therapeutic target for uterine leiomyoma. Current evidence from in vitro, in vivo, and epidemiologic studies suggests that simvastatin possesses anti-tumor effects on uterine leiomyoma. Our objectives in this study are to examine the effect of simvastatin on integrin-β1 expression and its downstream mediators in human leiomyoma cells.

DESIGN: In vitro laboratory study using human leiomyoma cells.

MATERIALS AND METHODS: Human leiomyoma (huLM) cells were treated with simvastatin (0.001 to 10 μM) for 24 to 72 hours. Anti-proliferative effect of simvastatin was determined by MTT assay. The effect of simvastatin on the expression of integrin-β1 and its downstream mediators p-FAK, AKAP13 and ROCK1 and MLCK were examined using western blotting after 48-hour treatment. Furthermore, the expression of cyclin D1, a downstream marker of FAK signaling, was evaluated. Student’s t-test was used to determine statistically significant differences (P<0.05).

RESULTS: Simvastatin exhibited significant anti-proliferative effects on leiomyoma cells in a dose- and time-dependent manner. At 48 hours, 85% and 51% proliferation inhibition were noted at 0.01 to 1 μM simvastatin, respectively. Simvastatin treatment at 1 μM for 48 hours was associated with 48% decrease in the expression of integrin-β1. The ratio of phosphorylated to total FAK (p-FAK/total FAK ratio) was reduced by 28% at 1 μM of simvastatin and there was a dose-dependent pattern. At 1 and 10 μM of simvastatin, the expression of AKAP13 was suppressed by 56% to 34% whereas the expression of ROCK1 and MLCK were decreased by 65% to 43% and 63% to 57%, respectively. Additionally, the expression of cyclin D1 demonstrated a 46% to 36% reduction at 1 and 10 μM simvastatin.

CONCLUSIONS: These encouraging results indicate that the simvastatin might have a significant therapeutic impact on uterine leiomyoma growth through modulating the ECM-integrin-β1 interaction in leiomyoma. Down-regulated p-FAK/FAK, AKAP13, ROCK1 and MLCK signaling molecules after simvastatin treatment may correct the mechanical signaling, already disordered in leiomyoma. Suppressing integrin-β1 and its downstream mediators after simvastatin treatment may serve as a promising approach for uterine leiomyoma treatment.

SUPPORT: Supported by NIH grant 1R01HD094380-01.

<table>
<thead>
<tr>
<th>Group A: Non-cavity distorting myoma (n=15)</th>
<th>Group B: No non-cavity distorting myoma (n=38)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>41.7 ± 3.2</td>
<td>37.3 ± 5.1</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.5 ± 7.9</td>
<td>22.2 ± 3.3</td>
</tr>
<tr>
<td>Gravidaity</td>
<td>1.5 ± 1.8</td>
<td>1.5 ± 1.3</td>
</tr>
<tr>
<td>Parity</td>
<td>0.33 ± 0.5</td>
<td>0.53 ± 0.8</td>
</tr>
<tr>
<td>Peak Endometrial Stripe (mm)</td>
<td>10.6 ± 2.4</td>
<td>9.4 ± 2.1</td>
</tr>
<tr>
<td>Positive Pregnancy Rate</td>
<td>0.73</td>
<td>0.79</td>
</tr>
<tr>
<td>Ongoing Pregnancy Rate</td>
<td>0.67</td>
<td>0.63</td>
</tr>
<tr>
<td>Miscarriage Rate</td>
<td>0</td>
<td>0.16</td>
</tr>
</tbody>
</table>
SIMVASTATIN INHIBITS RhoA ACTIVATION, COLLAGEN EXPRESSION AND GEL CONTRACTION IN HUMAN LEIOMYOMA CELLS. Sadia Afrin, PhD, Mostafa A. Borahay, MD, PhD Johns Hopkins University, School of Medicine, Baltimore, MD.

OBJECTIVE: There is a strong evidence that altered vascular homeostasis and signaling play a key role in uterine leiomyoma development and growth. Mechanical stress from disordered extracellular matrix (ECM) can initiate the activation of RhoA and its downstream signaling pathways. In turn, activated RhoA contributes to the production of collagen type I, alters the viscoelastic properties of tissue and contribute to increased ECM stiffness, a key feature of leiomyomas. Therefore, mechanical signaling pathway seems to be a conceivable pharmacologic target in leiomyoma. The objective of this study is to examine the effect of simvastatin on: i) RhoA activation; ii) collagen type I expression; iii) gel contraction; and iv) cell migration in human leiomyoma cells.

DESIGN: In vitro laboratory study using immortalized human leiomyoma cells.

MATERIALS AND METHODS: Human leiomyoma (huLM) cells were treated with simvastatin (0.001 to 10 μM) for 48 hours. RhoA activation was measured using the Rhotekin RBD Agarose beads to selectively isolate and pull-down the active (GTP-bound) form of RhoA, to be quantified by western blot. Simvastatin effect on collagen gel contraction was measured by culturing the leiomyoma cells in three-dimensional (3D) condition. Photographs were taken at the end of treatment. Simvastatin effect on cells migration were observed by wound closure assay and the wound areas were analyzed by Image J software. Western blot analysis was performed for examining the effect of simvastatin on collagen type I expression. Student’s t-test was used to determine statistically significant differences (P<0.05).

RESULTS: Simvastatin significantly decreased RhoA activation (active/total RhoA ratio) at 1 μM by 33% compared to control. Furthermore, simvastatin suppressed collagen type I expression by 58% at 10 μM. In addition, simvastatin inhibited 3D collagen gel contraction at as low concentrations as 0.001 μM with the higher concentrations of simvastatin (1 and 10 μM) inducing maximal gel relaxations, similar to collagen gel without cells. Finally, simvastatin decreases the migration ability of leiomyoma cells up to 43% compared to control cells.

CONCLUSIONS: Simvastatin has significant attenuating effects on RhoA activation, a key mediator of leiomyoma mechanical signaling that contributes to its development and growth. Also, simvastatin inhibits the expression of type I collagen. Additionally, the remarkable gel contraction noted in leiomyoma 3D culture was inhibited by simvastatin, which also reduced the migration ability of leiomyoma cells. These findings indicate the therapeutic efficacy of simvastatin for the treatment of uterine leiomyoma by targeting its disordered mechanical signaling.

SUPPORT. Supported by NIH grant 1R01HD094380-01.

P-602 Wednesday, October 16, 2019 6:30 AM

EXPRESSIONS OF VASCULAR ENDOTHELIAL GROWTH FACTOR AND ANGIopoietin-1 in MED12 MUTATED AND WILD-TYPE UTERINE LEIOMYOMAS. Ryoko Asano, MD, PhD, a Mikiko Asai-Sato, MD, PhD, a Taichi Mizushima, MD, PhD, b Koichi Nagai, MD, PhD, a obtained from all subjects. The leiomyoma tissue samples and clinical data of over a hundred of uterine leiomyoma patients who underwent surgery in our hospital were collected. The mutations in MED12 exon 2, the mutation hotspot of MED12 gene, were analyzed by Sanger sequencing. The mRNA expression levels of VEGF and Ang1 of leiomyoma tissue were measured by real-time reverse transcription-polymerase chain reaction. The relationship between MED12 gene mutation statuses, mRNA expression levels, and clinical backgrounds were analyzed. Mann-Whitney U test or χ² test for trend were performed for statistical analyses and P-values of less than 0.05 were considered statistically significant.

RESULTS: Fifty-two MED12 mutated and 56 wild-type leiomyomas were included in this study. The MED12 wild-type leiomyomas were confirmed to be 1.66-fold larger compared to MED12 mutated leiomyomas. Larger leiomyomas had the trend to be MED12 wild-type (P = 0.004). VEGF mRNA was 1.3-fold higher in MED12 mutated leiomyomas (P = 0.024); however, Ang1 mRNA and other clinical backgrounds did not have difference between MED12 mutated and wild-type leiomyomas.

CONCLUSIONS: Contrary to our expectation, MED12 mutated leiomyomas expressed higher VEGF mRNA levels. We speculate that MED12 wild-type and mutated leiomyomas grow in different mechanisms including angiogenesis and vessel maturation. The growth of MED12 mutated leiomyomas may be supported by the angiogenic effect of VEGF rather than EPO and MED12 wild-type leiomyomas may have an advantage in increasing tumor size by reinforced vessel maturation due to EPO.

P-603 Wednesday, October 16, 2019 6:30 AM

MULTI-OMIC ANALYSIS OF UTERINE LEIOMYOMAS FROM HEREDITARY LEIOMYOMATOSIS AND RENAL CELL CANCER PATIENTS. Thomas Conrads, PhD, a Anthony R. Soltis, PhD, b Nicholas Bateman, PhD, d Matthew Wilkerson, PhD, d Kathleen M. Darcy, PhD, d Additional variability was assessed using ANOVA. Multivariate linear mixed-effects models were used to estimate the effects of simvastatin on collagen gel contraction. The differences in the parameters were evaluated with a two-way ANOVA and Tukey’s post-hoc test. The results showed that simvastatin significantly decreased RhoA activation, collagen type I expression, gel contraction, and cell migration in huLM cells. These findings indicate that simvastatin can be a potential therapeutic agent for the treatment of uterine leiomyoma by targeting its disordered mechanical signaling.
previously described as being modified by 2SC in FH-mutated cancer cell lines (Ternette N, 2013 and Yang M, 2014). Pathway analysis of 2SC-modified proteins revealed altered regulation of cytoskeletal organization, cell death and cell migration signaling in HLRCU ULMs. Quantitative analyses revealed 63 unique 2SC-modified peptides were 2.45 (± 0.03)-fold elevated in HLRCU versus non-syndromic patients. These candidates included a peptide modified on C106 of Parkin 7 ( PARK7), a potent cellular deglycase and sensor of oxidative stress.

CONCLUSIONS: Multi-omic revealed protein alterations and post-translational modifications impacting mitochondrial and oxidative stress signaling in HLRCU versus non-syndromic ULMs. These findings define proteogenomic alterations that may better support the treatment of ULMs in HLRCU patients.

P-604 Wednesday, October 16, 2019 6:30 AM

REPROGRAMMING OF ESTROGEN SIGNALING BY MLL1 LINKS DEVELOPMENTAL EXPOSURE TO THE RISK OF UTERINE FIBROIDS. Mohamed Ali B, Pharm, M.Sc., Ayman Al-Hendy, MD PhD, Qiwei Yang, PhD.

University of Illinois at Chicago, Chicago, IL; University of Illinois College of Medicine, Chicago, IL; University of Illinois at Chicago (UIC), Chicago, IL.

OBJECTIVE: Environmental exposure to endocrine disrupting chemicals (EDCs) reprograms developmental organs, which leads to their predisposition to tumorigenesis later in life. Uterine fibroids (UFs) are monoclonal tumors arising from aberrant stem cells (SCs) in the myometrium (MM). We have previously demonstrated that MMSCs are the targets for epigenome reprogramming, and the expression of estrogen responsive genes (ERGs) was altered in response to early life exposure to EDCs. However, the mechanism responsible for initiation of this persistent EDCs-induced epigenetic alteration is unknown.

DESIGN: Laboratory research studies using Eker rat fibroid model MM tissue as well as MMSCs.

MATERIALS AND METHODS: Female newborn rats were treated S.C. with vehicle (VEH) or 10 μg/kg of diethylstilbesterol (DES-a tool compound of environmental EDCs) on postnatal days 10-12, a key period of uterine development. MMSCs were isolated from 5 month adult MM tissue (N=5 for each group) using Stro-1 and CD44 surface markers. To determine the role of MLL1 for changes in H3K4me3 in response to DES, knockdown (KD) of Taspase 1 (Tasp1) was performed using 3 lentiviral particles. To identify targets of epigenomic reprogramming in MMSCs, whole genome RNA-sequencing and ChIP-sequencing (using H3K4me3 antibody) was performed in DES- and VEH-MMSCs. Protein and gene expressions have been measured using Western blot (WB), immunofluorescence (IF) and qRT-PCR. Prime-PCR array of estrogen receptor (ER) signaling has been used. Ingenuity Pathway Analysis (IPA) software was used.

RESULTS: Our previous findings showed that DES exposure increased the expression of ERGs via epigenetic active marker H3K4me3. In this study, IPA analysis of RNA-seq data demonstrated that β-estradiol and ESR1 upstream regulators were highly activated, which was tightly correlated to the diseases of endocrine and reproductive systems . Also, ER signaling involving 47 molecules was activated in DES-MSMSCs. By WB and IF analyses, the expression levels of H3K4me3 and activated form of MLL1 were increased in DES- vs. VEH-MMSCs. To identify that MLL1 activates H3K4me3 mediated reprogramming, we inactivated MLL1 by knockdown of the Tasp1 protease, which KD abrogated the increase in expression of Tasp1, MLL1 heterodimer. WB demonstrated kD of Tasp1 protease, which was 0.05). To determine the additional estrogen pathway related molecules, which can be altered by MLL-1, Prime-PCR array of ER signaling was performed in Tasp1 KD and scramble DES-MMSCs. The data showed that the c-terminal fragment of MLL1 cleaved by Tasp1 is responsible for regulating ER signaling via direct and indirect epigenetic mechanism.

CONCLUSIONS: Our data demonstrate novel findings that MLL1 activation is required for H3K4me3 regulated ER expression that are vulnerable to disruption by environmental exposures. Tasp1 KD reverses the DES exposure-induced ERG reprogramming and modulates the ER signaling.


SUPPORT: NIH grants: R01 ES028615, U54 MD007602.

P-605 Wednesday, October 16, 2019 6:30 AM

SINGLE CELL RNASEQ ANALYSES OF UTERINE FIBROIDS AND FIBROID-FREE MYOMETRIA REVEAL PREVIOUSLY UNIDENTIFIED CELL TYPE AND STATE. Wanxin Wang, PhD, candidate, Aymara Mas, PhD, Javier Monleón, MD, Stephen Quake, DPhil, Carlos Simon, MD, PhD. Stanford University, Stanford, CA; Igenomix Foundation, Valencia, Spain; Servicio de Ginecología, Hospital Universitario y Politécnico La Fe, Valencia, Spain; Stanford University; Chan Zuckerberg Biohub, Stanford; San Francisco, CA; University of Valencia; Igenomix Foundation-INCLIVA, Valencia, Spain.

OBJECTIVE: Whole tissue studies of uterine fibroids provided information on transcriptomic and genomic signatures of the tumor, but were limited in providing mechanistic and therapeutic insights due to the undefined intra- and inter-tumor heterogeneity. We performed single-cell RNA-seq analyses on uterine fibroids (uF) and fibroid-free myometria (uM) at both expression and mutation level to better understand the molecular and cellular origin of the tumor and to identify targets for less invasive treatments.

DESIGN: Single cell RNAseq analyses on both expression and mutation level were performed on 5582 single cells from uF and matched uM from 6 patients with uF diagnosed, as well as uM from patients with no uF diagnosed.

MATERIALS AND METHODS: uF and uM were dissected after hysterectomy and dissociated separately into single cell suspension. Single cells were index-sorted into 384 well plates containing lysis buffer and ERCC. Single cell RNA was reverse transcribed and amplified (23 cycles) following an adapted SmartSeq2 protocol. Dual-indexed cDNA libraries were sequenced on a Novaseq to ~1e06 reads/cell. Mutations were called using an adapted GATK pipeline. Downstream analyses such as quality control, dimension reduction, and differential expression were performed using custom R scripts. Cell type and state validation was performed via RNA FISH.

RESULTS: uF and uM consist of cell types and states that are more complex than previously known. While both are composed of the primary hierarchy of smooth muscle cells, fibroblasts, blood vascular endothelia, and immune cells, in uF we identified previously unreported lymphatic vascular endothelia as well as further heterogeneity in fibroblasts and immune cells that does not exist in uM. For uM we report a previously uncharacterized ion-responding cell state. In addition, we observe an overall inflammatory state in uF, manifested as the transcriptomic signature of the immune cells, the presence of lymphatic system, and the interplay between the two via CCL21-CCR7 ligand-receptor pair. This state and the mutation load in the uF suggest a tumorigenic scheme that might differ between this benign tumor and cancer.

CONCLUSIONS: Our comprehensive single-cell hierarchy of uF reveals a previously unidentified cell type and state for both. The difference in the cellular hierarchy between the two and the differentially expressed genes in cell types that are common to both provide cellular and molecular targets for less invasive treatment for the tumor.

VITAMIN D3 AND ITS ANALOGUE PARICALCITOL REVERSE DNA DAMAGE IN HUMAN UTERINE FIBROID STEM CELLS: MECHANISM FOR POTENTIAL PREVENTIVE THERAPY. Mohamed Ali B Pharm, M.Sc., Lauren Prusinski Fernung, PhD, Ayman Al-Hendy, MD PhD, Qiwei Yang, PhD. "University of Illinois at Chicago, Chicago, IL; "Medical College of Georgia at Augusta University, Augusta, GA.

OBJECTIVE: The prevailing model for Uterine Fibroids (UFs) pathogenesis invokes the genetic transformation of a single myometrial stem cell (MMSC) into a tumor-initiating cell (UFSC) that seeds and sustains clonal tumor growth. UFSC are known to have higher prevalence in African American (AA) women, which is related in part to their vitamin D deficiency, yet its exact preventive mechanism of action has not been fully revealed yet. Growing body of evidence showed chemopreventive effect of vitamin D. We have recently demonstrated increased DNA repair defect in UFSCs compared to MMSCs. Collectively, we hypothesize that vitamin D3 or its potent analogues, through reparation of an impaired DNA damage response, will provide therapeutic benefits for UFs.

DESIGN: Laboratory research using Stro-1+/CD44+ MMSCs and UFSCs.

MATERIALS AND METHODS: Surgically removed fresh human UF and adjacent MM tissues were collected from two AA patients, and subjected to MM and UFSC isolation using dual Stro-1 and CD44 surface markers. Human UFSCs were treated with concentration ranges (10 nM-1000 nM) of 1, 25 dihydroyvitamin D3 and its three analogues (Paricalcitol, Doxercalciferol and Eocalcitol). The growth inhibitory effect was measured by MTT for 24, 48 and 72 hr. To determine the role of vitamin D and Paricalcitol on DNA damage repair system, UF SCs from 2 AA patients were treated with 100 nM of 1, 25 dihydroxyvitamin D3 or Paricalcitol for 3 days. Total RNA was extracted and DNA damage signaling pathway was examined using Prime-PCR array including 84 genes. The expression levels of 6 DNA double strand breaks repair genes including BRCA1, CHEK1, RAD50, RAD51, NBS1 and MRE11 were validated using RT-qPCR. In addition, protein lysates were extracted from treated and untreated cells and expression levels of DNA damage marker γH2AX as well as RAD51, NBS1 and MRE11 were measured by Western Blot (WB). Unpaired Student t-test was used to measure statistical significance. (P<0.05) was considered significant.

RESULTS: Using MTT assay, Vitamin D3 and its analogues treatment showed a potent significant anti-proliferative effect on human UFSCs in a concentration and time dependent manner (P<0.05). Using Prime-PCR array of DNA damage signaling, Vitamin D induced upregulation of 67 DNA repair genes while seven were downregulated and one was unchanged. Paricalcitol showed similar results by inducing the expression of several DNA related genes. Using RT-qPCR, expression of BRCA1, CHEK1, RAD50, RAD51, NBS1, MRE11 were validated in response to Vitamin D3 and paricalcitol treatment in favor of significant upregulation as compared to untreated control. WB analysis showed that both treatments significantly decreased protein expression of γH2AX while increased the protein levels of key DNA repair defect members including RAD51, NBS1 and MRE11. CONCLUSIONS: Our studies demonstrate a tight link between DNA damage and vitamin D in UFSCs. Vitamin D3 and its analogue(s) suppress the UF phenotype via targeting DNA damage repair pathway, therefore providing a novel mechanistic insight into clinical effectiveness of VitaminD3 and analogues on UF.

SUPPORT: National Institutes of Health grants R01 HD089553-01 and U54 MD007602.

VERTEPORFIN INHIBITS FIBROSIS, INFLAMMATION AND ANGIogenesis RELATED GENES IN UTERINE FIBROID CELLS. Md Soriful Islam, PhD, Jacqueline Yano Maher, MD, Sadia Afrin, PhD, Szu-Chi Su, MS, James Segars, MD, Johns Hopkins University, School of Medicine, Baltimore, MD.

OBJECTIVE: Uterine fibroids are characterized by abnormal cell proliferation and apoptosis, leading to excessive growth and secretion of an altered extracellular matrix (ECM). A key signaling pathway controlling cell proliferation and apoptosis is the Salvador/Warts/Hippo pathway. Hippo signaling is mediated by the TEAD domain family members (TEADs) and Yap-associated protein (YAP)<transcriptional co-activator with PDZ-binding motif (TAZ) transcription factors. Verteporfin, a benzoporphyrin derivative, is known to inhibit the interaction between TEAD and YAP/TAZ. We previously reported that Hippo signaling was altered in fibroid cells compared to myometrium and that verteporfin reduced expression of YAP responsive genes (CTGF and MMP-1). Here we tested the hypothesis that inhibition of Hippo targets by verteporfin would alter expression of key genes involved in uterine fibroid pathogenesis.

DESIGN: Translational research study with Human uterine fibroid (P53F) cells.

MATERIALS AND METHODS: Human myometrial and fibroid tissues were used to assess the expression levels of YAP and TAZ by immunohistochemistry (IHC). Next, we tested the effect of verteporfin on key ECM-related genes involved in fibroid formation and growth: collagen1A1; versican; integrin α6; matrix metalloproteinase (MMP)-14; the proliferative growth factors transforming growth factor (TGF)-β1, and TGF-β3; inflammation related gene, interleukin (IL)-8; and the angiogenesis related gene, endothelin1 in uterine fibroid cells. Cells were treated with vehicle or verteporfin at 0.5 or 1 μM for 24 hr. Viability curves showed >90% viability at 1 μM concentration. RNA was extracted using an RNAeasy Plus Mini Kit and converted to cDNA using iScript CDNNA Synthesis Kit. Real-time qPCR was performed on LightCycler 96 System, using FastStart Essential DNA Green Master Kit and gene-specific primers. Prior experiments confirmed activation of Yap phosphorylation by verteporfin in P53 myometrial cells. P<0.05 was considered as significant.

RESULTS: YAP and TAZ were differentially expressed in human myometrial and fibroid tissues as assessed by IHC. Treatment of fibroid cells with verteporfin significantly reduced steady-state mRNA levels of versican and MMP-14 in a dose-dependent manner in uterine fibroid cells, compared to control. Integrin α6 transcript levels were not affected, but IL-8 levels were reduced. Verteporfin also decreased fibroproliferative growth factors, TGF-β1, and TGF-β3 mRNA expression levels in fibroid cells, compared to untreated controls. Furthermore, we found that endothelin1 mRNA levels were reduced in response to verteporfin treatment in fibroid cells, compared to controls.

CONCLUSIONS: Inhibition of Hippo signaling by inactivation of nuclear YAP with verteporfin led to a reduction in mRNA expression levels of key genes involved in fibroid pathogenesis. These data support the possibility that altered Hippo signaling may contribute to the altered fibrosis, inflammation and angiogenesis of fibroids.

NAV2: A NOVEL NEURONAL PROTEIN AND REGULATOR OF THE CYTOSKELETON IS UPREGULATED IN LEIOMYOMA AND MYOMETRIUM. Jasmine Aly, MD, Joy L. Britten, M.D., Minnie Malik, Ph.D., Toral Parikh, M.D., Justin Pilgrim, M.D., Jacques Arisendi, Ph.D., Praphertino, M.D., Ph.D. a Program in Reproductive Endocrinology and Gynecology, NICHD, NIH, Bethesda, MD; bUniformed Services University of the Health Sciences, Bethesda, MD.

OBJECTIVE: Uterine leiomyoma are common reproductive-age benign tumors that contribute to severe morbidity and infertility, and account for 40% of gynecologic tumors in the US. Developing potential drug targets for medical treatment is of clinical importance. We have identified several neural genes present in leiomyoma tissue, including members of the neuron navigator (NAV) family. NAV2 plays a role in migration, cellular outgrowth and F-actin tethering to the myoskeleton in other tissues. However, its function is unknown in leiomyoma. The objective of this study is to assess NAV2 expression and its role in human uterine leiomyoma, and to identify potential oral medications that affect its expression.

DESIGN: Laboratory Study.

MATERIALS AND METHODS: RNA sequence (RNAseq) analysis was performed on placebo-treated patient matched leiomyoma and normal myometrium samples from a prospective, randomized, placebo-controlled clinical trial. These results were confirmed with qRT-PCR, western blotting, and immunohistochemistry (IHC). RESULTS: RNAseq analysis of placebo-treated fibroids compared to myometrium demonstrated the presence of transcripts encoding for several neuronal proteins. For NAV2, RNA sequence analysis demonstrated increased expression in leiomyoma as compared to myometrium (2.78 fold ±0.32, p<0.0001). Confirmatory qPCR results on leiomyoma and myometrial patient samples demonstrated an increase in expression of NAV2 in fibroids (3.86 fold ±0.98, p<0.005). Additionally, qRT-PCR on immortalized leiomyoma and myometrial cell lines similarly demonstrated an increase in expression of NAV2 in leiomyoma (3.06 fold ±1.02.
p=0.034. Western blot analysis on patient matched leiomyoma and myometrium supported these findings. IHC demonstrated a qualitative increase of NAV2 protein in fibroids as compared to myometrium by visual examination in morphologic appearance and staining intensity in 75% of patients examined.

CONCLUSIONS: NAV2, a member of the neuron navigator family, is identified in leiomyoma and myometrial tissue. NAV2 RNA and protein is elevated 2-3 fold in leiomyoma compared to myometrium. NAV2 is associated with F-actin and actin tethering, providing a novel target for compounds that regulate the cytoskeleton.

**SUPPORT:** This research was supported by Uniformed Services University of the Health Sciences, Department of Obstetrics and Gynecology and a research grant from Allergan.

The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of Defense, or the United States Government.

**P-609 Wednesday, October 16, 2019 6:30 AM**

IL6 AND STAT-3 PATHWAY HIGHLIGHT THE DIFFERENCES IN MOLECULAR RESPONSES IN MYOMETRIUM AND UTERINE FIBROIDS. Minnie Malik, Ph.D., Joy L. Britten, M.D., William Catherino, M.D., Ph.D., Uniformed Services University of the Health Sciences, Bethesda, MD.

**OBJECTIVE:** Human fibroids are highly prevalent and symptomatic uterine tumors. Phenotypically, they are different from normal myometrium because of massive production of extracellular matrix (ECM), which is a hallmark of these benign tumors resulting in symptoms including abnormal bleeding and pain. Dysregulated production of inflammatory cytokine, IL6 and its regulated JAK/STAT-3 pathway are known to contribute to the fibrotic process. Our objective was to test the effect of IL6 on fibroid and myometrium cells and the role of JAK/STAT-3 pathway in production of matrix proteins that play a major role in fibroid pathogenesis.

**DESIGN:** Laboratory study.

**MATERIALS AND METHODS:** Leiomyoma and patient-matched myometrium cell lines exposed to different concentrations of IL6 and JAK/STAT-3 modulators for various exposure time periods, in a 2D culture model system. Changes in expression of ECM proteins and regulating pathways were assessed using western blot.

**RESULTS:** In leiomyoma cells, IL6 activation of STAT-3 peaked (2.32+/−0.21 fold) as early as 1.5 hr of continuous exposure, and was 1.4+/−0.04 fold increased at end of 3 hr of exposure. The maximum increase (1.59+/−0.07 fold) in the feedback loop protein, Suppressor of cytokine Signaling (SOCS3) required a short exposure to IL6 (30 min) followed by collection after 3 hr. We also observed an increase (1.9+/−0.11 fold) in the ECM structural collagen-1 after continuous exposure to IL6 (3 hr) in leiomyoma cells. No significant effect of IL6 was observed in myometrium cells. Collagen-1 protein was also affected significantly in the leiomyoma cells on use of JAK/STAT-3 modulators. Increased levels of IL6 in the pathway in leiomyoma cells led to increased collagen-1 protein while the maximum increase (1.73+/−0.06 fold) in transforming growth factor beta3 (TGFβ3) protein, involved in fibrotic specific pathway, on use of JAK/STAT-3 modulators indicated that both pathways may interact to regulate the production of the ECM proteins in leiomyomas.

**CONCLUSIONS:** Direct effect of inflammatory cytokine IL6, on leiomyoma and not myometrium cells indicate that this differential response to IL6 and JAK/STAT3 pathway may be the key to increased ECM production and growth in uterine leiomyomas.

**SUPPORT:** USUHS Military Women’s Health Award OBG6422-309325.

**GENETIC COUNSELING**

**P-610 Wednesday, October 16, 2019 6:30 AM**

OFFERING UNIVERSAL CARRIER SCREENING TO WOMEN OF REPRODUCTIVE AGE SEEKING ROUTINE GYNECOLOGIC CARE. Carleagh B. Nesbit, DO, Ivy Wilkinson-Ryan, MD, Elisabeth D. Erekson, MD MPH, Valerie H. Lacroix, MSc LGIC, Devin M. Applebee, MS LGIC, Amy W. Bosco, MS LGIC, Catherine C. Pollock, BS, Rebecca H. Evans, MD Dartmouth Hitchcock Medical Center, Lebanon, NH.

**OBJECTIVE:** To investigate differences in demographic and clinical characteristics of reproductive age women who express interest in carrier screening consultation with genetic counseling offered as part of routine gynecologic care and those who do not.

**DESIGN:** Cross-sectional implementation study at a tertiary care gynecology practice.

**MATERIALS AND METHODS:** Women ages 18-40 years presenting for routine gynecologic care were eligible for participation. Women were given a packet with information about the benefits of genetic evaluation and assessment prior to conception and offered referral for genetic counseling consultation with the possibility of opting for carrier screening. Interested women were scheduled for comprehensive genetic counseling appointments which included evaluation, assessment, and discussion of available testing options. Demographic and clinical characteristics were obtained by review of the electronic medical record and a survey completed by women at the time of gynecologic visit. The electronic medical record was also reviewed to obtain information on the genetic counseling appointment, type of testing ordered, and test results. Statistical analysis were performed as appropriate with p < 0.05 to compare relevant characteristics.

**RESULTS:** From October 2018 to March 2019, 131 women were screened for participation. 105 women consented to participate, of which 4 were excluded due to participant or partner having undergone permanent surgical sterilization. Of the 101 women included in this study, 41 expressed interest in genetic counseling referral. Women most likely to express interest were those presenting for infertility evaluation (75.0%) and those presenting for preconception counseling (66.7%). Women presenting for other visit types were less likely to express interest (33.3% for annual exams, 28.6% for problems of reproductive age, and 26.7% for contraceptive counseling). Women of higher educational level were also more likely to express interest with least likely groups being those with high school degree or equivalent (30.7%) or associate’s degree (14.3%) and most likely groups being those with a master’s degree (88.9%) or professional degree/doctorate (60.0%) (p < 0.05). No significant differences were seen between differing age, race, ethnicity, employment status, marital status, insurance type, or past history of carrier screening. Of women who expressed interest, 13 (31.7%) attended their scheduled genetic counseling visit and 7 (53.8%) opted to undergo carrier screening.

**CONCLUSIONS:** After a brief introduction to genetic counseling services during routine gynecologic care in a single tertiary care clinic, nearly half of reproductive age women expressed interest in referral with possibility of carrier screening prior to conception. Nulliparous women, women of higher level of education, and women presenting for infertility evaluation or preconception counseling may be more likely to express interest in these services.

**SUPPORT:** None.

**P-611 Wednesday, October 16, 2019 6:30 AM**

PATERNAL ADVANCED AGE AND MALE FACTOR ARE INDICATORS FOR PRE-IMPLANTATION GENETIC TESTING IN EGG DONATION CYCLES. Jeimy Yesenia Pedraza, BsC,6 Hugo Sierra, BsC,6 Yadira Del Carmen Diaz, BsC,6 Jacqueline Cordero, Biología, Esther López-Bayghen, PhD6 Ingenes Mexico, Mexico City, DF, Mexico; aAffiliation not provided; 6Centro de Investigación y Estudios Avanzados IPN, México, EM, México

**OBJECTIVE:** Oocyte donation in fertility programs has become the most effective alternative to achieve pregnancy, mainly in women with low or no ovariian reserve as well as other complications. It has been shown that the use of young donors in oocyte donation cycles tends to increase success in pregnancy and live birth rates. Although there is a wide variety of studies that demonstrate the influence of the oocyte source’s age on the success of assisted reproduction treatments, the effect of paternal age has been studied to a lesser extent. Therefore, our goal was to assess semen quality between the spouse and donors and in vitro fertilization outcomes.

**DESIGN:** Retrospective.

**MATERIALS AND METHODS:** 394 IVF cycles in 5 different Mexican IVF labs where egg donation (age range: 18-35 years) was performed were considered. All donors underwent similar IVF stimulation protocols. The oocytes were aspirated and fertilized using ICSI technique. Biopsies were performed on Day 5 or Day 6, and chromosome integrity was determined by Next-Generation Sequencing. Insemination was performed with both spusal semen (n=332) and donor semen (n=62). Semen characteristics were evaluated by seminalogram, and seminal quality was assessed by measuring the total amount of normal progressive motile sperm (TNPm). Associations were determined using logistic regression.
OBJECTIVE: Expanded carrier screening (ECS) is a method of identifying individuals that are carriers for recessively-inherited genetic disorders with the goal of reducing the risk of having a child affected by a genetic disease. While some couples are screened in tandem, others may be screened sequentially to reduce need for a second individual’s test if a partner is found not to carry any mutations. However, it is unknown how often partners of individuals found to be carriers complete the recommended testing with a sequential approach. The goal of this study was to determine the frequency with which the partner of an individual identified as a carrier chooses to undergo testing and what factors may influence that decision.

DESIGN: Retrospective cohort chart review.

MATERIALS AND METHODS: All individuals at a university-affiliated reproductive endocrinology and infertility practice identified to be carriers of a recessively inherited mutation using the Counsyl/Foresight ECS between 9/1/2013 and 4/1/2019 were included. Conditions were categorized by severity (profound, severe and moderate) according to the classification system previously described by Lazarin et al. If an individual screened positive for more than one condition the category corresponding to the more severe condition was used.

RESULTS: A total of 544 cycles proceeded to biopsy with 2573 embryos biopsied. Of those, 368 (67.6%) cycles had at least one euploid embryo per cycle. Four patients had a transfer and biopsy remaining embryos within the same cycle. The percentage of cycles with euploid embryos decreased by age group from 86.1% of cycles in women less than 35 years old to 23.4% of cycles in women over age 42. Extrapolating data from the number of euploid embryos per cycle by age group, the estimated number of cycles to achieve at least one euploid blastocyst varies by cycle age group. The estimated number of cycles required to attain at least one euploid blastocyst decreases with increasing utilization of PGT-A technologies, the ability to counsel patients as to the number of expected cycles required to produce a euploid embryo is an important tool. This study aims to provide such a counseling tool utilizing retrospective outcomes data.

CONCLUSIONS: Though the greatest utility of ECS is when the carrier status of both reproductive partners is known, not all patients that carry recessively-inherited genetic disorders choose to have their reproductive partner screened. Patients found to be carrier of more debilitating genetic disorders may be more likely to screen their reproductive partners. The emphasizes the importance of the role of the provider in counseling patients prior to performing ECS, as well as genetic counseling after results are received.


P-613 Wednesday, October 16, 2019 6:30 AM

AGE BASED COUNSELING FOR WOMEN PLANNING TO UNDERGO IVF WITH PGT-A.


OBJECTIVE: Aging leads to both a decrease in embryo yield and euploid embryo frequency. With increasing utilization of PGT-A technologies, the ability to counsel patients as to the number of expected cycles required to produce a euploid embryo is an important tool. This study aims to provide such a counseling tool utilizing retrospective outcomes data.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: A total of 614 IVF cycles with intent for PGT-A from January 1, 2015 to March 15, 2019 at a single institution were reviewed. All cycles proceeding to oocyte retrieval were included, even if no embryos were available to biopsy. Patients who had an oocyte thaw with subsequent embryo biopsy were excluded. Cycles were analyzed to determine number of embryos biopsied, number of euploid embryos, and number of cycles with at least one euploid embryo. These data were utilized to obtain number of euploid embryos per cycle and calculate the estimated number of cycles required to attain at least one euploid blastocyst.

RESULTS: A total of 544 cycles proceeded to biopsy with 2573 embryos biopsied. Of those, 368 (67.6%) cycles had at least one euploid embryo per cycle. Four patients had a transfer and biopsy remaining embryos within the same cycle. The percentage of cycles with euploid embryos decreased by age group from 86.1% of cycles in women less than 35 years old to 23.4% of cycles in women over age 42. Extrapolating data from the number of euploid embryos per cycle by age group, the estimated number of cycles to achieve at least one euploid blastocyst varies by cycle age group. The estimated number of cycles required to attain at least one euploid blastocyst decreases with increasing utilization of PGT-A technologies, the ability to counsel patients as to the number of expected cycles required to produce a euploid embryo is an important tool. This study aims to provide such a counseling tool utilizing retrospective outcomes data.

CONCLUSIONS: Managing patient expectations during IVF treatment is critical. Clinicians and patients alike frequently underestimate the likelihood of not having embryos available for biopsy as well as the chance of having a euploid embryo with each cycle. With increasing utilization of PGT-A technology, a tool for estimating the number of cycles anticipated to achieve at least one euploid blastocyst can prove useful to set expectations with preparation for the possibility of multiple cycles.

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**TABLE 1. Cycle characteristics and biopsy results by patient age**

<table>
<thead>
<tr>
<th>Age Group</th>
<th>&lt;35</th>
<th>35-37</th>
<th>38-40</th>
<th>41-42</th>
<th>&gt;42</th>
<th>All Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Number of Cycles (%)</td>
<td>115 (19)</td>
<td>111 (18)</td>
<td>194 (32)</td>
<td>117 (19)</td>
<td>77 (13)</td>
<td>614 (100)</td>
</tr>
<tr>
<td>Cycles with No Biopsy (%)</td>
<td>8 (7)</td>
<td>10 (9)</td>
<td>17 (9)</td>
<td>21 (18)</td>
<td>14 (18)</td>
<td>70 (11)</td>
</tr>
<tr>
<td>Number Embryos Biopsied</td>
<td>702</td>
<td>553</td>
<td>736</td>
<td>404</td>
<td>178</td>
<td>2573</td>
</tr>
<tr>
<td>Number Euploid Embryos (%)</td>
<td>299 (43)</td>
<td>180 (33)</td>
<td>198 (27)</td>
<td>85 (21)</td>
<td>22 (12)</td>
<td>784 (30)</td>
</tr>
<tr>
<td>Cycles with at Least One Euploid per Cycle (%)</td>
<td>79 (66)</td>
<td>79 (71)</td>
<td>67 (60)</td>
<td>57 (49)</td>
<td>18 (23)</td>
<td>70 (60)</td>
</tr>
<tr>
<td>Number of Embryos Biopsied per Cycle</td>
<td>6.10</td>
<td>4.98</td>
<td>3.79</td>
<td>3.45</td>
<td>2.31</td>
<td>4.19</td>
</tr>
<tr>
<td>Number Euploid Embryos per Cycle</td>
<td>2.60</td>
<td>1.62</td>
<td>1.02</td>
<td>0.73</td>
<td>0.29</td>
<td>1.28</td>
</tr>
<tr>
<td>Number of Cycles to Euploid</td>
<td>1.16</td>
<td>1.41</td>
<td>1.66</td>
<td>2.05</td>
<td>4.28</td>
<td>1.66</td>
</tr>
</tbody>
</table>
IMPORTANCE OF EXPANDED CARRIER SCREENING IN THE ASHKENAZI JEWISH POPULATION.
Shelley N. Dolitsky, MD,a Shama Khan, MPH, MS, LGCa, Elena Ashkinadze, MS, LCGB,b Robert Wood Johnson School of Medicine, New Brunswick, NJ; Rutgers- Robert Wood Johnson Medical School, New Brunswick, NJ.

OBJECTIVE: Compared to the general population, patients of Ashkenazi Jewish descent have an increased risk of being genetic carriers for certain diseases, with an overall carrier rate ranging from 1 in 4 to 1 in 5. Therefore, the American College of Obstetricians and Gynecologists (ACOG) strongly recommends this population be offered carrier screening for four conditions: Tay Sachs, Cystic Fibrosis, Familial Dysautonomia, and Canavan Disease. Some experts have advocated for a more comprehensive screening panel, and subsequently, ACOG has emphasized the need for the following Jewish Genetic Diseases to be offered to patients: Bloom syndrome, Familial hyperinsulinism, Fanconi anemia, Gaucher disease, Glycogen storage disease type I, Joubert syndrome, Maple syrup urine disease, Mucolipidosis type IV, Niemann-Pick disease, and Usher syndrome. Given the genetic risks inherent in this population, carrier screening programs have been created to test for these founder mutations and have been successful in significantly decreasing the incidence of certain autosomal recessive conditions. Recently, however, with the advent of pan-ethnic, expanded carrier screening, we have the means to identify carriers for a broader array of conditions beyond the fourteen aforementioned. The objective of this study is to assess whether the current screening recommendations are sufficient in diagnosing carrier status in the Ashkenazi Jewish population.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: This was a retrospective chart review. Students at a single institution underwent genetic testing with expanded carrier screening through an outreach program at Rutgers University Hillel in October 2015. All the students were of Jewish descent. The genetic conditions tested in the expanded carrier screening were grouped into the following three categories based on ACOG’s 2017 committee opinion regarding carrier screening: the four strongly recommended genetic conditions, the fourteen recommended genetic conditions that can be offered, and the genetic diseases that are not specifically mentioned for screening in this population. The results were then divided according to this categorization.

RESULTS: A total of 81 patients were screened. Of these, 36 (44.4%) were found to be carriers of at least one disease. Out of the 36 patients, 28 were found to be a carrier for one disease, 7 for two diseases, and 1 for three diseases, representing 45 total identified mutations. The carrier rate was 7/45 (15.6%) for the four recommended Jewish Genetic Diseases, 20/45 (44.4%) for the fourteen offered conditions, and 25/45 (55.6%) for genetic diseases that were not recommended in this population.

CONCLUSIONS: If carrier screening for the Ashkenazi Jewish population was limited to only founder Jewish mutations in fourteen disorders, 44.4% of carriers would not have been identified. Our data supports that individuals of Ashkenazi descent should be offered pan-ethnic, expanded carrier screening.


SUPPORT: None.
PGT-M analysis and some offspring investigations often involve autosomal dominant conditions. Results of these investigations may have substantial implications for the donors’ own health and can more greatly disrupt the donor’s life, particularly if unexpected.

By engaging donors in the testing and informed consent process, gamete providers allow donors to be informed about risks, possible results, likelihood of positive results, and the potential implications to them and their own families, as with any other patient. Recipients and their providers are increasingly sending semen specimens for genetic testing without consent from donors or authorization from the gamete providers. Through this approach, well-informed clinicians and laboratory personnel place gamete providers in the difficult position of contacting donors regarding positive results for which they did not provide consent, and for which they may be greatly unprepared. For these reasons, and out of respect for autonomy of gamete donors, all testing on donors should be performed with consent and facilitated by the gamete provider.

SUPPORT: California Cryobank.

HEALTH DISPARITIES

P-617 Wednesday, October 16, 2019 6:30 AM

DETERMINANTS OF DISPARITIES IN MINIMALLY INVASIVE HYSTERECTOMY. Alicia Y. Christy, MD Veterans Administration, kensington, MD.

OBJECTIVE: Addressing racial disparities in access to minimally invasive surgery among women will require understanding factors that impact use of minimally invasive techniques for hysterectomy, the second most common surgery in women. Our objective was to identify trends in utilization of minimally invasive hysterectomy (MIH) among Black and White women over time in the Veterans Health Administration (VHA) and whether racial disparities in MIH varied by geographic region or whether they were performed at VA facilities or paid for by VA but performed at non-VA facilities.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: Using VA clinical and administrative data, we identified all women Veterans undergoing hysterectomy in fiscal years 2012–2014 with a diagnosis of fibroids (n=1714). We determined hysterectomy route (laparoscopic with/without robot assist, vaginal, abdominal) by International Classification of Diseases-9th edition codes. We employed multivariable logistic regression to estimate trends in racial disparities in MIH over time and to test whether racial disparities in MIH differed by geographic region or whether procedures were performed by VA or paid for by VA. Models adjusted for socio-demographic and health-related risk factors.

RESULTS: Disparities in the proportion of MIH decreased over time (p-value for interaction<0.001) primarily due to increases in MIH among Black women (Black: 26% to 39%; White: 50% to 40%). Disparities in the proportion of MIH procedures in Black versus White women did not differ by whether the procedure was performed by VA or paid for by VA, although the overall proportion of MIH was slightly higher within VA. The proportion of MIH procedures was highest in the Northeast (Black 45%, White 62%), but the disparity in MIH was also the greatest in this region (difference=16%). The proportion of MIH was lowest in the South (Black 34%, White 43%) but the disparity was smallest in this region (difference=9%).

CONCLUSIONS: In the enhanced access to care environment of the VHA, disparities in MIH appear to be narrowing over time. Variations existed in MIH proportion by geographic region, with observed Black-White disparities greatest in regions where MIH was more common overall. Efforts are needed to increase access to MIH in VHA in the Southern US in particular; however, any efforts to increase MIH must also address equity to avoid worsening racial disparities. Further studies, including qualitative research, are needed to determine optimal strategies for decreasing persistent racial disparities in access to new medical technologies, such as MIH.

Reference: None.

SUPPORT: None.

P-618 Wednesday, October 16, 2019 6:30 AM

ASSOCIATION OF PREGNANCY OUTCOMES WITH AREA DEPRIVATION INDEX. VINITA Alexander, MD, a Jean-Claire "Mandi" Powe Dillon, MD, b Emily S. Junghelm, MD, b MSCR, b Washington University in St. Louis, St. Louis, MO; bWashington University School of Medicine, St. Louis, MO.

OBJECTIVE: Living in a socioeconomically deprived neighborhood has been associated with an increased risk of adverse birth outcomes. However, variation in the effect of socioeconomic deprivation has not been studied in the U.S. population undergoing in vitro fertilization (IVF). In this study, we investigated the relationship between neighborhood-level socioeconomic status (SES) and clinical pregnancy rate, live birth outcomes, and preterm birth rates.

DESIGN: A retrospective cohort study of 516 women undergoing their first cycle of IVF at a single academic fertility center in St. Louis, MO from January 2015 to December 2018 was conducted.

MATERIALS AND METHODS: The Area Deprivation Index (ADI) has been validated to the neighborhood-level by Dr. Amy Kind at the University of Wisconsin-Madison. It facilitates the rankings of neighborhoods by socioeconomic status disadvantage. Using published ADI maps, neighborhood-level deprivation index was obtained per individual patient (from the 2013 American Community Survey). To construct a model with relevant factors, independent samples t-test were conducted for continuous variables of interest and chi-square analysis carried out for binary variables of interest. Logistic regression analysis was carried out to determine the relationship between clinical pregnancy (CP), live birth (LB), and preterm birth. Covariates included in the original model were: age, BMI, number of oocytes retrieved, intracytoplasmic injection (ICSI), number of 2PN embryos transferred, and anti-mullerian hormone (AMH) level.

RESULTS: Overall, there was no significant difference between the CP rate in the highest national quintile deprivation index group (most deprived) and those in the lowest (least deprived) group. Compared to the least deprived quintile, the OR for CP in second least deprived quintile was 1.34 (95% CI: 0.92-1.96, p=0.19) and in the most deprived group was 0.605 (95% CI: 0.212-1.723, p = 0.347). Factors significantly associated with CP in the studied cohort were: AMH, ICSI, and age at start of treatment. Overall, there was also no significant relationship between ADI and LB rate, with the most deprived group (compared to the least deprived quintile) having an OR of LB of 1.021 (95% CI 0.343-3.040, p = 0.970). Interestingly, the hazard ratio of preterm birth at <37 weeks was elevated in the second and third quintiles of deprivation compared to the areas with the lowest deprivation index; 1.626 (95% CI: 1.26-2.10) and 1.66 (95% CI: 1.25-2.2). Also interestingly, there was a nonsignificant trend in increasing odds ratio of multiple births in the most deprived quintiles compared to the least deprived quintile (OR 1.935, 95% CI: 1.440 to 8.509, p = 0.382).

CONCLUSIONS: We found no significant association between neighborhood deprivation index and probability of CP or LB after IVF. Given that the academic center is in St. Louis, MO and attracts many patients coming from Illinois, a state that mandates fertility coverage, it may be interesting to further investigate whether those in the most deprived ADI groups (and possibly fertility insurance coverage) are more likely to have multiples.

P-619 Wednesday, October 16, 2019 6:30 AM

EXPLORING THE INTERSECTION OF RACE, RELIGION, AND GENDER IN BLACK WOMEN WITH INFERTILITY. Nicolas A. Johnson, B.S., a David A. Grainger, M.D., b University of Kansas School of Medicine-Wichita, Wichita, KS.

OBJECTIVE: Investigating the cultural and psychosocial factors that affect Black women’s access to fertility treatment; including intraracial differences between infertile women who have accessed fertility treatment compared to women with infertility that have not accessed care.

DESIGN: Qualitative study in a community-based setting.

MATERIALS AND METHODS: The first author of the study consented participants via phone and conducted semi structured interviews with Black women with an ICD9 or ICD10 diagnosis of female factor or unexplained infertility. Interviews were audio recorded, transcribed, and analyzed in NVIVO using phenomenological methods.

RESULTS: Each of the 12 participants were married or partnered, and the mean age of the women was 39 years. Most women were college educated from working middle class households. All participants were insured. The matic analysis revealed each woman’s journey to motherhood, challenges navigating the healthcare system, and the value of their religion throughout their experience. Journey to Motherhood: Participants expressed their experience with pregnancy loss, delayed diagnosis, the anxiety around inheriting traits from an adopted child, and belief in the ultimate social importance of motherhood. Healthcare System: Challenges included; feelings of discrimination, high cost of fertility treatment, and lack of accessibility and knowledge about treatment. Religion: Emerging themes around religion included the belief in accepting God’s plan, using it as a form of solace. This belief did not impact their overall perception of fertility medication or the use of assisted reproductive technologies to build their families.
CONCLUSIONS: Black women face unique intersectional challenges in their experience living with infertility. The results of this study may serve as a tool for improving physician-patient interactions and foster a better understanding of modern reproductive health disparities and minority health outcomes.

P-620 Wednesday, October 16, 2019 6:30 AM

PROLONGED TIME TO DIAGNOSIS OF PRIMARY OVARIAN INSUFFICIENCY (POI) IN AN URBAN REPRODUCTIVE ENDOCRINOLOGY (RE) CLINIC. Shweta J. Bhatt, MD, a Valerie S. O’Besso, BA, a Nataki C. Douglas, MD, PhD, a Peter McGovern, MD, a Jacquelyn Loughlin, MD, a Sara S. Morelli, MD, PhD, a Rutgers New Jersey Medical School, New York, NY; a Rutgers New Jersey Medical School, Newark, NJ, a Associate Professor, Newark, NJ; a University Reproductive Associates, NJ; a Rutgers New Jersey Medical School, Newark, New Jersey, NJ.

OBJECTIVE: Prompt recognition of symptoms and subsequent diagnosis of POI are critical given its consequences on quality of life and long-term health. Poor access to care in low-income populations may contribute to delayed diagnosis. We previously demonstrated a dearth of board-certified RE physicians providing care for Medicaid patients in New Jersey (1). Given the adverse effects of prolonged hypoestrogenism, we aimed to evaluate length of time to diagnosis of POI in a low-resource/low-income population presenting to an urban university-based RE clinic.

DESIGN: Case series.

MATERIALS AND METHODS: All new patients seen at the RE clinic at University Hospital in Newark, NJ from June 2014 through June 2018 were included. POI was diagnosed in women with oligo/amenorrhea and menopausal levels of follicle stimulating hormone. The primary outcome was time to diagnosis from onset of symptoms.

RESULTS: Of 524 new patients seen, 19 (3.6%) were diagnosed with POI (Table 1). Mean time to diagnosis of POI from onset of symptoms was 6 years, 17/19 (89.5%) were Hispanic and/or Black. 13/19 (68.4%) reported hypoestrogenic symptoms at time of referral. 21.1% were diagnosed with Turner mosaicism. 14 patients completed DEXA scan, of which 35.7% were diagnosed with low bone mass or osteoporosis. Of those diagnosed prior to referral to RE (9/19, 47.4%), only 4 had initiated hormone therapy.

CONCLUSIONS: Prolonged time to diagnosis of POI has adverse effects, as reflected by hypoestrogenic symptoms and decreased bone mineral density. Our study demonstrates a need for more aggressive evaluation of oligo/amenorrhea in underrepresented minority women. Delayed diagnosis and management of POI may be related to health care disparities facing these women, and warrants action to improve access to care.


SUPPORT: None.

P-621 Wednesday, October 16, 2019 6:30 AM

IMPACT OF MATERNAL ETHNICITY ON PREGNANCY OUTCOME IN INFERTILE WOMEN WITH POLYCYSTIC OVARIAN SYNDROME. Fabiola D’Ambrosio, MD, Humberto Scoccia, MD. University of Illinois at Chicago, Chicago, IL.

OBJECTIVE: Polycystic ovarian syndrome (PCOS) is the most prevalent endocrine pathology seen among women of reproductive age. The objective of the study is to investigate the impact that ethnic background has on pregnancy outcomes, including live birth rates in infertile women with PCOS going through IVF compared to women without PCOS.

MATERIALS AND METHODS: This study used a coded REDCap data set of 486 women, 18-45 years of age who underwent IVF and embryo transfer between 1/1/2010 and 12/31/2015 at an academic IVF Center after IRB approval (IRB 2015-0623). Patients underwent their 1st IVF cycle following progesterone withdrawal (norethindrone acetate) using GnRH agonist or antagonist protocols with mixed gonadotropins and demographic data, including race and ethnicity was obtained. Data collected during the IVF process included peak estradiol, number of mature oocytes, fertilization rate, number of top quality embryos on Day 3 of development, number of embryos transferred, implantation rate, clinical pregnancy rate, live birth rate, clinical miscarriage rate, and ectopic pregnancy rate. In women, whose pregnancy resulted in a live birth, additional maternal and neonatal variables were collected, including estimated gestational age (EGA) at delivery, mode of delivery, and weight at birth. Using R analytics software, data was analyzed using logistic regression and linear models. For logistic regression, the estimated coefficient was the log-odds-ratio. A significant p value was considered <0.05.

RESULTS: Of the 486 initial women, 360 women were included in the final analysis. Only women with known-reported ethnicity were included. Not Hispanic is the referent cohort for ethnicity and non-PCOS is the referent group when comparing PCOS status. There was no significant difference found for implantation rate (p=0.53) and pregnancy rate (p=0.99) when comparing women without PCOS with the women with PCOS. When taking into account the ethnicity factor in PCOS and the women who conceived and had a live birth, there was no significant difference between being Hispanic with PCOS and the referent non-Hispanic group. However, when evaluating women who started the IVF cycle, women with PCOS are less likely to have a pregnancy that leads to a live birth compared to women without PCOS (p=0.046). Being Hispanic by itself does not seem to affect live birth (p=0.81). Hispanic women with PCOS have the same probability of having a vaginal delivery compared to the referent group (p=0.935). Women with PCOS are more likely to deliver ~2 weeks earlier than non-PCOS patients (p=0.038). Being Hispanic and having PCOS did not affect the EGA at delivery (p=0.83) or affected fetal weight compared to the referent group (p=0.58).

CONCLUSIONS: This pilot study did not find a significant difference in most of the variables studied comparing Hispanic PCOS women with non-Hispanic women without PCOS. However, further studies with a larger number of subjects are needed to assess the impact of ethnicity and PCOS on IVF pregnancy outcomes.

SUPPORT: None.

IMAGING

P-622 Wednesday, October 16, 2019 6:30 AM

ORAL DICLOFENAC POTASSIUM IS AN EFFECTIVE ANALGESIC DURING HYSTEROSALPINGOGRAPHY. Ahmed M. Abbas, MD, a Mohamed Khalaf, MD, a Ahmed Ali Abdelaleem, MD, a Tarek Farghaly, MD, a Ayman Shehata Dawood, M.D. a Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt; b Department of Obstetrics and Gynecology, Faculty of Medicine, Tanta University, Tanta, Egypt.

OBJECTIVE: The aim of the study was to investigate the effect of diclofenac potassium on pain during hysterosalpingography.

MATERIALS AND METHODS: A randomized, double-blind placebo-controlled trial study was conducted in a tertiary referral hospital in Tanta, Egypt. Patients who were scheduled for hysterosalpingography were randomized into two equal groups, the first was a diclofenac potassium group (n=61), and the second was a control group (n=61) who received saline as a placebo. The study was approved by the Research Ethics Committee of Tanta University Hospital. Patients were evaluated at 0, 2, 4, and 6 weeks after the procedure for pain using a visual analogue scale (VAS) and the effect was assessed by the patients themselves.

RESULTS: The VAS scores were lower in the diclofenac potassium group compared to the control group at all time points (p<0.05). The mean score of pain was significantly lower in the diclofenac potassium group compared to the control group at all time points (p<0.05).

CONCLUSIONS: Diclofenac potassium provides effective pain relief during hysterosalpingography.

SUPPORT: None.

TABLE 1. Patient Characteristics (n=19)

<table>
<thead>
<tr>
<th>Follicle Stimulating Hormone (M±SD)</th>
<th>82.0±31.5 mIU/mL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estradiol (M±SD)</td>
<td>12.3±17.5 pg/mL</td>
</tr>
<tr>
<td>Anti-Mullerian Hormone (M)</td>
<td>&lt;0.015 ng/mL</td>
</tr>
<tr>
<td>Age at Symptoms Onset in Years (M±SD)</td>
<td>25.1±10.0</td>
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<tr>
<td>Time to Diagnosis from Symptoms</td>
<td>72.4±61.3</td>
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<tr>
<td>Onset in Months (M±SD)</td>
<td></td>
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<tr>
<td>Ethnicity</td>
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</tr>
<tr>
<td>Hispanic, n (%)</td>
<td>6 (31.6)</td>
</tr>
<tr>
<td>Not Hispanic, n (%)</td>
<td>13 (68.4)</td>
</tr>
<tr>
<td>Race</td>
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<tr>
<td>White, n (%)</td>
<td>2 (10.5)</td>
</tr>
<tr>
<td>Black, n (%)</td>
<td>11 (57.9)</td>
</tr>
<tr>
<td>Other, n (%)</td>
<td>6 (31.6)</td>
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<tr>
<td>History of smoking, n (%)</td>
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<tr>
<td>BMI (M±SD)</td>
<td>25.6±5.4</td>
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<tr>
<td>Nulliparous, n (%)</td>
<td>14 (73.6)</td>
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<tr>
<td>Symptoms on Presentation to Reproductive Endocrinology</td>
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<tr>
<td>Vasomotor, n (%)</td>
<td>12 (63.2)</td>
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<td>Vaginal, n (%)</td>
<td>6 (31.6)</td>
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<tr>
<td>Hormone Therapy Initiated Prior to</td>
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<tr>
<td>Referral, n (%)</td>
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<td>Etiology Identified, n (%)</td>
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<td>Chemotherapy, n (%)</td>
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<td>Turner Mosaic, n (%)</td>
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<tr>
<td>Fragile X premutation, n (%)</td>
<td>14 (73.7)</td>
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<tr>
<td>Low Bone Mass or Osteoporosis, n (%)</td>
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<tr>
<td>Hormone Therapy</td>
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<td>Combined oral contraceptive pills, n (%)</td>
<td>6 (31.6)</td>
</tr>
<tr>
<td>Cyclic estrogen and progestin, n (%)</td>
<td>12 (63.2)</td>
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</table>
OBJECTIVE: Tubal abnormalities are found in 30-40% of cases of infertility and evaluation of tubal patency is so crucial in their diagnostic workup. Hysterosalpingography (HSG) is a reliable, simple and cost-effective method for evaluation of tubal patency. Our objective is to investigate the anaglesis effect of oral diclofenac potassium in pain alleviation during hysterosalpingography (HSG).

DESIGN: A randomized double-blinded controlled trial.

MATERIALS AND METHODS: Reproductive-aged infertile women scheduled for HSG were considered for enrollment Eligible women were recruited and randomized (1:1) to oral diclofenac or Placebo group. All women received oral 50 mg diclofenac potassium or placebo tablets one hour before HSG. The study outcomes were the participant’s self-rated pain perception using a 10-cm Visual Analogue Scale (VAS) during speculum application, cervical tenaculum application, injection of the dye, 5 minutes and 30 minutes post-procedure. A 2 cm difference in VAS score between both groups was considered a clinically significant difference. Other outcomes included the number of women who need additional analgesics and the adverse effects of the study medications. Mann Whitney test and Fisher’s exact test were used for the analysis of the outcomes.

RESULTS: Two hundred women were enrolled and randomized to diclofenac arm (n=100) or placebo (n=100). No difference between both groups in age, parity, BMI, type, duration of infertility and the prior mode of delivery. Women in the diclofenac group reported lower VAS scores during injection of the dye, 5 minutes and 30 minutes post procedure (median: 3 vs. 5.5, p=0.001; 2 vs. 4, p=0.001, 1.5 vs. 3, p=0.003, respectively). No significant difference was in VAS scores during speculum or tenaculum application. Additionally, twenty-five women asked for additional analgesics in the placebo group versus nineteen women in the diclofenac group (p=0.062). No difference in the rate of adverse effects.

CONCLUSIONS: oral diclofenac potassium one hour before HSG significantly alleviates the induced pain during and 30 min after the HSG procedure.

SUPPORT: None.

P-623 Wednesday, October 16, 2019 6:30 AM
UTERINE PERISTALSIS DURING IMPLANTATION PERIOD: EXPERIENCE OF 3,672 PATIENTS WITH 3 OR MORE FAIRULE OF EMBRYO TRANSFERS.
Hidehiko Matsubayashi, MD, a
Kotaro Kitaya, MD, a, Takumi Takeuchi, MD, PhD, b Masakazu Doshi, MD, a Kohei Yamaguchi, MD, a Tomomoto Ishikawa, MD a Reproduction Clinic Osaka, Osaka, Japan; bReproduction Clinic Tokyo, Tokyo, Japan.

OBJECTIVE: Uterine peristalsis caused by uterine contraction is thought to be one of the risk factor for implantation failure, because the uterus is quiescent in the time of implantation period. Previous studies suggested that more than 2 or 3 waves/min may be a threshold for implantation failure. Although those reports focused on frequency and direction of the uterine contraction, as far as we know, there were no reports regarding intensity and location of the uterine contraction. Therefore, we investigated intensity and location as well as frequency and direction of the uterine contraction in the largest number of patients with recurrent failure of embryo transfers.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Transvaginal ultrasonography scans of uterine peristalsis were performed at the mid luteal phase (7 days after gonadotropin administration = P+7 on hormone replacement cycle or 9 days after HCG administration = HCG+9 on natural cycle). The transvaginal probe (Logiq V5 Expert, 6 to 10 MHz, GE Healthcare) was introduced into the vagina as gently as possible to avoid stimulating the uterine cervix. After scanning, the uteri were considered to be quiescent as the previous examination while 3 min. video was recorded simultaneously. The video images were analyzed at 10 time the normal speed using Quick Time Player (Ver. 10.4) by a single observer. Frequency, intensity, location and direction of the uterine contractile activity were recorded and evaluated. Intensity was divided into 3 categories; movement with the whole endometrium (strong), with the middle and the surface of the endometrium (medium), and just the surface of the endometrium (weak). Direction was complicated with many patterns (e.g., lower→upper→lower).

RESULTS: Of 3671 patients (average age, 37.5), 1936 (52.7%) did not show any uterine peristalsis, 1735 (47.3%) had uterine peristalsis. In the peristalsis group, frequency was 55.2% for 1 to 3 times/3 min, 30.2% for 4 to 6, 10.8% for 7 to 9, and 3.8% for 10 or more. Intensity was almost equal among 3 categories (strong 34.1%, medium 37.4%, weak 28.5%). Most uterine peristalsis was observed in the whole uterine cavity (80.7%), whereas those in the upper, middle and lower part of the uterus were 9.7%, 1.6% and 8.1%, respectively. In terms of direction, about half (48.1%) of uterine peristalsis was observed as “lower→upper→lower”, followed by “upper→lower→upper” (16.9%), “lower→upper” (14.5%), “upper→lower” (14.3%), and unfocused (5.9%). Pregnancy outcome of patients (N=24) who had strong uterine peristalsis with 10 or more times/3 min was retrospectively evaluated after taking piperidolate hydrochloride (150mg/day). Patients with live birth or ongoing pregnancy with 22 weeks or more were 11 (45.8%), those with biochemical pregnancy or miscarriage were 6 (25.0%), and those without pregnancy were 7 (29.2%).

CONCLUSIONS: These data suggest that uterine peristalsis was frequently observed in patients with recurrent implantation failure. However, we have to determine the cutoff line that should be treated. Further studies will be required.

Reference: None.

SUPPORT: None.

P-624 Wednesday, October 16, 2019 6:30 AM
TRENDS IN EMERGENCY DEPARTMENT UTILIZATION IN WOMEN AGED 18-50 WITH OVARIAN CYSTS (2006-2014).
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OBJECTIVE: Ovarian cysts may be functional or non-functional with management ranging from expectant, to medical, or surgical. Clinical concerns regarding ovarian cysts include risk of torsion, rupture, hemorrhage, or underlying malignancy. Pain is often an associated feature prompting women to seek evaluation in the Emergency Department (ED), whereas other times ovarian cysts are identified incidentally. The aim of this study was to examine the frequency, trends, and associated features of women presenting to the ED with a diagnosis of an ovarian cyst.

DESIGN: Retrospective cross-sectional study.

MATERIALS AND METHODS: Data from the Nationwide ED Sample (NEDS) database of Health Cost and Utilization Project (HCUP; Rockville, MD), were queried for all ED visits of women aged 18-50 years old with a primary or secondary diagnosis (ICD-9) of ovarian cysts, between 2006-2014. Variables assessed included age, hospital type, medical insurance, household income quartile and disposition.

RESULTS: Between 2006 and 2014 the estimated number of ED visits for ovarian cysts increased (410,435 in 2006 to 628,425 in 2014). However, the percentage of patients admitted to the hospital for this condition decreased during the same time period (12.1% in 2006 to 7.3% in 2014). This decrease far outpaced the trend of decreased admission rates in age matched women who presented to the ED for all other diagnoses (8.2% in 2006 to 7.4% in 2014). Across the years analyzed, the 20-44 age category more frequently sought ED care for ovarian cysts while the older 45-50 age category was admitted at a higher rate. Overall, women that visited the ED for ovarian cysts were more likely to have private insurance or Medicaid, to live in zip codes of the bottom two income quartiles, to visit metropolitan EDs in areas with population >1M, and to live in the southern states. The most frequently associated secondary diagnoses, when ovarian cyst was the principal diagnosis for that ED visit, included tobacco disorder, abdominal pain and female genital symptoms.

CONCLUSIONS: While the total ED visits of women with a primary or secondary diagnosis of an ovarian cyst increased from 2006 to 2014, the proportion of women admitted during the same time period decreased. This decrease in admission rate may be attributed to a shift away from acute surgical management of ovarian cysts and/or an increased in the number of low-acute cases of ovarian cysts presenting to the ED. A disproportionate number of women evaluated in the ED for ovarian cysts were in the lowest two income quartiles highlighting a potential disparity in healthcare delivery and utilization.

P-625 Wednesday, October 16, 2019 6:30 AM
PREVENTING UNNECESSARY PITUITARY MAGNETIC RESONANCE IMAGING: PROLACTIN TO TESTOSTERONE RATIO PREDICTS PITUITARY ADENOMAS IN MALE PATIENTS WITH MILD HYPERPROLACTINEMIA.
Anup B. Shah, MD, MS, a Bryan Douglas Naelitz, BA, a Neel Parekh, MD, a Betul Hatipoglu, MD, a Daniel Shoskes, MD, a Sarah C. Vij, MD. aCleveland Clinic Foundation, Cleveland, OH; bCleveland Clinic, Department of Endocrinology, Diabetes and Metabolism, Cleveland, OH.

OBJECTIVE: Adenomas in male patients with mild hyperprolactinemia (PRL) are often discovered incidentally on Magnetic Resonance Imaging (MRI). It is unknown whether a high pituitary PRL to testosterone ratio (PRL/T) in the absence of symptoms justifies MRI. We investigated the cost and clinical utility of PRL/T cut off to avoid unnecessary MRI.

MATERIALS AND METHODS: A prospective series of 40 patients with mild hyperprolactinemia (PRL) (PRL >25 ng/ml) not on dopamine agonist therapy was recruited. Baseline PRL, free and total testosterone (T) and 24-hour urine free cortisol were measured. PRL/T was calculated. PRL/T was tested as a dichotomous variable with cut off point of 5 using receiver operating characteristic (ROC) curve analysis. The cut off point with maximum Youden index was used to calculate sensitivity, specificity, positive and negative predictive values (PPV, NPV) of PRL/T to predict an MRI positive result.

RESULTS: The mean baseline PRL, free and total testosterone (T) were 38.6 ± 4.1, 9.4 ± 1.2, 327 ± 36 ng/ml respectively. PRL/T had a mean of 0.27 ± 0.09. The cut off to predict MRI positive result was 1.5. The sensitivity, specificity, PPV and NPV for a PRL/T >1.5 to predict MRI positive result were 63%, 96%, 69% and 96%. The cost to perform MRI for patients with PRL/T >1.5 was $15,700.

CONCLUSIONS: A PRL/T >1.5 in male patients with mild hyperprolactinemia had high specificity (96%) and PPV (69%) to predict MRI positivity. Cost savings of $15,700 would be realized per patient screened with a PRL/T >1.5.

SUPPORT: None.

FERTILITY & STERILITY®
OBJECTIVE: Serum prolactin (PRL) levels are routinely obtained in men presenting with clinical hypogonadism or infertility with mild hyperprolactinemia, often prompting pituitary magnetic resonance imaging (pitMRI) to assess for adenoma. The utility of obtaining pitMRI in this population has not been adequately established and no society guidelines exist to inform this decision. We hypothesize that a combination of laboratory findings predicts positive pitMRI findings in patients with mild hyperprolactinemia and, given the high rate of negative pitMRIs among young men with mild hyperprolactinemia, sought to identify patients in whom pitMRI can safely be avoided.

DESIGN: Retrospective, case-control chart review.

MATERIALS AND METHODS: Male patients under the age of 50 with mild hyperprolactinemia (15-55 ng/mL) who presented with erectile dysfunction, low libido, hypogonadism, or infertility who had undergone pitMRI were included. Those with a prior diagnosis of prolactinoma, hormonal or dopaminergic therapy, or incomplete clinical data were excluded. Presenting symptoms, age, PRL, body mass index (BMI), testosterone (T), luteinizing hormone (LH), follicle-stimulating hormone (FSH), creatinine (SCR), all medications, and MRI findings were collected. Means of continuous variables were compared with Fisher Exact or Chi-squared tests. Fitted binomial distributions were used to generate Receiver Operating Characteristics (ROCs) and Area Under the Curve (AUC) calculations.

RESULTS: 62 men met inclusion criteria. Pituitary adenomas were identified in 18 patients (29%) with a mean adenoma size of 5.4 ± 5 mm. Mean PRL differed in men with and without adenomas (37.8 ng/mL vs 24.9 ng/mL, p < 0.001), as did mean T (198 ng/dL vs 301 ng/dL, p < 0.001) and mean LH (3.33 mIU/mL vs 8.21 mIU/mL, p < 0.001) in untreated patients with in untreated patients with adenomas. Statistical significance was determined with the Wilcoxon-Rank Sum test, and categorical variables were compared with Fisher Exact or Chi-squared tests. Fitted binomial distributions were used to generate Receiver Operating Characteristics (ROCs) and Area Under the Curve (AUC) calculations.

A novel ratio of PRL (ng/mL) to T (ng/dL) (PRL/T) was superior to PRL or T alone in predicting positive pitMRI findings. PRL/T outperformed PRL or T when PRL < 30 ng/mL (AUC 0.88 vs 0.76, 0.83 respectively) and when T < 300 ng/dL (AUC 0.83 vs 0.80, 0.73) with considerable overlap. Age, BMI, LH, FSH, and SCR were not associated with presence of adenoma (p > 0.05).

A novel ratio of PRL (ng/mL) to T (ng/dL) (PRL/T) was superior to PRL or T alone in predicting positive pitMRI findings. PRL/T outperformed PRL or T when PRL < 30 ng/mL (AUC 0.88 vs 0.76, 0.83 respectively) and when T < 300 ng/dL (AUC 0.83 vs 0.80, 0.73).

A PRL/T ratio > 0.1 identified adenomas (p < 0.001) with high sensitivity (89%, 16/18 adenomas identified). 43% of pitMRIs could have been prevented if this metric were applied. No patients had pituitary abnormalities when PRL/T < 0.1 and PRL < 30 ng/mL. A more conservative approach of ordering pitMRI when PRL/T ratio > 0.1 and/or PRL ≥ 30 retains 100% sensitivity for identifying adenomas (18/18, p < 0.01). This more conservative guideline would have prevented 32% of pitMRIs when applied to the study cohort.

CONCLUSIONS: The PRL/T ratio is a superior metric to PRL or T alone in identifying young male hypogonadal patients with mild hyperprolactinemia who have imaging-confirmed pituitary abnormalities. A conservative clinical heuristic of ordering pitMRI in patients with hypogonadism with PRL/T > 0.1 and/or PRL ≥ 30 ng/mL detects adenomas with 100% sensitivity and prevents 32% of pitMRIs without changing clinical management, thereby reducing healthcare costs.

P-265 Wednesday, October 16, 2019 6:30 AM

THE UTILITY OF PELVIC ULTRASOUNDS IN ADOLESCENTS PRESENTING TO THE EMERGENCY DEPARTMENT WITH HEAVY MENSTRUAL BLEEDING. Monica W. Rosen, MD, Sarah D. Rominski, PhD, MPH, Jenny S. George, MD, Victoria L. Stoffers, BS, Charlotte M. Bourdillon, MPH, Christine M. Pennesi, MD, Angela C. Weyand, MD, Elisabeth H. Quinl, MD University of Michigan, Ann Arbor, MI.

OBJECTIVE: Unlike in adults, the utility of pelvic ultrasounds (PUS) for heavy menstrual bleeding (HMB) in adolescents who seek care in the Emergency Department (ED) is not well known; therefore, this study was conducted to analyze both decision-making and data utilization around performing PUS in a gynecology setting.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: Patients between the ages of 11 and 19 years who presented to the ED at a tertiary care hospital from 2006-2018 were identified by ICD-9 and ICD-10 codes for HMB. Patients who had PUS were divided into three groups based on endometrial stripe measurement (EMS): EMS ≤ 5mm (group 1), EMS 6-9mm (group 2), and EMS ≥ 10mm (group 3). Patients were further divided into those admitted to the hospital versus those discharged from the ED. Outcome of treatment was evaluated in admitted patients by progress notes indicating when bleeding resolved. Statistical analysis was performed across all groups with cross tab and Chi-Square test, and logistic and linear regression analysis. Approval of this study was granted by the Institutional Review Board.

RESULTS: Two-hundred fifty-eight adolescent females presented to the ED with HMB during this timeframe, of which 113 (43.8%) had PUS. PUS were more likely to be performed if a patient was seen by gynecology, as opposed to hematology or both specialties together (p = 0.001). Additional predictors for obtaining the hormone value, the more likely PUS were to be performed (p < 0.003). The decision of whether or not to order PUS did not differ based on age (p = 0.1) or duration of bleeding (p = 0.1). There were no structural abnormalities noted on PUS. Forty-nine patients (43.4%) had an EMS that was ≤ 5mm (group 1), 32 (28.3%) had an EMS between 6-9mm (group 2), and 32 (28.3%) had an EMS ≥ 10mm (group 3). There was no difference between thickness of the EMS and duration of bleeding prior to presentation (p < 0.91). Among those who had PUS, 67 (59%) patients were treated with hormonal suppression and 46 (41%) were not. There were no significant differences in treatment choices across all EMS groups: 22, 13, and 16 patients were treated with oral contraceptive pills (OCP); 1, 1, and 4 patients used progesterone only pills (POP); and 3, 0, and 7 patients received IV estrogen in groups 1, 2, and 3 respectively (p = 0.061). To compare treatment outcomes, we analyzed the 44 patients who were admitted to the hospital, of which 34 (77.3%) had PUS. The distribution of treatments was evenly spread throughout the three EMS groups (p = 0.34). There were no significant differences with respect to the amount of time it took bleeding to either significantly taper down or stop completely after initiating treatment (p = 0.227, p = 0.211, p = 0.229, respectively for OCP, POP, and IV estrogen).

CONCLUSIONS: In adolescents with HMB in the ED, performing a PUS did not affect treatment decisions or outcomes. Providers may want to reconsider ordering PUS in adolescents who present for this purpose, as unlike in adults, structural abnormalities are rare and there does not appear to be utility in treating based on the EMS.
common urogenital sinus opening showed in imaging results. In 11 cases of DSD no vagina was displayed.

CONCLUSIONS: MRI and ultrasonography examination is effective at detection of dysplasia gonads, uterus and vagina, in combination with clinical manifestations, pathology is valuable in improving the diagnosis and treatment of patients with disorder of sex development.

THE UTILITY OF REPEAT SALINE INFUSION SONO-HYSTEROGRAM (SIS) IN THE INFERTILITY WORKUP. Andrey V. Dolinko, MD,1 Valery A. Danilack, PhD, MPH,2 Ruben J. Alvero, MD,3 Victoria V. Snegovskikh, MD.4 1Women and Infants Hospital and Warren Alpert Medical School of Brown University, Providence, RI; 2Stanford University, Palo Alto, CA.

OBJECTIVE: The purpose of this study is to evaluate the utility of repeat SIS prior to fertility treatment cycles (FTC) and to identify risk factors for uterine abnormality recurrence or the development of new abnormalities after initially normal imaging.

DESIGN: Retrospective cohort study of women undergoing initial infertility workup and treatment at a single institution who had at least two imaging studies performed 1/1/2007-12/31/2017.

MATERIALS AND METHODS: Initial imaging included hysterosalpingography and/or SIS, while repeat imaging ≥9 months later included only SIS. Patient characteristics, imaging results, and FTC data were abstracted from patient charts and a clinical IVF database. Analysis was stratified by initial imaging result: normal or abnormal. In each stratum, result of repeat imaging was compared to patient characteristics using Chi-square test, t-test, or Wilcoxon Rank Sum test.

RESULTS: Of 1163 patients identified, 436 were eligible for study inclusion. Of these, 318 (72.9%) had normal initial imaging and 118 (27.1%) had abnormal initial imaging. Among the former, 22% had an abnormal repeat SIS; among the latter, 54% had an abnormal repeat SIS (p < 0.0001, RR 2.39 (95% CI 1.83-3.12)). On average, 22.6±13.9 months passed between imaging studies. In both groups, women with abnormal repeat SIS were older than those with normal repeat SIS (p<0.01). Women with normal initial imaging were more likely to have had a live birth in the interim if their repeat imaging was normal (29.9 vs 6.7%, p<0.001), an association that did not hold for women with abnormal initial imaging (26.1 vs 18.0%, p=0.338).

Regardless of initial imaging outcome, there was no association found between repeat imaging outcomes and total number of FTCs [IVF, FET, ovulation induction, or natural cycle (timed intercourse or IUI)] performed, max total gonadotropins used, or maximum peak estradiol level between imaging studies.

FERTILIZATION AND EMBRYO TRANSFER. Yunfei Long, PhD,1 Rong Liang, PhD,2 Jiabin Zhang, PhD,1 Fang Fang, MD,1 Cheng Cheng, MB,1 Qun Lu, MD,1 Jue Zhang, PhD,1 Jiachen Zhang, PhD,1 College of Engineering, Peking University, Beijing, China; 2Center of Reproductive Medicine, Peking University People’s Hospital, Beijing, China; 3Academy for Advanced Interdisciplinary Studies, Peking University, Beijing, China.

OBJECTIVE: Uterine peristalsis has been reported to influence pregnancy chances in both natural and artificial cycles, but it is not convenient to observe clinically. Moreover, there is no tool for evaluating endometrial receptivity by invisible peristalsis of the uterus. We aim to identify the existence of a new phenomenon which is defined as uterine micro-peristalsis (UMP) by ultrasound video features, and to investigate the association between UMP and outcome of in vitro fertilization and embryo transfer (IVF-ET).

DESIGN: A prospective research study.

THE UTILITY OF REPEAT SALINE INFUSION SONO-HYSTEROGRAM (SIS) IN THE INFERTILITY WORKUP. Andrey V. Dolinko, MD, Valery A. Danilack, PhD, MPH, Ruben J. Alvero, MD, Victoria V. Snegovskikh, MD. Women and Infants Hospital and Warren Alpert Medical School of Brown University, Providence, RI; Stanford University, Palo Alto, CA.

OBJECTIVE: The purpose of this study is to evaluate the utility of repeat SIS prior to fertility treatment cycles (FTC) and to identify risk factors for uterine abnormality recurrence or the development of new abnormalities after initially normal imaging.

DESIGN: Retrospective cohort study of women undergoing initial infertility workup and treatment at a single institution who had at least two imaging studies performed 1/1/2007-12/31/2017.

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Regardless of initial imaging outcome, there was no association found between repeat imaging outcomes and total number of FTCs [IVF, FET, ovulation induction, or natural cycle (timed intercourse or IUI)] performed, max total gonadotropins used, or maximum peak estradiol level between imaging studies.

FERTILIZATION AND EMBRYO TRANSFER. Yunfei Long, PhD, Rong Liang, PhD, Jiabin Zhang, PhD, Fang Fang, MD, Cheng Cheng, MB, Qun Lu, MD, Jue Zhang, PhD, College of Engineering, Peking University, Beijing, China; Academy for Advanced Interdisciplinary Studies, Peking University, Beijing, China.

OBJECTIVE: Uterine peristalsis has been reported to influence pregnancy chances in both natural and artificial cycles, but it is not convenient to observe clinically. Moreover, there is no tool for evaluating endometrial receptivity by invisible peristalsis of the uterus. We aim to identify the existence of a new phenomenon which is defined as uterine micro-peristalsis (UMP) by ultrasound video features, and to investigate the association between UMP and outcome of in vitro fertilization and embryo transfer (IVF-ET).

DESIGN: A prospective research study.
CONCLUSIONS: Despite overall low fertility rates, IUI remains a common first step in the management of infertility given ease of treatment and low cost. Our device and study design failed to show a significant increase in sperm retention above conventional IUI technique. Notable, and not a surprising finding, is a decrease in semen reflux (sperm loss) after routine IUI; suggesting further research is warranted to improve IUI efficiency. Guiding future efforts, the finding of a significant correlation of sperm retention with extended device placement suggests a need to place and retain a therapeutic device for a prolonged period. Further, this study design suggests viability of using pre- and post-IUI vaginal washing technique for future studies.


SUPPORT: NA.

P-631 Wednesday, October 16, 2019 6:30 AM

A MULTI-CENTRIC, PROSPECTIVE TEST OF CAP-SCORE™ ABILITY TO PREDICT A MAN’S PROBABILITY OF GENERATING PREGNANCY. Jay S. Schinfeld, MD, FACOG,1 Randy S. Morris, MD,1 Giampiero D. Palermo, M.D., Ph.D.2 Zev Rosenswaks, M.D., John E. Nichols, Jr., MD,3 Fady I. Sharara, M.D.4 Eric K. Seaman, MD, Cristina Cardona, Ph.D.5 G Charles Ostermeier, PhD,6 Alexander J. Travis, VMD, PhD.7 Abington Reproductive Medicine, Abington, PA;8 TVF1, Naperville, IL; 9 The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weil Cornell Medicine, New York, NY; 10Piedmont Reproductive Endocrinology Gynec, Greensville, SC; 11Virginia Center for Reproductive Medicine, Reston, VA; 12New Jersey Urology, Short Hills, NJ; 13Androvia LifeSciences, Mountainside, NJ; 14Cornell University, Ithaca, NY.

OBJECTIVE: Semen analysis lacks an evaluation of fertilizing ability, and fails to diagnose many cases of male factor infertility. Previously, Cap-Score™, the percentage of sperm that can capacitate, showed strong correlations with male fertility (retrospective and cohort comparison studies), and prospectively identified low versus normal fertility using a simple cut-off. However, male fertility is a continuum; logistic regression based on clinical pregnancy outcomes related how Cap-Score relates to the probability of generating a pregnancy (PGP) in 3 cycles (Schinfeld et al, 2018; n=124; 5 clinics). Here, we prospectively tested the relationship between the predicted PGP and actual intratubal insemination (IUI) outcomes.

DESIGN: A multicentric prospective test of the PGP model’s ability to predict pregnancy. IUI was used as the experimental model to ensure collection of outcomes and provide control over number and timing of inseminations relative to ovulation. For inclusion, men had to have ≥ 3 million cells post-wash, and female partners could not have factors precluding IUI, e.g., tubal occlusion, hydroosalpinges.

MATERIALS AND METHODS: Studies approved by Weill Cornell’s IRB (1210013187) or WIRB (20152233). Cap-Score and outcomes were obtained from 6 clinics (n=292). A total of 128 finished treatment (pregnant or ≥ 3 IUIs). The PGP model was tested in two ways. First, the new outcomes were added to the prior 124 and the model was calculated to determine change. Second, the 128 new outcomes were divided into rank-ordered groups of roughly equal size. When split into 5 groups, each had 25-26 observations; when split into 6 groups, each contained 21-22 observations. The proportion of individuals successfully generating pregnancy within a group was compared to the average predicted PGP within a group (linear regression).

RESULTS: Only a slight change (average 2.6%) from the original model (PGP=1/[1+exp[-2.86+0.08*Cap-Score]]; n=124; p<0.01) was noted when new data were added (PGP=1/[1+exp[-2.26+0.06*Cap-Score]]; n=252; p<0.001), and fit improved. When predicted PGP were compared to observed pregnancies, significant linear relationships were seen for n=5 (y=0.81x+0.10; R²=0.84; p=0.03) and n=6 (y=0.69x+0.14; R²=0.86; p<0.01). The slopes were not different from 1 and intercepts were not different from 0 (p>0.05; t-tests).

CONCLUSIONS: Despite the potential for introducing noise when using cases from diverse settings, there was no significant change upon doubling the data set. A 1:1 relationship was detected between predicted PGP and the observed proportion of men generating pregnancy. These results further demonstrate the strong association between Cap-Score, sperm function/fertilizing ability, and the ability to generate pregnancy.


LGBTQ REPRODUCTIVE ISSUES

P-632 Wednesday, October 16, 2019 6:30 AM

QUALITY OF LIFE AFTER FERTILITY PRESERVATION AMONG TRANSGENDER PEOPLE. Amanda Adeleye, MD,1 Garrett Michael Reid, BS,2 Yiu Ho Au, B.S,3,4 J. A. M. E. S. F. SMITH, M.D.5 Evelyn Mok-Lin, MD6 UCSF REI fellow, San Francisco, CA; 7REI UCSF, Center for Reproductive Health, San Francisco, CA; 8University of California, San Francisco, SAN FRANCISCO, CA.

OBJECTIVE: There are limited data on the quality of life among transgender people who sought fertility preservation or family building. This pilot study sought to describe the quality of life among transgender people who sought fertility services through the Gender Expansive Attitudes about Reproductive Health (GEAR) study.

DESIGN: Cross-sectional survey.

MATERIALS AND METHODS: This survey queried transgender people who underwent ovarian stimulation or semen cryopreservation at an academic medical center between January 1, 2015 and March 31th, 2019. Enrollment is ongoing. Primary outcomes included the number of healthy days and depressed/anxious days as measured by the CDC health related quality of life survey and whether or not ovarian stimulation or semen cryopreservation was emotionally challenging. Primary outcomes were compared by gender identity and ease of gamete collection using a Fisher’s Exact or Wilcoxon Rank-Sum test when appropriate.

RESULTS: Among 40 transgender people who presented for care, 18 initiated the survey and 16 completed the survey (n=12 transfeminine people, n=4 transmasculine people). The median number of healthy days for the entire cohort was 21 (IQR 15.5-25.5). Transmasculine people experienced more healthy days than transfemini- nite participants (p<0.01). There were no associations between gender identity and the number of depressed or anxious days (p=0.09 and 0.14 respectively.)

Fourteen participants completed the survey about the ease of gamete collection. The majority of people, 64.3% (n=8 transfeminine women, n=1 transman) found the process of ovarian stimulation or sperm cryopreservation “not at all difficult” or “neither difficult or easy.” Five participants (n=4 transfeminine women, n=1 transman) found the process “somewhat difficult” or “very difficult.” The ease or difficulty of fertility preservation was not associ- ated with either gender identity (p=0.604) nor the number of healthy days, depressed days or anxious days (p=0.688, 0.528 and 1.00 respectively).

CONCLUSIONS: In this pilot study, transmasculine people experienced more healthy days compared to transfeminine people. Gender identity was not associated with the number of depressed or anxious days. Whether or not participants found the process of ovarian stimulation or sperm cryopreservation emotionally difficult, was not associated with quality of life metrics.

SUPPORT: None.

P-633 Wednesday, October 16, 2019 6:30 AM

IUD CHOICE IN TRANSGENDER AND GENDER DIVERSE INDIVIDUALS. Lauren Abern, MD,1 Glen DeGuzman, MD,2 Jake Cook, BA,3 Kristen Kiely, WHNP-BC,4 Karla Maguire, MD, MPH,4 Harvard Vanguard Medical Associates, Somerville, MA; 5University of Nevada Las Vegas School of Medicine, Las Vegas, NV; 6Phillly FIGHT, Philadelphia, PA; 7University of Miami, Miami, FL.

OBJECTIVE: Although use of the intrauterine device (IUD) is increasing, the appeal among transgender and gender diverse individuals is unknown. Our objective is to assess the reasons IUD users in this population are choosing one of the five FDA-approved devices available and if they are satisfied.

DESIGN: Cross-sectional, survey-based study.
MATERIALS AND METHODS: Transgender and gender diverse individuals assigned female at birth age 18 and older that currently have an IUD participated in an online survey about reproductive history, rationale for IUD choice, unwanted side effects, and satisfaction.

RESULTS: The mean age was 25.8 (SD 4.7) (14 (16%) identified as transgender, 70 (82%) as genderqueer or non-binary, and 1 (1%) as agender. The majority (71 (85%)) was white and had minimum of a college education (47, 55%), 72 (85%) were sexually active, and 63 (88%) were at risk for pregnancy. 62 (73%) chose a 52mg-Levonorgestrel (LNG) IUD (Mirena®/Liletta®), 5 (6%) the lower dose IUDs (Kyleena®/Skyla®), and 17 (20%) the copper IUD (Paragard®).

Menstrual manipulation was the main reason for choosing a 52mg-LNG IUD (35, 56%). Other influential factors included how long the IUD lasted (39, 63%), provider recommendation (28, 45%), and to avoid side effects experienced from other methods of contraception (28, 45%). (49, 33%) experienced unwanted side effects including missing cramping (8, 33%), pelvic pain (7, 29%), bloating (7, 29%) and weight gain (7, 29%). 6 (25%) reported these side effects within the first 0-6 months. 6 (25%) desired removal. Of those that desired removal, 2 (33%) would opt for another IUD.

The main reasons for choosing the lower dose IUDs were the size of IUD (2, 40%), and lower hormone dose (2, 40%). Other influential factors included insurance coverage (4, 80%), how long the IUD lasted (4, 80%), and menstrual manipulation (3, 60%). 2 (40%) experienced unwanted side effects including heavy bleeding (2, 100%), worsening cramping (2, 100%), and pelvic pain (2, 100%). 1 (50%) reported these side effects within the first 3-6 months. Neither (2, 100%) desired removal.

The majority of participants selecting the copper IUD did so to avoid hormones (12, 71%). Other influential factors included how long the IUD lasted (12, 80%), to avoid side effects experienced by other methods of contraception (9, 60%), and provider recommendation (6, 40%). 10 (67%) stated they were experiencing unwanted side effects including irregular bleeding (7, 70%) and worsening cramping (5, 50%). 4 (40%) reported these side effects in the first 0-6 months. However, only 12 (20%) desired removal, and both would opt for another type of IUD.

CONCLUSIONS: Of the IUD options available, the majority of transgender and gender diverse individuals surveyed opted for a 52mg-LNG IUD and chose this specific IUD type for menstrual manipulation. Although side effects were experienced with all options, many occurred within the first 6 months, and few desired removal. As a result, providers should counsel this population about the benefits of an IUD as well as expected side effects including those that should resolve over time.

P-634 Wednesday, October 16, 2019 6:30 AM

FERTILITY PRESERVATION KNOWLEDGE AMONG TRANSGENDER WOMEN: PRELIMINARY FINDINGS FROM THE GEAR STUDY. Amanda Adeeleye, MD, Garrett Michael Reid, BS, Yi-Ho Au, B.S., J. A. M. E. S. F. Smith, M.D., a Evelyn Mao Lin, MD, a REI UCSF, Center for Reproductive Health, San Francisco, CA; bUniversity of California, San Francisco, SAN FRANCISCO, CA.

OBJECTIVE: The American Society of Reproductive Medicine and the Endocrine society guidelines recommend a discussion about fertility prior to the commencement of gender affirming hormonal therapy (HT). There are limited data about how transgender people obtain this information and their understanding of HT on their fertility. This pilot study sought to describe transgender and gender diverse individuals surveyed for a 52mg-LNG IUD and chose this specific IUD type for menstrual manipulation. Although side effects were experienced with all options, many occurred within the first 6 months, and few desired removal. As a result, providers should counsel this population about the benefits of an IUD as well as expected side effects including those that should resolve over time.

RESULTS: Among 40 eligible patients, 12 transgender women completed the survey. Seventy-five percent (n=9) of transgender women cited the internet as their most useful resource, however there was no difference in the preferred educational resource and the answer to this question (p=0.545). Although sperm can be retrieved through surgical means when necessary, the majority of participants 83.3% (n=10) believed that ejaculation was required for sperm cryopreservation. There were no differences in participant answers by their preferred educational resource.

CONCLUSIONS: In this pilot study, the majority of transgender women obtained their information about fertility preservation from the internet. A minority of transgender women had misconceptions about their fertility potential after starting HT. Future studies may consider targeting the fertility knowledgebase among transgender women.

SUPPORT: None.

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IN VITRO FERTILIZATION (IVF) OUTCOMES IN GAY AND SINGLE WOMEN USING DONOR SPERM. Sara E. Barton, M.D., Sue McCormick, BS, William B. Schoolcraft, MD, Mandy G. Katz-Jaffe, Ph.D., Colorado Center for Reproductive Medicine, Lone Tree, CO.

OBJECTIVE: To describe the IVF outcomes in gay and single women using donor sperm.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: The first IVF oocyte retrieval in women using donor sperm due to lack of a male partner from January 1, 2016 to December 31, 2018 were reviewed at a single IVF center. Women with ≥ 3 failed IVF attempts at a previous clinic or >1 failed IVF attempt at our center, oocyte donation, and transfers to a gestational carrier were excluded.

The primary outcome was ongoing pregnancy rate. Secondary outcomes are listed in Table 1. Additionally, we calculated the odds of having no embryo transfer [women with failed blastocyst development or no euploid embryos in cycles where preimplantation genetic testing for aneuploidy (PGT-A) was performed]. Results are expressed as odds (%) and in median (range) where applicable.

RESULTS: 90 women met study inclusion criteria (n=32 gay women with a female partner; n=58 single women). The median maternal age was 40.0 (25-47) years. 28 women (31.1%) did not have an embryo transfer. The ongoing pregnancy rate was 45.6% (41/90) per oocyte retrieval and 66.1% (41/62) per transfer. One patient experienced a pregnancy loss after fetal cardiac activity was detected (2.4%) (Table 1).

Of the 90 women included, 86 women had a freeze-all cycle (84 for PGT-A; 2 for other indications) and the remaining 4 women had a fresh transfer. In the freeze-all group for PGT-A, 21.4% (18/84) had no euploid embryos, and 11.9% (10/84) had no blastocyst development; therefore 32.6% (28/86 freeze all cycles) did not have a transfer. The median maternal age of those with no blastocyst development was 43 (range 40-45) years and no euploid embryos 42.5 (35-47) years, significantly older than women who had an embryo transfer [39 (25-45) years, P<0.05].

CONCLUSIONS: It is possible that women using IVF for lack of a male partner presented at advanced maternal age. While the outcomes of this study suggest this population may have favorable livebirth rates compared to infertile women of the same age, female age remains a strong predictor of a failed cycle. Women presenting to infertility clinics at advanced reproductive ages should be counseled regarding the negative impact of age on fertility, regardless of previous fertility attempts. These data should be useful to guide counseling in gay and single women pursuing IVF treatment without prior infertility.

REFERENCE: None.

SUPPORT: None.

TABLE 1. Outcome variable

| N=90 | # oocytes retrieved | 16 (2-44) | # fertilized oocytes (2PN) | 8 (1-28) | # usable blastocysts | 2 (0-15) | Positive HCG | 82.5% | Implantation rate (FHT) | 62.3% | Ongoing pregnancy rate per FET | 66.1% | Ongoing pregnancy rate per retrieval | 45.6% | Miscarriage rate | 2.4% |

*results displayed as median (range) or odd (%)
MALE REPRODUCTION AND UROLOGY

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DELTA-9 THC CAN BE DETECTED AND QUANTIFIED IN THE SEMINAL FLUID OF MEN WHO ARE CHRONIC USERS OF INHALED CANNABIS. Malinda S. Lee, MD, MBA, Andrea Lanes, PhD, Elizabeth S. Ginsburg, MD, Janis H. Fox, MD, Brigham and Women's Hospital, Boston, MA.

OBJECTIVE: To detect whether delta-9-tetrahydrocannabinol (THC) and THC metabolites can be identified and quantified in human seminal fluid.

DESIGN: Proof-of-concept study in which serum, urine and semen testing was conducted in 12 male chronic users of inhaled cannabis.

MATERIALS AND METHODS: Healthy men aged 18-45 years who identified as chronic and heavy users of inhaled cannabis (at least 4 times per week for at least one year) were eligible to participate. Eligibility screening took place via structured phone interviews and preceded a single study visit performed at Brigham and Women's Hospital, Boston, Massachusetts. Participants were asked to abstain from ejaculation for 48-72 hours prior to their study visit, and to use cannabis within 24 hours of their visit. After informed consent was obtained, participants provided urine, semen and serum samples on site. 

Seminal analyses were performed as standard practice, using a Hamilton-Thorn IVOS Semen Analyzer. The remaining ejaculate, as well as the urine and serum samples, were frozen and stored at -80 degrees C. Cannabinoid assay testing in all three fluid matrices was performed through high performance liquid chromatography/tandem mass spectrometry by NMS Labs (Wilton, PA). Serum and semen were tested for THC (the primary active component of cannabis), 11-hydroxy delta-9 THC (11-OH-THC, the main psychoactive metabolite of THC), and delta-9 carboxy THC (THC-COOH, an inactive metabolite of THC). Urine was tested for THC-COOH, the main metabolite of THC in urine, as well as creatinine to provide a normalized ratio.

RESULTS: The median age and BMI of participants was 27.0 years and 24.7 kg/m2, respectively. Over half the participants were daily users of cannabis and had been using cannabis marijuana for over five years. On average, participants used cannabis 10 hours prior to their study visit and abstained for 53 hours from their last ejaculation. The median sperm concentration, motility and morphology was 75.5 million/mL, 69.5% and 5.5%, respectively. Urinary THC-COOH was detected in all 12 participants, whereas at least one serum THC metabolite was present in 10 of 12 participants. Two semen samples had insufficient volume to be analyzed. Delta-9 THC was above the reporting level of 0.50 ng/mL in the seminal fluid of two of the remaining ten participants. The major downstream THC metabolites were not detected in any of the semen samples. Seminal delta-9 THC was moderately correlated with serum levels of delta-9 THC (r = 0.66), serum 11-OH-THC (r = 0.57), and serum THC-COOH (r = 0.67). Seminal delta-9 THC was not correlated with urinary cannabinoid levels or semen analysis parameters.

CONCLUSIONS: This is the first study to report that delta-9 THC can be identified and quantified in human seminal fluid. Seminal delta-9 THC was found to be moderately correlated with serum THC and THC metabolites.

SUPPORT: This study was funded by the Expanding the Boundaries Grant from the Dept. of Obstetrics, Gynecology & Reproductive Biology, Brigham and Women’s Hospital.

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COMPREHENSIVE GENE EXPRESSION ANALYSIS BY RNA SEQUENCING OF TESTICULAR TISSUE EXOSOMES IN AZOOSPERMIC MEN: PREDICTING THE PRESENCE OF SPERM. Joshua Stewart, M.D., Michael H. Dahan, MD, a Jacques Balayla, M.D., a Naama Steiner, M.D., a Alexander Volodarsky-Perel, M.D., a Weon-Young Son, Ph.D, Alexander Volodarsky-Perel, M.D., a Weon-Young Son, Ph.D, a Malin Salomon-Dixon, Ph.D, a McGill University, Montreal, QC, Canada; aAffiliation not provided; aMcGill University Health Centre, Montreal, QC, Canada; aDivision of Reproductive Endocrinology and Infertility, McGill University Health Care Centre, Montreal, QC, Canada; aSenior Lecturer, Ariel, Israel.

OBJECTIVE: To isolate and characterize exosomes1, extracellular vesicles containing functional biomolecules, from testicular tissue in azoospermic men and to perform gene expression analysis in order to classify exosomes within the testicular germinal epithelium to predict spermatogenic reserve.

DESIGN: A case and control prospective study.

MATERIALS AND METHODS: A total of 17 surgically retrieved testicular specimens from 17 subjects (13 non-obstructive azoospermia (NOA); 7 with sperm identified at testicular biopsy and 6 with no sperm identified; 4 obstructive azoospermia (OA), all with retained spermatogenesis) were obtained from consenting men from March 2018 to August 2018. Exosome isolation was performed by a standardized differential ultracentrifugation protocol. Nanoparticle tracking analysis was used for characterization of exosome size and concentration. Protein concentration was measured by BCA assay and mass spectrometry proteomics analysis was performed. Gene expression was determined by RNA sequencing. Sequences were queried against the Homo sapiens reference genome and filtered of contaminants. The Wald test and ANOVA were used to determine significance.

RESULTS: The total number of isolated exosomes was 71×10^9/mL specimen volume with a mean size of 129 nm. Global transcriptional change in men with OA (retained spermatogenesis) was compared to men with NOA and no sperm identified at the time of testicular biopsy by analysis of 17,571 genes. A single gene (POS) was found to be significantly upregulated in the exosomes of men with retained spermatogenesis as compared to those without sperm identified (log fold change: 5.89, p-value 0.049). Paradoxically, within the overall NOA cohort, the majority of genes were significantly upregulated in the testicular exosomes of men that had no sperm identified at the time of biopsy compared to those with sperm identified (1,005 genes significantly upregulated, 147 significantly downregulated, p-value <0.05), including retinoic acid signaling mediators and regulators of the self-renewal capacity of germline cells. Furthermore, both groups within the NOA cohort had unique protein expression profiles with 1,926 proteins specific to men with NOA and retained spermatogenesis as compared to men with no sperm identified at the time of biopsy.

CONCLUSIONS: Investigators have identified many potential biomarkers in male infertility and spermatogenesis, few clinical applications have been identified currently. We show that the testicular germinal epithelium secretes exosomes, which carry unique gene expression profiles in azoospermic men with and without retained spermatogenesis. Specifically, we identify a single gene (POS) essential for germine specification which is significantly upregulated in the exosomes of men with retained spermatogenesis. These transcripts may serve as a biomarker for spermatogenesis, as well as the functional capacity of spermatogenesis. Furthermore, the molecular expression of testicular tissue exosomes indicates that these extracellular vesicles may interact with the germinal epithelium in order to ordain new waves of spermatogenesis.


SUPPORT: None.

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AN AGE-BASED NOMOGRAM BASED ON CUT OFF VALUES OF SEMEN ANALYSIS RESULTS, FROM 2010 WHO REFERENCE VALUES FOR SEMEN CHARACTERISTICS. Guy Shrem, M.D., a Michael H. Dahan, MD, a Jacques Balayla, M.D., a Naama Steiner, M.D., a Alexander Volodarsky-Perel, M.D., a Weon-Young Son, Ph.D, a Malin Salomon-Dixon, Ph.D, a McGill University, Montreal, QC, Canada; aAffiliation not provided; aMcGill University Health Centre, Montreal, QC, Canada; aDivision of Reproductive Endocrinology and Infertility, McGill University Health Care Centre, Montreal, QC, Canada; aSenior Lecturer, Ariel, Israel.

OBJECTIVE: To create a nomogram for sperm parameters along with the male life.

DESIGN: A retrospective evaluation of all records of Computer-Assisted Semen Analysis (CASA) (and human-verified) performed between January 2009 to December 2018 at a University Health Center.

MATERIALS AND METHODS: We encountered 17,915 CASA at all centers. Samples that did not meet the WHO lower reference limit [1] (concentration ≥15 million/mL, motility ≥40%, morphology ≥4%) were excluded, leaving 8045 samples.

RESULTS: For concentration, percentiles 25th to 75th of the population had a three-phasic pattern reflecting an increase in sperm concentration until around age 30 years, followed by a plateau in sperm concentration until age 45 years, and then a decrease in sperm concentration begins. For sperm motility, 50-95th percentiles demonstrate a triphasic distribution with an increase until 30 years of age, a plateau until the age of 40 years and...
then a decrease in motility. In the groups of two lowest percentiles (10th and 25th), a modest decrease begins at age 30 years, whereas a steeper slope is seen after the age of 40 years.

For sperm morphology, there are two different phasic trends. The 50th percentile and above exhibit a decrease in normal morphology throughout the twenties, subsequently values stabilize. Opposed to this trend, the groups of two lowest percentiles (10th and 25th) have stable low morphology values up to the 7th decade. CONCLUSIONS: Males have the best semen parameters from age 30-40 years. This may be acting as a compensatory mechanism to obtain pregnancy with female fertility falling at this age.


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YO® HOME SPERM TEST’S MOTILE SPERM CONCENTRATION AND YO SCORE™ CORRELATES WITH AUTOMATED SEMEN ANALYSIS™

RESULTS. Stan Honig, MD, a Lev Rabinovitch, PhD, b Natan Bar-Chama, MD. a Yale University, New Haven, CT; b Medical Electronic Systems, Caesarea Industrial Park, Israel; c Icahn School of Medicine at Mount Sinai, New York, NY.

OBJECTIVE: To evaluate the accuracy of the YO® Home Sperm Test (“YO”) motile sperm concentration (MSC) and YO SCORE™ results in the hands of TRAINED professionals as compared to the SQA-V automated laboratory sperm analyzer (Medical Electronic Systems).

DESIGN: Multi center, Double-blind prospective study.

MATERIALS AND METHODS: 316 human semen samples were tested by TRAINED professionals at three sites utilizing the YO Home Sperm test kit. In parallel, the same samples were tested on the SQA-V automated semen analyzer (Medical Electronic Systems). Samples were collected, liquefied, split and run in a blinded fashion. TRAINED professionals ran the YO test using the YO device (mini-microscope) on either a Galaxy or iPhone Smartphone following the YO app. instructions. YO automatically reports (a) LOW MSC <6m/mL or MODERATE/NORMAL MSC ≥ 6m/mL, and (b) a YO SCORE displayed as a two-digit integer, from 10 to 90+. MSC centile levels derived from the 2010 WHO 5th edition Table A1-2 of semen parameter centile distribution for recent fathers. The YO MSC results from the TRAINED professionals were analyzed statistically vs. the SQA-V based on negative and positive percent agreement (NPA and PPA). The TRAINED professional YO SCORE results were analyzed for accuracy vs. SQA-V semen quality groupings with an allowance of ± one YO SCORE deviation.

RESULTS: The YO device demonstrated high levels of PPA, NPA and accuracy when TRAINED professional MSC levels were compared vs. SQA-V results: 97.6%, 97.0% and 97.3% respectively with inter-site CV ≤ 2%; YO SCORE results obtained by TRAINED professionals demonstrated an overall accuracy of 94.3% for distinguishing between MSC semen quality groups which were established based on SQA-V MSC.

CONCLUSIONS: Using the YO® Home Sperm Test TRAINED professionals showed a high level of accuracy for motile sperm concentration when compared to the SQA-V automated laboratory sperm analyzer in 316 semen samples. This study also demonstrated that the YO SCORE is a reliable tool for defining different motile sperm concentration categories.

TABLE 1

<table>
<thead>
<tr>
<th>Site Name, Location</th>
<th>N</th>
<th>PPA</th>
<th>NPA</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Xytext Corporation, Augusta, GA</td>
<td>82</td>
<td>100.0%</td>
<td>98.2%</td>
<td>99.1%</td>
</tr>
<tr>
<td>Xytext Corporation, New Brunswick, NJ</td>
<td>136</td>
<td>97.0%</td>
<td>97.1%</td>
<td>97.1%</td>
</tr>
<tr>
<td>Medical Electronic Systems, Caesarea, IL</td>
<td>98</td>
<td>96.2%</td>
<td>95.8%</td>
<td>96.0%</td>
</tr>
<tr>
<td>OVERALL</td>
<td>316</td>
<td>97.6%</td>
<td>97.0%</td>
<td>97.3%</td>
</tr>
</tbody>
</table>

YOUTH SCORE Agreement TRAINED vs. SQA-V

<table>
<thead>
<tr>
<th>SQA-V Semen Quality Group</th>
<th>SQA-V MSC Range, 10^6/mL</th>
<th>YO SCORE</th>
<th>YO SCORE Accuracy vs. SQA-V</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOW (n = 90)</td>
<td>0 - &lt;6</td>
<td>0</td>
<td>96.7%</td>
</tr>
<tr>
<td>LOW NORMAL (n = 55)</td>
<td>6 – 30</td>
<td>10 – 30</td>
<td>94.5%</td>
</tr>
<tr>
<td>AVERAGE NORMAL (n = 78)</td>
<td>32 – 60</td>
<td>40 – 60</td>
<td>93.6%</td>
</tr>
<tr>
<td>HIGH NORMAL (n = 93)</td>
<td>63 – &gt;94</td>
<td>70 – &gt;90</td>
<td>92.5%</td>
</tr>
<tr>
<td>OVERALL (n = 316)</td>
<td></td>
<td>70 – &gt;94</td>
<td>94.3%</td>
</tr>
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</table>

Reference: None.

SUPPORT: Medical Electronic Systems.

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FERTILITY AND INFERTILITY TREATMENT KNOWLEDGE AMONG MEN AGED 18-50 IN THE U.S.

Parker H. Murray, MS4, a Rashmi Kudesia, MD, b Texas College of Osteopathic Medicine, UNTHSC, Fort Worth, TX; c CCRM Fertility Houston, Houston, TX.

OBJECTIVE: To validate the Fertility and Infertility Treatment Knowledge Scale (FIT-KS) among men aged 18-50 in the United States, and to assess fertility knowledge among men in the general population, with comparison to the female population in the original validation study.

DESIGN: Cross-sectional web-based survey study.

MATERIALS AND METHODS: An online survey with format identical to that previously constructed for the original FIT-KS validation study was administered to English-fluent men aged 18-50 residing in the United States. STATA v15.1 was used to compute descriptive statistics, and conduct analyses, including the Student’s t, Pearson’s r, and Kruskal-Wallis tests, to assess for correlation to demographics and comparison between the male and female cohorts. The study received IRB exemption.

RESULTS: In preliminary analysis, 99 men completed the survey, with median age 30 [28, 37]; 50 (50.5%) were single, with 14 (14.1%) in a relationship, 33 (33.3%) married, 2 (2%) divorced. Most (65.7%) had no children, and identified as White (74.8%), with 9.1% Hispanic or Asian, and 7.1% Black. The majority (89.9%) reported an annual household income at or below $100k, and 60.6% held a college or higher degree.

The mean FIT-KS score was 12.3 +/- 0.34 (out of 29, 42.4% correct). Increasing age was the only significant demographic predictor of higher FIT-KS score (p = 0.002). In item analysis, notable findings include: though 74 (74.8%) knew at which ages women are most fertile, many (48.5%) overestimated age of maximal fertility decline, fecundability at age 50 (63.6%) or at age 40 (71.7%), and 74.7% underestimated the spontaneous miscarriage rate. Only 6.1% agreed that men can contribute to a couple’s infertility, though 25.3% acknowledged male age could impact fertility. Only 17.2% knew how long sperm survive in the female reproductive tract. A majority were generally aware of lifestyle issues that impact fertility, though 31.3% knew about lubricants. When asked about IVF, 19.2% overestimated success rates at female age 35 and 85.9% at age 44. The twin rate was underestimated by 70.7%, and 95% overestimated success rates for oocyte cryopreservation.

When compared to the original validation cohort, men in this sample scored lower than women on total FIT-KS score (12.3 +/- 0.34 vs. 16.2 +/- 0.32), as well as in natural fertility and infertility treatment sub-sections (all p < 0.0001).

CONCLUSIONS: These preliminary results uphold the conclusion that fertility knowledge in the general population is low. Though the validation analysis for the FIT-KS in men is ongoing, these findings suggest that men also tend to overestimate natural fertility and infertility treatment success rates and underestimate risks and impact of lifestyle. Most surprising, the low rate of acknowledging the male role in infertility suggests a particular need for education in this area. Outreach efforts aimed at educating the public about fertility must target both men and women to sufficiently penetrate the general population and correct gaps in knowledge.

SUPPORT: None.

FERTILITY & STERILITY®

e361
Efficacy of antioxidant supplementation on conventional and advanced sperm function tests in patients with idiopathic male infertility. Mohamed Arafa, MD, a Ashok Agarwal, PhD, c Ahmad Majzoub, MD, c Kareem Khalafalla, MD, c Sami Alsaied, MD, c Haitham Elbardishi, MD, c Hamad Medical Corporation, Doha, Qatar; c Cleveland Clinic, CLEVELAND, OH.

OBJECTIVE: Antioxidants have long been used in the empirical treatment of infertile men. While a positive effect has been reported by a number of studies, others have failed to reproduce any benefit leading to controversy regarding their efficacy in the treatment of infertility. The aim of the present study was to evaluate the effects of antioxidant combination therapy on conventional semen parameters and advanced sperm function tests in men seeking fertility.

DESIGN: Prospective clinical trial.

MATERIALS AND METHODS: 148 patients presenting with male factor infertility to a tertiary medical center with at least one abnormal semen parameter over a period of 6 months were included. Patients with varicoceles, leukocytospermia, history of genitourinary infections, any febrile illness and exposure to chemotherapeutics were excluded.

All participants were treated with the antioxidant supplement FH-PRO (1000 mcg B12, 30mg Zinc, 140mcg Selenium, 350mg Arginine, 2000mg, 200mg Co-Q10, 120mg Vitamin C, 200IU Vitamins E) (Fairhaven Health, Bellingham, WA) for a period of 3 months. Semen analysis, sperm DNA fragmentation (SDF) (Halosperm kit, Halotech, Madrid, Spain), oxidation reduction potential (ORP) (MiOXSYS, Ayu BioScience, Englewood, CO) and hormone levels (estradiol, FSH, LH, prolactin, and testosterone) were performed on all participants initially and following treatment. Numbers (percentages) were used to report categorical values while mean ± SE to report numerical values. Results were compared using Wilcoxon Signed Ranks Test and a p value of <0.05 was considered statistically significant.

RESULTS: The mean age of study participants was 35.9 ± 0.5 years and body mass index 29.6 ± 0.4 kg/m². Compared to the pretreatment test results, there was statistically significant improvement in conventional semen parameters including sperm concentration, total and progressive motility and normal morphology after 3 months of treatment with FH-PRO. Furthermore, a significant improvement in advanced sperm function tests (SDF & ORP) was also observed following antioxidant supplementation.

CONCLUSIONS: Treatment of patients with idiopathic male infertility with FH-PRO antioxidant regimen for 3 months resulted in significant improvement in conventional semen parameters and advanced tests of sperm function. It may offer promise to the medical treatment of idiopathic male infertility.

<table>
<thead>
<tr>
<th>Table</th>
<th>Parameters</th>
<th>Pre-treatment</th>
<th>Post-treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Semen volume (ml)</td>
<td>3.18 ± 0.12</td>
<td>3.12 ± 0.11</td>
</tr>
<tr>
<td></td>
<td>Sperm concentration (10⁶/ml)</td>
<td>22.23 ± 2.01</td>
<td>30.57 ± 2.26*</td>
</tr>
<tr>
<td></td>
<td>Total motility (%)</td>
<td>34.59 ± 1.43</td>
<td>38.47 ± 1.54*</td>
</tr>
<tr>
<td></td>
<td>Progressive motility (%)</td>
<td>4.00 ± 0.61</td>
<td>8.06 ± 0.81*</td>
</tr>
<tr>
<td></td>
<td>Normal morphology (%)</td>
<td>2.86 ± 0.19</td>
<td>3.98 ± 0.26*</td>
</tr>
<tr>
<td></td>
<td>SDF (%)</td>
<td>38.63 ± 2.10</td>
<td>32.04 ± 1.82*</td>
</tr>
<tr>
<td></td>
<td>ORP (mV/10⁶ sperm/mL)</td>
<td>10.26 ± 1.29</td>
<td>6.21 ± 1.18*</td>
</tr>
</tbody>
</table>

*P<0.05.

VARICOCELE AND TESTICULAR HYPERTHERMIA: INFRARED DIGITAL THERMOGRAPHIC MEASUREMENT OF SCROTAL AND INGUINAL TEMPERATURES AMONG VARICOCELE PATIENTS AND NORMAL CONTROLS. Kareem Khalafalla, MD, Mohamed Arafa, MD, Haitham Elbardisi, MD, Sami Alsaied, MD, Ahmad Majzoub, MD, Mohammed Mahdi, MD Hamad Medical Corporation, Doha, Qatar.

OBJECTIVE: Testicular hyperthermia has been considered the primary pathophysiology leading to spermatogenic dysfunction in patients with varicocele. This study aims to compare scrotal and inguinal temperature measurements between varicocele patients and normal controls linking such measurement with semen parameter results.

DESIGN: Prospective comparative study.

MATERIALS AND METHODS: Patients presenting with left clinical varicocele to our male infertility unit over a period of 1 year were included. The exclusion criteria were history of genitourinary infections/surgery and prior infertility related treatment. Conventional semen analysis (WHO 2010) and oxidation reduction potential (ORP) measurement (MiOXSYS, Ayu BioScience, Englewood, USA) were performed on all study participants. Controls (group I) with no varicocele and normal semen (sperm concentration ≥ 15×10⁹/ml + total motility ≥ 40% + normal morphology ≥ 4%) were recruited (n=32). Varicocele patients were classified into normal semen (group II; n=57); and abnormal semen (group III; n=22) (≥ 1 abnormal parameter). Bilateral scrotal and inguinal infrared digital thermographic imaging (FLIR E6, FLIR systems, Wilsonville, USA) was performed on patients and controls. Temperature measurements were compared between all study groups using ANOVA. Pearson’s correlation was performed to examine the link between temperature findings and different variables.

RESULTS: The study population’s mean age was 33 ± 4.5 years. Left scrotal, inguinal & right scrotal temperatures were significantly higher in varicocele patients compared to normal controls. Temperature measurements were compared between all study groups using ANOVA. Pearson’s correlation was performed to examine the link between temperature findings and different variables.

<table>
<thead>
<tr>
<th>Table</th>
<th>Parameters</th>
<th>Pre-treatment</th>
<th>Post-treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left Scrotal temp (°C)</td>
<td>33.1 ± 0.8*</td>
<td>33.2 ± 0.7</td>
</tr>
<tr>
<td></td>
<td>Right Scrotal temp (°C)</td>
<td>32.9 ± 0.9*</td>
<td>33.1 ± 0.7</td>
</tr>
<tr>
<td></td>
<td>Left Inguinal temp (°C)</td>
<td>34.3 ± 1.0*</td>
<td>34.5 ± 0.9</td>
</tr>
<tr>
<td></td>
<td>Right inguinal temp (°C)</td>
<td>33.9 ± 1.1</td>
<td>33.9 ± 0.8</td>
</tr>
<tr>
<td></td>
<td>Left Testicular size (cm³)</td>
<td>16.5 ± 5.1*</td>
<td>15.1 ± 4.8*</td>
</tr>
<tr>
<td></td>
<td>Right Testicular size (cm³)</td>
<td>16.9 ± 5.7</td>
<td>19.3 ± 7.2</td>
</tr>
<tr>
<td></td>
<td>sORP (mV/10⁶ sperm)</td>
<td>2.2 ± 1.5*</td>
<td>1.8 ± 1.2*</td>
</tr>
</tbody>
</table>

*Significance between (III) & (II); † Significance between (III) & (I).
Left scrotal temperature was significantly negatively correlated with sperm concentration (\(r = -0.268, p = 0.004\)), total motility (\(r = -0.337, p < 0.001\)), normal morphology (\(r = -0.282, p = 0.003\)) & left testicular size (\(r = -0.292, p = 0.002\)). While it was significantly positively correlated with ORP (\(r = 0.371, p = 0.001\)), left testicular temperature (\(0.521, p < 0.001\)) & right scrotal & inguinal temperatures (\(0.843, p < 0.001\); 0.521, \(p < 0.001\)).

CONCLUSIONS: Increased scrotal and inguinal temperatures are detected in patients with testicular dysfunction secondary to clinical varicocele.

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IMPACT OF COMMERCIAL SPERM SUPPLEMENTATION ON SEMINAL PARAMETERS. Megan Goodwin, MS, Kaci D. Rogers, MS, Fady I. Shara, M.D., Virginia Center for Reproductive Medicine, Reston, VA.

OBJECTIVE: Various products on the market claim to improve seminal parameters, but the impact of such supplements has not been well studied in a clinical setting. We sought to evaluate the effects of a new commercially available supplement on patients with male factor infertility.

DESIGN: Prospective.

MATERIALS AND METHODS: An initial semen analysis (SA) was performed and, if abnormalities were noted, men were started on Androferti (Innovus Pharmaceuticals, San Diego, CA), a commercial supplement in powder form, taken twice daily. Androferti is a blend of nutrients including L-Carnitine, Vitamin C, Selenium, Co-Q10, Zinc, Vitamin E, Foliate, and Vitamin B12. A second SA was then performed after a minimum of 30 days to evaluate the results of supplementation.

RESULTS: A total of 120 male patients with an abnormal initial SA and at least 30 days of taking Androferti (149.15 ± 146.26 days on average) were prospectively evaluated. Of these patients, 94 had been on Androferti for 60 or more days. There were no differences in average semen volume (2.93 vs 2.80 cc, P = NS) or concentration (46.2 vs 42.1 x10^6/cc, P = NS) between the first and second SA, but there were significant increases in sperm motility and progression (36.6% vs 40.2%, P = 0.023; 2.19 vs 2.35, P = 0.034, respectively). The average number of total motile sperm per ejaculate, however, did not differ between the first and second SA (39.6 vs 39.6 Millions, P =NS). There was also a trend towards improved strict sperm morphology after 30 days on Androferti (1.935 vs 2.74%, P = 0.061).

CONCLUSIONS: Supplementation with Androferti significantly improved sperm motility and progression, with a trend to improve strict morphology, as early as 30 days after supplementation. Future studies will evaluate whether such supplementation will improve spontaneous conception or IUI success rates.

Reference: None.

SUPPORT: None.

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REPEAT SEMEN ANALYSIS – AN UNNECESSARY DELAY IN UROLOGIC EVALUATION? Lauren Ursillo, MD, Arielle S. Yeshua, MD, Christine Mullin, MD, Avner Hershlag, MD, Weiwei Shan, MS PhD, Baruch Abittan, MD, Sarah Girardi, MD, Randi H. Goldman, MD, NYU Winthrop Hospital, Mineola, NY; Northwell, Manhasset, NY; Northwell Fertility, Zucker School of Medicine at Hofstra/Northwell, Manhasset, NY; Northwell Health Department of Biostatistics, New Hyde Park, NY; Northwell Fertility, Manhasset, NY.

OBJECTIVE: Most conventionally accepted guidelines recommend obtaining a repeat semen analysis (SA) following an abnormal initial test. The objective of this study is to determine if repeating a SA when one or more abnormal values is identified may unnecessarily delay REI referral to a Urologist by determining the likelihood that a patient with an abnormal SA will have an entirely normal SA with subsequent tests.

DESIGN: Retrospective cohort study at a single academic medical center.

MATERIALS AND METHODS: All men who underwent two or more SA (one to six months apart) from January 2016 to December 2018 at one large academic fertility center were included. Semen samples were analyzed manually by trained technicians according to 2010 World Health Organization (WHO) criteria. Normal values included concentration ≥ 15 million/mL, motility ≥ 40%, and Kruger morphology ≥ 4%. Total motile sperm concentration (TMC) was calculated by multiplying the concentration x volume x motility divided by 100 and considered normal at >20 x10^6 per ejaculate. SA parameters were sequentially analyzed for differences between the first and any subsequent SA to determine how often an abnormal SA becomes entirely normal with additional tests. We assumed that abnormalities in any SA parameter would result in Urology referral and analyses were performed with and without consideration of morphology defects.

RESULTS: Five hundred fifty first and second SA from 275 men were analyzed, each of whom had at least one defect in the first SA (Table). The most common abnormality was morphology defects. Seventy-nine percent (N=217) of men had at least one abnormality on the second test as well, while the remaining 21% had SA that normalized entirely with a second
SA, including morphology defects. When morphology defects were excluded, approximately 3/4 (73.3%) of men with an initial abnormal SA had persistently abnormal results on a second test, while the remaining 26.7% had a normal second SA. Among patients with at least two initial defects, only 8.1% had a normal second SA; when morphology defects were excluded, this figure increased to 16.4%.

CONCLUSIONS: The majority of men with abnormal semen analyses on initial testing have persistent abnormalities on repeat testing that warrant referral to Urology. Less than than 1 in 10 men with two or more defects on initial testing had a normal second SA. These results suggest that referral to a Urologist may be considered after a single abnormal SA to expedite male-factor infertility workup and treatment.

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LONG TERM SAFETY AND EFFICACY OF CLOMIPHEN CITRATE FOR THE TREATMENT OF MALE HYPOGONADISM. Devang Sharma, MD, a Sarah C. Krzastek, MD, b Natasha Abdullah, BA, c Mark I. Sultan, BS, d G Lake Machen, MD, e Jessica L. Wennel, BS, f Alex M. Ellis, BS, g Xizhao Chen, BS, h Mehraban Kavoussi, BS, j Raymond A. Costabile, MD, k Ryan P. Smith, MD, l Parviz K. Kavoussi, MD m University of Virginia, Charlottesville, VA; n Affiliation not provided; o Medical College of Wisconsin, Milwaukee, WI; p UT Austin Dell Medical School, Austin, TX.

OBJECTIVE: The aim of our study was to assess the ability of clomiphene citrate (CC), a selective estrogen receptor modulator, to maintain eugonadal testosterone levels and improve the symptoms of hypogonadism in men being treated with CC for extended periods of time.

DESIGN: A retrospective chart review was performed to identify all patients treated with CC for hypogonadism from two institutions from 2010-2018. Duration of CC therapy, serum testosterone levels, improvement in hypogonadal symptoms, and side effects while on CC were assessed.

MATERIALS AND METHODS: Hypogonadism was defined as a baseline serum testosterone < 300ng/dL. Side effects while on CC were subjectively reported by patients. As the longest duration of CC treatment in the literature to date is 3 years, patients were divided into those on CC treatment for ≤ 3 years, and those on treatment for > 3 years. Unpaired t-test was used to evaluate changes in testosterone and estradiol between groups. Fisher’s exact test was used to compare side effects, symptom improvement, and requirement for anastrozole between groups.

RESULTS: 400 patients were treated with CC from 2010-2018. Mean patient age was 39 ± 11 years. Mean length of CC treatment was 25.5 ± 20.48 months with a range of 0-84 months. 280 patients were treated with CC for ≤ 3 years (mean CC duration 12.75 ± 9.52 months), and 120 patients were treated with CC for > 3 years (mean CC duration 51.93±10.52 months). Following treatment with CC for > 3 years, 106 patients (88%) achieved eugonadal testosterone levels, 92 patients (77%) reported improvement in hypogonadal symptoms, and 10 patients (8%) reported side effects on CC. There was not a statistically significant difference in the results between patients treated > 3 years and patients treated ≤ 3 years. The most common side effects reported by patients treated > 3 years included changes in mood (N=5), blurred vision (N=3), and breast tenderness (N=2). There were no significant adverse events with long term sequelae in any patients treated with CC.

CONCLUSIONS: Testosterone replacement therapy (TRT) has traditionally been the primary treatment for hypogonadism in men. However, exogenous testosterone disrupts the hypothalamic-pituitary-gonadal (HPG) axis and suppresses intratesticular testosterone production and spermatogenesis. CC is commonly used to treat hypogonadism in men desiring to preserve spermatogenesis and fertility, and may be used as an off-label primary treatment for hypogonadism. There is a paucity of long-term data on the efficacy and safety of CC, with no published data with the use of CC in men for durations longer than three years. CC has not historically been offered as a primary treatment for hypogonadism in men who do not desire fertility preservation, perhaps in part due to the lack of data regarding long term safety and efficacy of CC. This data demonstrates that CC is safe and effective with few side effects when used as a long-term treatment for hypogonadism.

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PATERNAL AGE IS A PREDICTOR OF ELEVATED SPERM DNA FRAGMENTATION IN INFERTILE MEN. Julie Sroga Rios, MD, a Robert M. Coward, MD, b Fanghai Sun, MPH, c Heping Zhang, PhD, c Nanette Santoro, M.D, d Anne Z. Steiner, MD, MPH e University of Cincinnati and Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; f University of North Carolina, Chapel Hill, NC; g Yale University School of Public Health, New Haven, CT; h University of Colorado Denver, Aurora, CO; i Duke University Medical Center, Durham, NC.

OBJECTIVE: Increased sperm DNA fragmentation (DF) has been associated with reduced embryo quality and pregnancy rates, and increased miscarriage rates. The underlying cause of increased SDF is unknown. Our objective is to examine clinical factors associated with abnormal DF in infertile men.

DESIGN: Cross sectional study.

### Table 1. Characteristics of males by level of DF

<table>
<thead>
<tr>
<th></th>
<th>0≤SCSA ≤ 30 % (n=119)</th>
<th>SCSA &gt; 30% (n=28)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sperm concentration (million/ml)</td>
<td>20.0 (11.0, 40.0), n=119</td>
<td>18.0 (12.0, 51.5), n=28</td>
<td>0.624</td>
</tr>
<tr>
<td>Normal morphology (%)</td>
<td>5.0 (3.0, 8.5), n=104</td>
<td>5.0 (2.0, 11.0), n=19</td>
<td>0.666</td>
</tr>
<tr>
<td>Total motility (%)</td>
<td>45.2 ± 15.6, n=119</td>
<td>38.2 ± 20.5, n=28</td>
<td>0.040</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>33.0 (30.0, 36.0), n=119</td>
<td>36.0 (32.5, 40.0), n=28</td>
<td>0.009</td>
</tr>
<tr>
<td>BMI (mg/kg2)</td>
<td>27.7 (24.2, 31.3), n=118</td>
<td>28.0 (24.3, 30.9), n=27</td>
<td>0.994</td>
</tr>
<tr>
<td>History of Smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>71/119 (59.7)</td>
<td>17/28 (60.7)</td>
<td>0.748</td>
</tr>
<tr>
<td>Current</td>
<td>106/119 (89.1)</td>
<td>2/28 (7.1)</td>
<td></td>
</tr>
<tr>
<td>Former</td>
<td>5/119 (4.2)</td>
<td>9/28 (32.1)</td>
<td></td>
</tr>
<tr>
<td>History of Alcohol Use</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>8/119 (6.7)</td>
<td>0/28 (0.0)</td>
<td>0.476</td>
</tr>
<tr>
<td>Current</td>
<td>106/119 (89.1)</td>
<td>27/28 (96.4)</td>
<td></td>
</tr>
<tr>
<td>Former</td>
<td>5/119 (4.2)</td>
<td>1/28 (3.6)</td>
<td></td>
</tr>
<tr>
<td>Varicocele (self-reported)</td>
<td>Yes 11/119 (9.2)</td>
<td>2/28 (7.1)</td>
<td>1.000</td>
</tr>
<tr>
<td>No</td>
<td>108/119 (90.8)</td>
<td>26/28 (92.9)</td>
<td></td>
</tr>
<tr>
<td>Duration of Infertility (months)</td>
<td>24.0 (16.0, 36.0), n=116</td>
<td>24.0 (13.0, 36.0), n=26</td>
<td>0.951</td>
</tr>
</tbody>
</table>

Wilcoxon’s rank-sum test, Chi-square, or Fisher’s exact test were used where appropriate.
MATERIALS AND METHODS: A secondary analysis of 147 infertile males enrolled in the Male, Antioxidant, and Infertility (MOXI) Trial, MOXI participants, who were 18-40 years old with at least one abnormal semen parameter, provided a semen sample and completed questionnaires including baseline demographics, health and lifestyle factors. Semen samples underwent standard semen analysis and DF testing using sperm chromatin structure assay. Abnormal DF was defined as >30%. Bivariate analysis and subsequent multivariable regression analysis were performed. Variables were introduced to the multivariable regression analysis in a step-wise fashion, using a p-value of <0.10 on the bivariate analysis to enter and a p-value of <0.05 to remain.

RESULTS: Nineteen percent of subjects had DF >30%. Males with abnormal DF were older and had lower total sperm motility compared to controls (Table 1). No differences were seen in environmental or lifestyle exposures between groups (data not shown). Only male age remained a significant predictor of abnormal DNA fragmentation in the regression model (OR 1.16; 95% CI 1.03,1.32; p=0.02).

CONCLUSIONS: Older male age and lower sperm motility, but not smoking, obesity, or environmental or lifestyle exposures are associated with increased DF among infertile males. Longitudinal studies are needed to confirm causal inference. The role of abnormal DF during infertility treatment as well as optimizing treatment options in men with abnormal DF is worthy of further study.

SUPPORT: R25 HD 075735; U10HD077844, U10HD077680, U10 HD077841, U10HD027049; U10HD038992; U10HD039005; and U10HD055925.

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ANTIOXIDANT COMBINATION THERAPY: A NEW HOPE FOR OLIGOATHENOTERATOSPERMIC PATIENTS. Kareem Khalafalla, MD,1 Mohamed Arafa, MD,2 Ahmad Majzoub, MD,3 Haitham Elbardsi, MD,4 Sami Alsaid, MD,5 Ashok Agarwal, PhD,6 Hamad Medical Corporation, Doha, Qatar; 2Cleveland Clinic, CLEVELAND, OH.

OBJECTIVE: Idiopathic oligoasthenoteratospermia (iOAT) is a challenging condition often seen in up to 40% of infertile men and has been linked with increased seminal oxidative stress. This study aims at evaluating the effect of antioxidant combination formula (FH PRO) on the semen parameters and advanced sperm function tests in patients with iOAT.

DESIGN: Prospective clinical trial.

MATERIALS AND METHODS: Patients presenting to the Male infertility clinic with semen parameters showing iOAT (sperm concentration < 1, and ≤15 million/ml, motility ≤ 40%, normal forms ≤ 4.0%) were included in the study. Patients with clinical varicocele, epididymo-orchitis, irradiation or chemotherapy, history of recent STDS infection, malignancy and recent antioxidant use were excluded. Study subjects received antioxidant formula FH PRO, Fairhaven Health (1000 mcg B12, 30mg Zinc, 140mcg Selenium, 350mg Arginine, 2000mg, 200mg Co-Q10, 120mg Vitamin C, 200IU Vitamins E) (Fairhaven Health, Bellingham, WA) daily for 3 months.

Semen samples were collected before and after treatment and analyzed according to WHO 5th edition guidelines and for oxidation reduction potential (ORP) (MIOXSYS analyzer, Ayu Bioscience, Englewood, USA) and sperm DNA fragmentation (Halosperm kit, Halotech, Madrid, Spain). Numbers (percentages) were used to report categorical values while mean ± SE was used to report numerical values. Results were compared using Kruskal Wallis Test and a p value of <0.05 was considered statistically significant.

RESULTS: 52 infertile patients completed the study with a mean age 35.7±6.6 years and a mean infertility duration 5.9±2.4 years. There was a significant improvement in semen parameters including sperm count (p<0.001), progressive motility (p<0.002) and normal morphology (p<0.001) compared to pre-treatment results. Significant decrease in seminal oxidation reduction potential was observed (p 0.001), as well as significant decrease in sperm DNA fragmentation (p 0.007).

CONCLUSIONS: Medical treatment of infertile men with idiopathic OAT by Fairhaven Pro resulted in a significant improvement in semen parameters, reduction in seminal oxidative stress and sperm DNA fragmentation. We conclude that these changes should lead to improvement in men’s fertility and better outcome in natural conception as well as in assisted reproduction.

THE VALUE AND USAGE OF DNA BANKING ON SEMEN DONORS. Lauren Isley, M.S., L.C.G.C., Kara Baldwin, M.S., Pamela Callum, M.S., California Cryobank, Los Angeles, CA.

OBJECTIVE: To illustrate the uses and benefits of banked extracted DNA on semen donors based on our experience with genetic evaluation needs after the donor’s initial qualification.

DESIGN: Data was compiled for all additional genetic evaluation needs on California Cryobank (CCB) semen donors from 2017 to 2018 following the donor’s initial qualification. Cases involving stored DNA as the utilized sample type were identified. The data was then evaluated based on the specific indication for the additional testing.

MATERIALS AND METHODS: Not applicable.

RESULTS: Banked extracted DNA was utilized for genetic evaluation purposes in 24 cases involving 19 donors. In the majority of cases (13/24), the additional testing was performed based on a recipient’s request to evaluate the donor’s carrier status for an autosomal recessive condition for which the recipient was a carrier. One case involved a request to perform HLA testing for compatibility purposes. In seven cases, extracted DNA was utilized for preimplantation genetic testing (PGT) assay creation based on recipient need. Three cases involved additional genetic testing on the donor prompted by the report of a genetic condition in a donor-conceived offspring. In 2 of these 3 cases, testing confirmed the donor’s carrier status for an autosomal recessive condition for which he was not previously tested, resulting in restricted distribution of remaining vials and recipient notifications.

CONCLUSIONS: Banking extracted DNA on gameote donors is advantageous both for gamete donor facilities and recipients. Banked DNA is valuable when a donor is unavailable for sample collection and may serve multiple purposes, including additional evaluations to investigate reports of genetic diagnoses in donor-conceived offspring. Given the rapid evolution and availability of genetic testing, gamete donor facilities may consider a uniform approach to DNA banking on donors with careful attention to the initial consent process for DNA collection and re-contacting donors to discuss requests for specific uses of their DNA samples.

SUPPORT: California Cryobank.

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COMPARISON OF SEMEN QUALITY IN NORTHERNTAIWAN BETWEEN 2017 AND 2001-2010. Shang-Yu Tzeng, Master, Chii-Ruey Tzeng, MD, MPH, Chi-Huang Chen, MD, PhD, Taipei Medical University Hospital, Taipei, Taiwan.

OBJECTIVE: Semen quality is a crucial indicator of male reproductive ability. This study aimed to show the trend of men sperm quality in northern Taiwan in the year of 2017.

DESIGN: We recruited 1125 male samples in 2017 from Center of reproductive Medicine, Taipei Medical University Hospital. The semen data of 2017 were compared to the semen data from 2001 to 2010.

MATERIALS AND METHODS: Semen analysis was performed through standardized methods outlined in the World Health Organization laboratory manual. Furthermore, sperm sample of low quality rate was calculated.

RESULTS: The median of sperm volume, total sperm count, progressive sperm motility and rapid progressive sperm motility in 2017 was decreased by 0.23±1.07 ml, 8% and 3% respectively, compared to the data of 2001-2010. Low quality rate of sperm concentration, volume, total sperm count, progressive motility and rapid progressive motility in 2017 were increased significantly.

CONCLUSIONS: These finding shows the fact that man sperm parameter values were significantly decreased in the year of 2017 in comparison with the data in 2001-2010. Moreover, it was estimated that total sperm count was decreased by 2.85×10^9/ml annually.
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PERSISTENT GENDER GAP AND A TREND TOWARDS SUBSPECIFICATION: CHARACTERISTICS OF SURGEONS PERFORMING VASECTOMY IN THE UNITED STATES. Joshua A. Halpern, MD, MS, a Mary Kate Keeter, MPH, b Alexander J. Tatem, MD, b Katelyn Zumpe, MS, b Leah J. Wlery, PhD, b Nelson E. Bennett, Jr., MD, c Robert E. Brannigan, MD. a Northwestern University Feinberg School of Medicine, Chicago, IL; b Northwestern University, Chicago, IL; c Men’s Health Center, Indianapolis, IN.

OBJECTIVE: We sought to characterize trends in the characteristics of urologic surgeons performing vasectomy over time.

DESIGN: Retrospective, cross-sectional study.

MATERIALS AND METHODS: We examined surgeon characteristics for cases from American Board of Urology (ABU) certifying urologists between 2004 and 2013, which included information on surgeon age, gender, certification cycle, self-reported subspecialty, and practice area population. We used generalized estimating equations (GEE) with a log link and negative binomial distribution to determine whether the association between a surgeon characteristic, such as gender, and the count of vasectomies, changed over time. Analyses were conducted in R version 3.4.3 and SAS 9.4.

RESULTS: A total of 115,146 vasectomies were performed by 5,415 individual certifying urologists. Mean surgeon age was 43.9±8.3 years, which remained stable throughout the study. The majority of surgeons self-identified as general urologists (80.6%). A small proportion identified as andrology and infertility specialists (1.7%), pediatric urologists (1.4%), and other specialists (16.4%). Surgeons were equally distributed across the various certifying cycles.

Most number of vasectomies performed per certifying surgeon during the study period was 12 (interquartile range [IQR] 5-23), ranging from 10 to 12.5 for each individual certifying year. Based on the distribution of vasectomies performed per cycle year, The majority of vasectomies were performed by high-volume surgeons (≥ 23 vasectomies) ranging from 51.5% - 66.0%, whereas the proportion performed by low-volume (≤ 5 vasectomies) surgeons ranged from 4.2% - 6.13%. The maximum number of vasectomies performed by a single certifying surgeon was 1,183. Female surgeons accounted for approximately 7.0% of all certifying urologists. Over time, the percent of female surgeons performing vasectomies increased from 2.9% in 2004 to 9.2% in 2013. Male surgeons performed vasectomies 2.33 times more frequently than female surgeons (CF: 2.05 to 2.65; p<0.001). There was no statistical evidence to suggest this gap has changed over time. In other words, the interaction between year and surgeon gender on the count of vasectomies was not found to be statistically significant.

CONCLUSIONS: While the majority of surgeons performing vasectomy identify as general urologists, there are clear trends towards subspecialization of vasectomy among a small number of high-volume surgeons. Furthermore, while the proportion of vasectomies performed by female surgeons has increased over time, a gender gap persists.

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UTILIZATION OF EJACULATED SPECIMEN AFTER ICSI FAILURE WITH TESTICULAR SPERMATOZOA FROM MEN WITH HIGH DNA FRAGMENTATION. Alessandra Parrella, M.Sc., Derek Keating, B.A., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D. The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To assess the benefit of using ejaculated spermatozoa from men with high DNA fragmentation in their ejaculate after intracytoplasmic sperm injection (ICSI) failure with testicular specimen.

DESIGN: CONsenting couples with a history of assisted reproductive technology (ART) failure, and male partners with elevated DNA fragmentation in their ejaculate, were treated by testicular biopsy and underwent a subsequent ICSI cycle with ejaculated spermatozoa. Embryology and clinical outcome were compared between the two semen origins.

MATERIALS AND METHODS: A total of 43 couples had their ejaculate assessed for DNA fragmentation by terminal deoxynucleotidyl dUTP nick-end labeling (TUNEL). A threshold of <15% was considered normal, with at least 500 spermatozoa assessed per patient. ICSI and testicular biopsy were performed in the standard fashion.

RESULTS: A total of 43 couples (maternal age, 36.6±6; paternal age, 41.3±10) underwent 65 cycles with testicular biopsy due to a prior history of ART failure and high DNA fragmentation in the male partners’ ejaculate. The parameters for the testicular specimens were an average concentration of 1.8±4 million and 5.0±11 motility. ICSI with testicular spermatozoa (ICSI-TESE) had a fertilization rate of 53.0%, an implantation rate of 13.2%, and a clinical pregnancy rate (CPR) of 23.8%, which led to a delivery rate of 21.1%. The pregnancy loss rate was 1.9%. Subsequently, these couples attempted cycles (n=85) with ejaculated spermatozoa. These specimens were characterized by an average volume of 2.6±1 mL, a concentration of 12.6±23 million, and 16.9±20% motility. The resulting fertilization rate was 62.7% (P < 0.001), the embryo implantation rate was 17.0%, and the CPR was 31.9%, which resulted in a delivery rate of 29.0%. The pregnancy loss rate was 2.9%.

When we consider as a denominator only the couples that failed to achieve a pregnancy with testicular biopsy, the actual fertilization rate was 64.2% (P < 0.0001), with an embryo implantation rate of 19.4% and a CPR of 35.3%, which resulted in a delivery rate of 31.4%. The pregnancy loss rate was 3.9%.

CONCLUSIONS: It has been recently proposed that couples with recurrent ART failure and male partners with high DNA fragmentation in their ejaculate to attempt ICSI with testicular spermatozoa. In these couples, if the ICSI-TESE fails, it seems reasonable to make an additional ICSI attempt with ejaculated spermatozoa. This prevents the surgical risk of TESE and reduces the potential financial and emotional hardships related to the procedure.

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PREDICTIVE BIOMARKER AS MICROBIOMES IN THE SEMINAL PLASMA ASSOCIATED WITH SPERMATOGENESIS STATUS. HyoJeong Kwon, MS, a Boyoung Jeon, BS, a Eunji Lee, MS, a Hyoeun Kang, MS, a TaEun Shin, MS, b Kyu Bum Kwack, Ph.D., b Jung-Jae Ko, Ph.D. b Dae Koun Kim, M.D. Ph.D. b, Jae Ho Lee, Ph.D. b, c CHA Fertility Center in Seoul, Seoul, Korea, Republic of (South); cDepartment of Biomedical Science, CHA University, Seoul, Korea, Republic of (South); cCHA Fertility Center, Seoul, Korea, Republic of (South).

OBJECTIVE: Whether microbiota in seminal plasma has a specific co-relationship with spermatogenesis status on male fertility or not?

DESIGN: Andrology at the in vitro fertilization center.

MATERIALS AND METHODS: We investigated whole microbiome screen in the seminal plasma of normal group (4 cases), abnormal group (4 cases; sertoli cell only syndrome (SCO) 2 cases, hypospermatogenesis 2 cases) using next generation sequencing (NGS). We harvested normal semen and azospermia semen by SCO, Klinefelter’s syndrome, and hypospermatogenesis cases. And we performed microbiome analysis used by NGS for identification of microbiome in the seminal plasma of normal and azospermia patients. Therefore, we analyzed microbiome’s taxonomic composition of each sample from phylum to genus level.

RESULTS: Based on the metagenomics-NGS, we found that total 638 microbe genome counts in the seminal plasma. Therefore, non-obstructive azospermia present 437 genomes count number and normal spermatozoa presented 384 genomes count number of microbes. We investigated specific microbiome on the genus level in the azospermia patient compared to normal group. Azospermia group present a significantly higher population of Prevotellaceae, Prevotella, Porphyromonas, Streptococcus, and Sutterellaceae compared to normal spermatozoa group. In the case of hypospermatogenesis group showed a specifically more abundant Prevotellaceae, Prevotella, Streptococcus than Porphyromonas, Sutterellaceae in the seminal plasma. Normal group revealed more variable microbiota regarding family and genus bacteria compared to azospermia patients and have no major dominant microbiota.

CONCLUSIONS: Specific microbiome profiling data may be valuable for prediction of normal spermatogenesis. The small sample size used in the present study may be insufficient to clarify the role of microbiota in this preliminary study. However, this data showed possibility for the external validation study of seminal plasma microbiota. Male infertility may be associated with the residential bacterial flora as microbiomes microenvironment.

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SUB-FERTILITY AND ITS PSYCHOLOGICAL IMPACT ON MEN. Pranav Dadhich, MD, Garrett K. Berger, PharmD, Peter N. Dietrich, MD, Johnathan Doolittle, MD, Abbey Kruper, PsyD, Jay I. Sandlow, MD. Medical College of Wisconsin, Milwaukee, WI.

OBJECTIVE: Infertility affects an estimated 15% of couples attempting to conceive. Of these couples, male factor etiology is thought to play a part in
50% of cases. While practitioners strive to provide comprehensive care to these men, the psychologic impact of subfertility on individuals has not traditionally been addressed, and there is a dearth of data on the subject, particularly in regards to the experience of men.

**DESIGN:** At our institution, men presenting for an infertility evaluation are routinely administered a survey assessing their psychological well-being and concerns at their initial visit. This study aims to assess the results of these surveys as a means to quantify the psychological impact of sub-fertility on men.

**MATERIALS AND METHODS:** This single-center prospective study utilized a questionnaire containing both narrative questions and a Likert survey to probe several psychological and emotional domains relevant to the their impact of sub-fertility on males. Specifically, the effects of sub-fertility on mood, marital relations and sexual experience were assessed. The Likert survey was utilized to better characterize patient’s abilities to cope with subfertility as well as the desire for additional resources in regards to its impact. Data were analyzed using SPSS v24.

**RESULTS:** One hundred sixty-four men completed the questionnaire. Of those, 83 men (51.6%) reported a negative effect on their relationship and 40 (24.8%) described a negative effect on their sexual experience. Approximately one third of men (34.6%) doubted their ability to manage the emotional impact of this pathology. Lastly, around one-fourth of men (25.7%) requested additional resources to aid in coping with these psychological impacts.

**CONCLUSIONS:** Sub-fertility has a significant impact on the emotional and psychological well-being of men who presented to our infertility clinic. As indicated above, one in four men feel the need for additional resources or treatment to address the psychological impact of this pathology. When encountered in clinic, these particular individuals are provided pamphlets and/or appropriate referrals when indicated. While the medical management of infertility remains paramount, it is important to consider the emotional toll this pathology has on patients and possible need for further resources.

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**THE OVERALL HEALTH STATUS OF INFERTILE MEN IN THE UNITED STATES IS SIMILAR TO THAT OF FERTILE MEN.** Jesse Benjamin Persily, BA, Bobby B. Najari, MD, MSc. New York University School of Medicine, New York, NY.

**OBJECTIVE:** Epidemiologic studies have found that a greater degree of comorbidity is associated with worse fertility potential. However, these findings are largely based on retrospective studies of men interacting with the health care system. Our objective was to evaluate the association of fertility and health status in men in the United States using a nationally representative survey.

**DESIGN:** We compared the demographics, healthcare utilization, and overall health status of fertile and infertile men in the National Survey for Family Growth (NSFG).

**MATERIALS AND METHODS:** We performed an analysis of the male 2011-2017 cycles of the NSFG, a nationally representative survey of family planning. Infertile men were defined as men who had ever used infertility services or men who self-reported as non-surgically sterile. Men who reported completed pregnancies were considered fertile.

**RESULTS:** Of the 13,861 men surveyed, 1,071 men were infertile, and 5,661 men were known to be fertile. Projecting to the national population, this translates to 5,205,771 infertile men and 26,577,702 fertile men. Of the total population of sexually active men aged 15-49, roughly 8.5% (95% CI: 7.8-9.3) of men were infertile. Compared to known fertile men, infertile men had significant demographic and healthcare utilization differences (Table). Infertile men were wealthier, better educated, more likely to be white, more likely to be married, and more likely to have private insurance. Importantly, infertile men and fertile men had similar overall health status. On multivariate analysis, differences in income, marital status, and usual healthcare place remained significant.

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**TABLE. Demographics, Healthcare Utilization, and Overall Health Status of Fertile and Infertile Men**

<table>
<thead>
<tr>
<th></th>
<th>Infertile</th>
<th>Fertile</th>
<th>Bivariate Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>34.1</td>
<td>34</td>
<td>0.867</td>
</tr>
<tr>
<td>Income, % of poverty level</td>
<td>318.5</td>
<td>263.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Religion, %</td>
<td>0.017</td>
<td>0.05</td>
<td>0.001</td>
</tr>
<tr>
<td>No Religion</td>
<td>25</td>
<td>25.9</td>
<td>0.259</td>
</tr>
<tr>
<td>Catholic</td>
<td>23.5</td>
<td>22.4</td>
<td>0.867</td>
</tr>
<tr>
<td>Protestant</td>
<td>40.2</td>
<td>44.6</td>
<td>0.267</td>
</tr>
<tr>
<td>Other Religions</td>
<td>11.2</td>
<td>7.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Race, %</td>
<td>0.001</td>
<td>0.59</td>
<td>0.001</td>
</tr>
<tr>
<td>Hispanic</td>
<td>18.8</td>
<td>24.4</td>
<td>0.267</td>
</tr>
<tr>
<td>White</td>
<td>61.9</td>
<td>53.1</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>12.2</td>
<td>14.8</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>7.2</td>
<td>5.6</td>
<td></td>
</tr>
<tr>
<td>Marital Status, %</td>
<td>&lt;0.001</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>66.7</td>
<td>57.9</td>
<td></td>
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<tr>
<td>Widowed</td>
<td>0.1</td>
<td>0.2</td>
<td></td>
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<tr>
<td>Divorced/Seperated</td>
<td>5.9</td>
<td>11.9</td>
<td></td>
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<tr>
<td>Never Married</td>
<td>27.3</td>
<td>30.1</td>
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<tr>
<td>Education, %</td>
<td>0.001</td>
<td>0.267</td>
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<tr>
<td>Less than High School</td>
<td>12.7</td>
<td>17.5</td>
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</tr>
<tr>
<td>High School</td>
<td>64.7</td>
<td>67.7</td>
<td></td>
</tr>
<tr>
<td>College</td>
<td>22.6</td>
<td>14.9</td>
<td></td>
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<tr>
<td>Health Insurance Status</td>
<td>&lt;0.001</td>
<td>0.259</td>
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<tr>
<td>Private</td>
<td>69.8</td>
<td>59.2</td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
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<td>10.1</td>
<td></td>
</tr>
<tr>
<td>Military</td>
<td>4.9</td>
<td>4.9</td>
<td></td>
</tr>
<tr>
<td>Uninsured</td>
<td>15.6</td>
<td>25.7</td>
<td></td>
</tr>
<tr>
<td>Usual Place for Healthcare, %</td>
<td>79.2</td>
<td>69.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Health Status, %</td>
<td>0.378</td>
<td>0.472</td>
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<tr>
<td>Excellent</td>
<td>24.5</td>
<td>27.7</td>
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<tr>
<td>Very Good</td>
<td>42.6</td>
<td>39.3</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>26.2</td>
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</tr>
<tr>
<td>Fair</td>
<td>5.9</td>
<td>6.5</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>0.8</td>
<td>1.2</td>
<td></td>
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</tbody>
</table>

**FERTILITY & STERILITY®**

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CONCLUSIONS: While infertile men do have significant demographic and healthcare utilization differences compared to fertile men, the overall health status of both infertile and fertile men appear similar.

P-658 Wednesday, October 16, 2019 6:30 AM
AN EVIDENCE-BASED ANALYSIS OF INGREDIENTS IN POPULAR MALE FERTILITY SUPPLEMENTS. Manish Kuchakulla, B.S., Yash Soni, B.S., Premal Patel, MD, Ranjith Ramasamy, MD University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: To study the level of evidence available for ingredients of popular over-the-counter male fertility supplements.

DESIGN: Systematic review

MATERIALS AND METHODS: We performed a systematic search using the terms “male fertility supplement”, “male sperm supplement”, and “male reproductive supplement”. We identified the top male fertility supplements available from the most commonly used online retailers in the United States: AI Supplements, Amazon, Vitamin Shoppe, and Walmart. The ingredients of each of these supplements were identified and a systematic review was performed to identify randomized controlled trials studying each ingredients impact on sperm parameters and/or live birth rates using search terms, “Xingredient and sperm,” “Xingredient and male fertility,” and “Xingredient and sperm parameters.” A score was assigned to each ingredient based on its available evidence using The American Heart Association Evidence-Based Scoring System. Subsequently, a composite level of evidence score was calculated for each supplement to assess its overall level of evidence.

RESULTS: Ninety unique ingredients were identified from the top 17 listed male fertility supplements. The most commonly used ingredients were Vitamin E, Folic Acid, Zinc, Vitamin C, Selenium, Vitamin B12, L-Carnitine, and Maca. Only 17% of ingredients had published data showing positive effect on semen parameters, of these, the most studied ingredients are L-Carnitine, Vitamin E, Vitamin C, CoQ10, and Zinc. None of the supplements had any published evidence of their use in a randomized controlled trial. Our scoring system gave an average composite rating of 1.66 (on a scale to 5) for the evidence level of the popular supplements. Evolution 60 and Conception XR had the highest composite scores with 3.6 and 3.5, respectively. Mitamen and Standard Process scored the lowest with 0 and -3.3, respectively. Mitamen and Standard Process scored the lowest with 0 and -3.3, respectively.

CONCLUSIONS: Many fertility supplements claim to improve fertility; however, their promises are rarely backed by evidence. Very few ingredients used in popular fertility supplements had positive evidence demonstrated in randomized clinical trials. These findings can help providers counsel men attempting conception about the use of the over-the-counter supplements.

P-659 Wednesday, October 16, 2019 6:30 AM
ELEVATED BLOOD SUGAR PARAMETERS IN YOUNG INDIAN MEN ATTENDING OUR FERTILITY CLINIC. Madhavi M. Panpalia, MS,a Sujatha Reddy, MD,a Chitra Ishwar, MD,b Meenal Khandeparkar, MS,a Dattatrjay Naik, MSc,a Suresh Dhumal, MSc,a Prashant Makwana, MSc,a Firuza Rajesh Parikh, MD DNB PhD,a Jaslok Hospital and Research Centre, Mumbai, India; bGenexplore Diagnostics and Research Centre Pvt. Ltd., AHMEDABAD, India.

OBJECTIVE: India is considered the diabetic capital of the world (1). This study aims to review the levels of high blood sugar parameters for the incidence of Type 2 Diabetes in young male partners of Indian couples seeking fertility treatment since there is a paucity of studies documenting blood sugar levels in young Indian men.

DESIGN: Retrospective observational study in the young Indian male visiting our Fertility Centre.

MATERIALS AND METHODS: Over a 6 month period, 727 male partners of Indian ethnicity (median age 35 years, range 24 - 45 years) of couples visiting our fertility clinic for the first time were investigated for blood sugar levels with one or more of the following parameters: a) Fasting plasma glucose (FPG) with no calorie intake for at least 8 hours. b) 2 hours plasma glucose (2 hr PG) during oral glucose tolerance test (OGTT) using a glucose load containing 75 gm glucose. c) Glycosylated Haemoglobin (HbA1C).

RESULTS: Of the 727 young male partners, while 62 (8.5%) were diabetic, 279 (38.4%) were pre-diabetic. The remaining 386 (53.1%) were normal.

CONCLUSIONS: Our study found that Indian men showed deranged blood sugar parameters indicating the prevalence of diabetes in young Indian men. Furthermore it highlights the importance of screening male partners prior to fertility treatment. In India, a trend indicates that there is a rapid increase in the number of individuals becoming diabetic and a decline in the mean age of onset of Type 2 Diabetes. This is a disturbing trend as Type 2 Diabetes is seen in Indian males a decade earlier than in Caucasian males (2).


P-660 Wednesday, October 16, 2019 6:30 AM
HIV/OTHERSTD INFECTIONS AMONG 338,432 INFERTILE POPULATIONS SHOULD RECEIVE MORE ATTENTION IN HUNAN, CHINA, 2012-2018: A CROSS-SECTIONAL STUDY. Gang Liu, PhD,a Weina Li, PhD, a Institute of Reproduction and Stem Cell Engineering, Central South University, changsha, China; bReproductive and Genetic Hospital of CITIC-Xiangya, changsha, China.

OBJECTIVE: Although infertile populations were not at high risk for HIV compared with sex workers and MSM groups, they do not adjust their high risk practices in natural pregnancies for reproduction. However, data regarding HIV/STD testing, infections and coinfections among infertile couples are limited. This study aimed to assess HIV/otherSTD prevalence among infertile populations in China.

DESIGN: This study was performed as a retrospective survey of 338,432 infertile populations in Hunan, China, from 2012-2018 in our hospital.

MATERIALS AND METHODS: A cross-sectional hospital-based study was conducted to evaluate the prevalence of HIV/other STDs (HBV, HCV, syphilis, Chlamydia trachomatis, Neisseria gonorrhoeae, Mycoplasma genitalium (MG)) among 338,432 infertile populations. We calculated linear trends in prevalence using bivariate linear regression.

RESULTS: The overall prevalence rates of HIV, chlamydia, gonorrhea, MG, syphilis, HBV and HCV antibody positivity in this study were 0.04%, 1.73%, 0.05%, 2.60%, 2.15%, 12.01% and 0.56%, respectively. The predominant infection was HBV, followed by MG, syphilis, and chlamydia. Of those participating, 16.65% (5636/ 338432) had at least one positive test; 0.59% (1999/338432) had more than one positive test. Only 1.13% of participants (382/338432) reported STD signs and symptoms suggesting genital tract infection. However, the variation in HIV prevalence was not significant (β=0.000, P TRENDS = 0.907) during this period. From 2012-2018, the characteristics of the HIV-infected infertile population had not shifted dramatically: women composed 32.56% of HIV cases in China, and the incidence rate for men was 2 times the rate in women. Concordant infections were found in 4.65% of infertile couples (6/129).

The highest incidence of 54.26% (70/129) was found at 30-39 years of age. Overall, 87.60% of the HIV-infected population had a relatively low education. All HIV-positive women discontinued treatment, but 45.98% (40/87) of HIV-positive men continued their assisted reproductive therapy with donor semen.

CONCLUSIONS: Therefore, screening for STDs should be emphasized regardless of symptoms in the clinical setting, and targeted interventions

Criteria by the American Diabetes Association (ADA) for the diagnosis of Diabetes

<table>
<thead>
<tr>
<th></th>
<th>Fasting plasma glucose (FPG)</th>
<th>2 hrs plasma glucose in OGTT</th>
<th>HbA1C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetic</td>
<td>≥ 126 mg/dl</td>
<td>≥ 200 mg/dl</td>
<td>≥ 6.5%</td>
</tr>
<tr>
<td>Prediabetic</td>
<td>100 - 125 mg/dl</td>
<td>140 - 199 mg/dl</td>
<td>5.7 - 6.4%</td>
</tr>
<tr>
<td>Normal</td>
<td>&lt; 100 mg/dl</td>
<td>&lt; 140 mg/dl</td>
<td>&lt; 5.7%</td>
</tr>
</tbody>
</table>
A significant positive correlation was noted with age & serum estradiol levels, normal morphology, and serum testosterone levels. While a weak correlation was noted between BMI & sperm concentration, progressive motility, and normal morphology when BMI increased. A significant increase in estradiol and a decrease in testosterone were noted as BMI increased.

OBJECTIVE: To characterize the prior evaluation and intervention that infertile couples received prior to male evaluation.

DESIGN: Retrospective review of couples presenting for male infertility evaluation by fellowship-trained male reproductive urologists.

MATERIALS AND METHODS: Couples presenting for infertility to a male infertility specialist were identified and charts were reviewed for duration of attempting pregnancy, prior reproductive workup, and prior use of assisted reproductive technology (ART). Variables were compared between couples presenting for primary versus secondary infertility and between couples who had undertaken ART and those who had not. Physical exam findings at evaluation, and subsequent therapeutic interventions were recorded.

RESULTS: A total of 806 patients were included for analysis. The mean age at presentation was 36.2 (range 20–73) years for men, and 32.42 (range 19–53) years for women (p < 0.001). 39% (312/799) of couples were first evaluated by a gynecologist only, 25% (200/799) a reproductive endocrinologist (REI) only, 18% (147/799) presented without a female workup, and 18% (140/799) of couples saw both a gynecologist and REI prior to presentation at our clinic. In total, 14% previously attempted ART: 6% (46/776) underwent intrauterine insemination (IUI) (range 1-8 cycles); 6% (43/776) underwent invitro fertilization (IVF) (range 1 to 8 cycles); 3% (20/776) underwent both IUI and IVF. Couples who had undertaken ART were attempting pregnancy for 39 months versus 22 months for those who had not undergone ART (p < 0.001). The majority (63%) of females had no abnormality in their workup. 72% (78/109) of men undergoing ART had at least one abnormality diagnosed at examination. Varicocele was the most common abnormality diagnosed amongst these men (Table 1). Varicocele repair (VR) (41%, 45/109) and testicular sperm extraction (11%, 12/109) were the most common interventions pursued following evaluation.

CONCLUSIONS: Our findings highlight that a male workup for infertile couples often lags behind a female workup and sometimes even ART. We
identified that undergoing a simple, inexpensive male workup composed of scrotal ultrasound, semen analysis and hormone levels identifies several correctable forms of male infertility and prompt surgical interventions such as VR that can potentially improve outcomes.

**SUPPORT:** A.W.P. is a National Institutes of Health (NIH) K08 Scholar supported by a Mentored Career Development Award (KO8DK115835-01) from the National Institute of Diabetes and Digestive and Kidney Diseases. This work is also supported in part through a Urology Care Foundation Rising Stars in Urology Award (to A.W.P.) and NIH grant K12 DK0083014, the Multidisciplinary K12 Urologic Research (KURE) Career Development Program awarded to DJL (NT is a K12 Scholar) from the National Institute of Kidney and Digestive Diseases to Dolores J Lamb. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

**P-663** Wednesday, October 16, 2019 6:30 AM

**MALE MULTIVITAMIN USE AND SEMEN QUALITY.** Sydney K. Willis, M.P.H., a Elizabeth Hatch, Ph.D., a Greg Sommer, PhD, b Michael L. Eisenberg, M.D., c Tanran Wang, MPH, c Lauren A. Wise, Sc.D. a b c Boston University School of Public Health, Boston, MA; c Sandstone Diagnostics, Livermore, CA; c Stanford University, Stanford, CA.  

**OBJECTIVE:** To prospectively evaluate the association between male multivitamin use and semen quality. Male factors contribute up to 50% of couple infertility, but few modifiable factors have been identified. Several studies have examined the influence of male multivitamin use on semen quality, but findings have been inconsistent.  

**DESIGN:** Prospective cohort study.  

**MATERIALS AND METHODS:** Pregnancy Study Online is a web-based preconception cohort of North American pregnancy planners. At baseline, female participants completed a questionnaire on demographics, lifestyle, and reproductive history, including multivitamin use. Multivitamin use was ascertained by asking “Which of the following vitamins and/or minerals did you take on a regular basis (daily or almost every day)?” with “multivitamins” as a response option. Female participants invited their male partners to complete a similar baseline questionnaire. During October 2015 through April 2019, a subset of male participants from the U.S. whose partners reported regular menstrual cycles were invited to use Trak, an FDA-approved device that measures sperm concentration and semen volume at home. Men were instructed to provide up to two semen tests, with at least 3 days of abstinence time, and upload their results online via self-report and smartphone photo images. We used generalized estimating equations, accounting for within-person correlation, to estimate risk ratios (RR) and 95% confidence intervals (CI) for the association between male multivitamin use and low semen volume (≤2 vs >2 ml), low sperm concentration (≤20 vs >20 million/ml), and low total sperm count (TSC, ≤50 vs >50 million). The analysis included 223 men who provided a total of 375 samples. The median and interquartile range of attempt time for men at study enrollment was 1 (1-3 cycles). We adjusted for abstinence time, age, body mass index (BMI), and lifestyle and socio-demographic factors.  

**RESULTS:** At baseline, 34% of male participants reported taking multivitamins on a regular basis. Nearly 14% of samples had semen volume ≤2 ml, 18% had sperm concentration ≤20 million/ml, and 14% had TSC ≤50 million. Compared with men not taking multivitamins regularly, RRs for men reporting regular multivitamin use were 0.98 (CI: 0.54-1.78) for low semen volume, 0.74 (CI: 0.40-1.31) for low TSC, and 0.74 (CI: 0.4-1.31) for low TSC.  

**CONCLUSIONS:** In a geographically heterogeneous cohort of U.S. men, we observed slight inverse associations between regular multivitamin use and semen volume, 0.66 (CI: 0.40-1.09) for low sperm concentration, and 0.74 (CI: 0.40-1.31) for low TSC. Compared with men not taking multivitamins regularly, RRs for men reporting regular multivitamin use were 0.98 (CI: 0.54-1.78) for low semen volume, 0.74 (CI: 0.40-1.31) for low TSC, and 0.74 (CI: 0.4-1.31) for low TSC.  

**SUPPORT:** This research was supported by R01HD086742, R21HD094322, and R21HD072326.

**P-665** Wednesday, October 16, 2019 6:30 AM

**EFFECT OF MEDICAL COMORBIDITIES OVER SEMINAL PARAMETERS AND SPERM DNA FRAGMENTATION.** Cristian R. Alvarez Sedo, PhD, Heydy W. Uriondo Boudri, MSc., Lourdes Correa Brito, BS, Federico Bleckwelder, BS, Carolina Salazar, MD, Natalia Vic, MD, Carlos Sancho Minano, MD FERTILIA, TUCUMAN, Argentina.  

**OBJECTIVE:** Several publications have been shown that it could be a relationship between male infertility and general health status. The aims of this study were to investigate the prevalence and effect of some medical comorbidities over sperm parameters and DNA fragmentation in an Argentinian population.  

**DESIGN:** Retrospective controlled cohort study.  

**MATERIALS AND METHODS:** Under the approval of the institutional ethics committee, a retrospective study was performed for 1,092 men who were examined due to infertility between August 2017 and April 2019. The initial evaluations were comprised of a complete medical history, a physical examination, endocrine assessment, and at least two semen analyses. Sperm parameters and DNA fragmentation were compared between men with and without medical comorbidities.
RESULTS: Significant medical comorbidities were found in 112 of 1092 (10.3%) men, including 3.6% with hypertension, 2.3% with hypothyroidism, 2% with mental, 2% with diabetes/dyslipemia and 0.6% with respiratory disease.

Semen volume, sperm count and progressive motility were significantly lower in men with comorbidities than in men without comorbidities (p=0.045, p=0.036 and p=0.025, respectively). Regarding sperm DNA fragmentation, it was higher in patients with comorbidities (p=0.018). Sperm viability and strict morphology were not significantly different. Within patients with comorbidities, patients with diabetes/dyslipemia and anxiety disorders presented significantly higher levels of DNA fragmentation (p=0.001).

CONCLUSIONS: After this preliminary study, we can conclude that medical comorbidities are associated with the impairment of sperm production and function. It has been published that obesity and metabolic disorders could be associated with impaired sperm function by altering physical and molecular structure of germ cells. A complete male infertility evaluation, including an exhaustive anamnesis, could offer the possibility of specific therapy in order to improve some semen parameters. We didn’t assess this theoretical benefit, however it would be very interesting to evaluate if that therapy, despite the improvement of the general health status, could improve the spermatogenesis.

MALE REPRODUCTION AND UROLOGY - BASIC

P-666 Wednesday, October 16, 2019 6:30 AM

ROLE OF LEPTIN AS A PARACRINE FACTOR CRITICAL FOR HUMAN LEYDIG STEM CELL FUNCTION AND DIFFERENTIATION. Himanshu Arora, PhD, Ranjith Ramasamy, MD. University of Miami Miller School of Medicine, Miami, FL.

OBJECTIVE: Impaired testosterone production as a result of Leydig cell loss or dysfunction can occur in men with testicular failure. Although several testosterone formulations are available, none are capable of replicating the physiological pattern of testosterone secretion. We have shown in our recent study conducted in murine models that, Leydig stem cell transplantation along with peritubular myoid cells and Sertoli cells could be used to physiologically increase serum testosterone thereby potentially minimizing the adverse effects. However, in order to optimize the function of Leydig stem cells, we need to understand the paracrine factors released by myoid and Sertoli cells. In the present study we evaluated the significance of paracrine factors secreted by human peritubular myoid cells and Sertoli cells on Leydig stem cell function.

DESIGN: A total of 8 men with testicular failure underwent testes biopsies for sperm retrieval. Using an IRB approved protocol, about 10mg of testicular tissue from each of these men were processed for Leydig stem cell isolation, culture and characterized.

MATERIALS AND METHODS: The presence of Leydig stem cells (LSCs), Sertoli cells (SCs) and peritubular myoid cells (PMCs) in the harvested testis were evaluated by immunohistochemical and real time PCR (qPCR) using PdgfRα, 3bHSD and Sox9. PZL, respectively. After stimulation by Luteinizing hormone (LH), the levels of 3bHSD mRNAs were increased. Additionally, the CD146 (+) cells representing LSCs were sorted using MACS kit and maintained along with unsorted cells in charcoal stripped medium. Condition media was collected from both the cell types and screened for secreted protein using RayBio Human Antibody Array for a total of 80 molecules.

RESULTS: We successfully isolated and cultured LSCs from all 8 testis biopsies. We were able to culture up to 3 million cells / biopsy. Of the cells cultured, up to 70% of the cells were Leydig stem cells and 10% of them were Sertoli-cell in origin on day 14. IF and qPCR data showed as the majority of cell population was undifferentiated (PdgfRα-). Upon stimulation by LH, the expression of 3bHSD (mature Leydig cells) was increased and that of PdgfRα- was decreased. Importantly, human antibody protein array demonstrated increased expression of one cytokine - LEPTIN in the media of LSC's that were co-cultured with Sertoli cells and myoid cells compared to the media from purified LSCs cultures (CD146 positive). Further results confirmed that Leptin is upstream of desert hedgehog signaling in regulation of LSC differentiation.

CONCLUSIONS: Our results indicate that LSCs can be isolated and cultured from men with testicular failure. Leptin is a specific paracrine factor which can be released by myoid and SCs which could be required for LSC differentiation and testosterone production. Further studies are ongoing to validate the implications of Leptin in terms of their role in LSCs function, differentiation and survival.

SUPPORT: Supported by the American Urological Association Research Scholar Award and Stanley Glaser Award to RR. J.M.H. is supported by NIH grants IR01 HL137355, IR01 HL107110, IR01 HL134558, SR01 CA136387, 5UM1 HL113460 and Soffer Family Foundation.

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IDENTIFICATION OF TWO NOVEL SEMINAL PEPTIDES, WHICH ACT AS NEUTRAL ENDOPEPTIDASE INHIBITORS AND MODULATE SPERM MOTILITY. Alexander Kucherev, MD, Kelvin Davies, PhD. Albert Einstein College of Medicine / Montefiore Medical Center, Hartsdale, NY; Albert Einstein College of Medicine, Bronx, NY.

OBJECTIVE: Poor sperm motility is highly predictive of male factor infertility. Semenogelins, and their peptide products, are recognized as important determinants of sperm motility; most research suggests they act as inhibitors of sperm motility. Peptidomic analysis of semen identified several semenogelin-derived peptides. Based on sequence analysis, these peptides may act as substrates, and thereby inhibitors, of neutral endopeptidase (NEP). Since inhibition of NEP activity has been associated with increased sperm motility, this raises the intriguing possibility that certain semenogelin-derived peptides may activate sperm motility. The present study determined if two novel seminal semenogelin-derived peptides, (RSIY-15 and SSII-15), were indeed NEP inhibitors and if they had a positive effect on sperm motility.

DESIGN: A colorimetric assay was performed using recombinant human NEP enzyme at 0.1 µg/ml and fluorogenic NEP peptide substrate. RSIY-15 and SSII-15 were synthesized and the colorimetric assay was performed to evaluate their inhibitory nature and Ki. Sperm analysis was undertaken in order to determine the effects of RSIY-15 and SSII-15 on sperm motility.

MATERIALS AND METHODS: 50µL of substrate, at a range of concentrations, was added to 50µL of NEP enzyme followed by 50µL of a range concentrations of RSIY-15 and SSII-15. Dixon and Lineweaver Burk plots were generated to evaluate the inhibitory nature of RSIY-15 and SSII-15. Sperm samples from patients presenting for routine semen analysis were collected; semen from each patient was divided into aliquots and motility analyzed following addition of 1µL of 75µM RSIY-15 or SSII-15. Addition of 1µL 75µM RSIY-11 or 200 µM Opiorphin (peptides previously identified as NEP inhibitors) were utilized as positive controls, and vehicle (PBS) was utilized as negative control. Additionally, 1 aliquot was set aside without addition. 2µL of semen was then placed into a 4-chamber microcell disposable counting chamber slide. Progressive and non-progressive motility was assessed at 0, 30, and 60 minutes after the addition of peptide. Wilcoxon Rank-Sum Tests were used to evaluate differences in sperm motility between groups.

RESULTS: Colorimetric assays indicate that RSIY-15 and SSII-15 both act as competitive inhibitors of NEP. Both peptides appear to have Ki similar to Ki of RSIY-11 (12.58± 3.75 µM and 13.69± 5.44 µM, respectively). Semen analysis for 30 patients was undertaken. Compared to PBS controls, the addition of RSIY-15 and SSII-15 lead to improved progressive and total sperm motility (p < 0.05).

CONCLUSIONS: The novel seminal semenogelin-derived peptides RSIY-15 and SSII-15 act as competitive inhibitors of NEP. Both peptides increased progressive and total sperm motility when added to semen samples. Contrary to the prevailing viewpoint that semenogelin is primarily an inhibitor of sperm motility, our observations demonstrate that semenogelin and its peptide products both activate and inhibit sperm motility. Further studies are underway to investigate the breakdown products of these peptides, and to compare the peptidomic profiles of fertile and infertile men.

SUPPORT: NIH/NIDDK (DK107807 awarded to KD).

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SUBTLE SIGNATURES OF AGING PERSIST OVER TWO GENERATIONS THROUGH THE PATERNAL GERM LINE. Timothy G. Jenkins, PhD, Emma James, B.S., Kenneth I. Aston, PhD, James Hotaling, MD, Douglas T. Carrell, PhD. University of Utah School of Medicine Andrology and IVF Laboratories, Salt Lake City, UT.

OBJECTIVE: Determine if epigenetic signatures of aging in sperm persist over multiple generations.

DESIGN: DNA methylation analysis of stored sperm samples.
CONCLUSIONS: Male hormones, Bcl-2, Cytochrome C and Caspase gene expression were altered in men with impaired fertility possibly via their associations with sperm count, motility and morphology.

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FAM9B WAS ASSOCIATED WITH HUMAN SPERMATOGENESIS AND MALE-SPECIFIC STERILITY. Xinjie Zhang, Dr., Ping Liu, prof., Reproductive Medicine Center, Department of Obstetrics and Gynecology, Peking University Third Hospital, Beijing, China.

OBJECTIVE: Spermatogenesis is the process of gamete formation, which includes mitosis in spermatogonia, meiosis in spermatocytes, and spermiation. A key event is the formation of the synaptonemal complex (SC). Mutations of genes encoding SC components (such as SYCP3, synaptonemal complex protein 3) lead to infertility or sub fertility due to germ cell death. Fam9B mapped on the human chromosome X (Xp22.3) was more similar to SYCP3 in their amino acid sequences and expressed in human testis. However, the expression and precise underlying mechanisms of Fam9B have not been clearly in testes during the spermatogenesis and infertility. And Fam9B mutation associated with sterility?

DESIGN: This study was an analysis of azoospermia, sertoli cell only syndrome (SCOS) and proven fertile patients, including 162 patients diagnosed with azoospermia, 65 patients diagnosed with SCOS and 10 proven fertile patients at the Reproductive Medical Center of Peking University Third Hospital between January 2015 and January 2019. Fam9B was cloned, expressed and identified. Genome DNA sequencing analysis, RT-PCR, Western-blot, Immunohistochemistry and immunocytochemistry were performed.

MATERIALS AND METHODS: Fam9B was analyzed with blood and testicular biopsy samples from azoospermia patients by genome DNA sequencing analysis. These likely mutations were further screened in SCOS patients and in men proven to be fertile. And Fam9B was cloned, expressed and identified with testicular samples using RT-PCR, western blot, Immunohistochemistry and immunocytochemistry. The concentration of testosterone in azoospermia and SCOS patients were determined, and their relativity was studied by statistical methods.

RESULTS: Fam9B mRNAs and protein were detected in human testis, and Fam9B was expressed at different levels in men and patients at the Reproductive Medical Center of Peking University Third Hospital.

CONCLUSIONS: Male hormones, Bcl-2, Cytochrome C and Caspase gene expression were altered in men with impaired fertility possibly via their associations with sperm count, motility and morphology.

P-669 Wednesday, October 16, 2019 6:30 AM

TO STUDY OF APOPTOTIC GENE EXPRESSION THROUGH HYPOTHALAMUS-PITUITARY-CONDONAL AXIS IN. Kamla Shukla Shukla, PhD. All India Institute of Medical Sciences, Jodhpur, India.

OBJECTIVE: To investigate the apoptotic gene expression of Bcl-2, Cytochrome C, Caspase and procaspase with male hormone profile in infertile subjects for their relationship to sperm quality and cell death parameters.

DESIGN: We undertook gene expression on a total of 400 individuals, including 100 fertile donors as controls and three subgroups of infertile men, normozoospermic (idiopathic unexplained; n=100), oligozoospermic (n=100) and asthenozoospermic (n=100). These participants were selected from Departments of Urology, King George’s Medical University, Lucknow, India.

MATERIALS AND METHODS: We used ELISA, quantitative real time PCR (qPCR) with lightCycler Fast Start DNA PLUS SybrGreen kit for IL-6 and TNF alpha, Bcl-2, Cytochrome C, Caspase and procaspase mRNA and their relation to male fertility.

RESULTS: We found decreased sperm motion kinetics and altered male hormone profile associated with increased (p<0.05) procaspase expression and increased of Cytochrome C expression was significantly increased in the oligozoospermic and asthenozoospermic infertile subjects compared to healthy fertile subjects.

CONCLUSIONS: Previous assessments of this data set from our lab have failed to show significant results due to the fact that only conventional approaches were employed. Due to the extremely small changes identified and lack of consistency between samples, the findings reported herein were never previously identified. When thresholds for magnitude were removed and averages generated across each group we began to see subtle but clear signals commonly observed in “aged” sperm. It is clear that the aging signal is nearly all removed through the epigenetic reprogramming process in the embryo, but the fact that some very subtle signals remain suggests that this process is incomplete or susceptible to some degree of error. Perhaps some of this subtle epigenetic transmission over multiple generations plays a small role in previously identified patterns of increased incidence of neuropsychiatric disease in the grand offspring of older grand fathers.

Reference: None.

SUPPORT: None.
OBJECTIVE: Sperm DNA fragmentation is one of the major cellular mechanisms of male infertility and can be observed in 20% to 25% of infertile men. An earlier study has found that RARRES1 and PSM4A5 proteins are altered in seminal plasma in men with high DNA fragmentation. Another study has shown that smokers present high sperm DNA fragmentation. Therefore, in this study, we wanted to evaluate whether these proteins are also altered in other causes of infertility, such as smoking.

RESULTS: Control and smokers groups did not differ regarding DNA fragmentation (mean; standard deviation of 40.5; 17.45 and 47.3; 15.97 respectively). On the other hand, sperm concentration, count, and morphology were lower in the smoking group (p = 0.005, p = 0.002, p = 0.019, respectively). There was no difference between groups for PSM4A5/mL (median; interquartile range of 0.23;0.18 and 0.17;0.21) and PSM4A5/ejaculate (0.65;0.62 and 0.65;0.65). There was no difference between groups for RARRES1/mL (1.15;0.87 and 1.32;1.00) and RARRES1/ejaculate (4.07;3.64 and 4.57;4.79).

CONCLUSIONS: Seminal levels of PSM4A5 and RARRES1 are not altered due to smoking. It is an important finding because it corroborates our hypothesis that these proteins are exclusively associated with sperm DNA fragmentation, but not with other infertility conditions, such as smoking.

FERTILITY & STERILITY®

P-673 Wednesday, October 16, 2019 6:30 AM

IMPACT OF INTERACTION BETWEEN OXIDATIVE STRESS ADDUCTS (OSA) LEVELS AND ACCESSORY CELLS ON SPERM DNA INTEGRITY AND COMPLEMENT REGULATORY PROTEIN. Denis Vaughan, MD, MRCP1,6 Denny Sakkas, PhD,6 Edna E. Tirado, PhD,6 Beth Israel Deaconess Medical Center, Boston, MA;6 Boston IVF, Waltham, MA;6 ReproSource-Quest Diagnostics, Woburn, MA.

OBJECTIVE: Factors present in the semen such as Zinc (Zn), white blood cells (WBC), Round (RC) and epithelial cells (EC) may increase the levels of oxidative stress (OS) and consequently, the formation of oxidative stress adducts (OSA) which may interact with sperm key biomolecules such as complement regulatory proteins required (CRP) for acrosome reaction and DNA producing sperm defective function. The aims of this study were (i) to determine if OSA levels are associated with concentrations of Zn, WBC, RC, and EC and (ii) to compare OSA levels induce both the increased of DNA fragmentation and loss of expression of CRP.

RESULTS: The sperm DFI scores were increased both BL and Abnormal categories when were compared to Normal OSA (Normal 12.75 ± 3.39 BL 24.45 ± 2.19 Abnormal 38.59 ± 8.16 p<0.001). The concentrations of leukocytes were different for BL 0.8 ± 0.2 and Abnormal 6.8 ± 2.3 when were compared to Normal 0.4 ± 0.1 (p<0.01). The values of CRP measured as expression of CD46 indicated that BL 12.73 ± 3.07 and Abnormal 11.32 ± 4.07 are significant different when compared to Normal 15.48 ± 5.18 (p<0.05). Although no differences were found an increasing tendency are observed when the OSA levels are increasing for Zn (Normal 24.1 ± 17 μM BL 256.4 ± 19 μM and Abnormal 261.4 ± 18.4 μM), RC (Normal 3.06 ± 1.55 BL 4.55 ± 3.67 and Abnormal 5.26 ± 5.74 x 10^6/mL) (HDS) Normal 5.06 ± 2.12 BL 8.72 ± 3.27 and Abnormal 9.45 ± 3.60) and no differences were found among the 3 OSA groups for sperm and EC concentrations.

CONCLUSIONS: The levels of oxidative stress measured as (OSA) are associated with DNA fragmentation (DFI) and the loss of expression of (CRP). These results also suggest a possible role for OSA in sperm function, in generating the stress, and demonstrate the application of CD45 staining and flow cytometry to identify leukocytes.

OBJECTIVE: To Investigate a possible correlation between the glycoprotein subunit 130 (gp130) gene adenine (A) > thymine (T) (rs1900173) polymorphism and semen quality or sperm DNA damage.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: A prospective cohort study enrolled 364 men seeking fertility care. DNA was extracted from peripheral blood, and the gp130 gene A>T (rs1900173) polymorphism was genotyped using real-time PCR with the Taqman Universal PCR Master Mix and Taqman SNP genotyping assays. Patients were genotyped for the gp130 polymorphism and were categorized as follows: A/A, A/T, T/T. The remainder of the semen samples were tested for sperm DNA fragmentation using TUNEL assay; sperm morphology examination (MSOME). The remainder of the semen samples were compared between genotype groups.

A portion of each semen sample was used for analysis according to the WHO guidelines/morphological analysis by motile sperm organellae morphology examination (MSOME). The remainder of the semen samples were tested for sperm DNA fragmentation using TUNEL assay; sperm apoptosis was analyzed using the annexin V assay; sperm chromatin packaging/proteination was assessed using chromocycin A3 (CMA3) staining; and sperm mitochondrial membrane potential (MMP) was analyzed using Mitotracker Green. At least 200 spermatozoa were examined in each evaluation.

RESULTS: No correlation was observed between gp130 gene genotypes and semen quality or sperm DNA damage. Table 1 shows the data. CONCLUSIONS: There appears to be no association between gp130 gene A>T single nucleotide polymorphism (SNP) and semen quality or sperm DNA damage. However, more studies stratified for different ethnic background should be performed in the future to clarify the possible roles of gp130 gene SNPs in the pathogenesis of male infertility.

SUPPORT: Merck Grant for Fertility Innovation (GFI-2014).

<table>
<thead>
<tr>
<th>Semen parameter</th>
<th>A/A</th>
<th>A/T</th>
<th>T/T</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>8.1±0.2</td>
<td>8.1±0.2</td>
<td>8.0±0.2</td>
<td>0.59</td>
</tr>
<tr>
<td>Volume (ml)</td>
<td>2.8±1.5</td>
<td>2.8±1.2</td>
<td>1.4±0.8</td>
<td>0.12</td>
</tr>
<tr>
<td>Concentration (mlx10^6)</td>
<td>62.4±50.4</td>
<td>64.2±56.4</td>
<td>90±78.6</td>
<td>0.82</td>
</tr>
<tr>
<td>Progressive motility (%)</td>
<td>53.0±16.5</td>
<td>53.6±16.0</td>
<td>68.3±8.1</td>
<td>0.16</td>
</tr>
<tr>
<td>Total motility (%)</td>
<td>60.1±16.4</td>
<td>60.9±16.0</td>
<td>74.7±8.5</td>
<td>0.17</td>
</tr>
<tr>
<td>Leukocytes (x10^3/ml)</td>
<td>0.4±0.8</td>
<td>0.3±0.3</td>
<td>0.2±0.2</td>
<td>0.19</td>
</tr>
<tr>
<td>Vitality (%)</td>
<td>61.6±15.9</td>
<td>64.3±14.4</td>
<td>73.0±7.1</td>
<td>0.26</td>
</tr>
<tr>
<td>Normal spermatozoa (%)</td>
<td>0.6±0.8</td>
<td>0.7±0.5</td>
<td>1.2±0.3</td>
<td>0.23</td>
</tr>
<tr>
<td>DNA fragmentation (%)</td>
<td>13.7±7.7</td>
<td>13.5±8.0</td>
<td>8.5±0.7</td>
<td>0.59</td>
</tr>
<tr>
<td>Apoptosis (%)</td>
<td>19.5±8.5</td>
<td>19.9±6.1</td>
<td>21.5±2.1</td>
<td>0.54</td>
</tr>
<tr>
<td>CMA3 positivity (%)</td>
<td>55.1±17.1</td>
<td>58.1±16.0</td>
<td>56±26.9</td>
<td>0.56</td>
</tr>
<tr>
<td>Abnormal MMP (%)</td>
<td>25.8±17.4</td>
<td>26.4±16.0</td>
<td>22.5±14.8</td>
<td>0.95</td>
</tr>
</tbody>
</table>

Table 1: gp130 gene A>T (rs1900173) genotypes vs. population and semen parameters

P-674 Wednesday, October 16, 2019 6:30 AM

KARYOTYPING SINGLE SPERM: TARGETED NEXT GENERATION SEQUENCING ALLOWS FOR ACCURATE CHROMOSOME COPY NUMBER ANALYSIS OF HAPLOID GENOMES. Diego Marin, M.S., a Yiping Zhan, Ph.D., a Richard Thomas Scott Jr., MD, a Xin Tao, Ph.D. a TVI-RMA New Jersey, Basking Ridge, NJ; b The Foundation for Embryonic Competence, Basking Ridge, NJ; c Foundation for Embryonic Competence, Basking Ridge, NJ.

OBJECTIVE: Available NGS-based PGT-A platforms have been validated and clinically implemented for karyotyping of trophoectoderm biopsies, where at least 5 cells are available for DNA amplification. However, their application on single cells remains challenging, especially when dealing with haploid genomes. Given the current urge to investigate genetics at a single cell level and the promising advances of in vitro generated gametes, this study aimed to evaluate the performance of a targeted NGS-based PGT-A platform in single spermatozoa, an application that could be extended to any haploid genome.

DESIGN: Experimental and methodology validation study.

MATERIALS AND METHODS: Surplus washed sperm samples from two subjects undergoing an IVF-ICSI cycle were used in this study. For sperm isolation, single spermatozoa with progressive motility were immobilized with an ICSI pipette under a microscope and placed on a 2 μl microdrop of loading buffer, then the microdrop was loaded into a PCR tube. Finally, all samples were subjected to a targeted 2-step PCR protocol for DNA amplification before undergoing NGS. The targeted nature of DNA amplification of this platform results in higher sequencing depth, which allows for accurate single nucleotide polymorphism (SNP) genotyping across all chromosomes. Therefore, if complete loss of heterozygosity was evidenced by more than 95% of SNPs across the whole genome being homozygous, the sample was called haploid. In addition, NGS allele frequency patterns provided further evidence to detect chromosomal abnormalities. For instance, the presence of heterozygous SNPs demonstrates an imbalance of two chromosomes in single sperm, whereas a total absence of SNP data would indicate a chromosome nullisomy.

RESULTS: 52 single spermatozoa (20 from subject 1 and 32 from subject 2) were isolated and subjected to DNA amplification and sequencing. One sample from each subject did not show DNA amplification. In total, 39 samples (Subject 1 = 15, subject 2 = 24) retrieved a haploid genome. Of these, 21 (53.8%) samples presented the X chromosome and 18 (46%) the Y. Based on SNP data and heterozygosity plots, the remaining 11 samples were not categorized as pure haploid, which could be indicative of sample contamination, presence of more than one spermatozoon or suboptimal DNA amplification. Furthermore, 1 in 15 sperm karyotypes from subject 1 and 1 in 24 from subject 2 presented both a nullisomy of chromosome 15, which indicates a sperm aneuploidy rate of 6.67% and 4.17% respectively for each subject.

CONCLUSIONS: This NGS-based PGT-A platform is coupled with targeted DNA amplification, thus resulting in sufficient sequencing depth to allow genotyping that can be used to evaluate abnormality rates in sperm.
with higher precision. This application also highlights its ability to be used in other haploid samples such as second polar bodies or in vitro-generated gametes. In addition, our data supports the fact that aneuploidy rates in human sperm are low.

**P-676 Wednesday, October 16, 2019 6:30 AM**

**EFFECT OF OXIDATION-REDUCTION POTENTIAL ON MITOCHONDRIAL MEMBRANE POTENTIAL AND VITALITY OF PHYSIOLOGICALLY NORMAL HUMAN SPERMATOZOA.** Manesh Kumar Panner Selvam, PhD,a Ashok Agarwal, PhD,b Renata Finelli, PhD,c Christopher M. Douglas, B.A., M.S.,d Ralf Henkel, PhD,e Sajal Gupta, MD,a Rakesh Sharma, PhD,a American Center for Reproductive Medicine, Cleveland Clinic, Cleveland, OH; dUniversity of the Western Cape, Bellville, South Africa.

OBJECTIVE: Physiological levels of reactive oxygen species (ROS) are necessary for optimal sperm functions such as total and progressive motility. In our previous study, we have demonstrated that higher levels of seminal oxidation-reduction potential (ORP) negatively affects total and progressive motility. Furthermore, motility is directly related to sperm vitality and mitochondrial membrane integrity. The objective of the present study was to investigate the effect of ORP on vitality and mitochondrial membrane potential (MMP) of physiologically normal spermatozoa.

DESIGN: Physiologically normal sperm from donor semen samples (n=8) were exposed to different titrated levels of oxidative stress (ORP; 1.48 and 2.75 mV/10⁶ sperm/ml) in sperm wash medium (SWM). MMP and sperm vitality were measured at different time intervals (0, 60 and 120 minutes). The sample size for this study was calculated with an 80% power and a significance of P<0.05.

MATERIALS AND METHODS: ORP of SWM was taken as baseline (control) and the different ORP levels (1.48 and 2.75 mV/10⁶ sperm/ml) were generated by titrating SMW with defined concentrations of the oxidative stress inducer, cumene hydroperoxide. Equal concentrations (≈20 μM) of double-density gradient centrifugation-selected sperm (motility >90%) were incubated in SMW with different ORP levels for up to 120 minutes. Eosin-nigrosin staining was performed to evaluate the vitality; whereas, JC-1 dye was used to stain the sperm cells (≈1 x 10⁶) to evaluate the depolarization of mitochondrial membrane. MMP was analyzed using flow cytometry after 60 and 120 minutes. Pairwise comparison analysis was carried out to determine the statistical significance.

RESULTS: MMP remained unchanged after sperm exposure for 60 minutes. MMP decreased to 2.5% (P=0.0014) and 61.1% (P<0.0001) at 120 minutes when sperm was exposed to ORP values of 1.48 mV/10⁶ sperm/ml and 2.75 mV/10⁶ sperm/ml, respectively. Vitality decreased to 21.2% (P<0.0001) at 60 minutes and 41.1% (P<0.0001) at 120 minutes when sperm were exposed to ORP values of 2.75 mV/10⁶ sperm/ml.

CONCLUSIONS: The current findings demonstrate that spermatozoal MMP and vitality were affected at ORP levels of ≥1.48 mV/10⁶ and ≥2.75 mV/10⁶ sperm/ml, respectively. Hence, high seminal ORP may have a negative effect on sperm functionality and therefore on the fertilizing ability of spermatozoa.

Reference: None.

SUPPORT: None.

**P-677 Wednesday, October 16, 2019 6:30 AM**

**MAPPING EVOLUTION OF MAMMALIAN SPERM-ATOSIS VIA HIGH RESOLUTION TRANSCRIPTOMICS.** Adrienne N. Shami, B.S., a Adrienne N. Shami, B.S., a Sarah Munyoki, B.A., a Xianing Zheng, B.S., a Jun Z. Li, Ph.D., a Kyle E. Orwig, Ph.D., b Sue Hummood, Ph.D. c University of Michigan, Ann Arbor, MI; dUniversity of Pittsburgh School of Medicine, Pittsburgh, PA.

OBJECTIVE: Sperm are unique, highly specialized cells that carry genetic information from father to offspring and provide a continuous link between the past, present, and future of a species. In all mammals, the foundational unit of fertility is the spermatogonial stem cell (SSC), which must balance self-renewal with differentiation to ensure continuous sperm production. This is reliant on coordinated intrinsic (germ-cell mediated) and extrinsic (some mediated) regulation to guide differentiation, commitment to meiosis, and morphological maturation. While decades of research in mice have provided a critical foundation of data, studies in primates have been limited to targeted subtypes based on a priori knowledge applied from rodents. However, fundamental differences exist between lineages, limiting the ability to use mouse models. As a result, these processes are not well understood in humans and efforts to restore impaired spermatogenic function have had limited success. Here, we aim to identify key differences among species in these processes by conducting unbiased global evolutionary comparisons of expression between rodents and primates in the germline and soma throughout the course of spermatogenesis.

DESIGN: Single cell RNA sequencing was performed on adult human and nonhuman primate testis, and datasets were analyzed both individually and also globally compared with our previously published mouse single cell atlas.

MATERIALS AND METHODS: Cryopreserved testes samples from 4 human and 5 macaque individuals were dissociated to single cell suspensions and isolated via microfluidics using the Drop-seq platform to conduct single-cell sequencing on multiple technical replicates.

RESULTS: The data revealed a continuous developmental progression from spermatogonia to spermatids in adult humans (n=4, ~14,000 cells) and rhesus macaques (n=5, ~22,000 cells), thus capturing the complete germ cell differentiation process and analogous somatic cell types across all three species. Comparing pseudotime alignments of germ cell trajectories across species identified areas of similarity and dis-synchrony of germ cell maturation program, including differences in starting and ending states and a variable “clock rate” within the trajectories. Targeted analysis of spermatogonia computationally aligned discrete molecular states between species, revealing a unique undifferentiated population in primates, potentially containing SSCs. Characterization of underlying transcriptional programs and somatic cell inputs identified additional features of divergence.

CONCLUSIONS: Our datasets provide new insights into differences in the intrinsic germ cell program and extrinsic signals required to promote germ cell differentiation in human, nonhuman primate, and rodent testes.

**P-678**

WITHDRAWN

**P-679 Wednesday, October 16, 2019 6:30 AM**

**COMPARATIVE PROTEOMIC ANALYSIS REVEALS DIFFERENTIAL REGULATION OF REDOX HOMEOSTASIS AND PURTURBED OXIDATIVE PHOSPHORYLATION PATHWAY IN UNILATERAL COMPARED TO BILATERAL VARICOCELE CONDITION.** Manesh Kumar Panner Selvam, PhD,a Ashok Agarwal, PhD,b Ralf Henkel, PhD,e Sajal Gupta, MD,a American Center for Reproductive Medicine, Cleveland Clinic, Cleveland, OH; dUniversity of Pittsburgh School of Medicine, Pittsburgh, PA.

OBJECTIVE: Sperm are unique, highly specialized cells that carry genetic information from father to offspring and provide a continuous link between the past, present, and future of a species. In all mammals, the foundational unit of fertility is the spermatogonial stem cell (SSC), which must balance self-renewal with differentiation to ensure continuous sperm production. This is reliant on coordinated intrinsic (germ-cell mediated) and extrinsic (some mediated) regulation to guide differentiation, commitment to meiosis, and morphological maturation. While decades of research in mice have provided a critical foundation of data, studies in primates have been limited to targeted subtypes based on a priori knowledge applied from rodents. However, fundamental differences exist between lineages, limiting the ability to use mouse models. As a result, these processes are not well understood in humans and efforts to restore impaired spermatogenic function have had limited success. Here, we aim to identify key differences among species in these processes by conducting unbiased global evolutionary comparisons of expression between rodents and primates in the germline and soma throughout the course of spermatogenesis.

DESIGN: Single cell RNA sequencing was performed on adult human and nonhuman primate testis, and datasets were analyzed both individually and also globally compared with our previously published mouse single cell atlas.

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CONCLUSIONS: Our datasets provide new insights into differences in the intrinsic germ cell program and extrinsic signals required to promote germ cell differentiation in human, nonhuman primate, and rodent testes.
TABLE 1. Proteins involved in oxidative phosphorylation pathway

<table>
<thead>
<tr>
<th>DEPs</th>
<th>Unilateral varicocele (Z-score)</th>
<th>Bilateral varicocele (Z-score)</th>
<th>Combined varicocele (Z-score)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SDHA</td>
<td>2.27</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>COX4A1</td>
<td>-2.33</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>ATP5F1B</td>
<td>-3.25</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>UQCR2C</td>
<td>-1.96</td>
<td>0</td>
<td>-1.63</td>
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<tr>
<td>CYC1</td>
<td>-4.71</td>
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<td>0</td>
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<tr>
<td>NDUF53</td>
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<td>0</td>
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<tr>
<td>COX5B</td>
<td>-4.89</td>
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<tr>
<td>NDUF51</td>
<td>-5.77</td>
<td>-2.78</td>
<td>-3.76</td>
</tr>
</tbody>
</table>

*Considered significant when Z score is >2 or < -2.

RESULTS: Seminal plasma proteomic analysis revealed the presence of cellular proteins particularly of mitochondrial origin in seminal plasma. Proteins involved in the oxidative phosphorylation pathway of spermatozoa were present (Z score = -3.5) in unilateral varicocele patients. Whereas, the Z-score was not available for combined varicocele and bilateral varicocele groups (Table 1). In addition, proteins regulating the cellular antioxidant mechanism such as SOD1 (Z score = 3.94) and SOD2 (Z score = 8.08) were detected in unilateral varicocele patients. Whereas, IL-8 signaling pathway was activated in bilateral varicocele group (Z score = 2.236) compared to unilateral varicocele group (Z score = 1.342).

CONCLUSIONS: Our proteomic result implies release of spermatozoal proteins into seminal plasma of unilateral varicocele patients may be due to oxidative damage of sperm membrane or inflammation originating from mitochondrial dysfunction. On the other hand, in case of bilateral varicocele it may due to apoptosis which might have been phagocytized thereby, no cellular content is released into seminal plasma.

Reference: None.

SUPPORT: None.

P-680 Wednesday, October 16, 2019 6:30 AM

EXOME SEQUENCING IDENTIFYING ADDITIONAL QRICH2 MUTATIONS IN OLIGO-ASTHENO-TERATOZOSPERMIA AND ASTHENOSPERMA PATIENTS. Wenming Xu, Ph.D. Xiao Liang Li, Ms., American Society of Human Genetics, Chengdu, China.

OBJECTIVE: Our recent study has shown that loss-of function of QRICH2, a testis specific expressed gene, is associated with male infertility with multiple morphological abnormalities of the flagella (MMAF), the current study aim to determine whether QRICH2 mutations were associated with other more common forms of male infertility, such as oligo-astheno-teratozoospermia and asthenospermia

DESIGN: Experimental study recruited from male infertility clinic and human samples of case and control were collected.

MATERIALS AND METHODS: 84 cases of male infertility patients were recruited. WES was performed for all subjects. All identified variants were confirmed by Sanger sequencing. Immunostaining result was used to determine the specific localization of QRICH2 in human sperm. Western blot were used to determine the expression of QRICH2 in oligo-astheno-teratozoospermia. Co-Immunoprecipitation (Co-IP) with QRICH2 antibody in human testis and proteomics analysis were conducted to identify the binding partner. IVF/ICSI outcome were followed to determine whether the mutation of QRICH2 have effect on the normal development of offspring.

RESULTS: We identified five unrelated patients (5/84, 5.9%) with homozygous and compound heterozygous mutations in the QRICH2 gene, which is specifically expressed in human and mouse testis. Five of the samples harbor a recurrent deletion, (g.17:74288566_74288568del.c.1742_1744del.p.581_582del) None of these mutations were reported in control sequence databases. 4 of mutation is located in the SNC-N domain, while one mutation is located in the Glutamine rich domain. Co-IP result indicated that mitochondrial proteins, such as VDAC1 is associated with QRICH2. Western blot result shows that QRICH2 expression is down-regulated in patients. And IVF/ICSI outcome analysis indicates that normal offspring development could be observed in the patients.

CONCLUSIONS: Compared with other reported genes associated with male infertility, high frequency of QRICH2 mutations were detected with WES. QRICH2 is important for sperm motility. The mutation of QRICH2 gene, especially high frequency mutations of SMC_N domain are likely responsible for the phenotypes of both oligo-astheno-teratozoospermia and asthenospermia.
ASSOCIATION OF MENTAL HEALTH DIAGNOSES AND UTERINE ENDOMETRIAL THICKNESS IN WOMEN UNDERGOING IN-VITRO FERTILIZATION. Anna K. Knight, PhD, a Heather S. Hipp, MD, b Laurie McKenzie, MD, c Jessica B. Spencer, MD, MSC, c Sabrina A. Gerkowicz, MD. aEmory University School of Medicine, Atlanta, GA; bBaylor College of Medicine, Houston, TX; cEmory University School of Medicine, Department of Gynecology and Obstetrics, Atlanta, GA.

OBJECTIVE: To assess the association between mental health diagnoses and uterine receptivity, operationalized as endometrial thickness.

DESIGN: Due to the lack of data regarding the impact of mental health diagnoses on intermediate outcomes of in vitro fertilization (IVF), we performed an exploratory retrospective cohort study of women undergoing IVF at an academic medical center from 2018 to 2019.

MATERIALS AND METHODS: A total of 101 patients undergoing IVF were recruited and underwent controlled ovarian hyperstimulation with an antagonist protocol. Women on clomiphene or letrozole, those seeking fertility preservation and those with uterine factor were excluded. Mental health diagnoses and medications were abstracted from chart review. Endometrial thickness was assessed via transvaginal ultrasound on the final day of stimulation. We used linear regressions to assess the associations between 1) anxiety 2) depression 3) any psychiatric diagnosis 4) current treatment with antidepressant or anxiolytic medications. Women had a mean of 35.1 years of age, a mean BMI of 26.3±5.6 kg/m², and a mean endometrial thickness of 10.3±2.7 mm. Women self-reported as Caucasian (52.5%), Asian (24.8%), or African American (15.8%). A mental health diagnosis (p = 0.002) were negatively associated with endometrial thickness. All associations remained significant after controlling for BMI. Endometrial thickness was not associated with cycle characteristics (peak estradiol level, total gonadotropin dose, or number of oocytes retrieved).

CONCLUSIONS: Mental health diagnoses and current antidepressant or anxiolytic treatment are associated with a thinner endometrial thickness, a marker of uterine receptivity. Prior studies have indicated women with history of anxiety and depression may have lower live birth rates; this is perhaps due to the influence of stress on endometrial thickness and interaction with the reproductive hormonal axis. These findings are important given the strong association of mental health diagnoses and infertility, with anxiety and depression often exacerbated by the stress of fertility treatment. Future studies will examine biochemical markers of stress to further explore the mechanism behind this finding.

PATH TO PREGNANCY: A MULTINATIONAL SURVEY OF WOMEN’S EXPERIENCES AND EXPECTATIONS WHEN PLANNING PREGNANCY. Sarah Johnson, PhD.a, b Sarah Weddell, BSc.c Support: Study funded by SPD Swiss Precision Diagnostics GmbH.

OBJECTIVE: Limited scientifically rigorous research exists on decisional distress and uncertainty experienced by individuals considering preimplantation genetic testing (PGT), and no questionnaire (Q) exists to measure these constructs. This study assessed the psychometric properties of the new Preimplantation Genetic Testing (PGT) Decisional Distress Q and the PGT Decisional Uncertainty Q.

DESIGN: Prospective online Q’s and associated psychometric evaluation of the Q’s.

MATERIALS AND METHODS: The Q’s were developed by the investigative team based on a careful review of the relevant literature and our prior experience with questionnaire design for aspects of reproductive health. A semi-structured interview was conducted to assess face validity. Eligibility required women had used or considered using PGT in the previous 6 months. The new Distress Q has 22 items. The new Decisional Uncertainty Q has 13 items and assesses (through three subscales): clarity of the perceived benefits/drawbacks of testing (5 items), degree of input by respondent in the decision (1 item), and decision certainty (7 items). Means, variances (SD), and ranges were calculated, followed by Cronbach’s alpha, and correlation between the Q’s. Estimated sample size of n = 100 was based on alpha = 0.05 and 80% power to detect correlations of r = 0.28 between the contributors and the Q scores.

RESULTS: N = 106 females (mean age 36.5±4.8 years, range 26–45 years; 15% non-Caucasian; 9% Hispanic) completed the online questionnaire, and 17 states were represented. All scales had excellent internal consistency (Cronbach’s α = 0.92-0.94). Distress levels were low (mean 1.00 [SD = 0.75] on a 0–4 scale, higher score = greater distress). Decision clarity and decision certainty were good (mean 3.26 and 3.06 [SD = 0.79 and 0.89] respectively on a 0–4 scale, higher score = greater clarity/certainty). Distress was inversely correlated with decision clarity (r = 0.34, p < 0.01) and decision certainty (r = 0.65, p < 0.01). Decision clarity was positively correlated with decision certainty (r = 0.73, p < 0.01). For degree of input in the testing decision, more than half (62%) indicated that they and their partner would have equal input, and 32% said that they would have more input than their partner.

CONCLUSIONS: Infertility patients must call through many clinical and personal factors prior to making the decision to utilize PGT, and modern
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IS A DIAGNOSIS OF UTERINE FIBROIDS WORSE THAN A DIAGNOSIS OF CONGESTIVE HEART FAILURE OR CHRONIC LUNG DISEASE? Bhuchitra Singh, M.D., MPH, MS,a Martha C. Thomas, M.D., M.S.,b Holly Sims, RN, BSN,c James Segars, M.D.,ca Johns Hopkins School of Medicine, Baltimore, MD; b University of Mississippi Medical Center, Jackson, MS; c Johns Hopkins University, School of Medicine, Baltimore, MD.

OBJECTIVE: More than 80% of African American women and 70% of white women have detectable uterine fibroids by age 50. Despite the high prevalence of disease, the psychosocial impact of fibroid disease has not been quantitatively compared to other chronic conditions. Here we rigorously used published standardized, validated questionnaires of the effect of fibroids at baseline and after treatment. We evaluated women's health-related quality of life (HRQoL) using the SF-36, UFS-QoL, and SAQ questionnaires. We considered women eligible if they met the criteria of being diagnosed with fibroids and met clinical indices, such as increase in hemoglobin levels or decrease in fibroid size.

RESULTS: Of the 2,422 articles identified, 21 studies met inclusion/exclusion criteria, representing a total of 2,361 patients. Of note, the data showed that for 7 out 8 categories on the SF-36 (Short Form 36) Health Survey questionnaire, a diagnosis of uterine fibroids was accompanied by a disability score that exceeded (i.e., was a greater psychosocial stressor) than the diagnosis of congestive heart failure (CHF), diabetes mellitus (DM), or chronic lung disease (CLD). At baseline, quality of life scores were considerably lower in all instruments measuring these variables in women with uterine fibroids, indicating significantly impaired psychosocial functioning. Uterine fibroids were associated with significant patient-reported health disabilities related to bodily pain, emotional and mental health, social functioning, and satisfaction with life. Women with symptomatic fibroids regarded an improvement in quality of life as a major driver of decision making, more so than clinical indices, such as increase in hemoglobin levels or decrease in fibroid size.

CONCLUSIONS: The level of disability associated with uterine fibroids exceeded that of chronic diseases such as CHF, DM and CLD. Attention to the impact of uterine fibroids on the quality of life in women affected by fibroids will lead to increased patient satisfaction.

SUPPORT: This effort is supported in part by the Howard and Georganna Jones Research Endowment.

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THE PSYCHOLOGICAL IMPACT OF SURROGACY ON THE FAMILIES OF GESTATIONAL CARRIERS: IMPLICATIONS FOR CLINICAL PRACTICE. Mary P. Riddle, Ph.D., Stephanie C. Michaud, B.S., Quenell D. Redden, B.S., Olivia R. Pozza, B.A., Brendan L. Scanlan, B.S., The Pennsylvania State University, University Park, PA.

OBJECTIVE: ASRM has issued ethics and practice committee guidelines for gestational carriers (GCs) that include recommendations for the psychological consideration of a GC's own family. At present, there are no studies on the impact of surrogacy within GC family systems that can offer guidance to mental health professionals (MHPs) who counsel potential GCs. This study seeks to explore the psychological impact of surrogacy on families in order to guide MHPs in educating GCs on how this experience might affect their families.

DESIGN: IRB approved, cross-sectional survey study.

MATERIALS AND METHODS: Participants (n = 53) were recruited via an ad posted on surrogacy websites and forums. Research packets were mailed to GC families with designated questionnaires for each family member to fill out and return. All family members filled out a detailed questionnaire on the experience of surrogacy along with the Family Assessment Measure, Version III (FAM-III). Children were asked to fill out the Piers-Harris Children’s Self-Concept Scale, 2nd Edition (Piers-Harris 2). Data was entered and analyzed by SPSS software.

RESULTS: Children of GCs (n = 23) endorsed excitement, curiosity, surprise, and pride at the highest rate amongst emotions experienced from surrogacy. 74% of children reported the experience as having a positive impact on their life. Children scored within normal limits on all domain scales on the Piers Harris 2, including behavioral adjustment, freedom from anxiety, and male infertility stigma as well as infertile women’s internalized experiences of stigma.

SUPPORT: This research was funded by Modern Health, Inc.

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A COMPREHENSIVE EXAMINATION OF INFERTILITY STIGMA AMONG FERTILE AND INFERTILE WOMEN IN THE UNITED STATES. Amber K. Worthington, PhD,a Erin E. Burke, PhD,a Carly Leahy, B.A.b Penn State University, University Park, PA; bModern Fertility, San Francisco, CA.

OBJECTIVE: Infertility impacts 1 in 6 couples; however, having children is a social norm, potentially stigmatizing infertile individuals. This research expands previous qualitative and small-scale studies with a large-scale survey of both fertile and infertile women’s societal perceptions of female

and male infertility stigma as well as infertile women’s internalized experiences of stigma.

DESIGN: A national, cross-sectional survey.

MATERIALS AND METHODS: 327 women were recruited through an e-newsletter in March 2019; no incentive was provided. Eligible participants were ages 18 to 59, identified as women, and lived in the USA. After providing informed consent, participants completed an online survey to assess societal perceptions of female and male infertility stigma. The survey also assessed infertile women’s internalized experiences of stigma and emotions. The data were analyzed using one-sample and independent sample t-tests and bivariate correlations; the power for these analyses was excellent (>.99).

RESULTS: Participants ranged in age from 18 to 59 (M = 34.11, SD = 6.64). The majority identified as heterosexual (95%) and had a partner (81%). Infertility was defined as a diagnosis of infertility or 12 months of unprotected sex without becoming pregnant; 33% of the participants were infertile.

An examination of societal perceptions of infertility stigma revealed that both fertile (M = 2.90, SD = 0.76) and infertile women (M = 2.76, SD = 0.81) felt that female infertility was stigmatized (the means were statistically higher than the midpoint of the 5-point scale; fertile women, t(217) = 4.89*; infertile women, t(108) = 5.48*). Fertile (M = 2.56, SD = 0.73) and infertile women (M = 2.49 SD = 0.71) did not believe male infertility was stigmatized (the means were not statistically higher than the midpoint; fertile women, t(217) = 0.15, ns; infertile women, t(108) = 0.95, ns). A comparison of societal perceptions of female and male infertility stigma revealed that both fertile (r(217) = 0.45*) and infertile women (r(108) = 0.40*) felt infertility stigma was significantly higher than male infertility stigma (fertile women: r(217) = 0.56*; infertile women: r(108) = 0.80*). Infertile women indicated feeling internalized stigma, as the mean (M = 4.18, SD = 0.84) was significantly higher than the midpoint of the 5-point scale, t(108) = 3.04*. Internalized stigma was associated with feeling afraid (r = .25*), uncertain (r = .22*), anxious (r = .23*), stressed (r = .45*), ashamed (r = .48*), and guilty (r = .52*).

CONCLUSIONS: Despite the increased awareness of infertility and emergence of new technologies increasing treatment success, infertility stigma persists, particularly for women. The results suggest that women believe infertile women are stigmatized, and there is greater stigma for infertile women than men. Further, infertile women report feeling stigmatized, which is related to negative emotions. Infertility stigma puts strain on relationships, may lead individuals to hide their diagnoses from friends or family and delay or avoid treatment. In turn, this could lead to worse prognoses for these patients.

Note *p < .05; ns = not significant.

SUPPORT: This research was funded by Modern Health, Inc.
The small size could have contributed to the lack of significant differences short recruitment phase and the sample size was thus smaller than planned. Groups at follow-up but the increase in stress level was significantly greater lifestyle, was significant (P < .05). Each of the FPI five domain-specific scores in the group had a five point decrease, changing from extremely high to moderately high, but not significant. The FPI five domain-specific scores in the intervention group decreased at follow up and one, Rejection of Childfree lifestyle, was significant (P = 0.03). Several statements increased in both groups at follow-up but the increase in stress level was significantly greater in the control group than the intervention group (P = 0.02).

CONCLUSIONS: Recruitmen
t was challenging for this study due to the short duration of the FertiStrong app and the sample size was thus smaller than planned. The small size could have contributed to the lack of significant differences in the HADS. However, despite the small sample size, there were several significant improvements noted in the intervention group and on all testing, the intervention group trended to less distress. More research is needed on convenient interventions for men experiencing infertility.

SUPPORT: This study was supported by an unrestricted educational grant from Ferring Pharmaceuticals.

MOTIVATING FACTORS AND QUALITY OF LIFE FOR MALE PARTNERS OF INFERTILE COUPLES. Rachel Blair Danis, MD,a Semara A. Thomas, MD,a Richard J. Paulson, MD, MS,b Kristin Bendikson, M.D.,c Jacqueline Ho, MD MS,a Mary Katherine Samplaski, MD,a Rachel S. Mandelbaum, MD,a University of Southern California, Los Angeles, CA; bKeck School of Medicine, University of Southern California, Los Angeles, CA.

OBJECTIVE: Motivating factors for pursuing fertility treatment may be difficult to ascertain, as there may be fear of a “wrong” answer. Given that infertility is a couples’ condition, it is important to understand the male’s perspective. We sought to assess the male motivations and quality of life (QoL) during fertility treatment.

DESIGN: Cross-sectional survey study.

MATERIALS AND METHODS: 2 anonymous paper surveys were given to 70 male partners after providing a semen sample for assisted reproductive technology at a fertility clinic. Men were alone during this time. 1st, a questionnaire assessed demographics, motivating factors, and fertility history. 2nd, the fertility quality of life (FertiQoL) survey assessed the impact of infertility on the male partner. FertiQoL contained 2 QoL domains: Core (with Mind-Body, Emotional, Relational, and Social subdomains) and Treatment (with Tolerability and Environmelt subdomains). Responses were scaled 0-100. A higher score indicated higher QoL. Eligible respondents included men receiving treatment as part of an infertile couple. Responses were analyzed via descriptive statistics, chi-square analysis, and multivariable regression analysis.

RESULTS: Out of 70 anonymous surveys, 61 (87.1%) and 52 (74.3%) completed the 1st and 2nd surveys entirely. 62 (88.6%) men were married, 51 (75.0%) did not have prior children, and 19 (27.9%) reported prior in vitro fertilization (IVF). 23 (33.8%) men had been trying to conceive for <12 months, 20 (29.4%) for 12-24 months, and 25 (36.8%) for >24 months. When asked, “Why are you pursuing a fertility evaluation?”, 89.6% (60/67) said it was “because both my partner and I want a child.” When asked, “Do you want children?” 91.0% (61/67) said “yes,” but 9.0% (6/67) said “no.” Of these men, 4/5 were planning to undergo IVF. In contrast, 66.7% (40/60) of men who did desire children were planning to undergo IVF. Duration of infertility, age, income, and marital status were not related to male desire for a child (p > 0.05). Not having a prior child was related to male desire for wanting children (p = 0.003).

Mean FertiQoL scores were: Overall 78.9 +/- 9.9, Core 79.0 +/- 9.6, and Treatment 78.5 +/- 14.4. Men who did not want children scored lower in the Core interpersonal subgroups (Relational and Social) than those who did want children, but this was not significant (p > 0.05). CONCLUSIONS: 9% of males self-reported that they did not want a future child, yet 4/5 were planning to undergo IVF. Not having a prior child was related to desire for future children. Understanding these motivations provides an opportunity to better care for male partners.

KNOWLEDGE, ATTITUDES AND CONCERNS TOWARDS SINGULAR SINGLE EMBRYO TRANSFER (SET) IN COUPLES UNDERGOING FRESH/FROZEN EMBRYO TRANSFER CYCLES IN ASIAN POPULATION. Hema Vaithianathan, MD MRCONG,a P. M. Ganipathi, MD, DGO, FMMC, FICS, FICOG, MBSA(b) S. S. Gayathri Devi, MD(OG), FRM. "Postdoctoral Fellow, Chennai, India; Director & Senior Consultant, Chennai, India; "Consultant - Reproductive Medicine, Chennai, India.

OBJECTIVE: With increasing trend towards elective single embryo transfer (SET), it is essential to explore crucial questions like how patients perceive, understand and decide for these options. In countries where the number of embryos transferred is still unregulated and left for clinician’s discretion, there is a need to reduce couples desire for multiple embryo transfer. Particularly, in a patient population with poor health literacy and mostly
taking self-funded treatment, understanding how patient balances the risks and benefits of single embryo transfer is vital. The purpose of this study is to assess the patients’ and spouses’ knowledge, attitude and concerns regarding single embryo transfer.

**DESIGN:** Prospective questionnaire study at a tertiary-care, university-affiliated teaching hospital.

**MATERIALS AND METHODS:** 240 couples participated in this 25 item questionnaire survey at their routine counselling visit before embryo transfer. The common practice in the centre during the study period was double embryo transfer (DET). The treatment cycles were self-funded and the patients received no reimbursements. All couples received a psychological counseling session, written information as brochure and consultation with ART clinician, explaining DET, SET and Multiple pregnancy, before responding to questionnaire. Descriptive statistics were computed, chi square tests were performed to compare the frequencies according to population demographics and response characteristics.

**RESULTS:** 240 women and 232 men answered the questionnaire for analysis. 62% preferred singleton conception in their next embryo transfer cycle. Yet, 92% of men and 93% of women indicated that they would happily accept if conception resulted in twins in the current IVF attempt. Cancelled cycle (82%) was perceived as unacceptable risk followed by failed cycle (67%) and multiple pregnancy (45%). Twin conception risks are perceived as important by the couples but still prefer two embryo transfer stating ‘Have a positive attitude and wouldn’t happen to all’ (76%).87% of men and 89% of women would prefer SET if results unchanged and comparable to DET.

The top concerning factor for choosing DET over SET was ‘understand the benefits but feel it will prolong the time to conceive’ (69% men and 74% women). Compared to women, men were more likely to choose SET over the factor ‘less risks to mother’ in singleton conception (63% Vs 35%, P=0.04). About 74% choose DET over SET in the next cycle even after feeling well informed and understood benefits.

**CONCLUSIONS:** Twin conception risks were perceived as important by the couples but still prefer double embryo transfer. Couples believe accepting SET would prolong the time to conceive. These results could help in counselling patients addressing their concerns and specific information provision about risks. Couples would prefer SET programs if it may provide comparable success rates and time to conception which would require careful patient selection. Thus, strategies to maintain existing rates of successful conception per oocyte recovery may reduce couples desire to choose multiple embryo transfer.

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**LIFESTYLE RELATED FACTORS ASSOCIATED WITH PREGNANCY OUTCOME AFTER IN VITRO FERTILISATION-EMBRYO TRANSFER CYCLES.** Hema Vaithianathan, MD MRCCOG, P. M. Gopinath, MD, DGO, FMMC, FICS, FICOG, MBA(HSM), S. S. Gayathri Devi, MD(OG), FRM. 2Postdoctoral Fellow, Chennai, India; 2Director & Senior Consultant, Chennai, India; 2Consultant - Reproductive Medicine, Chennai, India.

**OBJECTIVE:** Lifestyle factors have a dramatic impact on the reproductive performance of infertile population undergoing Assisted Reproductive Technology. The present study focused on IVF population and explored association between lifestyle factors primarily during the implantation window and implantation success. This study aims at determining the independent contribution of female lifestyle related factors following embryo transfer leading to ART success. Also, the secondary aim is to compare the differences between pregnant and non-pregnant cycles and to draw strategies to improve ART outcome.

**DESIGN:** Cross sectional questionnaire based study.

**MATERIALS AND METHODS:** This study was undertaken in our university affiliated and tertiary referral private hospital. We recruited 130 women who underwent frozen/fresh embryo transfer (IVF/ICSI cycles) over a period of 12 months. We categorized lifestyle factors into diet and nutrition related, physical activity related and emotional support related behaviours. A structured questionnaire with 13 questions was framed. The survey was conducted using the computer assisted telephone interviewing system. The women completed the questionnaire based on their lifestyle factors from the time of embryo transfer to serum pregnancy testing. The primary outcomes were the result of Serum beta hCG (>25mIU/mL considered to be positive) on day 14 after embryo transfer.

**RESULTS:** Among the 130 women receiving ET, 50/130(38%) resulted in implantation. The mean age of the study population was 31.23±3.21 years with a mean BMI of 25.2±3.2kg/m². Age, duration of infertility, previous IVF attempts all showed a correlation with negative outcome. A BMI consistent with being overweight (BMI 25-29 kg/m2) and obese (BMI >30 kg/ m2) was associated with a lower pregnancy rate compared with women of a BMI of 19 - 24.9(Implantation rate - 23%). A comparison of the physical activity variables among the pregnant and non-pregnant groups yielded no significant differences among them in logistic regression analysis. There was a significant association between plant based diet and inclusion of fresh fruits to successful outcome (P = 0.043). All women responded that they had received adequate emotional/psychological support and there was no statistical differences between two groups (P = 0.521).

**CONCLUSIONS:** Women had a tendency to limit physical activity levels post embryo transfer and bed rest has no correlation with ART success and there is a clinical need to emphasize that prolonged bed rest following ET is not necessary. Women maintained a plant based diet showed an association to positive pregnancy outcome. A structured counselling to facilitate lifestyle changes may optimise reproductive performance and improve their chance of success.

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**P-692 Wednesday, October 16, 2019 6:30 AM**

**FAMILY-BUILDING AFTER CANCER: UNDERSTANDING PATIENT SUPPORT NEEDS, PREFERENCES FOR SUPPORT, AND RECOMMENDATIONS FOR CARE.** Catherine Benedict, PhD, Alexandria Louise Hahn, MSc, Alyssa McCready, LMSW, Michael A. Diefenbach, PhD, Jennifer S. Ford, PhD, Stanford University School of Medicine, Palo Alto, CA; Feinstein Institute for Medical Research, Manhasset, NY; Hunter College and The Graduate Center, City University of New York (CUNY), New York, NY.

**OBJECTIVE:** Fertility is one of the most distressing issues for adolescent and young adult female (AYA-F) cancer survivors. Family-building often requires reproductive medicine, with associated challenges (e.g., high cost). This study examined AYA-F survivors’ fertility experiences and perceptions of care related to family-building after cancer treatment.

**DESIGN:** Semi-structured interviews (45-60 minutes) were conducted with AYA-F cancer survivors (N=25) exploring themes related to fertility and family-building.

**MATERIALS AND METHODS:** Coding categories were derived based on the Ottawa Decision Support Framework and augmented by grounded theory. The coding team (n=3) completed an iterative process of coding and review, resulting in adequate inter-rater reliability (alpha>.7).

**RESULTS:** Participants averaged 29 years old (SD=6.2; range, 15-39) and were primarily White and well educated: 32% had undergone fertility preservation. Three main themes were identified: Unmet Needs, Preferences for Support Delivery, and Recommendations for Providing Support. Multiple support needs were described, including lack of informal support, fertility and family-building options (36%), psychological support (16%), and logistical help navigating access to care and resources (32%). AYA-Fs believed the best way to learn about resources was through online platforms (72%) or doctor-initiated discussions during clinic visits (40%). Their preferred format for receiving in-depth information and counseling was through face-to-face interactions (80%). Thus, a combined approach was preferred such that information (via web-based communication) should be provided first, with follow-up in-person visits and referral to fertility specialists available when needed. AYA-Fs wanted providers to communicate with more empathy, spend more time discussing fertility and family-building, and initiate honest, open dialogues that could continue throughout care (40%). They also wanted to be referred to trusted resources tailored to their age group for informational and emotional support (36%). Specific recommendations to address family-building costs and financial planning were identified (16%).

**CONCLUSIONS:** Informational and psychological support services are needed to better educate patients about gonadotoxic effects and options to have children after cancer and address the emotional burden. Future work should evaluate how multidisciplinary care between cancer and reproductive medicine may inform the development of interactive web-based patient resources, coupled with in-person supportive interventions, and referrals.

**SUPPORT:** This research was supported by a grant from the National Cancer Institute (NCI: R03CA212924-02, PI: Benedict).
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**INSIGHTS FROM WOMEN WITH FERTILITY CONCERNS ABOUT THEIR CHOICES WHEN ATTEMPTING TO IMPROVE THEIR ABILITY TO CONCEIVE.** Alice D. Domar, Ph.D.,* Elizabeth A. Grill, PsyD,† Mary Christ, MD, MBA,‡ Evgenii Malikov, MBA,' Boston IVF, Waltham, MA; †Weill Cornell Medical Center, Rye Brook, NY; ‡Nestle Health Science, Bridgewater, NJ.

**OBJECTIVE:** The goal of this survey-based research was to gather additional information from women who have been actively trying to conceive, on barriers to access of fertility-related treatment and perception of value of such services.

**DESIGN:** Three online surveys of women who were trying to conceive and voluntarily responded to a request for participation.

**MATERIALS AND METHODS:** 330 women ages 18-44 completed the first questionnaire on their overall feelings towards fertility. 132 unique women completed the second questionnaire on emotional state. 93 unique respondents answered questions regarding their interest in various fertility related services and sources of information.

**RESULTS:** 65% (214/330) had been trying less than seven months, 17% (55/330) more than a year, 34% (127/336) had not yet seen a physician in relation to fertility concerns. The two most common reasons for not seeing a physician were ‘feeling they could get pregnant on their own’ (42%; 96/230) and ‘wanting to try a more natural approach’ (23%; 53/230). 80% (180/224) believed that their emotions could have an impact on their fertility. When asked about most helpful fertility-related services, which could be made available to them, access to certified reproductive experts (39%; 36/92) was followed by nutrition-related services and sources of information.

**CONCLUSIONS:** Most of the research available to fertility specialists is conducted on women already seeking consultation. A significant number of women not yet under fertility treatment prefer to seek out natural means of conception and believe in the importance of their emotional state in improving their chances of conception. Educating women about real options to increase chances of conception should be a priority.

**SUPPORT:** This research was sponsored by Nestle Healthcare Nutrition.

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**ASSOCIATIONS BETWEEN PSYCHOLOGICAL STATUS AND SEMEN QUALITY PARAMETERS AMONG MALE PARTNERS OF COUPLES ATTEMPTING FERTILITY.** Jiahui Qiu, PhD,* Jichun Tan, PhD,§ Shengjing hospital of China medical university, Shenyang, China; §Key Laboratory of Reproductive Dysfunction Diseases and Fertility Remodelling of Liaoning Province, Shenyang, China.

**OBJECTIVE:** To study associations of semen quality parameters with psychological status including depression, stress and anxiety.

**DESIGN:** A cross-sectional single-center study.

**MATERIALS AND METHODS:** A total of 412 men attending fertility centers from 2017 to 2018 were investigated. Participants completed a questionnaire on lifestyle factors, self-rating depression scale, self-rating anxiety scale and perceived stress scale. Semen samples were collected to test semen volume, sperm concentration, progressive motility rate, vitality, normal forms rate.

**RESULTS:** Men with depression symptoms were detected to have lower sperm vitality ($p=0.026$) and progressive motility rate ($p=0.01$). Higher anxiety scores were accompanied with decreased sperm vitality ($p=0.03$). While no significant associations between self-reported stress and semen parameters were found.

**CONCLUSIONS:** Depression and anxiety are associated with lower levels of semen quality, which may lead to infertility of men.

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**EFFECT OF PHYSICIANS’ PERSONAL REPRODUCTIVE EXPERIENCES ON COUNSELING INFERTILITY PATIENTS.** Jenna M. Turcocy, MD,* Leslie V. Farland, Sc.D.,* Elizabeth S. Ginsburg, MD,* Paula C. Brady, MD,§* Columbia University Medical Center, New York, NY; §University of Arizona, Tucson, AZ; *Brigham & Women’s Hospital, Boston, MA.

**OBJECTIVE:** Physicians’ personal medical experiences have been shown to affect patient counseling and management. Our objective was to assess whether reproductive endocrinologists’ personal experience with infertility and multiple gestation correlate with clinical counseling and treatment recommendations.

**DESIGN:** A web-based cross-sectional survey.

**MATERIALS AND METHODS:** An anonymous survey was emailed to Society for Reproductive Endocrinology and Infertility members, regarding personal and close contacts’ experience with infertility and multiple gestation, and factors influencing embryo transfer (ET) number and twin risk counseling. Responses were compared using Fisher exact and Mann-Whitney U tests as appropriate, with significance at $p<0.05$.

**RESULTS:** Responses were provided by 109 physicians, who were 51% female, 85% white and 56% age 50 years or older. Most (91%) reported being parents, and 28% had a personal history of infertility. Among respondents, 12% reported they or their partners had conceived multiples (83% using assisted reproduction), and half had family or close friends with multiples. Physicians with a history of infertility regularly shared their experiences with multiples more often than those without infertility (50% vs. 16%, $p=0.01$). Twins were considered an adverse outcome by 86%, regardless of their reproductive experiences. When counseling about multiples, physicians rated their concern for preterm birth and neonatal morbidity highest (mean 4.9 on a scale of 1 [not at all] to 5 [to a large extent]); familial stress and maternal mental health were rated lowest (3.6%). Incidence of preterm birth in twins was underestimated by 34% of physicians, and 44% underestimated twin infant mortality, irrespective of personal or close contacts’ multiple gestations (including preterm deliveries). Most (79%) “encourage SET whenever possible.” In deciding ET number, avoidance of multiples and patients’ obstetrical history were rated highest (mean 4.4) while self-pay status (2.5) and body mass index (BMI, 2.3) were rated lowest. These ratings did not vary by reproductive history, though physicians reporting strong influence of patient BMI on ET number had significantly lower BMI than those reporting little to no effect (22.8 vs. 25.0 kg/m², $p=0.05$).

**CONCLUSIONS:** There is a high incidence of infertility diagnoses (28%) and multiple gestation (12%) among reproductive endocrinologists. Physicians reported strongly advocating for SET to reduce risk of multiples, which were widely considered an adverse outcome, independent of personal experience with infertility or multiple gestation. This is despite at least one-third of respondents underestimated twin morbidity or mortality.

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**AN ANALYSIS OF THE CORRELATION BETWEEN MATRITAL ADJUSTMENT TEST AND SELF-EsteEM AND DEPRESSION IN CHINESE INFERTILE WOMEN.** Qingwen He, MA, Xihong Li, MD,Ph.D, Yan Ouyang, MD/Ph.D, Qingqing Wu, Bachelor’s degree Reproductive and Genetic hospital of Citic-Xiangya, Changsha, China.

**OBJECTIVE:** To investigate the status of marital adjustment test and self-esteem and depression in the Chinese infertile women and to explore the mediating effect of self-esteem on the relationship between marital adjustment test and depression.

**DESIGN:** A cross-sectional descriptive study was conducted with 244 Chinese infertile women from February 2019 to April 2019 in our reproductive center. All included women had voluntarily participated in this self-evaluation and the informed consents were obtained from all participants.

**MATERIALS AND METHODS:** This study was conducted at the Reproductive and Genetic Hospital of CITIC-Xiangya (Changsha, China). The 244 Chinese infertile women who had completed 4 questionnaires were recruited by simple random sampling. The questionnaires included (a) General information (made by the author), (b) Locke-Wallace marital adjustment Test(MAT), (c) Self-Esteem Scale (SES) and (d) Center for Epidemiological Studies Depression Scale (CES-D). Pearson’s correlation was used to investigate the relationship. Structural equation model (SEM) was constructed by AMOS 22.0.

**RESULTS:** The mean scores of these Chinese infertile women were 101.42 ± 20.76, 28.24 ± 4.96 and 17.82 ± 10.47 based on MAT, SES and CES-D, respectively. The total mean score of CES-D was found to have a significant negative correlation with the score of MAT ($r=-0.609$, $p<0.01$) and CES-D ($r=-0.548$, $p<0.01$). While the total mean score of MAT was found to have a significant positive correlation with the score of SES ($r=0.441$, $p<0.01$). SEM indicated that marital adjudistic test had significant direct effects on self-esteem ($β=0.44$, $P<0.01$) and depression ($β=-0.35$, $P<0.01$); self-esteem had a significant direct effect on marital adjustment test ($β=-0.46$, $P<0.01$). Furthermore, self-esteem partially mediated the relationship between marital adjustment test and depression.
CONCLUSIONS: The depression level of infertile women was higher, and was negatively correlated with marital adjustment test and self-esteem. The mediating role of self-esteem may provide a potential mechanism for exploring the relationship between marital adjustment test and depression. These results suggested that medical staff should pay attention to the patients’ depression, especially to the infertile women with marital disorders and low level of self-esteem. And then, humanistic care which helps the patients to vent their inner depression in a variety of ways could be implemented during treatment. In addition, we should actively carry out health education for infertile women and their families, so that they could have an enhanced understanding of reproductive knowledge, and gradually improved psychosociality and coping ability to deal with various problems arising in the course of treatment.

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DOES DURATION OF INFERTILITY AFFECT THE MALE’S FERTILITY QUALITY OF LIFE? Rachel Blair Danis, MD, Semara A. Thomas, MD, Rachel S. Mendelbaum, MD, Richard J. Paulson, MD, MS, Kristin Bendikson, MD, Jacqueline Ho, MD MS, Mary Katherine Samplaski, MD. University of Southern California, Los Angeles, CA; USC Keck School of Medicine, Los Angeles, CA; Keck School of Medicine, University of Southern California, Los Angeles, CA.

OBJECTIVE: An infertility diagnosis can confer a significant amount of personal stress and strain on a couple. There is limited data on how infertility affects quality of Life (QoL) and the male’s perspective on his relationship with his partner. The purpose of this study was to determine if duration of infertility affects males’ QoL and partner intimacy.

DESIGN: Cross-sectional survey study.

MATERIALS AND METHODS: 2 anonymous paper surveys were given to 70 male partners after providing a semen sample for assisted reproductive technology at a fertility clinic. Men were alone during this time. 1, a questionnaire assessed demographics, motivating factors, and fertility history. 2, the fertility quality of life (FertiQoL) survey assessed the impact of infertility in diverse life areas. The FertiQoL contained 2 QoL domains: Core and Treatment. The Core consisted of 4 subscales, each focusing on psychosocial QoL factors. Treatment consisted of 2 subscales: environment and tolerance (of treatment). Responses were scored 0-100; a higher score indicated higher QoL. Eligible respondents included men receiving treatment as part of an infertile couple. Responses were analyzed via descriptive statistics, chi-square analysis, and multivariable regression analysis.

RESULTS: Out of 70 anonymous surveys, 61 (87.1%) and 52 (74.3%) completed the 1st and 2nd surveys in their entirety. 62 (88.6%) men were married, 51 (75.0%) did not have prior children, and 19 (27.9%) reported prior infertility. Mean FertiQoL scores for all men were: Overall 78.9 +/- 9.9, Core 79.0 +/- 9.4, Treatment 78.5 +/- 9.5. For infertility duration <12 months, scores were 81.8 +/- 6.5, 83.1 +/- 6.4, and 78.7 +/- 13.9, respectively. For infertility duration 12-24 months, scores were 79.7 +/- 11.0, 79.6 +/- 10.8, and 79.5 +/- 15.4, respectively. For infertility duration >24 months, scores were 76.1 +/- 10.8, 75.5 +/- 9.9, and 77.4 +/- 14.9, respectively. There were no significant differences between overall or domain scores and the duration of infertility groups (p>0.05). However, there was a downward trend in scores the longer the couple was trying to conceive, and duration of infertility >24 months was significantly related to one’s Relational score (subscale of the Core domain, p=0.019).

CONCLUSIONS: For most FertiQoL domains, duration of infertility did not affect scores. This is reassuring that longer durations of infertility do not seem to impact male QoL. Infertility for at least a 2-year period did affect the Relational score, which may suggest that the longer durations of infertility >2 years may cause stress on a couple’s intimate relationship. Awareness of how infertility affects the male partner’s quality of life and relationship with his partner provides an opportunity to enhance our care of the infertile couple.

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PREVALENCE OF INFERTILITY TREATMENT IN PATIENTS WITH VULVODYNIA. Jenny S. George, MD, Ashley Hesson, MD, PhD, Natalie A. Saunders, MD, Hope K. Haefner, MD. University of Michigan, Ann Arbor, MI; University of Michigan, Obstetrics and Gynecology, Ann Arbor, MI.

OBJECTIVE: There is a paucity of data on the fertility desires of patients with vulvodynia, and if pain associated with vaginal intercourse limits these patients’ reproductive goals. Thus, the objective of this study was to determine the prevalence of infertility treatment in patients with vulvodynia. We hypothesized that patients with vulvodynia who would have higher rates of infertility treatment compared to the general public and that, of those seeking infertility treatment, uptake of intrauterine insemination (IUI) would be higher compared to uptake of oral or gonadotropins cycles requiring vaginal intercourse, given the potential barrier of painful intercourse.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: Self-administered questionnaires detailing symptom history, vulvar pain characteristics, pregnancy desires, and history of infertility treatment, were completed by patients seeking evaluation at an ambulatory vulvar disorders clinic from 1996 to 2018. Patients with diagnoses other than vulvodynia were excluded. Primary outcome was prevalence of infertility treatment, defined as use of oral induction agents, gonadotropins, IUI, in-vitro fertilization (IVF), or surgical procedures for tubal factor infertility. Secondary outcomes included desire for pregnancy and frequency of vaginal intercourse. Descriptive statistics were used to characterize these distributions. Approval of this study was granted by the Institutional Review Board.

RESULTS: 379 patients diagnosed with generalized or localized vulvodynia were included in this study. Mean age of patients was 40.3 years (SD 14.9), 30.3% (N=115) patients reported desiring pregnancy, and 81.7% (N=94) of their partners were in agreement with this desire. 7.65% (N=29) patients had sought or were seeking infertility treatment, compared to 12.5% reported in population prevalence studies. 35.6% (N=135) patients reported having vaginal intercourse at least once weekly, while 0.53% (N=20) patients reported never having vaginal intercourse. Of the patients who sought infertility treatment, 10 (32.0%) received oral induction agents, 3 (9.6%) utilized gonadotropins, 5 (16.0%) employed IUI, 4 (12.9%) underwent surgical procedures for tubal factor infertility (9.6%) received IVF, and 6 (19.3%) were unaware of treatment modality.

CONCLUSIONS: Prevalence of infertility treatment in patients with vulvodynia is similar to that of the general public. A large proportion of patients with vulvodynia desire pregnancy; these patients do not refrain from vaginal intercourse and do not have higher rates of IUI uptake compared to other treatment modalities.

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SPOUSAL CONCORDANCE IN ASSISTED CONCEPTION: PROSPECTIVE COHORT STUDY OF COUPLES UNDERGOING THEIR FIRST IVF CYCLE. Karema Alrashid, MD, Scott M. Nelson, MD, PhD. University of Glasgow, Glasgow, United Kingdom.

OBJECTIVE: Assortative mating and cohabitation concordance cause married/cohabiting couples to share similar traits, with spousal concordance known to contribute to cardiovascular disease and be associated with worse treatment outcomes in other medical specialities. Maternal and paternal characteristics/behaviors are known to affect both natural fertility and success of infertility treatment outcomes in other medical specialities. Maternal and paternal characteristics/behaviors are known to affect both natural fertility and success of infertility treatment but the contribution of concordance is unknown. This study was designed to examine the extent to which heterosexual couples undergoing IVF are concordant with respect to baseline characteristics/behaviors and whether this impacts upon outcome?

DESIGN: Prospective cohort study of consecutive couples undertaking their first IVF cycle.

MATERIALS AND METHODS: Couples were assessed prior to undertaking NHS Scotland funded IVF treatment, with assessment of demographic, anthropometric, lifestyle and medical factors. Spousal concordance was assessed by sparsian correlation for continuous variables, whilst kappa analysis was employed for categorical variables, with regression modelling for their association with outcomes.

RESULTS: There were 306 couples with complete baseline data, of which 264 underwent fresh embryo transfer, with 125 ongoing pregnancies (47.3%). Couples were strongly concordant for age (r=0.59 p<0.000), alcohol consumption (k=0.661), educational attainment (k=0.655) and smoking status (k=0.45) but not BMI (r=0.11, p=0.44). Only exercise concordance was significantly associated with outcome, with exercise discordance a predictor of biochemical pregnancy (OR: 1.86; 95% CI 1.18-2.92 p=0.008). Furthermore, females in discordant couples were significantly less physically active than females in concordant couples (mean difference = 0.4527 times/week, p=0.003).
CONCLUSIONS: Couples undertaking assisted conception are concordant for many baseline characteristics, with couples with discordant exercise habits having increased rates of biochemical pregnancy. Shared education and public health initiatives to attain spousal concordance of lifestyle factors may be beneficial for overall health outcomes if they converge towards healthier behaviors, but concordance per se had limited impact on clinical ART outcomes.

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ATTITUDES TOWARDS PREGNANCY IN PATIENTS WITH VULVODYNIA. Jenny S. George, MD, Ashley Hesson, MD, PhD, Natalie A. Saunders, MD, Hope K. Haefner, MD, University of Michigan, Obstetrics and Gynecology, Ann Arbor, MI.

OBJECTIVE: Qualitative studies indicate that vulvodynia affects women’s reproductive desires and timing [1]. However, little is known about the prevalence of these attitudes amongst patients with vulvodynia, or the relationship between pain severity and reproductive planning. We aimed to further characterize the effects of vulvodynia on women’s reproductive wishes, hypothesizing that desire for pregnancy would decrease with increasing pain score and fear of pregnancy would increase with worsening pain score.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: We retrospectively analyzed patient intake questionnaires completed prior to evaluation at an ambulatory vulvar disorders clinic from 1996 to 2018. Questions addressed symptom history, vulvar pain characteristics, and pregnancy desires. Only those diagnosed with vulvodynia in their subsequent clinic visit were included in our sample. Patients with incomplete questionnaires were excluded. Our primary outcomes were pain severity and unpleasantness scores (0-100) compared between women reporting presence versus absence of desire for pregnancy, as well as between those noting fear of pregnancy or lack thereof. Descriptive statistics and Student’s t-tests were used as appropriate. This study was approved by the University of Michigan Institutional Review Board.

RESULTS: 424 patients diagnosed with vulvodynia (generalized or localized) were eligible for analysis. Their mean age was 40.2 years (SD 15.1); 13.2% (N=56) of them had never had a pregnancy. Nearly one third of the sample (27.8%, N=118) reported a desire for pregnancy. Of those desiring pregnancy, 63.6% (N=75/118) were having at least weekly vaginal intercourse. Mean pain intensity score among those desiring pregnancy was not different between those having and not having at least weekly intercourse (67.1 vs 71.1, p=0.38). Similarly, mean pain unpleasantness was comparable between these groups (78.1 vs 79.0, p=0.81). Of the total 424 patients, 15.1% (N=64) feared pregnancy. This fear was not associated with increased pain intensity (p=0.99) or unpleasantness scores (p=0.28).

CONCLUSIONS: Although vulvodynia has far-reaching effects on women’s quality of life, our study suggests that women with more intense or unpleasant pain do not avoid or fear pregnancy more than those with less pain.


SUPPORT: None.

NUTRITION

P-701 Wednesday, October 16, 2019 6:30 AM

GLYCEMIC LOAD, DIETARY FIBER, AND ADDED SUGAR AND SPONTANEOUS ABORTION. Sydney K. Willis, M.P.H., Lauren A. Wise, Sc.D., Amelia K. Wesselink, Ph.D., Katherine L. Tucker, Ph.D., Ellen M. Mikkelsen, RN, MPH, Ph.D., Elizabeth E. Hatch, Ph.D. “Boston University School of Public Health, Boston, MA; Boston, MA; University of Massachusetts Lowell, Lowell, MA; Aarhus University, Department of Clinical Epidemiology, Aarhus, Denmark.

OBJECTIVE: To prospectively evaluate the association between preconception dietary factors including glycemic load (GL), dietary fiber (DF), and added sugar, and spontaneous abortion (SAB). To the authors’ knowledge, there have been no studies of the association between GL and SAB.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Pregnancy Study Online is a web-based preconception cohort study of pregnancy planners in North America. At baseline, female participants completed a questionnaire providing data on demographic, lifestyle, medical, and reproductive histories. Ten days after enrollment, participants completed the National Cancer Institute’s Dietary History Questionnaire II, a validated food frequency questionnaire. Participants were followed with bi-monthly questionnaires for up to 12 months or until a reported conception. Data on SAB, first positive pregnancy test date, due date, and gestational weeks at loss were ascertained from follow-up questionnaires, an early pregnancy (~12 weeks’ gestation) and a late pregnancy (~32 weeks’ gestation) questionnaire. We calculated GL (glycemic index times portion size); DF, soluble fiber, insoluble fiber (grams/g/day); and added sugar (teaspoons (sp)/day), based on reported frequencies of individual foods, standard recipes for mixed foods, and average serving size. We used Cox proportional hazards regression to estimate hazard ratios (HR) and 95% confidence intervals (CI), using gestational weeks as the time scale. We adjusted for age, body mass index (BMI), healthy eating index score (HEI-2010), energy intake, and lifestyle and demographic factors.

RESULTS: Of the 3,565 female participants included in this analysis, 75% (21%) had a SAB over the course of follow-up. The median gestational week at loss was 6 weeks (interquartile range: 5-9 weeks). Compared with an average daily GL ≤100, HRs for GL of 101-114, 115-125, 126-140, and ≥141 were 0.95 (CI: 0.77-1.18), 0.80 (CI: 0.64-1.01), 0.89 (CI: 0.71-1.12), and 1.07 (CI: 0.84-1.35), respectively. Compared with daily total DF intake of 10-12, 13-17, and ≥18 g/day, HRs for 17-20, 21-24, and ≥25 g/day were 1.05 (CI: 0.85-1.30), 1.13 (CI: 0.90-1.43), 0.83 (CI: 0.64-1.07), respectively. Relative to soluble fiber intake of ≤4 g/day, HRs for 5-6, 7-8, and ≥9 g/day were 1.04 (CI: 0.85-1.27), 1.02 (CI: 0.81-1.27), and 0.86 (CI: 0.68-1.08), respectively. Relative to insoluble fiber intake of ≤10, HRs for 11-13, 14-17, and ≥18 g/day were 1.19 (CI: 0.96-1.48), 1.03 (CI: 0.80-1.33), and 1.02 (CI: 0.77-1.33), respectively. Compared with added sugar intake of ≤1 tsp/day, HRs for 7-9, 10-13, 13-17, and ≥18 tsp/day were 0.98 (CI: 0.77-1.24), 0.96 (CI: 0.75-1.22), 1.00 (CI: 0.78-1.28), and 1.04 (CI: 0.80-1.36), respectively. Results were similar for early (<8 weeks’ gestation) and late (≥8 weeks’ gestation) SAB.

CONCLUSIONS: GL, total DF, insoluble fiber, and added sugar intakes were not appreciably associated with SAB. A slight inverse association was seen for higher intake of soluble fiber and SAB risk. Chance remains a plausible explanation of these associations.

SUPPORT: This research was supported by NIH/NICHD grants R01HD086742 and R21HD072326.

HIGH-FAT DIET LEADS TO INCREASED OVARIAN LIPID DEPOSITION EVEN IN THE ABSENCE OF OBESITY. Natalie M. Hohos, PhD, Emily M. Elliott, BS, Jennifer Monks, PhD, Malgorzata E. Skaznik-Wiikiel, MD UNIVERSITY OF COLORADO - ANSCHUTZ MEDICAL CAMPUS, Aurora, CO.

OBJECTIVE: We have previously shown that high-fat diet (HFD) feeding leads to depletion of the ovarian reserve, subfertility, and altered expression of key ovarian genes, irrespective of the development of obesity. It has been proposed that HFD-induced ovarian dysfunction is due to increased lipid accumulation in the ovary, however, it is currently unknown if there is increased HFD-induced lipid accumulation in the ovary in the absence of obesity. We hypothesized that HFD exposure would increase ovarian lipid deposition regardless of the induction of obesity.

DESIGN: Prospective laboratory animal study.

MATERIALS AND METHODS: 5-week-old C57BL/6j mice were fed either a 60% HFD or standard chow (N = 15) for 10 weeks. After 10 weeks body weights were determined. Lean and fat mass were measured by quantitative MRI. HFD mice were divided into HFD-lean (HFLn, N = 11) and HFD-obese (HFOb, N = 9) groups based on body weight: mice < 26 g were considered HFLn and mice ≥ 26 g were considered HFOb. Ovaries were collected, one for qRT-PCR analysis of the lipid droplet protein plin2 and the other for immunohistochemical analysis of lipid droplets via anti-plin2 stain. A one-way ANOVA (Tukey’s post hoc) was used for statistical analysis.

RESULTS: After 10 weeks of diet HFOb mice weighed more and had a higher percentage of body fat (33.2 ± 0.9 g, 37.2 ± 1.2%, respectively) than both HFLn mice (23.5 ± 0.6g, 17.7 ± 1.5%, respectively) and Chow controls (21.6 ± 0.3g, 11.2 ± 0.6%, respectively) (p < 0.0001). Ovarian expression of plin2 was dramatically increased after HFD, with a 5-fold increase observed in HFLn mice and a 4.7-fold increase observed in HFOb mice (p < 0.05).
Two distinct cohorts of animals were identified based on their IBIs. While the majority of animals (n = 44) had IBIs less than 16 months (13.3 ± 0.2 months), which was common for rhesus macaques, IBIs of 9 animal groups were longer than 20 months (24.1 ± 0.8 months; p < 0.001). After being normalized by animal age and body weight, serum VD concentrations of animals in the short IBI group (166 ± 6 ng/ml) were higher (p < 0.05) than those of the long IBI group (143 ± 6 ng/ml). The offspring birth weight values were comparable (p > 0.05) between animals in the short (0.51 ± 0.01 kg) and long IBI groups (0.46 ± 0.05 kg). For animals with short IBIs, the serum VD concentrations correlated negatively with the length of their IBIs when animal age and body weight were taken into account (r = -0.48; p < 0.01). There was no significant correlation between maternal serum VD concentrations and the offspring birth weight (r = -0.24; p > 0.05). CONCLUSIONS: These data demonstrate a relationship between maternal serum vitamin D levels and pregnancy outcomes. Macaques with relatively low serum vitamin D levels require more time to achieve spontaneous pregnancy, though the offspring birth weight does not appear to be affected by maternal serum vitamin D levels. The findings are consistent with previous observations of improved ovulation and menstrual cyclicity via vitamin D supplementation in patients with polycystic ovary syndrome.

SUPPORT: The study was supported by NIH OD P51OD011092.
OBJECTIVE: To evaluate pregnancy outcomes following IUI in young women with low ovarian reserve compared to age-matched controls.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: Patients aged <35 years undergoing their first IUI cycle with a documented anti-mullerian hormone (AMH) level at a single large IVF center between 1999 and 2018 were included. All patients had evidence of patent fallopian tubes and severe male factor infertility (total motile sperm count < 10 million on IUI) was excluded. Patients with AMH <1.0 ng/mL were compared to those with levels >1.0 ng/mL. The primary outcome was positive pregnancy test. Secondary outcomes included live birth, biochemical loss, clinical miscarriage (loss after visualized gestational sac) and ectopic pregnancy. Student’s t-tests and chi square testing were used where appropriate.

RESULTS: There were 3438 patients included. 428 with AMH <1.0 ng/mL, and 3010 with AMH >1.0 ng/mL. Mean AMH values were 0.63 ± 0.26 vs 5.7 ± 5.6 ng/mL, respectively. Mean antral follicle count was 10.6 ± 5.2 vs 22.9 ± 12.7. There were no differences in age (31.6 ± 2.4 vs 30.6 ± 2.7 years), body mass index (26.0 ± 6.4 vs 26.3 ± 6.5 kg/m²) or infertility diagnosis (54% vs 51% with unexplained or ovulatory dysfunction excluding polycystic ovarian syndrome) between patients with decreased ovarian reserve compared to those without. Reproductive outcomes are depicted in Table 1.

CONCLUSIONS: Young patients (<35 years) with decreased ovarian reserve conceived less often after IUI as compared with age-matched controls. However, once pregnant, such patients had fewer biochemical losses and similar live birth and clinical miscarriage rates as compared to controls. These data imply a quantitative, not qualitative, distinction between groups. Future prospective studies carefully controlling for infertility diagnosis are required to confirm these relationships.

SUPPORT: None.

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THE RATE OF ANTRAL FOLLICLE COUNT DECLINE DECREASES WITH OLDER AGE AND LOWER ANTRAL FOLLICLE COUNT. Xiaojie P. Zhou, M.D.,a Charles E. McCulloch, PhD.b Mitchell P. Rosen, MD, HCLDb, Marcelle I. Cedars, MD.c aUniversity of California - San Francisco, San Francisco, CA; bIVF-RMA New Jersey, Basking Ridge, NJ; cUniversity of North Carolina, Raleigh, NC.

OBJECTIVE: To investigate the underlying molecular mechanisms associated with DOR in young women’s reproductive lifespan. While this is common as women age, about 10% of younger women will be impacted by premature DOR, resulting in reduced oocyte quality and quantity, impacting reproductive potential. To confirm these relationships, we performed exome sequencing and identified deleterious DNA variants associated with premature Ovarian Reserve.

MATERIALS AND METHODS: Whole peripheral blood was collected from IRB consented female patients and donated to research: young, fertile, oocyte donor controls (CONT ≤ 31 years; n=11), and age-matched young women presenting with diminished ovarian reserve (DOR ≤ 31 years; n=11). DNA was isolated using the QIAamp DNA Mini kit (Qiagen). Exome sequencing libraries were prepared using SureSelectXT (Agilent) and sequenced on the Illumina NovaSEQ 6000. Sequences were processed using the GATK4 Best Practices exome analysis pipeline. Functional and rare variants found exclusively in DOR samples were evaluated for pathogenicity and corresponding genes were tested for pathway enrichment using Ingenuity Pathway Analysis (Qiagen). Sequencing validation was performed using qPCR with Taqman SNP Genotyping Assays (Applied Biosystems).

RESULTS: Exome sequencing revealed 730 significant DNA variants across the genome that were observed exclusively in the young DOR sample set (P<0.01). Bioinformatic analysis revealed the top significantly enriched signaling pathways associated with young DOR: Glucocorticoid receptor (GR) and Notch (P<0.01). The GR signaling pathway had 32 deleterious DNA variants within 16 different genes, all of which would significantly affect protein function (P<0.01).

FERTILITY & STERILITY®

TABLE. Yearly AFC Change by Baseline Age and AFC Groups

<table>
<thead>
<tr>
<th>Baseline Age Group</th>
<th>(Years)</th>
<th>N</th>
<th>Yearly AFC Change</th>
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<th>95% CI</th>
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<td>0.19</td>
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<td>-0.67</td>
<td>0.15</td>
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</table>

SUPPORT: Grant Support:Â R01 HD044876; 1R01AG053332-01A1.
Each young DOR patient had an average of 2.9 different deleterious DNA variants impacting the GR signaling pathway. Glucocorticoid receptors are crucial for the establishment and maintenance of reproductive function and stress response, influencing oocyte maturation and developmental potential. The Nocti pathway had 5 missense DNA variants observed in young DOR patients (P < 0.01), which could be responsible for abnormal folliculogenesis and affect meiotic spindle assembly. To date, DNA variant validation has been performed on 5 genes in the GR signaling pathway, including AGT which has been implicated in reduced ovulatory capacity, and KRT19, involved in proliferation of the surface epithelium during ovarian development.

CONCLUSIONS: A case study of 19 young DOR patients revealed significant deleterious DNA variants in genes crucial to ovarian function, folliculogenesis and oocyte maturation. The combination of these adverse hits across key signaling pathways would impact the reproductive stress response, growth and maturation of ovarian follicles, as well as downstream oocyte quality. Identifying the underlying molecular mechanisms responsible for premature DOR could lead to preventative treatments that slow the process of early ovarian aging.

SUPPORT: None.

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INTEREST OF THE USE AUTO-TRANSPLANTATION OF THE OVARIAN CORTEX AFTER DORMANT FOLLICLES IN VITRO ACTIVATION (IVA) IN PATIENTS WITH PREMATURE OVARIAN INSUFFICIENCY (POI). Khaled Mahmoud, Dr. a Hanen Eloumi, Dr. a Mohamed Khrouf, Dr. b MED Habib Ben Aribia, Dr. a Khaled Tarek, Dr. a Sonia Mnaillah, Dr. a Mariem ben Khelifa, Ph.D. a Fathi Ziboua, Dr. a clinique La Rose, Centre FERTILLIA, jardins du lac 2, Tunisia; clinique la rose, Tunis, Tunisia; clinique la rose, centre FERTILLIA, Tunis, Tunisia.

OBJECTIVE: In women with POI, spontaneous conception and response to ovarian stimulation are considerably limited; oocyte donation is therefore the only effective treatment. But in some social cultures, like ours, egg donation is forbidden. The aim of this study is to evaluate the efficacy of autotransplantation of the ovarian cortex after in vitro activation of dormant follicles in these patients in order to have their own genetic children.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: From September 2018 to February 2019, 19 patients with POI according to the Bologna criteria agreed to participate in this study on IVA treatment. The main characteristics of women are: age (35.4 ± 2.9 years), duration of amenorrhea: (2.6 ± 1.9 years), FSH (51.5 ± 20.3 IU/L), E2 (13.0 ± 3.6 pg/ml) and AMH: (0.04 ± 0.03 ng/ml). all women received pretreatment with an oral estrogen/progesterone (OEPP). on days 20 to 22 of this pretreatment, a first laparoscopy is performed to remove an entire ovary which will immediately be transferred to the IVF laboratory. The biologist separates the ovarian cortex from the medulla and cuts it into small cubes (0.5–1 cm²; 1-2 mm thickness). 10 to 20% of this ovarian cortex is used to histological analysis to determine the presence of residual primordial follicles (RPF), the rest is cultured for 48 hours with a PI3K stimulator and a PTEN inhibitor. A second laparoscopy is performed to auto-transplant 20 to 30 of the cultured cortex ovarian cubes, in each of the 2 peritoneal pockets created to ovarian stimulation are considerably limited; oocyte donation is therefore the only effective treatment. But in some social cultures, like ours, egg donation is forbidden. The aim of this study is to evaluate the efficacy of autotransplantation of the ovarian cortex after in vitro activation of dormant follicles in these patients in order to have their own genetic children.

CONCLUSIONS: In our country oocyte donation is prohibited, it would be interesting to better develop this technique for not only women with premature ovarian insufficiency but also for those who have ovarian failure due to age in order to have legitimately their own genetic children.

P-709 Wednesday, October 16, 2019 6:30 AM

DECLINING TREND OF AMH LEVELS IN INDIAN WOMEN OF REPRODUCTIVE AGE GROUP: THE JASLOK EXPERIENCE. Jyotsna Palgamkar, DGO, DNB, a Sapna Agarwal, MD, b Nilesh J. Shah, Ph.D, c MDDeeepak Ramniklal Sanghavi pathology, Sr., c Flavia D. Almeida, MBA BSc, c Trupti Mehta, DNB, d Dhananjay Kulkarni, Ph.D, d Arundhati Athalye, Ph.D, d Firuza Rajesh Parikh, MD DNB PhD d Jaslok Hospital and Research Centre, MUMBAI, India; dMetropolis Healthcare Ltd, MUMBAI, India; Metropolis Healthcare Ltd, mumbai, India; dJaslok Hospital and Research Centre, Mumbai, India.

OBJECTIVE: To study the declining trend of AMH levels in young Indian women visiting our Fertility Center.

DESIGN: Retrospective case control study of AMH levels in Indian women visiting our Fertility Center.

MATERIALS AND METHODS: AMH (n=800) of these women was measured (ng/ml) using Electro-chemiluminescence Immuno Assay (Roche machine e601 ECLIA). Their age and AMH values were compared.

RESULTS: Of the 800 women (Table 1), 31 % of women in < 30 years of age group and 51 % of women in the 31 to 35 age group had AMH levels < 2 ng/ml as compared to 18 % and 35 % in the fertile control groups respectively (p < 0.05). It is interesting to note that 13.9 % of women in < 30 years age group and 26 % of women in 31-35 year age group had AMH of < 1 ng/ml as compared to 2.6 % and 13.4 % respectively in the control group. This study indicates the troubling trends of low AMH in Indian women in the reproductive age group.

CONCLUSIONS: Young Indian women in their late 20’s and early 30’s visiting our center for infertility treatment showed a worrisome declining trend of AMH. Speculation can point towards the ubiquitous role of plastics and Endocrine Disrupting Chemicals (EDCs) that entered the Indian environment 30-35 years ago.

**TABLE 1**

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>AMH (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.55</td>
<td>0.56-1.0  Total (&lt;1)</td>
</tr>
<tr>
<td>&lt;30 (n=215)</td>
<td>6.0% 7.9%</td>
</tr>
<tr>
<td>&lt;31-35 (n=327)</td>
<td>(0%)</td>
</tr>
<tr>
<td>&lt;35-40 (n=52)</td>
<td>(0%)</td>
</tr>
<tr>
<td>&lt;40 (n=56)</td>
<td>44.6%</td>
</tr>
<tr>
<td>Total (n=800)</td>
<td>(0%)</td>
</tr>
</tbody>
</table>

*(Within parenthesis is the value from fertile control group) *p value (<0.05) from respective fertile control group
THE EFFECT OF THE RELATIVE DEGREE OF HOW LOW IS THE SERUM ANTI-MULLERIAN HORMONE (AMH) LEVEL IN WOMEN AGED <39 ON OUTCOME FOLLOWING IN VITRO FERTILIZATION-EMBRYO TRANSFER (IVF-ET). Jerome H. Check, M.D., Ph.D.,¹ Rachael Cohen, D.O.,² Eric Chang, D.O.,³ Jung Choe, M.D.,¹ Carrie K. Wilson, B.A.¹ ¹Cooper Medical School of Rowan University, Camden, NJ; ²Cooper Institute for Reproductive Hormonal Disorders, P.C., Mt. Laurel, NJ.

OBJECTIVE: To determine the relative adverse effect of decreasing levels of AMH on IVF-ET in women aged ≤39 with diminished oocyte reserve.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: Women with diminished oocyte reserve, as evidenced by a serum AMH <1 ng/mL, who were undergoing IVF-ET during a finite time period, were divided into 4 subcategories: grp 1 – AMH ≤0.39, grp 2 – AMH 0.40 to 0.59, grp 3 – AMH 0.60 to 0.79, and grp 4 – AMH 0.80 to 0.99 ng/mL. Only mild gonadotropin stimulation was used. All transfers were on day 3. A couple was included only one time. Power analysis suggested a study group size of 75 patients having oocyte retrieval with marked DOR (AMH <0.39) and 75 with AMH 0.4 to 0.99 considering that the very low AMH group would be less likely to have oocyte retrieval result in embryo transfer.

RESULTS: Pregnancy rates following IVF-ET (day 3 transfers) according to serum AMH levels in women aged ≤39 with diminished oocyte reserve are seen in the table below.

<table>
<thead>
<tr>
<th>AMH Levels (ng/mL)</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;0.39</td>
<td>13</td>
<td>27</td>
<td>24</td>
<td>20</td>
</tr>
<tr>
<td>0.40-0.59</td>
<td>36</td>
<td>18</td>
<td>17</td>
<td>16</td>
</tr>
<tr>
<td>0.60-0.79</td>
<td>36.0</td>
<td>38.4</td>
<td>35.9</td>
<td>36</td>
</tr>
<tr>
<td>0.80-0.99</td>
<td>11.1%</td>
<td>27.8%</td>
<td>47.1%</td>
<td>21.4%</td>
</tr>
<tr>
<td>% Clinical/pregnancies/transfer</td>
<td>5.6%</td>
<td>16.7%</td>
<td>17.6%</td>
<td>21.4%</td>
</tr>
<tr>
<td>Avg. no. embryos transferred</td>
<td>1.47</td>
<td>1.7</td>
<td>1.9</td>
<td>1.6</td>
</tr>
<tr>
<td>Implantation rate</td>
<td>6.7%</td>
<td>22.6%</td>
<td>27.3%</td>
<td>26.1%</td>
</tr>
</tbody>
</table>

Live deliveries are possible even in women aged ≤39 with the lowest serum AMH levels (<0.39 ng/mL). Overall, the live delivered pregnancy rate following day 3 embryo transfer was 13%/transfer (11/85) in women with diminished oocyte reserve as evidenced by serum AMH <1 ng/mL. Overall, oocyte retrieval led to an embryo transfer 53% of the time. Even grp 1 (AMH <0.39) had an embryo transfer 50% of the time and had 1.7 embryos transferred. Excluding grp 1, the live delivered pregnancy rates for groups 2-4 was 18.3% (9/49).

CONCLUSIONS: Knowledge of the likelihood of success based on the degree of oocyte deficiency can help a couple aged ≤39 with diminished oocyte reserve to decide to try IVF with their own oocytes or choose donor oocytes. Comparing a 5.6% live delivered pregnancy rate in grp 1 vs. 18.3% for groups 2-4, with the same average number of embryos transferred, it would seem that oocyte quality is markedly reduced with serum AMH extremely low, but otherwise oocyte quality is only mildly to moderately compromised with serum AMH levels of 0.4 to 0.99 ng/mL.

PCOS/ANDROGEN EXCESS

P-712 Wednesday, October 16, 2019 6:30 AM

BROWN ADIPOSE TISSUE IN WOMEN WITH POLYCYSTIC OVARY SYNDROME: RELATIONSHIP WITH BODY MEASURES, PLASMA IRISIN LEVELS AND THE USE OF METFORMIN. Flavia R. Oliveira, MD, PhD,a Marcelo Mamede, MD, DMSc,b Mariana F. Bizzi, M.Sc.,b Ana Luiza L Rocha, MD, PhD,b Claudia N. Ferreira, PhD,b Karina B. Gomes, PhD,b Ana L. Candido, MD, PhD,b Fernando M. Reis, MD, PhD,b Universidade Federal de Minas Gerais, Belo Horizonte, Brazil;

AFFILIATION not provided; UFMG, Belo Horizonte, Brazil.

OBJECTIVE: Brown adipose tissue (BAT) has been recently identified in adult humans through positron emission tomography-computed tomography (PET-CT). Irisin is a myokine that can induce BAT formation. Polycystic ovary syndrome (PCOS) is a chronic dysfunction associated with obesity and metabolic disorders. The aim of this study was to evaluate whether BAT activity in women with PCOS differs from controls, correlates with plasma irisin levels and can be rescued by metformin.

DESIGN: Prospective cross-sectional study and randomized controlled trial.

MATERIALS AND METHODS: In the cross-sectional study, we included women aged 18-45 years with PCOS (n=45) and a healthy control group (n=25) matched by age and body mass index (BMI). The 45 participants of the PCOS group were subsequently randomized into a metformin subgroup (1500 mg/day during 60 days, n=21) and a placebo subgroup.
RESULTS: Of the 466 women evaluated, 62% (n = 287) were White, 15% (n = 71) were Hispanic, 11% (n = 52) were East/Southeast Asian, 7% (n = 32) were South Asian (SA), and 5% (n = 23) were African American (AA). The cohort was notable for AA patients being older (p = 0.02), and Hispanic and AA patients having higher BMI (p < 0.01) and waist circumference (p < 0.01) compared to other remaining ethnic groups. Overall prevalence of adequate physical activity was 66% in our cohort. Logistic regression analysis was used to identify correlates of adequate physical activity after controlling for age (SAS v9.4). Further, we used the Kruskal-Wallis test to compare the distribution of METs from moderate-intensity, vigorous-intensity, and total (moderate-plus vigorous-intensity) exercise between ethnic groups.

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matched for sex, birth place (Utah or elsewhere), and 5-year birth cohort. In addition, controls were required to have had at least one child. Children born to PCOS cases and controls, and maternal age at each birth, were determined using birth certificate data. We report mean values, standard deviation (SD) and range using conventional methods. As the data were not normally distributed, the Mann-Whitney U test was used to compare age and number of children between the PCOS cases and matched controls.

RESULTS: A total of 1,022 PCOS cases who had given birth to at least child 1,022 matched population controls were used in this analysis.

<table>
<thead>
<tr>
<th>TABLE 1. Fecundity patterns in women with and without PCOS</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCOS cases: mean (SD), range</td>
</tr>
<tr>
<td>Age at censoring (yrs)</td>
</tr>
<tr>
<td>Number of children born</td>
</tr>
<tr>
<td>Age at first birth (yrs)</td>
</tr>
<tr>
<td>Age at last birth (yrs)</td>
</tr>
</tbody>
</table>

CONCLUSIONS: The mean number of births for both PCOS cases and matched controls in this high fecundity population was greater than 2 for both groups. PCOS cases had significantly lower parity on average than matched controls. PCOS cases were an average of 2.7 years older at the birth of their first child and 1.5 years older at the birth of their last child. As only women with at least one live birth were included, the detrimental impact of PCOS on lifetime fecundity may be greater than estimated here.


P-716 Wednesday, October 16, 2019 6:30 AM

IS HIRSUTISM A MARKER OF METABOLIC DYSFUNCTION? Sahar Z, Wertheimer, MD, Jessica L. Chan, MD, MSCE, Erica T. Wang, MD, MAS, Ricardo Azziz, MD, MPH, Margaretta D. Pisarska, MD, Cedars-Sinai Medical Center, Los Angeles, CA; University at Albany, SUNY, Albany, NY.

OBJECTIVE: To determine if hirsutism alone is a marker of metabolic dysfunction.

DESIGN: Prospective community-based cohort study.

MATERIALS AND METHODS: Women (age > 14) with a modified Ferriman-Gallwey (mFG) score and markers of metabolic dysfunction were included. Hirsutism was defined by an mFG score ≥ 8 and oligomenorrhea as < 8 cycles/year. Markers of metabolic dysfunction included body mass index (BMI), waist to hip ratio (WHR), high-density and low-density lipoprotein (HDL, LDL), insulin and glucose levels during a 2-hr oral glucose tolerance test (OGTT), Categorical variables were compared using χ² tests and continuous variables were compared using Kruskal-Wallis or ANOVA, as appropriate. Linear regression models were used to determine correlation of degree of hirsutism with severity of metabolic dysfunction.

RESULTS: 497 hirsute patients were identified, of which 236 were oligomenorrheic (H/O) and 261 were eumenorrheic (H/NO); 303 non-hirsute controls (CONTROLS) were included. The groups were similar in race and age, WHR, LDL and HDL. Hirsute groups had higher BMI values (Table 1). Fast- ing, 1- and 2-hr insulin values were significantly higher for hirsute groups vs controls. In H/O women, mFG scores negatively correlated with HDL (β= -0.94% 95% CI -1.82% to -0.06), and positively correlated with 1- and 2-hr insulin levels (1-hr: β= 6.1% 95% CI 1.1-11.0, and 2-hr: β= 4.3% 95% CI 0.97-7.62). These relationships were not significant after adjusting for BMI. In H/NO women, mFG scores positively correlated with 1- and 2-hr insulin values (1-hr: β= 5.38% 95% CI 1.7-9.1; and 2-hr: β= 4.27% 95% CI 0.67-7.88), even after adjusting for BMI.

CONCLUSIONS: Hirsutism is associated with a higher BMI and markers of metabolic dysfunction. In hirsute women with oligo-ovulation, evidence of metabolic dysfunction appears to be primarily associated with BMI. However, in eumenorrheic hirsute women, increasing mFG scores correlate with markers of metabolic dysfunction, even after adjusting for BMI. Thus, both increasing BMI and hirsutism alone may be suggestive of metabolic derangement and should be used as a marker for metabolic screening.

P-717 Wednesday, October 16, 2019 6:30 AM

BONE MORPHOGENETIC PROTEIN SUPPRESSES THE ANDROGEN PRODUCTION IN PCOS THECA IN-VITRO CELL MODEL. Rishi Man Chugh, PhD, Hang-Soo Park, PhD, Amro Elsharoud, MD, Mara Ulin, MD, Hajra Takala, MD, MPH, Ayman Al-Hendy, MD PhD. The University of Illinois College of Medicine, Chicago, IL; University of Illinois College of Medicine, Chicago, IL.

OBJECTIVE: Polycystic Ovarian Syndrome (PCOS) is a metabolic disorder characterized by inflammation, infertility and excess ovarian androgen production by theca cells in the ovary. Though its etiology is not fully understood, women with PCOS exhibit the increased expression of steroidogenic pathway genes (CYP17A1, and CYP11A1) involved in androgen production. Most available therapies aim to decrease ovarian androgen production to enhance fertility. The Bone morphogenetic proteins (BMPs) which are members of the transforming growth factor β (TGFβ) family plays a significant role in controlling the enzymes of the steroidogenic pathway which suppresses the androgen production. Our previous study showed the effect of mesenchymal stem cells (MSCs) secretome on steroidogenic pathway genes. It is reported in the literature that MSCs also secrete BMPs in its secretome. In this study, we evaluated the utility of BMPs on Human H295R adreno-carcinoma cell line, an in-vitro model for the investigation of the steroidogenic pathway. The H295R cell line expresses genes that encode for the key enzymes for the steroidogenesis.

DESIGN: We hypothesize that bone morphogenetic proteins are able to inhibit the androgen biosynthesis in PCOS in-vitro cell model by affecting the steroidogenic pathway genes expression.

MATERIALS AND METHODS: Human adreno-carcinoma cell line (H295R), purchased from ATCC and cultured as per the protocol. Cells were seeded on six-well plates at a density of 1.8 x10^6 cells per well and cultured for 60 hours. Cells were treated with BMP 6 and 7 with different concentrations 25, 50, 100 ng per ml with respective control (without BMP) for 48 hours. After 48 hours the media was removed and cells were washed with PBS and serum free media were added for further 24 hours. After 24 hours incubation, cells and media were collected for analysis.
expression of mRNA for CYP17A1, CYP11A1, and DENND1A genes was decreased significantly (P < 0.003). 8-OHdG exhibited a decrease from a median of 34.62 (27.7–45.4) to 31.94 (23.18–42.10), 29.96 (21.21–39.09), and 18.57 (12.14–31.15) at 3, 6 and 12 months, respectively (p < 0.001). A higher BMI was considered to be a significant factor affecting the changes in mtDNA copy number over time (P = 0.017).

CONCLUSIONS: Metformin treatment is associated with decreased markers of oxidative stress in patients with PCOS. BMI appears to play a role in the change in mtDNA copy number, while changes in 8-OHdG appears to be unaffected.

SUPPORT: This study was supported by grant MOST 105-2628-B-004-MY4 from the Ministry of Science and Technology of Taiwan.

P-719 Wednesday, October 16, 2019 6:30 AM

ANDROGEN ALTERS SENP3 EXPRESSION AND INDUCES AUTOPHAGY IN GRANULOSA CELLS: A NOVEL MECHANISM INVOLVED IN POLYCYSTIC OVARY SYNDROME. Dongmei Sun master, Wei Ren Chai Doctor. Shanghai Ninth People’s Hospital, Shanghai JiaoTong University School Of Medicine, Shanghai, China.

OBJECTIVE: Polycystic ovary syndrome (PCOS) is a common endocrine disorder in reproductive-aged women, which is mainly associated with androgen excess[1]. Autophagy is responsive to energy stress and is activated in the ovarian tissue of PCOS [2]. The role of autophagy in PCOS related metabolic disorders is increasingly recognized [3-4]. Small ubiquitin-like modifier (SUMO) modification is an important post-translational protein modification in various cell types and is associated with autophagy activation[5]. SENP3, one ofSentrin/SUMO-specific proteases (SENP s) family members, can remove SUMO2/3 from proteins and SENP3 expression is closely related to oxidative stress[6]. Therefore, this study was designed to research the relationship between testosterone, SENP3 and autophagy in PCOS granulosa cells.

DESIGN: We collected granulosa cells of patients treated by in vitro fertilization with the same controlled ovarian stimulation protocol and were divided into two groups between January 2017 to January 2018. Group A included 75 PCOS patients and group B included 75 tubal-factor infertile patients. Cultured human ovarian granulosa-like tumor cell line (KGN cells) were treated or not with testosterone.

MATERIALS AND METHODS: Granulosa cells were isolated by gradient centrifugation from the follicle fluid aspirated during oocyte retrieval. Western blotting, quantitative PCR analysis were used to detect the SENP3, LC3 and p62 levels in human granulosa cells and KGN cells.

RESULTS: In group A, LC3II/I expression (1.00 ± 0.05 vs 0.5 ± 0.04, P < 0.01) was significantly higher than group B, whereas p62 (0.69 ± 0.02 vs 0.78 ± 0.01, P = 0.01) expression significantly decreased. After granulosa cells were treated by testosterone for 24 hours, the LC3II/I expression (1.5± ± 0.08 vs 1.0 ± 0.05, P = 0.02) was significantly higher than control group, whereas the expression of P62 levels (1.35 ± 0.08 vs 1.0 ± 0.05, P = 0.02) were obviously lower, which showed that ovarian granulosa cell of polycystic ovary syndrome were hypothyroid, autophagy is activated and androgen excess is involved in the autophagy activation of granulosa cells in polycystic ovary syndrome patients. In KGN cells, SENP3 expression declined as the dose of androgen increased (0.61± ± 0.01 vs 0.93± ± 0.04, P< 0.01); whereas LC3II/I expression significantly increased (2.62± ± 0.04 vs 1.5 ± 0.06, P< 0.01). LC3II/I expression and mRNA levels were decreased after SENP3 overexpression and were elevated after the transfection of siRNA(P<0.05). It suggested that SENP3 is involved in the process of hyperandrogenism induce autophagy in KGN, granular cell of two groups cultured and treated with 10 μM testosterone, SENP3 expression (1.13± ± 0.10 vs 1.54± ± 0.03 , P=0.02) was lower in PCOS group treated with testosterone, which suggested that SENP3 plays an important role in the autophagy activation of granulosa cells in patients with hyperandrogenism polycystic ovary syndrome.

CONCLUSIONS: Our results show that androgen excess alters SENP3 and granulosa cell autophagy, which may play a role in PCOS. This may shed some light on the pathogenesis of PCOS.

  2. Li Da,Yue Yue,Bi Fang-Fang et al. Autophagy is activated in the ovarian tissue of polycystic ovary syndrome.[J]. Reproduction, 2018, 155: 85-92.
P-720 Wednesday, October 16, 2019 6:30 AM

ESTABLISHING AN ANTI-MULLERIAN HORMONE (AMH) CUT-OFF TO DETERMINE POLYCYSTIC OVARIAN MORPHOLOGY (PCOM) SUPPORTING DIAGNOSIS OF POLYCYSTIC OVARIAN SYNDROME (PCOS): THE APHRODITE STUDY. Alexandra Dietz de Loos, PhD, a Martin Hund, PhD, b Katharina Buck, PhD, b Cindy Meun, MD, c Johanna Silliman, PhD, b Joop S. E. Laven, MD, PhD. d Erasmus University Medical Center, Rotterdam, Netherlands; e Roche Diagnostics International Ltd., Rotkreuz, Switzerland; f Roche Diagnostics GmbH, Penzberg, Germany.

OBJECTIVE: To derive and validate a cut-off for AMH to discriminate PCOM using the Elecsys® AMH Plus immunoassay.

DESIGN: APHRODITE is a case-control study of PCOS-positive (cases) and PCOS-negative (controls) women aged 25–45 years. Cases were defined using Rotterdam criteria, showing the full phenotype A (irregular cycles sometimes ovulatory dysfunction, clinical or biochemical hyperandrogenism and PCOM); controls had an antral follicle count (AFC) ≤20, based on the new international guideline for PCOS.

MATERIALS AND METHODS: The discovery cohort included 290 cases and 575 controls, whereas the validation cohort consisted of 455 cases and 500 controls. Serum levels of AMH were measured using the Elecsys® AMH Plus immunoassay; AFC was determined by transvaginal ultrasound. An AMH cut-off was optimised in the discovery cohort based on concordance analysis. Performance (sensitivity, specificity and area under the curve [AUC]) of the defined cut-off was evaluated in the validation cohort. Exploratory analyses in different subcohorts (including age groups) were also performed.

RESULTS: Compared with controls, PCOS cases were younger (median age 29.0 vs 34.0 years), with a higher body mass index (median 29.2 vs 23.8 kg/m²) and higher AMH level (median 6.23 vs 2.13 ng/mL). Good correlation was observed between AMH and AFC in the discovery and validation cohorts, with Spearman correlation coefficients of 0.83 and 0.84, respectively. A serum AMH cut-off of 3.5 ng/mL (25 pmol/L) was determined in the discovery cohort, which achieved 85.9% sensitivity and 89.8% specificity, respectively. A serum AMH cut-off of 3.5 ng/mL (25 pmol/L) was determined in the discovery cohort, which achieved 85.9% sensitivity and 89.8% specificity, respectively. A serum AMH cut-off of 3.5 ng/mL (25 pmol/L) was determined in the discovery cohort, which achieved 85.9% sensitivity and 89.8% specificity, respectively. A serum AMH cut-off of 3.5 ng/mL (25 pmol/L) was determined in the discovery cohort, which achieved 85.9% sensitivity and 89.8% specificity, respectively.

CONCLUSIONS: The Elecsys® AMH Plus immunoassay provides a robust method for identifying PCOM as part of PCOS diagnosis with a high specificity, with an AUC of 94.0% (95% CI 92.6–95.5). In women aged 29.0 vs 34.0 years, with a higher body mass index (median 29.2 vs 23.8 kg/m²) and higher AMH level (median 6.23 vs 2.13 ng/mL). Good correlation was observed between AMH and AFC in the discovery and validation cohorts, with Spearman correlation coefficients of 0.83 and 0.84, respectively. A serum AMH cut-off of 3.5 ng/mL (25 pmol/L) was determined in the discovery cohort, which achieved 85.9% sensitivity and 89.8% specificity, respectively.

P-721 Wednesday, October 16, 2019 6:30 AM

PROBIOTICS AND SYNBiotics FOR POLYCYSTIC OVARIAN SYNDROME: A SYSTEMATIC REVIEW AND META-ANALYSIS. Mauro Cozzolino, M.D., a Amerigo Vitagliano, M.D., b Fundacion IVI, Valencia, Spain; cUniversity of Padua, Padua, Italy.

OBJECTIVE: To evaluate the effectiveness of probiotics and synbiotics on metabolic, hormonal and inflammatory parameters of PCOS, to identify the effect on potential fertility mediators. Probiotics and synbiotics seems to have an effect on metabolic, hormonal and inflammatory aspect of PCOS.

DESIGN: Systematic review and meta-analysis of randomized controlled trials (RCTs). Electronic databases (MEDLINE, Scopus, EMBASE, ScienceDirect, The Cochrane Database of Systematic Reviews and ClinicalTrials.gov) were searched from their inception until May 2018. The review protocol was registered in PROSPERO before starting the data extraction (CRD42018111534).

MATERIALS AND METHODS: Randomized controlled trials (RCTs) of PCOS’s women undergoing a therapy at least of eight weeks with probiotics or synbiotics or without therapy. Primary outcomes were changes in anthropometric parameters, glucose/insulin metabolism, lipid profile, sex hormones profile, inflammation markers. Studies were assessed using the Cochrane Risk of Bias tool.

RESULTS: Nine RCTs were included; 294 women were assigned to the intervention group and 293 to the control group. The intervention was associated with a significant improvement in FPG, BMI, HOMA-IR, BMI and modified Ferriman-Gallway, serum triglycerides, testosterone, hs-CRP, NO, TAC, GSH and MDA. Subgroup analysis on the type of intervention showed that probiotics were associated with greater testosterone and FPG reduction, synbiotics administration resulted in a more pronounced decrease of BMI. Subgroup analyses on the duration of therapy showed that in the women with 12-weeks of therapy had a significantly greater effect on QUICK-I than the 8-weeks therapy, whilst no significant difference was observed in terms of BMI, HOMA-IR and FPG.

CONCLUSIONS: There is a need to structure a robust and well driven RCT that analyses pregnancy-related outcomes in PCOS women being treated with these substances to check their fertility-related effects, since previously available evidences point to recommend use of probiotic/synbiotic in the clinical practice.

SUPPORT: no financial support.
AMH/AFC is higher in Asians compared to Caucasians. Other factors stable: AFC is lower in African-Americans and Asians and controls. Age and BMI are significant independent negative predictors of the AMH/AFC ratio when compared with community-based controls. In ANCOVAs controlling for age, BMI, smoking, and race, a diagnosis of PCOS was an independent predictor of AMH and AFC but not of AMH/AFC. Age and BMI have a negative effect on AMH and AMH/AFC. African-Americans and Asians have a significantly lower AFC while Asians have a significant increase in their AMH/AFC compared to Caucasians.

OBJECTIVE: Although it is known that anti Mullerian hormone (AMH) levels are higher in polycystic ovary syndrome (PCOS), it is unclear if the elevated AMH is related to increased follicle number, over-production of AMH per follicle, or both. Thus, we sought to compare the AMH to AFC ratio in a population of PCOS and community-based controls.

DESIGN: Cross-sectional cohort study.

MATERIALS AND METHODS: Study participants were recruited at the multidisciplinary PCOS clinic following a diagnosis of PCOS by Rotterdam criteria between July 2010 and September 2015. Controls included healthy, normo-ovulatory women from a community-based cohort (Ovarian Aging Study) between November 2006 to November 2010. Clinical and laboratory data were collected for all patients. Serum AMH was assessed for both cohorts at a central laboratory. T-tests were used to assess for significance between demographics variables. AMH, AFC, and AMH/AFC were compared between the PCOS and control cohorts using analysis of covariance (ANCOVA), while controlling for age, body mass index (BMI), smoking status, and race. Pairwise comparisons were adjusted using the Bonferroni method when necessary.

RESULTS: 160 patients with a diagnosis of PCOS and 310 community-based controls were identified for inclusion. The PCOS patients were younger on average by 7 years (p < 0.001), had a higher BMI (p = 0.038), as well as significantly higher total cholesterol, fasting insulin, AMH, total AFC, and AMH/AFC compared to controls. In ANCOVAs controlling for age, BMI, smoking, and race, a diagnosis of PCOS was an independent predictor of AMH and AFC but not of AMH/AFC. Age and BMI have a negative effect on AMH and AMH/AFC. African-Americans and Asians have a significantly lower AFC while Asians have a significant increase in their AMH/AFC compared to Caucasians.

CONCLUSIONS: PCOS is an independent predictor of AMH and AFC but not of the AMH/AFC ratio when compared with community-based controls. Age and BMI are significant independent negative predictors of the AMH/AFC ratio. Interesting racial comparisons can be made while holding other factors stable: AFC is lower in African-Americans and Asians and AMH/AFC is higher in Asians compared to Caucasians.

TABLE 2. Predictors of Primary Outcome in Analysis of Covariance Multivariate Models

<table>
<thead>
<tr>
<th>Factor</th>
<th>Coefficient</th>
<th>95% Confidence Interval</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMH/AFC</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Have PCOS Diagnosis</td>
<td>0.04</td>
<td>-0.01, 0.08</td>
<td>0.162</td>
</tr>
<tr>
<td>Age (years)</td>
<td>-0.005</td>
<td>-0.008, -0.002</td>
<td>0.002</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>-0.004</td>
<td>-0.007, -0.001</td>
<td>0.005</td>
</tr>
<tr>
<td>Ever Smoked</td>
<td>-0.03</td>
<td>-0.08, 0.02</td>
<td>0.254</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td>&lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>African-American</td>
<td>-0.03</td>
<td>-0.10, 0.04</td>
<td>1.000</td>
</tr>
<tr>
<td>Asian</td>
<td>0.14</td>
<td>0.07, 0.21</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hispanic</td>
<td>-0.005</td>
<td>-0.08, 0.07</td>
<td>1.000</td>
</tr>
</tbody>
</table>

Predictors of Primary Outcomes in Analysis of Covariance Multivariate Models with Respect to Increasing Age

<table>
<thead>
<tr>
<th>Factor</th>
<th>PCOS</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMH</td>
<td>-0.038</td>
<td>0.794</td>
</tr>
<tr>
<td>AFC</td>
<td>-0.806</td>
<td>0.034</td>
</tr>
<tr>
<td>AMH/AFC</td>
<td>+0.00013</td>
<td>0.972</td>
</tr>
</tbody>
</table>

DIVERGENT INFLAMMATORY PATHWAYS MODULATE KEY ANDROGENIC GENE EXPRESSION IN OVARIAN THECA-INTERSTITIAL CELLS. Chelsea Webb Fox, M.D., Ph.D.;· Zhang Lingzhi, Ph.D.; Benjamin C. Moeller, Ph.D.; Antoni Duleba, M.D.· University of California San Diego, La Jolla, CA; University of California Davis, Davis, CA.

OBJECTIVE: Polycystic ovary syndrome is characterized by low-grade systemic inflammation and excessive androgen production by ovarian theca cells. This study evaluated the molecular mechanism through which inflammatory stimuli increase androgenic gene expression in theca-interstitial cells (TIC).

Vol. 112, No. 3, Supplement, September 2019
DESIGN: In vitro study exploring the mechanism of action of pro-inflammatory lipopolysaccharide (LPS) on androgenic gene expression in TIC.

MATERIALS AND METHODS: Isolated rat TICs were cultured in chemically defined media for 48 hours with or without LPS (100ng/mL) and/or TAK-242 (1μM; an inhibitor of TLR4), MCC950 (1μM; an inhibitor of the NLRP3 inflammasome) or ibuprofen (10⁻⁷ M), a non-selective inhibitor of cyclooxygenase (COX) enzymes. RNA was isolated and qPCR was performed to evaluate mRNA expression of Cyp71a1, Cyp11a1, Hsd3b, Ptgs2, Cebpd and Hprt (reference gene).

RESULTS: Compared to control cultures LPS increased Cyp71a1, Cyp11, Hsd3b, Ptgs2, and Cebpd by 4.7 fold (p<0.001), 7.1 fold (p<0.0001), 2.7 fold (p<0.0001), 5.6 fold (p<0.0001) and 3.2 fold (p<0.0001), respectively. These effects on androgenic gene expression were abrogated by ibuprofen (p<0.001) and TAK-242 (p<0.0001) treatment. The effect of LPS on Cyp71a1 expression was also abrogated by MCC-950 (p<0.0005); in contrast, effects of LPS on Cyp11a1, Hsd3b, Ptgs2, and cebpd were not significantly altered by MCC-950.

CONCLUSIONS: Collectively, our data demonstrate inflammatory stimuli affect androgen-synthesis and that the upregulation of key enzymes involved in androgen synthesis is mediated via activation of TLR4, and downstream effects mediated in part by NLRP3 inflammasome (MCC-950-sensitive pathway) and in part by other, NLRP3 independent pathway(s) including up-regulation of Cebpd (transcription factor involved in regulation of Ptgs2) and Ptgs2(COX-2). This data provides a mechanism through which inflammatory stimuli modulates androgen production in theca-interstitial cells.

SUPPORT: 5T2 HD007203 Training in Reproductive Sciences Grant.

P-726 Wednesday, October 16, 2019 6:30 AM

SEERUM OF POLYCYSTIC OVARY SYNDROME PATIENTS FROM THE PPCOSII TRIAL HAS HIGHER GONADOTROPIN RELEASING HORMONE RECEPTOR AUTOANTIBODY ACTIVITY THAN UNEXPLAINED INFERTILE CONTROLS FROM THE AMIGOS TRIAL. Elizabeth A. Weedin, DO, a Heather R. Burks, MD, b XiChun Yu, MD, b Hong Liang Li, MD, PhD, b Christopher E. Aston, PhD, b David C. Kem, MD, b LaTasha B. Craig, MD. a University of Oklahoma Health Sciences Center, Department of Pediatrics, Oklahoma City, OK; b University of Oklahoma Health College Medicine.

OBJECTIVE: Polycystic Ovary Syndrome (PCOS) is a complex disease of unknown etiology. We previously identified activating autoantibodies (AAb) to the second extracellular loop of the gonadotropin-releasing hormone receptor (GnRHR) in the serum of the PCOS patients. This AAb may provide a screening/diagnostic test for PCOS. We aimed to (1) confirm the increased GnRHR AAb activity in PCOS patients from a large, well-defined cohort, and (2) demonstrate the effectiveness of GnRHR antagonist in suppressing GnRHR AAb activity.

DESIGN: Cross-sectional, matched case-control study.

MATERIALS AND METHODS: Serum from 200 PCOS patients from the Pregnancy in Polycystic Ovary Syndrome II (PPCOS II) trial and from 200 race, parity, age, and body mass index (BMI) matched ovulatory, unexplained infertile control patients from the Assessment of Multiple Intrauterine Gestations from Ovarian Stimulation (AMIGOS) trial were obtained. All serum samples were tested with and without cetrotrexil, a GnRHR antagonist, for GnRHR AAb activity using the GeneBLAzer cell-based fluorescence resonance energy transfer (FRET) assay. AAb activity values are expressed as percent change from baseline to the individual values. Statistical analyses in R included paired t-tests and linear regression.

RESULTS: There were no statistically significant differences between groups for race (91% white) or parity (65% nulliparous), however, significant differences were observed in the AMH, GnRHR AAb, GnRHR AAb activity levels in the PCOS group were significantly higher than in the control group, P<0.0001. With cetrotrexil, GnRHR AAb activity was largely suppressed in the PCOS group (p<0.0001) but not in controls (p=0.93). These differences remained significant after adjusting for within pair differences in age, BMI, and AMH.

CONCLUSIONS: We have confirmed higher GnRHR AAb activity levels in the serum of an independent cohort of PCOS patients compared to unex-plained infertile controls. Addition of cetrotrexil resulted in significant suppression of AAb activity levels in PCOS patients but controls were unaffected. The GnRHR AAbs we have identified may provide a future screening/diagnostic test for PCOS or a target for treatment.

SUPPORT: College of Medicine Alumni Association (COMAA) Grant, University of Oklahoma Health College Medicine.

P-727 Wednesday, October 16, 2019 6:30 AM

PREGNANCY OUTCOMES WITHIN A PROSPECTIVE COHORT OF WOMEN WITH POLYCYSTIC OVARY SYNDROME (PCOS). Avanthi S. Ajjarapu, BA, a Karen M. Summers, MPH CHES, b Bradley J. Van Voorhis, MD, b Rachel Mejia, D.O. c University of Iowa, Iowa City, IA; aUniversity of Iowa, Iowa City, OR.

OBJECTIVE: To assess treatment course, treatment outcomes and time to pregnancy following participation in the “Combined Letrozole and Clomid in Women with infertility and PCOS Randomized Control Trial” (NCT02802865) among women who were not pregnant following the study treatment cycle.

DESIGN: Prospective Cohort Study.

MATERIALS AND METHODS: 63 participants in the NCT02802865 who did not conceive, had a biochemical pregnancy, or miscarriage at the end of the active study period were followed for 9 months after first menses following the treatment cycle. Chart abstraction was completed to follow fertility treatment, type and number of treatment cycles, ongoing clinical pregnancy, as well as time to pregnancy for those participants that had positive results. SPSS was used for statistical analysis.

RESULTS: The cohort consisted of women with a mean age of 30.4±4.1 with a mean BMI of 34 ±7.3. Within the cohort, the treatments received and the per cycle clinical pregnancy rate of those treatments are presented in Table 1. For oral ovulation induction, many of the participants used letrozole monotherapy 44/63 (70%). During the follow up window 37/63 (59%) of the participants conceived one or more pregnancies. Of these 6 (16%) resulted in miscarriage, 2 (6%) had biochemical pregnancies, 1 (3%) ectopic pregnancy. The clinical pregnancy rate per participant was 31/63 (49%).

Six participants conceived spontaneously with no treatment. The mean time to clinical pregnancy was 3 ±2.5 months.

CONCLUSIONS: This prospective cohort provides valuable information for patient counseling for women with PCOS. About half of the women who conceived conceived with spontaneous unexplained infertility.
conceived within a 9-month period with mean time to clinical pregnancy of 3 months. This demonstrates an overall good prognosis for patients with PCOS and continued efforts with low intervention treatments such as oral ovulation induction can still be effective and worth pursuing.

P-728 Wednesday, October 16, 2019 6:30 AM

INFLUENCE OF OBESITY ON CLINICAL OUTCOME IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME. Run-Xin Gan, M.S.a Fei Gong, PhD.b *Reproductive and Genetic Hospital of CITIC-Xiangya, Changsha, China; *Reproductive and Genetic Hospital of CITIC-Xiangya, Changsha, Hunan, China.

OBJECTIVE: To determine the effect of obesity in patients with Polycystic Ovary Syndrome (PCOS).

DESIGN: Analysis of clinical outcome, immune status of serum and endometrium between obesity and normal weight patients with PCOS.

MATERIALS AND METHODS: A total of 1738 normal weight patients with PCOS and obesity patients with PCOS who received routine IVF or intracytoplasmic sperm injection (ICSI) in the first cycle from August 2015 to March 2017 at Reproductive and Genetic Hospital of CITIC-XIANGYA were included in the study. The clinical outcome was analyzed between obesity and normal weight patients with PCOS. Meantime, There were 67 patients to examine C-reactive protein, Interleukin-18, and white blood cell index from the blood samples. Interleukin-18 and percentage of endometrial Natural Killer cells were also examined from the endometrial sample. Two independent samples were compared using the test. If the normal distribution is not (Gomez mediant interquartile range is used), and the two independent samples were compared using the Wilcoxon rank-sum test. Count data were used to describe the rate, comparative by chi-square test. A correlation between the indicators was drawn using linear correlation analysis.

RESULTS: There were no differences in first-trimester rate (6.91% vs. 5.63%, p = 0.44); ectopic rate (1.1% vs. 0.47%, p = 0.304) and live birth rate (65.4% vs. 65.3%, p = 0.954) between normal body weight group and obesity group. However, The clinical pregnancy rate in the PCOS normal body weight group was higher (78.2% vs. 72.2%, p = 0.017) in the PCOS normal body weight group. Serum levels of C-reactive protein and White blood cell in the early follicular and secretory phases were significantly higher in the PCOS obesity group (n = 24) compared with the PCOS normal body weight group(n = 43). However, there was no significant difference in serum and endometrial Interleukin-18 between the two groups in the early follicular phase and the luteal phase. uNK cells in the PCOS obesity group were significantly lower than those observed in the PCOS normal body weight group (p < 0.05). No correlation was found between TC and endometrium of inflammatory status.

CONCLUSIONS: Clinical pregnancy rate decreased in obese patients with PCOS, whose serum inflammatory response and endometrial immune status may be disrupted by obesity.

Reference: N/A.

SUPPORT: This study was funded by the National Science Foundation of China (81501328).

P-729 Wednesday, October 16, 2019 6:30 AM

ASSESSMENT OF PSYCHOLOGICAL DISTRESS IN POLYCYSTIC OVARIAN SYNDROME INFERTILE PATIENTS AT A TERTIARY LEVEL INFERTILITY CARE CENTRE IN INDIA. Kanad Dev Nayar, M.D., DOO., FI. COG, P. Raman Nayar, Ph.D., Sweta Gupta, M.D., MRCOG, Minal Singh, DGO, DNB, Monica Gupta, MD, FRM, Rahul Gahlot, M.D., Dip Clinical Embryology, Kapil Dev Nayar, MBBS Akanksha IVF Centre, Delhi, India.

OBJECTIVE: Polycystic ovarian syndrome (PCOS) is the commonest endocrine disease affecting young women. Thirty percent of infertile women are diagnosed with PCOS as a cause of infertility. Apart from infertility, PCOS has huge long term metabolic consequences that affects patient’s quality of life (QOL). Co-existing psychological distress have also been shown to impair patient’s QOL. However it is difficult to say if they are particularly attributable to some clinical-biochemical features of PCOS per se. The present study was undertaken to assess the prevalence of psychological distress among PCOS infertile patients and its association with clinical-biochemical features of the syndrome.

DESIGN: A single centre cross sectional study was carried out at a tertiary care infertility centre in India from 1st January 2018 through 31st March 2018. Three hundred infertile patients consented to participate in the study.

One hundred and fifty PCOS infertile patients were matched to one hundred and fifty infertile controls.

MATERIALS AND METHODS: Hamilton’s Rating Scales (HAM-A and HAM-D) were used for assessing levels of anxiety and depression. Fertility and Quality of Life Questionnaire (Ferti QoL) was used to index the quality of life. Body Image distress was measured by Feel Ideal Discrepancy (FID) Score using Stunkard Figure rating Scale. Hirsutism score (calculated using Modified Ferriman Gallyway score) and body mass index (BMI) were determined. Primary outcome measured was the prevalence of psychological disorders in PCOS infertile patients and their comparison with non PCOS infertile controls. Secondary outcome was association between psychological distress with BMI and hyperandrogenism.

RESULTS: The baseline prevalence of anxiety in PCOS infertile patients was 40.32% and in non PCOS infertile controls was 28.86% (p = 0.039); baseline prevalence of depression in PCOS patients was 38.2% and in controls was 24.82% (p = 0.018), both were statistically significant. The HAM-A scores in PCOS and non-PCOS infertile controls (14.58 ± 7.46 vs. 11.95 ± 7.45; p = 0.002) and HAM-D scores (14.18 ± 7.16 vs. 11.39 ± 6.95; p < 0.001) in PCOS and non-PCOS infertile controls; the difference was clinically significant. There was no difference in FertiQoL scores for both the groups. Both groups showed comparable reduced quality of life and increased overall life stress. FID scores were higher in PCOS patients (1.2 ± 1.4) compared to non PCOS infertile controls (0.5 ± 1.4, p < 0.001). BMI and Hirsutism score were associated with depression in these patients (p < 0.001).

CONCLUSIONS: PCOS is a complex disorder associated with alarming levels of psychological distress which is much greater when compared to infertile controls. Clinicians should routinely evaluate all infertile patients, especially PCOS from a mental health perspective otherwise their hidden psychological stress would remain undiagnosed. Psychotherapy in addition to pharmacotherapy would help improve quality of life thus helping patients cope up with financial and emotional burden of their treatment.


SUPPORT: NIL.

P-730 Wednesday, October 16, 2019 6:30 AM

HOMOZYGOUS ANTI-MULLERIAN HORMONE (AMH) GENE MUTATION rs10417628 IN A POLYCYSTIC OVARY SYNDROME (PCOS) WOMAN WITH EXAGERATED HYPERANDROGENISM. Luis R. Hoyos, M.D.,a Jenny A. Visser, Ph.D.,b Anke McLuskey, B.A.S.,b Gregorio Chazenbalk, Ph.D.,c Tristan R. Grogan, M.S.,c Daniel A. Dumesc, M.D.,c “UCLA, Los Angeles, CA; cAffiliation not provided.

OBJECTIVE: Gene mutations of anti-Müllerian hormone (AMH) have been reported in approximately 3% of women with polycystic ovary syndrome (PCOS), in whom impaired AMH inhibition of CYP17 transcription could occur, leading to enhanced androgen production (1, 2). We report an AMH gene mutation in a normal-weight PCOS woman with undetectable serum AMH levels. The purpose of this study was to determine whether AMH mutation in this PCOS woman was associated with hyperandrogenemia in excess of that from a cohort of normal-weight PCOS women and, if so, whether it was accompanied by exaggerated LH hyperscertainment.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Twelve normal-weight PCOS women (by 1990 NIH criteria), ages 18-35 years, and 19 age-and body mass index (18.5-25 kg/m²)-matched controls underwent serum hormone and metabolic measures as part of a NIH-funded study. Serum AMH levels were measured by ELISA (Ansh Labs, Webster, TX) in all subjects and were undetectable in the PCOS woman with a homozygous missense gene variant in exon 5 (T/C [A/a]515Val); rs10417628). Serum androgen and LH levels were measured by LC-MS/MS (Quest Diagnostics, San Juan Capistrano, CA) and chemiluminescence, respectively. Outcome variables between the cohorts of PCOS and control women were compared by the Wilcoxon rank-sum test. The same outcome variables of the PCOS woman with the AMH gene mutation were ranked in order of magnitude relative to those of the cohort of PCOS women.

RESULTS: Undetectable serum levels of AMH immunoreactivity occurred in this PCOS woman with homozygous AMH gene mutation.
rs10417628 and could reduce its bioactivity to exaggerate the PCOS phenotype through impaired AMH inhibition of CYP17 transcription, promoting androgen induced loss of steroid negative feedback on LH.

References: Å
SUPPORT: NIH P50 HD071836; NIH P51 OD011092; UL1TR001881; Santa Monica Bay Woman’s Club.

P-731 Wednesday, October 16, 2019 6:30 AM
EXPRESSION PROFILES OF miRNA -369-5P AND miRNA-671-3P IN THE PLASMA OF PREGNANT WOMEN WITH POLYCYSTIC OVARY SYNDROME VERSUS NORMAL PREGNANCIES. Meryem Hoçaoglu, M.D.a, b Selin Demirer, Specialist,a Eser Kaynak, Student,a Erkut Altar, M.D., a Sibel Bulucuoğlu Kuran, Ph.D.b Ayse Altun, specialist,b Abdullahir Turgut, M.D., Ph.D.a Ervin Komurcu Bayrak, Ph.D.b aObstetrics and Gynecology, Goztepe Training and Research Hospital, Istanbul Medeniyet University, Istanbul, Turkey; bObstetrics and Gynecology, Reproductive Endocrinology and Infertility, Istanbul Medical Faculty, Istanbul University, Istanbul, Turkey; cGenetics, Aziz Sancar Institute of Experimental Medicine, Istanbul University, Istanbul, Turkey.

OBJECTIVE: Women with polycystic ovary syndrome (PCOS) exhibit increased risk of pregnancy complications (1). MicroRNA-369-5p (miRNA) and miR-671-3p were associated with adipogenic differentiation of mesenchymal stromal cells (2), diabetes (3) and insulin secretion (4, 5). The aim was to determine if there are differences in expression levels of miR-369-5p and miR-671-3p in the cell free plasma samples between pregnant women with PCOS and healthy controls.

TABLE 1. Patient demographics, clinical and biochemical characteristics

<table>
<thead>
<tr>
<th>Index Characteristics</th>
<th>PCOS (n=14) Mean ± SD</th>
<th>Control Group (n=12) Mean ± SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>29.6 ± 4.34</td>
<td>26.6 ± 4.9</td>
<td>0.561</td>
</tr>
<tr>
<td>Gestational age at sampling (weeks)</td>
<td>29.1 ± 5.1</td>
<td>28.9 ± 0.2</td>
<td>&lt;0.0001</td>
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<td>Pre-Pregnancy</td>
<td>28.3 ± 6.1</td>
<td>23.6 ± 2.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BMI (kg/m2)</td>
<td>31.2 ± 5.7</td>
<td>26.4 ± 2.9</td>
<td>0.004</td>
</tr>
<tr>
<td>Systolic blood pressure at sampling (mmHg)</td>
<td>106.4 ± 10.1</td>
<td>101.7 ± 5.8</td>
<td>0.028</td>
</tr>
<tr>
<td>Diastolic blood pressure at sampling (mmHg)</td>
<td>62.8 ± 7.3</td>
<td>60.0 ± 6.0</td>
<td>0.106</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.3 ± 0.2</td>
<td>5.1 ± 0.3</td>
<td>0.844</td>
</tr>
<tr>
<td>Fasting glucose (mg/dl) at sampling</td>
<td>76.0 ± 9.1</td>
<td>75.9 ± 8.7</td>
<td>0.670</td>
</tr>
<tr>
<td>1-h glucose (mg/dl) at sampling following a 75-g OGTT</td>
<td>139.7 ± 27.5</td>
<td>122.7 ± 28.9</td>
<td>0.952</td>
</tr>
<tr>
<td>2-h glucose (mg/dl) at sampling following a 75-g OGTT</td>
<td>108.0 ± 24.4</td>
<td>97.5 ± 19.0</td>
<td>0.386</td>
</tr>
</tbody>
</table>

PCOS, polycystic ovary syndrome; SD, standard deviation; BMI, body mass index; GA, gestational age; OGTT, oral glucose tolerance test Data presented as mean ± SD and compared using unpaired t-test *p < 0.05.

DESIGN: A pilot prospective cohort study.
MATERIALS AND METHODS: Singleton and spontaneous pregnancies were enrolled this study. Using real-time quantitative PCR, the expression level of miR-369-5p and miR-671-3p in the plasma were analyzed in pregnant women with PCOS were diagnosed before pregnancy according to the Rotterdam criteria, and had no obstetrical or medical complications (n=14) compared to healthy pregnant women (n=12). The relative expression of the target miRNAs in samples was compared to the calibrator and the results were expressed as relative quantification (RQ) values.

RESULTS: The characteristics of patients are listed in (Table 1). The expression levels of miR-671-3p were significantly increased in the pregnant patients with PCOS (RQ value= 5.53±2.98) versus healthy controls (RQ value= 1.20±0.64) (p=0.0001). One receiving operator characteristic analysis, areas under the curve of the expression ratio of miR-671-3p in PCOS was 0.96 (95%CI: 0.88-1.00). At a cut-off value of 1.89 for this miRNA, sensitivity and specificity values were 92% and 93%, respectively. There was no difference in the expression levels of miR-369-5p between PCOS and controls.

CONCLUSIONS: Our results indicated miR-671-3p has a candidate for diagnosis for PCOS and could be a potential biomarker during pregnancy.

**THE IMPACT OF A BRIEF INTERVENTION ON RETENTION RATES WITH PATIENTS WHO DID NOT RETURN TO CARE AFTER AN INITIAL PHYSICIAN VISIT.** Alice D. Domar, Ph.D., Kristin L. Rooney, BA, Dan W. Duvall, Jr., BA, Denny Sakkas, PhD. Boston IVF, Waltham, MA.

**OBJECTIVE:** The goal of this study was to determine a) if a follow-up email to selected patients who had an initial consult with an infertility specialist, but did not return for a second visit, would change return to care behavior and b) why patients had not returned.

**DESIGN:** Controlled prospective trial.

**MATERIALS AND METHODS:** From July 2017 to March 2018 all patients who had attended an initial visit with an infertility specialist at the clinic, but had not returned for at least three months were selected to receive a follow up email. Those selected for an email excluded patients who we knew had achieved a pregnancy, already had a plan for treatment, had visited for an egg freeze and all LGTPQ patients. The email asked if the patient had any questions about that visit, offered support to the patient and included contact information for the patient liaison sending the email. The email also asked each participant to indicate why they had not returned and were provided 4 options and an opportunity to write in a response. From April 2018 to December 2018 no emails were sent to patients. No other changes of patient contact practice was initiated during the trial period. All patients were then followed for 11 months after their initial visit to observe return to care behavior.

**RESULTS:** A total of 647 patients were selected to be sent 301 emails (Group 1) and 657 did not receive an email (Group 2). Forty-one percent of the patients in Group 1 returned to care, compared to 32% who did not (Group 2) (P < .0014). Of the Group 1 patients 116 replied (38.5%). For those who gave a reason why they hadn’t returned, 32% of the respondents (Group 2) (P < .0014). Of the Group 1 patients 116 replied (38.5%). For those who gave a reason why they hadn’t returned, 32% of the respondents (Group 2) (P < .0014). Of the Group 1 patients 116 replied (38.5%). For those who gave a reason why they hadn’t returned, 32% of the respondents (Group 2) (P < .0014). Of the Group 1 patients 116 replied (38.5%). For those who gave a reason why they hadn’t returned, 32% of the respondents (Group 2) (P < .0014). Of the Group 1 patients 116 replied (38.5%). For those who gave a reason why they hadn’t returned, 32% of the respondents (Group 2) (P < .0014). 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**CONCLUSIONS:** A simple follow-up email sent to patients who had an initial visit with an infertility specialist but did not return to the clinic within three months was associated with a significant increase in return to care when compared to patients who did not receive an email.
OBJECTIVE: To provide cumulative clinical pregnancy rates, time to pregnancy, and treatment discontinuation rates depending on initial fertility treatment and prognosis.

DESIGN: retrospective cohort.

MATERIALS AND METHODS: Electronic medical records data from 78958 treatment-naive infertile patients whose initial treatments were OI (with or without intrauterine insemination) with oral medication (clomiphene or letrozole), OI with gonadotropins (Gn), or IVF (fresh or cryopreserved embryo transfer) between Jul 2009 – Sep 2015 were analyzed. The overall population and pregnancy subgroups were studied and stratified by initial treatment type.

RESULTS: Patients with a good prognosis were more likely to begin treatment with OI oral, while patients with a poor prognosis were more likely to start with IVF. Regardless of prognosis, the proportion of patients who achieved a pregnancy was highest among those who initiated treatment with IVF rather than OI. Patients who started treatment with OI required more cycles to achieve pregnancy than those who started with IVF (mean 3.5 vs 1.8 cycles). A large percentage (26–48%) of pregnancies among patients who started with OI resulted from IVF after OI failed. Treatment discontinuation without a pregnancy was most common among patients who started with OI oral.

CONCLUSIONS: Beginning clinical treatment with IVF rather than OI resulted in higher cumulative pregnancy rates, fewer total treatment cycles, and lower rates of treatment discontinuation without a pregnancy. The advantage of IVF was greater among patients with a poorer prognosis (eg, diminished ovarian reserve ≥35 years). These results favor initiating treatment with IVF unless a patient has a strong personal preference for less invasive approaches.

SUPPORT: Study sponsored by EMD Serono, Inc. (a business of Merck KGaA, Darmstadt, Germany), Rockland, MA, USA.

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OBJECTIVE: To ascertain how often US IVF patients change clinics, what their underlying motivations are and how they perceive how much time and expense their initial choice of clinic may have cost.

DESIGN: 28,000 US IVF patients were surveyed on the number of clinics they received IVF treatment from. A sub-segment (1,000) of those who were treated at multiple clinics were re-surveyed on their reasons for switching and their perception of how being treated at multiple clinics impacted their financial and emotional well-being.

MATERIALS AND METHODS: Patients were surveyed at www.FertilityIQ.com and thereafter followed-up by email, whereby additional questions were posed using the the Qualtrics survey tool.

RESULTS: 48% percent of surveyed fertility patients are treated at one clinic, 27% at two clinics and 25% at three-or-more clinics. Of those who were treated at more than one clinic, 32% left their first clinic due to inadequate attention or service, 30% due to inadequate clinical results, 18% due to infertility requiring in-vitro fertilization at a public unit serving the general public and operating five days a week. MATERIALS AND METHODS: Included were women and couples with infertility requiring in-vitro fertilization at a public unit serving the general local population. Cycle data was recorded on an excel spread sheet prospectively and analyzed retrospectively following local ethics committee approval. Patient, treatment and outcome parameters were compared as a function of the day of the week menstruation began. Only antagonist cycles were included, each patient was included only once (the first treatment) and freeze all cycles were excluded.

SAS9.4 software was used for statistical analysis. Categorical data was analyzed with the chi-squared test while continuous data were compared between groups with the Kruskall-Wallis test. P<0.05 was considered significant.

RESULTS: Included were 676 cycles. The live birth rate for each weekday menstruation began is as follows: weekday 1 – 14.56%, weekday 2 – 14.56%, weekday 3 – 22.02%, weekday 4 – 26.99%, weekday 5 – 27.78%, weekday 6 – 15.38%, weekday 7 – 12.90% (P=0.0407). The treatment groups did not differ for age, infertility duration, BMI, FSH, parity, cause of infertility. The groups differed significantly for number of days of gonadotropin stimulation (P=0.0066), though they did not differ for the amount of gonadotropins administered, the numbers of oocytes aspirated, or the fertilization rate (P=0.0742). They differed significantly for pregnancy rate (P=0.0143), and clinical pregnancy rate (0.0292) as well.

In a subgroup of 363 ICSI cycles, the percent of M2 oocytes differed significantly among treatment groups (P=0.0383) but the live birth rate did not.

CONCLUSIONS: The study is limited by its retrospective nature. We are unaware of prospective randomized trials which compare a five-day work week to a six- or seven-day work week. Since the day menstruation begins is a rather random occurrence, the finding that there are differential results suggests that the lack of flexibility in scheduling the OPU after an ideal stimulation duration, may be compromising results.

Adding weekend OPU to the workschedule may improve outcomes but at considerable cost to the public sector. Alternatively, cycle scheduling using hormonal therapy may be considered. More research should be invested in exploring how work schedules may impact results.

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INSIGHTS INTO INFERTILITY PATIENT DISCONTINUATION OF CARE: RESULTS OF A NATIONWIDE SURVEY. Barbara Collura, MA, a Brooke Hayward, SM, MBA, a Krysten Modrzykiewski, PharmD, b Gilbert L. Mottila, MD, c Kevin S. Richter, PhD, d Allison B. Catherino, PhD, b RESOLVE: The National Infertility Association, McLean, VA; eEMD Serono, Inc., Rockland, MA; fShady Grove Fertility Center, Annapolis, MD; gFertility Science Consulting, Silver Spring, MD.

OBJECTIVE: To illustrate perspectives of patients on the infertility treatment journey, and their motivations for treatment discontinuation and return to care.

DESIGN: Online, cross-sectional, qualitative–quantitative patient survey.

MATERIALS AND METHODS: Participants were recruited from the infertility patient community and invited to complete the survey, administered in March–April 2019. Descriptive statistics were calculated for all survey items.

RESULTS: Among 359 respondents from 40 US states, 99% were female. Forty-one percent had earned a graduate degree (master’s or doctoral), and an additional 41% had a bachelor’s degree. Most (69%) were 31–40 years of age with 18% being 30 years of age and 18% being older than 40 years. The majority (51%) reported an annual household income of $100k or greater, while 7% reported an income below $50k. 180 patients who reported that they were done with treatment, 62% (n=111) completed treatment with a live birth and 38% (n=69) ended treatment without a live birth. 99% completed treatment with a live birth and 38% (n=69) ended treatment without a live birth.
birth. Of the 200 respondents who considered discontinuation of care, 30% (n=60) continued without ever stopping, 36% (n=71) stopped for a period of time and then restarted, and 35% (n=69) stopped with no plan to restart. Commonly cited reasons (patients could choose multiple reasons) for treatment discontinuation were financial (62%), psychological burden/treatment fatigue (58%), poor prognosis (26%), and natural conception (6%); the reasons most often cited for staying in treatment were patient’s desire for a family (47%), hope (21%), and partner’s desire for a family (13%). The expected vs actual time to pregnancy was vastly different. Of patients who thought it would take <1 year to become pregnant, 42% (78/185) reported it took >2 years before pregnancy while 45% (83/185) reported still being on their treatment journey.

CONCLUSIONS: Fertility patients predominantly cite psychological burden/treatment fatigue and cost as reasons for discontinuation, and hope and desire for family as reasons for staying in treatment. Fostering more realistic patient expectations by fertility providers regarding the time it often takes to achieve pregnancy may play a role in reducing treatment discontinuation and dropout.

SUPPORT: Study sponsored by EMD Serono, Inc. (A business of Merck KGaA, Darmstadt, Germany), Rockland, MA, USA.

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DETERMINING THE REASONS WHY INSURED WOMEN DROP OUT OF IVF TREATMENT AFTER ONE UNSUCCESSFUL CYCLE

Alice D. Domar, Ph.D.a Kristin L. Rooney, BAa Laura E. Dodge, ScD, MPHb

aBoston IVF, Waltham, MA;bHarvard Medical School, Boston, MA.

OBJECTIVE: To determine reasons why insured patients discontinue in vitro fertilization (IVF) treatment after a single unsuccessful cycle.

DESIGN: Cross-sectional study.

MATERIALS AND METHODS: Women whose first autologous IVF cycle began June 2014–October 2018, who did not have a live birth, and who did not return for treatment for at least four months were eligible. Women completed a survey regarding treatment termination either online or via phone. Results were compared to those from a prior study of 237 insured patients who discontinued treatment after more than one unsuccessful cycle, the last of which began January 2010–May 2014, and who did not return to care for a one-year period.

RESULTS: Of 262 eligible women, 93 (36%) completed surveys. Of these, 25 (27%) did not have insurance coverage for IVF treatment and were excluded. Of the remaining 68 participants, 14 (21%) sought care elsewhere after their single unsuccessful cycle, which was significantly fewer than participants who completed more than one unsuccessful cycle (37%; P=0.02). Those who sought care elsewhere after a single unsuccessful cycle reported doing so because they were unhappy with their care (50%), they had moved away (29%), they wanted a second opinion (21%), or they had heard good things about another center (21%); these reasons were similar to those who did multiple unsuccessful cycles, with the exception that those doing multiple cycles were more likely to want a second opinion (60%; P=0.01). Of the 54 participants who had not sought additional care after one unsuccessful cycle, over half (52%) reported that they were taking a break from treatment, and nearly one-quarter reported that they could not afford the out-of-pocket costs (24%). Other reasons included losing insurance coverage (22%) and conceiving spontaneously (22%). Participants not seeking care after multiple unsuccessful cycles were more likely to be pursuing or have adopted a child (23% vs. 4%; P=0.002), to report that further treatment was too stressful (45% vs. 20%; P=0.001), and to report that they had been advised to stop treatment (15% vs. 4%; P=0.03).

CONCLUSIONS: Half of participants who did not return to care within four months of a single unsuccessful IVF cycle reported that they were taking a break from treatment, and despite having partial or full insurance coverage, nearly one-quarter reported not returning due to financial difficulties. Treatment stress was less of an issue for participants who had undergone a single unsuccessful cycle compared to those who had undergone multiple unsuccessful cycles.

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DOES IN VITRO FERTILIZATION (IVF) INSURANCE COVERAGE CHANGE PRACTICE PATTERNS? Jenny S. George, MD.a Micaela J. Stevenson, BS,a Samantha B. Schon, MD, MTR.a Michael Lanham, MD.a Jim M. Dupree, IV, MD, MPH.a Molly B. Moravek, MD, MPH.a ‘University of Michigan, Ann Arbor, MI; ’University of Michigan Medical School, Ann Arbor, MI; ’Michigan Medicine, Ann Arbor, MI.

OBJECTIVE: On January 1, 2015, a single, large academic institution implemented self-directed IVF insurance coverage for employees and students with an infertility diagnosis; however intrauterine insemination (IUI) remained an uncovered benefit. The insurance benefit mandated single embryo transfer ≤35 years, single or double embryo transfer >35 years, and imposed a lifetime limit on gonadotropin prescription coverage, regardless of whether the gonadotropins were used for IVF. The objective of this study was to examine practice patterns within the context of this insurance change. We hypothesized that patients with IVF coverage would undergo fewer injectable (gonadotropin or hybrid) cycles prior to IVF, fewer IUI cycles prior to IVF, and have less embryos transferred overall, compared to patients without IVF coverage.

DESIGN: Retrospective chart review.

MATERIALS AND METHODS: We used ICD-9/10 and CPT codes to identify patients who underwent IVF from 1/1/15 through 4/28/18 (n=568). Exclusion criteria included initial evaluation prior to 1/1/15, history of IVF treatment at an outside facility, IVF for fertility preservation, severe male factor or tubal factor infertility necessitating IVF treatment, and use of preimplantation genetic testing for aneuploidy (PGT-A). Primary outcome was number of embryos transferred. Secondary outcomes included number of injectable cycles prior to IVF and number of IUI cycles prior to IVF. Descriptive statistics and Student’s t-test were used to characterize these distributions.

RESULTS: 321 patients met inclusion criteria (142 without insurance coverage and 179 with insurance coverage). Mean age in both the uncovered and covered groups was 33.3 years (SD = 4.26, NS). Mean number of embryos transferred was similar between uncovered and covered patients (1.42 vs 1.47, NS). Number of injectable cycles prior to IVF was similar between groups (3.82 vs 2.33, NS), as was the number IUIs prior to IVF (2.68 vs 2.64, NS). In patients with unexplained infertility, number of IUI cycles prior to IVF was similar between groups (3.31 vs 3.13, NS). In patients with a diagnosis of unexplained infertility, diminished ovarian reserve (DOR), or endometriosis, there were no significant differences in number of IUI cycles prior to IVF between groups (2.83 vs 2.6, NS).

CONCLUSIONS: Number of embryos transferred, number of IUI cycles prior to IVF, and number of injectable cycles prior to IVF was similar between patients with and without insurance coverage for IVF. These data provide reassurance that coverage status is unlikely to alter infertility provider practice and treatment strategy. Despite IUI being an uncovered benefit, providers still followed standard guidelines for care of treatment conditions such as unexplained infertility and endometriosis.

<table>
<thead>
<tr>
<th>Patient expectation</th>
<th>0.5 years</th>
<th>1 year</th>
<th>2 years</th>
<th>&gt;2 years</th>
<th>Still on journey</th>
<th>Completed family without live birth</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>I did not have an expectation</td>
<td>1</td>
<td>5</td>
<td>5</td>
<td>21</td>
<td>11</td>
<td>0</td>
<td>43</td>
</tr>
<tr>
<td>I would be pregnant in &lt;1 year</td>
<td>2</td>
<td>3</td>
<td>14</td>
<td>78</td>
<td>83</td>
<td>5</td>
<td>185</td>
</tr>
<tr>
<td>I would be pregnant in 1–2 years</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>8</td>
<td>40</td>
<td>4</td>
<td>56</td>
</tr>
<tr>
<td>I would never be pregnant</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Total</td>
<td>3</td>
<td>11</td>
<td>22</td>
<td>110</td>
<td>136</td>
<td>9</td>
<td>291</td>
</tr>
</tbody>
</table>

Italic = patient expectation aligned with actual time to pregnancy; bold = expectations and actual time to pregnancy not aligned.
OBJECTIVE: Current management of FET cycles in programmed cycles generally entails monitoring with sonography and/or hormonal measurements. Endometrial thickness has shown correlation with implantation rate, prompting many clinicians to attempt to detect and correct poor endometrial response. To date, however, no studies have demonstrated that monitoring and active management of endometrial response is beneficial. This is important because the monitoring requirements associated with FET cycles add to the complexity and decrease the predictability of the day of embryo transfer. In an effort to increase access to care, our clinic has recently implemented a programmed cycle protocol performed without monitoring for patients undergoing FET following intravaginal culture (IVC). We examined the pregnancy outcomes of these cycles compared to contemporaneous programmed cycles with conventional monitoring.

DESIGN: FET cycles between April 2017 and March 2019 were retrospectively analyzed. 74 patients underwent a FET cycle with no monitoring and 143 underwent an FET cycle with monitoring. Non-monitored cycles: Patients began 6 mg of oral estradiol on cycle day 1 and were instructed to call the IVF coordinator to schedule their FET. IM progesterone (PIO) was begun after 12 or more days of estradiol. No ultrasounds or hormonal testing was performed during the cycle. Monitored cycles: The cycle was timed with oral contraceptives. A sonogram was performed prior to starting leuprolide SQ daily. OCPs were discontinued after 5 days of leuprolide overlap. A second sonogram was performed after 7 to 8 days of leuprolide to assess endometrial thickness and ovarian suppression. Additionally, serum was obtained for an estradiol level. Oral estradiol 6 mg/d was begun daily if the serum E2 was <85 pg/ml and ovarian suppression. Additionally, serum was obtained for an estradiol level. Oral estradiol 6 mg/d was begun daily if the serum E2 <85 pg/ml and endometrial thickness <5 mm. A third sonogram was performed after 12 to 14 days of estradiol supplementation. If the endometrium was 8 mm in thickness and trilaminar in appearance, PIO was begun. If not, a fourth sonogram was performed 7 days later. All FETs were performed on the 6th day of PIO.

MATERIALS AND METHODS: Fisher Exact Test.

RESULTS: 72 women completed the survey, with 33% reporting a multifetal gestation of twins or greater as the ideal treatment outcome and 67% preferring a singleton gestation. There were no significant differences in mean age, partner age, marital status, education or religious affiliation between groups (Table). The ideal family size was significantly higher in women desiring a multifetal gestation, 2.5 children vs 2.2, p=0.03. Women who preferred multifetal gestation were less likely to have an income < $100,000 per year, 63% vs 85%, p=0.04. Women with insurance coverage for infertility who were aware of their benefits (n=32) were more likely to prefer a singleton gestation, with 22% desiring a multifetal gestation and 78% desiring a singleton.

CONCLUSIONS: Multifetal gestations have a significantly increased risk of maternal and neonatal morbidity and mortality. Despite this, one third of women presenting for infertility care reported multifetal gestation as the ideal treatment outcome. Interestingly, patients with a higher income and insurance coverage for fertility care are more likely to desire singleton gestation. This data suggests that patients perceive multifetal gestation as a cost-effective treatment strategy. Future research should evaluate if improved access to insurance coverage decreases multiple pregnancy rates.

CONCLUSIONS: Streamlined IVF processes offer the possibility to increase patient access to care through fewer visits and lower patient cost. FET cycles with no monitoring have comparable outcomes to FET cycles with conventional monitoring.

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IMPACT OF INSURANCE COVERAGE FOR FERTILITY TREATMENT ON PATIENT PREFERENCE FOR SINGLETON GESTATION. Seth J. Barishansky, MS, Anne Hutchinson, M.D, Dana B. McQueen, MD, Andrew C. Offord, BS, Angela K. Lawson, Ph.D, Mary Ellen Pavone, MD, MSCL. Northwestern University, Chicago, IL; Northwestern University Feinberg School of Medicine.

OBJECTIVE: To evaluate predictors for patient preference regarding multifetal or singleton gestation among women presenting for infertility care.

DESIGN: Cross-Sectional Study.

MATERIALS AND METHODS: IRB approval was obtained. Couples undergoing treatment at a university-based infertility clinic between February 2019 and April 2019 participated in a 40-question previously validated digital survey (Ryan et al, 2004). All patients received treatment in a location with state mandated infertility insurance coverage. The desire for singleton versus multifetal gestation was recorded. Baseline characteristics and demographic data compared between groups.

RESULTS: 72 women completed the survey, with 33% reporting a multifetal gestation of twins or greater as the ideal treatment outcome and 67% preferring a singleton gestation. There were no significant differences in mean age, partner age, marital status, education or religious affiliation between groups (Table). The ideal family size was significantly higher in women desiring a multifetal gestation, 2.5 children vs 2.2, p=0.03. Women who preferred multifetal gestation were less likely to have an income < $100,000 per year, 63% vs 85%, p=0.04. Women with insurance coverage for infertility who were aware of their benefits (n=32) were more likely to prefer a singleton gestation, with 22% desiring a multifetal gestation and 78% desiring a singleton.

CONCLUSIONS: Multifetal gestations have a significantly increased risk of maternal and neonatal morbidity and mortality. Despite this, one third of women presenting for infertility care reported multifetal gestation as the ideal treatment outcome. Interestingly, patients with a higher income and insurance coverage for fertility care are more likely to desire singleton gestation. This data suggests that patients perceive multifetal gestation as a cost-effective treatment strategy. Future research should evaluate if improved access to insurance coverage decreases multiple pregnancy rates.

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CUTTING THE COST OF PARENTHOOD: THE EFFICACY AND COST SAVINGS OF COMPOUNDED FOLLICLE STIMULATING HORMONE. Alexander J. Tatem, MD, J. Abram McBride, MD, Joie Guner, MD, MSc, Jonathan A. Beilan, e399
OBJECTIVES: Injectable follicle stimulating hormone (FSH) provides ovarian stimulation (OS) in women undergoing both in vitro fertilization (IVF) and oocyte cryopreservation (OCP). Brand FSH (B-FSH) is prohibitively expensive and can be a major roadblock to couples pursuing fertility treatment. Introduced in late 2017, compounded FSH (C-FSH) offers a cost-effective alternative to B-FSH with promising early clinical results. Here we provide the first analysis of the clinical efficacy and cost-effectiveness of C-FSH in women pursuing OCP and IVF.

DESIGN: Retrospective chart review identified all females receiving C-FSH for IVF or OCP from late 2017 to present.

MATERIALS AND METHODS: Clinical outcomes including oocyte retrieval rates, fertilization rates, blast/embryo yield, pregnancies and live births were evaluated. All C-FSH prescriptions were obtained through the same specialty compounding pharmacy in Houston, TX. The average cost of a typical course of therapy.

RESULTS: 34 female patients (mean age 35.3) initiated IVF or OCP. 29 women showed good response resulting in a mean retrieval of 12.75 (4-39) mature oocytes. Of the 21 women pursuing IVF, we observed a 74% fertilization rate and a mean yield of 4.3 (0-13) mature blastocysts per cycle. 8 total embryo transfers were performed. 6 of these were frozen transfers with single embryo transfers.

CONCLUSIONS: In this novel analysis, C-FSH therapy showed excellent OS of women undergoing IVF and yielded several pregnancies, validating the clinical effectiveness of C-FSH. Compared to B-FSH, C-FSH provides unprecedented cost savings to patients undergoing IVF therapy and may allow some couples to achieve parenthood who otherwise would be prohibited by cost.
PROTEOMIC SIGNATURES OF EPIGENETIC AND TRANSCRIPTION REGULATORS ARE PIVOTAL IN CONTROLLING PATERNFAL FACTORS IN RECURRENT PREGNANCY LOSS. Gayatri Mohanty, PhD, Soumya Ranjan Jena, M.Phil, Jasmine Narayan, M.Phil, Sujata Kar, MBBS, MD, DNB, Luna Samanta, PhD, Redox Biology Laboratory, Department of Zoology, Center of Excellence in Environment and Public Health, Ravenshaw University, Cuttack, Odisha, India; A-32, Unit-4, Kharvel Nagar, Bhubaneswar, India.

OBJECTIVE: Recurrent pregnancy loss (RPL) is a problem often experienced with embryo loss within first trimester of gestation while in fifty percent of cases the cause remains unknown [1]. The epigenetic machinery of the spermatozoa is tailored in a way to meet the demands of the highly specialised sperm cell while the integrity of the sperm epigenome is essential for initiation and maintenance of a successful pregnancy. Increased oxidative stress has been a cause for damaged chromatin, proteins and lipids [2]. The objective is to investigate and identify altered proteomic signatures that control paternal factors post-fertilisation in RPL patients.

DESIGN: Comparative proteomic analysis to identify epigenetic and transcriptional proteins in RPL patients.

MATERIALS AND METHODS: After excluding subjects with any kind of known abnormalities as well karyotype abnormalities, a total of 20 well phenotyped male partners of women with RPL less than 10 weeks of gestation were included in this study. The samples were homogenised and subjected to high-throughput proteomic analysis using in-gel digestion through 2D-DIGE MALDI-TOF as well as in-solution Q-TOF analysis. A p value < 0.05 was considered statistically significant. Key proteins after pathway analysis were validated by western blotting.

RESULTS: The findings of the study indicate six proteins to be differentially expressed during spermatogenesis and early development. In addition, although much of RPL may be attributed to aneuploidy, but that other factors also remain 3% higher than in infertile controls. These findings reflect that aneuploidy is not the sole source of RPL.

CONCLUSIONS: Although low sample size may be considered as a limitation of our study, our data suggests that altered proteins identified play a pivotal role in epigenetic programming and transcriptional regulation of paternal factors both during spermatogenesis and early development. In conclusion, although we cannot confirm these signature differences at proteomic level as an independent cause for unexplained RPL, the findings of the study are interesting and imply a better understanding of their biological implications.

Department of Science and Technology, Govt. of India.

Council for Scientific and Industrial Research.


SUPPORT: University Grants Commission, Govt. of India.

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HIGH ODDS OF ANEUPLOIDY IN RECURRENT PREGNANCY LOSS POPULATION IRRESPECTIVE OF FINDINGS ON TRADITIONAL EVALUATIONS. Ann Korkidakis, MD, MPH, Arianne Y. K. Albert, PhD, Mohamed Ali Bedaiwy, M.D., Ph.D, University Of British Columbia, Vancouver, BC, Canada; "Women’s Health Research Institute, Vancouver, BC, Canada; "University of British Columbia, Vancouver, BC, Canada.

OBJECTIVE: To predict the probability of aneuploidy in the products of conception (POC) in the recurrent pregnancy loss (RPL) population based on the gestational age (GA) of pregnancy loss, maternal age, and positive findings on traditional RPL investigations.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Women with 2 or more pregnancy losses that underwent cytogenetic testing on their POC were eligible for analysis. Exclusion criteria included induced abortions and pregnancies missing data on GA at time of loss. Cytogenetics on the POC was performed using 24-chromosome microarray analysis. Abnormal results on traditional RPL investigations included TSH >4.0 IU/mL, hemoglobin A1c >6.4%, prolactin >23.4ng/mL, positive anti-phospholipid antibodies (lupus anticoagulant, anticardiolipin, and anti-beta 2 glycoproteins antibodies), abnormal parental karyotypes, or uterine anatomical defects on hysterosalpingogram (HSG) or hysteroscopy (congenital uterine anomalies or intrauterine lesions). Mixed-effects logistic regression was used to compare the probability of

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PREIMPLANTATION GENETIC TESTING FOR ANEUPLOIDY (PGTA) REDUCES MISCARRIAGE AND IMPROVES LIVE BIRTH RATES IN RECURRENT PREGNANCY LOSS PATIENTS. Julia G. Kim, MD, MPH, Gayathree Murugappan, MD, Ruth B. Lathi, MD, Jonathan D. Kort, MD, Brent M. Hanson, MD, Ashley W. Tiegส, MD, Emily K. Osman, MD, Shelby A. Neal, MD, Richard Thomas Scott Jr., MD, IVI-RMA New Jersey, Basking Ridge, NJ; Stanford University Medical Center, Sunnyvale, CA; Stanford Fertility and Reproductive Medicine Center, Sunnyvale, CA; IVI/Reproductive Medicine Associates of Northern California, San Francisco, CA; Sidney Kimmel Medical College at Thomas Jefferson University, Philadelphia, PA.

OBJECTIVE: Recurrent pregnancy loss (RPL) is a diverse syndrome with many causes, the most common being embryonic aneuploidy. PGTA should thus improve outcomes in RPL patients, but studies conflict as to whether
aneuploidy by gestational age, maternal age, and positive findings on RPL investigations. A polynomial regression model was constructed based on the relationships of these variables.

RESULTS: A total of 604 miscarriages were included in the study. There was a significant relationship between the odds of aneuploidy and both maternal age and gestational age. There was a linear relationship between aneuploidy and maternal age, with a nearly 2-fold increase in the odds of aneuploidy with every 5-year increase in maternal age (OR 1.83, 95% CI 1.40-1.83). In contrast, the association between aneuploidy and gestational age was curvilinear, with a peak probability of aneuploidy with pregnancy losses at approximately 8 weeks gestation (p<0.02). While women with positive findings on RPL investigations had a slightly lower odds of aneuploidy as compared to those with a normal work-up, this difference was minimal and did not reach statistical significance (p=0.18).

CONCLUSIONS: There is an overall high rate of aneuploidy among the RPL population, even in women with positive findings on traditional RPL investigations. Across all maternal ages, the odds of aneuploidy significantly drop in pregnancy losses over 12 weeks gestation. These findings suggest that genetic testing on POC should be offered at the time of second and subsequent pregnancy losses <12 weeks gestation to all RPL patients.

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OBJECTIVE: The use of PGT-A and vitrification to select euploid embryos for transfer has led to improved live birth success in IVF; however, some euploid embryos fail to progress following implantation. Our objective was to compare parameters from 1) the retrieval cycle (IVF) in which blastocysts were biopsied and vitrified, 2) the frozen embryo cycle (FET) during which the uterus is prepared for transfer, 3) the embryo transfer (FETt), and 4) the embryology (Lab) records all consolidated to determine what best predicts pregnancy loss following establishment of pregnancy by euploid embryos. DESIGN: Multivariate analysis of 45 parameters from IVF, FETt, FET, and Lab and their association with loss of pregnancies after a positive pregnancy test (+hCG).

MATERIALS AND METHODS: Data were collected from our electronic records for patients with transfers of thawed single euploid embryos diagnosed as euploid by NGS during the IVF cycle. Parameters from IVF (17), FETt (5), FET, and Lab (19) were considered. All cases of STEET using euploid embryos tested with Next Generation Sequencing (908) were considered for analysis. Transfers without +hCG (204) and clinical pregnancies without +hCG (204) at the time of pregnancy test (+hCG) were excluded. The 499 remaining cases with a positive pregnancy test (+hCG >5 mIU/mL) and all the required fields. 144 cases failed to progress (75 biochemical pregnancies and 69 SABs). Stepwise multiple logistic regression (152 combinations of parameters) was performed using the Akaike Information Criterion (AIC) to select parameters associated with loss of pregnancy precluding live birth following +hCG. +hCGs were considered implantations since 1) patients believe they are pregnant when they have a +hCG result and 2) no interfering hCG was administered to these patients.

RESULTS: Parameters associated with increased pregnancy loss after positive +hCG (in descending magnitude of standard partial regression coefficient) were: more expansion of the trophectoderm prior to biopsy (IVF); more serum estrogen on the day prior to progesterone administration (FETt); and more difficulty of the embryo transfer procedure (FETt). Age at retrieval, embryo grades, as well as many other parameters were not associated with pregnancy loss.

CONCLUSIONS: Parameters from 3 categories were associated with loss of pregnancy as biochemical pregnancies or spontaneous abortions. Of these, some are under our control: serum estradiol levels on the day prior to progesterone administration and possibly the difficulty of the transfer and the expansion of the blastocyst prior to biopsy. However, it is possible that these parameters may be associated with other features such as rate of blastocyst development, patient weight, and/or uterine contractions or presence of blood in the cervix or uterus. No Lab parameters were associated with pregnancy loss. Also notable was the lack of association between embryo grades and pregnancy loss.

SUPPORT: None.

References:

OBJECTIVE: Chronic Intervillositis of Unknown Etiology (CIUE) is a poorly understood idiopathic process that leads to massive infiltration of mononuclear cells into the intervillous space, leading to recurrent pregnancy loss (RPL) and adverse pregnancy outcomes, such as intrauterine growth restriction (IUGR) and intrauterine fetal demise (IUDFD). One study suggests that a higher degree of CIUE leads to worse outcomes than a lower degree of infiltration1, and studies are conflicting on whether empiric treatment improves pregnancy outcomes or not2,3. The aim of this study was to calculate the incidence of CIUE at our institution, the one and only referral center for RPL in British Columbia, Canada, and to evaluate the pregnancy outcomes based on severity of lesions as well as different empiric treatments.

DESIGN: Retrospective cohort.

MATERIALS AND METHODS: The pathology database was queried for the keywords “intervillositis” and “CIUE” between February 2006 and 2018. Cases with a diagnosis of acute intervillositis were excluded. The histology and medical records for the cases were reviewed and pathology was re-evaluated using the diagnostic criteria set forth by Bos et al4 to confirm diagnosis. Cases that met the Bos et al5 criteria were categorized as low grade (<50% of intervillus space involved) or high grade (>50% involvement) using a modified grading scheme based on grading proposed by Rota et al6. The study was approved by the Children’s & Women’s Health Centre of British Columbia Research Ethics Board (H18-03623).

RESULTS: A total of 84 patients were diagnosed with intervillositis in the 12-year study period. Only 78 of these, CIUE was confirmed in 46 patients (54.8%) using the Bos et al4 diagnostic criteria. A total of 95 specimens had previously been diagnosed with CIUE, of which 51 (53.7%) met diagnostic criteria on review. Total incidence was 0.17% (51 cases out of 29592 specimens), with a significantly higher incidence seen in 1st trimester products of conception compared with 2nd and 3rd trimester specimens (0.34% vs 0.09%; p < 0.0001). 8 specimens had an abnormal karyotype (15.7%). 20 specimens were low grade, 11 of which were in the context of a first trimester loss, and 11 were losses after 20 weeks gestation. 27 cases were high grade, of which 21 were in the context of a first trimester loss, and 6 were 2nd and 3rd trimester losses. 29 (56.9%) CIUE diagnoses were made in the context of RPL, of which 4 had abnormal karyotype and one case was associated with multiple fetal anomalies. Empiric treatment was administered in 10 patients, including acetylsalicylic acid (ASA), low molecular weight heparin (LMWH), and dexamethasone. In our experience, empiric treatment was too low to make any generalized conclusions regarding treatment.

CONCLUSIONS: This is the largest original case series on CIUE reported to date. Incidence rate was lower than quoted in other studies, which may be due to our rigorous diagnostic criteria. This remains an important diagnosis to make especially in the early pregnancy loss population where the incidence is highest. The number of patients receiving empiric treatment was too low to make any generalized conclusions regarding treatment.

IS ANTIMULLERIAN HORMONE PREDICTIVE OF OUTCOMES AFTER PGT-A IN PATIENTS WITH RECURRENT PREGNANCY LOSS? Gayathree Murugappan, MD,a Lora K. Shashine, MD,a Ruth B. Lathi, MD,b 1Stanford University Medical Center, Sunnyvale, CA;2Pacific Northwest Fertility and IVF Specialists, Seattle, WA;3Stanford University Medical Center, SUNNYVALE, CA.

OBJECTIVE: Serum biomarkers of ovarian reserve have been utilized in non-RPL cohorts to stratify patients who may benefit from PGT-A. The goal of this study was to determine if AMH levels are predictive of outcomes in RPL patients pursuing PGT-A.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Unexplained RPL patients undergoing PGT-A at two fertility centers from 2009-2018 were included. All patients with the intent to perform PGT-A (propheticderm biopsy and 24 chromosome screening) were included regardless of final cycle outcome. Pregnancy loss was defined as loss of pregnancy from conception (bHCG level >5mIU/mL) through twenty weeks gestation.

RESULTS: 157 patients underwent 191 retrievals (RET), 146 of which completed PGT-A. Patient demographics and outcomes stratified by AMH <1 ng/mL and AMH ≥ 1 ng/mL are shown in Table 1. Patients with AMH <1 ng/mL were significantly older with similar BMI and number of prior losses compared to patients with AMH ≥ 1 ng/mL. Patients with AMH <1 ng/mL had fewer oocytes (p<0.01) and a higher average aneuploidy rate (p=0.02) compared to patients with AMH ≥ 1 ng/mL. In a regression model adjusting for age, AMH is not a significant predictor of having at least one euploid blastocyst (p=0.10, CI 0.97-1.43), reaching ET (p=0.07, CI 0.84-1.18), achieving pregnancy (p=0.42, CI 0.82-1.09), achieving live birth (p=0.12, CI 0.86-1.02) or undergoing pregnancy loss (p=0.42, CI 0.90-28).

CONCLUSIONS: Although ovarian reserve is associated with IVF success rates, we report that RPL patients with diminished ovarian reserve (DOR) have similar likelihood of achieving pregnancy and live birth with PGT-A compared to RPL patients with AMH > 1 ng/mL. Future studies should incorporate total cycle potential in evaluation of clinical outcomes and consider a lower AMH cutoff for evaluating DOR.

Reference: None.

SUPPORT: None.

<table>
<thead>
<tr>
<th>AMH &lt;1 ng/mL n=42 RET</th>
<th>AMH ≥ 1 ng/mL n=149 RET</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yrs (mean ± SD, range)</td>
<td>37.6±4.2 (28-44)</td>
<td>36.2±3.6 (29-43)</td>
</tr>
<tr>
<td>No. of prior losses (mean ± SD, range)</td>
<td>3.1±1.2 (2-6)</td>
<td>3.1±1.0 (2-7)</td>
</tr>
<tr>
<td>BMI, kg/m² (mean ± SD, range)</td>
<td>24.1±3.6 (18-31)</td>
<td>23.2±3.5 (17-39)</td>
</tr>
<tr>
<td>No. of oocytes (mean ± SD, range)</td>
<td>11.1±9.2 (1-41)</td>
<td>18.8±8.5 (4-43)</td>
</tr>
<tr>
<td>% of cycles reaching euploid ET (%), n</td>
<td>48% (n=20/42)</td>
<td>59% (n=88/149)</td>
</tr>
<tr>
<td>% of cycles transferring untested embryos (%), n</td>
<td>21% (n=9/42)</td>
<td>13% (n=20/149)</td>
</tr>
<tr>
<td>% of cycles not reaching ET (%), n</td>
<td>31% (n=13/42)</td>
<td>28% (n=41/149)</td>
</tr>
<tr>
<td>PR per RET (%), n</td>
<td>40% (n=17/42)</td>
<td>49% (n=73/149)</td>
</tr>
<tr>
<td>Avg. aneuploidy rate (mean ± SD)</td>
<td>69% ± 84%</td>
<td>53% ± 28%</td>
</tr>
<tr>
<td>PR per PGT-A cycle (%), n</td>
<td>52% (n=14/27)</td>
<td>50% (n=60/119)</td>
</tr>
<tr>
<td>PR per euploid ET (%), n</td>
<td>70% (n=14/20)</td>
<td>68% (n=60/88)</td>
</tr>
<tr>
<td>Pregnancy loss rate per pregnancy (%), n</td>
<td>35% (n=6/17)</td>
<td>30% (n=22/73)</td>
</tr>
<tr>
<td>LBR per RET (%), n</td>
<td>26% (n=11/42)</td>
<td>34% (n=51/149)</td>
</tr>
</tbody>
</table>

1Student’s T Test, 2-tailed, unpaired.

2Chi-squared analysis.

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MANAGEMENT OF EARLY PREGNANCY LOSS WITH MIFEPRISTONE AND MISOPROSTOL: CLINICAL PREDICTORS OF SUCCESS FROM A RANDOMIZED TRIAL. Sarita Sonalkar, MD MPH,a Nathanan C. Koelper, MPH,a Mitchell D. Creinin, MD,a Jessica M. Atrio, MD, MSC,b Mary D. Sammel, ScD,c Courtney A. Schreiber, MD, MPH,a 1University of Pennsylvania, Philadelphia, PA;2University of California - Davis, Sacramento, CA;3Montefiore Hospital & Albert Einstein College of Medicine, Bronx, NY.

OBJECTIVE: To evaluate characteristics associated with treatment success in women receiving medical management for early pregnancy loss (EPL).

DESIGN: We performed a secondary analysis of a randomized trial of 300 participants comparing mifepristone-misoprostol to misoprostol alone for EPL treatment.

MATERIALS AND METHODS: We tested the ability of characteristics associated with misoprostol success in a previous study, vaginal bleeding and parity of 0 or 1, to discriminate successful from failed treatment in each arm of our study population and in the combined cohort using receiver-operating characteristic curves. We calculated the area under the curve (AUC) to quantify the ability of the score to discriminate between treatment success or failure in each arm as well as in the entire cohort. Using multivariable logistic regression, we then assessed our study population for other predictors of treatment success in both treatment groups, with and without mifepristone.

RESULTS: The clinical characteristics of vaginal bleeding and parity of 0 or 1 did not predict success above chance alone in the misoprostol-alone arm (AUC=0.55, 95% CI 0.44-0.65), the mifepristone pretreatment arm (AUC=0.59, 95% CI 0.45-0.72) or the combined cohort (AUC=0.56, 95% CI 0.48-0.64). No other baseline clinical factors predicted treatment success in the misoprostol-alone or mifepristone pretreatment arms individually. In the full cohort, randomization to pretreatment with mifepristone was a positive predictor of treatment success (aOR 2.51, 95% CI 1.43-4.43), while smoking was a negative predictor (aOR 0.47, 95% CI 0.23-0.97).

CONCLUSIONS: Pretreatment with mifepristone is a more useful intervention than applying baseline clinical factors to maximize treatment success in women undergoing medical management of EPL with misoprostol.


SUPPORT: Supported by the National Institute of Child Health and Human Development of the National Institutes of Health (Eunice Kennedy Shriver award number R01-HD0719-20 [to Dr. Schreiber] and Women’s Reproductive Health Research award number K12-HD001265-18 [to Dr. Sonalakar]), and a Society of Family Planning Research Fund Midcareer Mentor Award (Schreiber).
DESIGN: RPL-serine protease A was investigated to identify its putative substrates using proteomics and bioinformatics tools. XIAP was identified to interact with the RPL-serine protease A. XIAP was differentially expressed in a dose-dependent manner of RPL-serine protease A. To check the effect of RPL-serine protease A on cell proliferation and cell invasion, RPL-serine protease A and its mutant form were transfection into BeWo cells, and knock-out BeWo cell line was established.

MATERIALS AND METHODS: Immunoprecipitation: Flag-RPL-serine protease A and myc-XIAP were transfected into 293T cells for performing immunoprecipitation. GST pull-down assay: Recombinant GST and GST-RPL-serine protease A proteins were incubated in cell lysates overexpressed with Myc-XIAP. The bound proteins were analyzed with an anti-Myc antibody. Cell Counting Kit (CCK-8): CCK-8 assay was performed to investigate effect of RPL-serine protease A on cell proliferation. Invasion assay: Overexpression RPL-serine protease A and its mutant form, and knock-out of RPL-serine protease A BeWo cells were divided into trans-well with the same numbers of cells to check the effect of RPL-serine protease A on cell invasion. To study the functions of RPL-serine protease A, CRISP-Cas9 system was applied for making the knock-out of RPL-serine protease A in reproductive cell lines.

RESULTS: In a previous study, we identified that an RPL-serine protease A gene is more expressed in chorionic villi from normal controls than in those from RPL patients. In this study, XIAP selected from candidate proteins identified from proteomics and bioinformatics tools, interacted with the RPL-serine protease A. Immunoprecipitation assay revealed that putative substrates such as XIAP and CPBP interacted with the RPL-serine protease A. Further investigation with GST pull-down assay indicates that RPL-serine protease A directly binds to XIAP. Exogenous and endogenous expression levels of XIAP were decreased by the RPL-serine protease A in a dose-dependent manner. It is of interest that RPL-serine protease A suppresses cell proliferation in vitro, and the proliferation rate of RPL-serine protease A knock-out cells was significantly higher than that of wild type cells. Over-expressed RPL-serine protease A stimulates BeWo cell invasion.

CONCLUSIONS: RPL-serine protease A interacts with XIAP, and expression of XIAP was decreased by RPL-serine protease A. Through these mechanisms, trophoblast apoptosis and proliferation may be regulated in placenta. The molecular functions of RPL-serine protease A in promoting cell proliferation needs to be investigated.

SUPPORT: This study was supported by the Ministry of Health & Welfare of the Republic of A Korea (grant numbers, H116C0378) through the Korea Health Industry Development Institute.

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ANTIMULLERIAN HORMONE (AMH) AND SPONTANEOUS ABORTION (SAB): IS AMH AN INDEPENDENT RISK FACTOR FOR SAB IN GONADOTROPIN-IUI CYCLES? Jennifer Y. Hsu, MD, a Kaitlyn E. James, PhD, a Irene Dimitriadis, MD, a Georgios Christou, MD, a Stylianos Vagios, MD, a Charles L. Bormann, PhD, a Irene Souter, MD, a Massachusetts General Hospital, Boston, MA; Albert Einstein College of Medicine, Bronx, NY.

OBJECTIVE: Emerging studies suggest that in infertile women undergoing IVF, AMH levels are associated with adverse obstetric outcomes, though the data remain inconclusive [1, 2]. Our objective was to evaluate if AMH is independently associated with risk of SAB among women undergoing gonadotropin-intrauterine insemination (Gn-IUI) cycles.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Intervention: 1861 Gn-IUI cycles from 821 women were analyzed (11/2007 to 3/2019). Cycles were stratified by the following AMH (ng/ml) serum concentration cutoffs, based on previously published literature [3]: LOW (<0.7), NORMAL (0.7-8.4), and HIGH (≥8.5). Outcome measures: Rate of SAB, defined as pregnancy loss following sonographic confirmation of clinical pregnancy, within each AMH group. Statistics: Fischer’s exact or x2 tests were used as appropriate. Multilevel mixed-effects Poisson regression models, adjusted for age, were used to determine the incidence risk ratios (IRR) for SAB within each AMH group. P-value <0.05 was considered significant.

RESULTS: The mean (SD) age of the study population was 35.4 (4.0) years with mean body mass index (BMI): 25.1 (5.2) kg/m2. The median (IQR) AMH value was 1.9 ng/ml (0.7, 4.5) with 24%, 64%, and 12% of the women categorized into the LOW, NORMAL, and HIGH AMH groups, respectively. Clinical pregnancy rates per cycle were: 8.2% 12.4%, and 19.0% for LOW, NORMAL, and HIGH AMH groups, respectively (p<0.001). The overall SAB rate was 18.1%. Women in the NORMAL and HIGH AMH groups had lower incidence of SAB (15.6% and 16.3%, respectively) compared to those in the LOW AMH group (29.7%). However, after adjusting for age, the risk difference was no longer statistically significant.

Table 1 summarizes the adjusted and unadjusted IRR for SAB utilizing the NORMAL group as a reference. After adjusting for age, AMH was not associated with risk of SAB. There was also a trend toward higher SAB risk in women with AMH below the 10th percentile (AMH ≤0.4), a finding that lost its significance in the adjusted models.

CONCLUSIONS: In women pursuing Gn-IUI treatment, lower AMH does not appear to be an independent risk factor for SAB. Therefore, younger women with lower ovarian reserve should not be counseled that they are at risk of worse early pregnancy outcomes compared to their age-matched counterparts with normal or high ovarian reserve.


SUPPORT: None.

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CHARACTERISTICS OF FIRST TRIMESTER MISCARRIAGES ASSESSED BY CHROMOSOMAL ANALYSIS OF PRODUCTS OF CONCEPTION WITH NEXT GENERATION SEQUENCING. Takumi Takeuchi, MD, PhD, a Masakazu Doshida, MD, a Yukiko Takaya, MD, b Kohei Yamaguchi, MD, b Hidetoshi Matsubayashi, MD, a Kotaro Kitaya, MD, a Yasuhisa Araki, PhD, b Tomomoto Ishikawa, MD, b Reproduction Clinic Tokyo, Tokyo, Japan; b Reproduction Clinic Osaka, Osaka, Japan; b Nippon Reprogenetics Inc, Maebashi, Japan.

OBJECTIVE: Chromosomal abnormalities are the major cause of early pregnancy loss. Chromosome testing of products of conception (POC) provides valuable information for counseling and clinical managing of patients. We previously showed that next generation sequencing (NGS) can be utilized as a technique demanding lesser specimen with a lower failure rate, higher resolution, and shorter turnaround time than conventional karyotyping which is requiring labor-intensive and time-consuming cell culture with possible maternal cell contamination. We aimed to assess the efficacy of NGS method for chromosomal analysis of POC. In addition, we attempted to identify any associations between the incidence of chromosomal abnormalities and the profile of patients as well as fetal development in an assisted reproductive technology (ART) program.

DESIGN: Retrospective study with a single reference genetic laboratory.

MATERIALS AND METHODS: Total of 131 consenting patients with first trimester miscarriages after vitrified-warmed embryo transfer were involved. POC samples were obtained bdylation and curettage between 7 to 10 gestational weeks. Chorionic villi were isolated under a dissecting microscopy, subsequently processed for NGS chromosomal analysis. Incidence of each chromosomal abnormality was reported and evaluated according to the patient profile, such as maternal age, previous history of miscarriage and fetal development. Finally, frequency of mosaics was also assessed.

TABLE 1. RISK OF SAB STRATIFIED BY AMH LEVEL

<table>
<thead>
<tr>
<th>AMH GROUP</th>
<th>UNADJUSTED IRR (95%CI)</th>
<th>ADJUSTED IRR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>1.9 (1.0, 3.6)*</td>
<td>1.6 (0.8, 3.1)</td>
</tr>
<tr>
<td>Normal</td>
<td>1.0 (0.5, 2.2)</td>
<td>1.3 (0.6, 2.8)</td>
</tr>
<tr>
<td>High</td>
<td></td>
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</tr>
</tbody>
</table>

<P>0.05

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RESULTS: After NGS analysis, 28 cases (21.4%) were found to be normal, and the remaining 103 (78.6%) were abnormal, including 10 (7.6%) mosaics. Among normal karyotypes, ratio of female to male was 1.15 (15/13). Trisomies were the most common abnormalities except for the chromosome X monosomy (10.7%). Aneuploidy of chromosome 22 (20/113, 17.7%), 15 (16/113, 14.2%), 16 (16/113, 14.2%), X (13/113, 11.5%) and 21 (21/113, 19.7%) including overlaps, were most frequently involved. Mean maternal age of chromosomally normal cases was significantly higher than that of normal karyotypes (39.0 ± 18.5 vs 36.9 ± 16.5 years, P < 0.05). Patients with more than equal 3 previous miscarriages showed a significantly lower rate of abnormalities than those with <3 miscarriages (28.6% vs 81.5%, P < 0.01). Rate of abnormalities with positive fetal cardiac activity was not different from that of anembryonic pregnancies (80.0% vs 76.1%), although fetal cardiac activity was detected in all the 45 XO cases. Interestingly, however, mosaic abnormalities were significantly more often detected in anembryonic pregnancies than the other (15.2% vs 3.5%, P < 0.05).

CONCLUSIONS: With more conclusive and accurate results and higher resolution by NGS, we were able to characterize early pregnancy loss after ART, demonstrating relatively high rate of abnormalities with gender ratio being close to 1. Patients with repeated pregnancy loss showed lower chromosomal abnormalities indicating other causes for miscarriages in this group of patients. A higher incidence of mosaics detected in anembryonic pregnancies warrants further investigation. SUPPORT: None.

P-754 Wednesday, October 16, 2019 6:30 AM
VITAMIN D INSUFFICIENCY IS THE RISK FACTOR FOR HYPERHOMOCYSTEINEMIA DERIVED FROM MTHFR C677T GENE POLYMORPHISM IN WOMEN WITH RECURRENT PREGNANCY LOSSES. Kuniaki Ota, M.D., a Toshifumi Takahashi, M.D., b Joanne Kwak-Kim, MD, MPH. c Fukushima Medical University, Fukushima, Japan; dChicago Medical School, Rosalind Franklin University of Medicine and Science, North Chicago, IL, Vernon Hills, IL.

OBJECTIVE: Vitamin D insufficiency, methylenetetrahydrofolate reductase (MTHFR) C677T gene polymorphism, and hyperhomocysteinemia have been reported as risk factors for recurrent pregnancy losses (RPL). However, the relationship among vitamin D, homocysteine, and MTHFR C677T gene polymorphism in women with RPL remain unknown. In the current study, we aim to investigate whether the MTHFR gene polymorphism affects the levels of homocysteine and 25 (OH) vitamin D as well as immune-parameters in women with RPL.

DESIGN: This study was a cross-sectional study of 837 women with RPL at a university hospital.

MATERIALS AND METHODS: Total 837 women with unexplained RPL were registered, and MTHFR C677T genotypes (homozygous (TT), heterozygous (CT) and wild (CC)) were investigated by PCR. Biochemical tests were used to determine plasma homocysteine and serum 25 (OH) vitamin D levels, and natural killer (NK) cell cytotoxicity was analyzed by the flow cytometry. Data were analyzed by MTHFR C677T genotypes.

RESULTS: The level of 25 (OH) vitamin D in the TT group was significantly lower compared to CT and CC groups (p < 0.05), while the level of homocysteine in the TT group was significantly higher than the CT and CC groups (p < 0.01). NK cytotoxicities of TT group was significantly higher than those of CC but not CT group (p < 0.01). There was a significant negative correlation between the levels of 25 (OH) vitamin D and homocysteine in the TT group (r=-0.257). In multivariate analysis, 25 (OH) vitamin D insufficiency (<30 ng/ml) was an independent risk factor for hyperhomocysteinemia (adjusted odds ratio 1.89, 95% CI 1.41-2.52).

CONCLUSIONS: Both MTHFR C677T gene polymorphism and vitamin D insufficiency may involve in the pathogenesis of unexplained RPL via hyperhomocysteinemia. It is speculated that lowering the homocysteine level may improve the reproductive outcome in women with RPL.

PROFESSIONAL DEVELOPMENT

P-755 Wednesday, October 16, 2019 6:30 AM
SURGICAL SIMULATION SUPPLEMENTS REI FELLOWSHIP TRAINING. Tess E. Chase, MD.a Stephanie J. Estes, MD.a Divya Kelath Shah, MD, MME,a Preston Parry, MD,a Balasubramanian Bhagavath, M.B.B.S.,a Steven R. Lindheim, MD.a John C. Petrozza, M.D.,a Samantha Pfeifer, M.D.b ePenn State Milton S Hershey Medical Center, Hershey, PA; fUniversity of Pennsylvania, Philadelphia, PA; gParity Fertility, Madison, MS, MS; hUniversity of Rochester Medical Center, Rochester, NY; iWright State University, Dayton, OH; jMassachusetts General Hospital Fertility Center, Boston, MA; kWeill Medical College of Cornell University, New York, NY.

OBJECTIVE: To characterize interest and skill in minimally invasive reproductive surgery among Reproductive Endocrinology and Infertility (REI) fellows and the utility of an intensive “boot camp” in improving performance of select surgical tasks.

DESIGN: Prospective evaluation of 40 REI fellows during the 2-day 2019 SRS-SREI boot camp.

MATERIALS AND METHODS: Surveys collected data on fellow demographics, prior surgical and IVF experience, and perceived competency with reproductive surgery. Surveys were administered before, immediately after, and 1 month after the boot camp. Simulations focused on laparoscopic suturing/knot tying using both box trainers and cadavers, robotic suturing, and operative hysteroscopy. Wilcoxon signed-rank tests and rank-sum tests were used to compare suturing times for a given fellow over time and changes in suturing time across fellows by year of training, respectively. Spearman correlation coefficients assessed associations between prior clinical experience and surgical skill.

RESULTS: Forty fellows (25 first, 11 second, and 4 third year) provided data, representing 72% of REI fellowship programs in the USA. Fellows reported an average of 15 hours of prior simulation experience for conventional laparoscopy, 8 hours for robotics and 5 hours for hysteroscopy. Prior to the boot camp, most fellows felt prepared to perform hysteroscopy (100%) and conventional laparoscopy (82%), but only a minority felt prepared to perform robotic surgery (46%) or tubal anastomosis (15%). Significant improvement was seen across all levels of training in laparoscopic suturing (boot camp trainers): by 44 seconds (seconds for running suture, 82 sec for intracorporeal knots, and 71 sec for extracorporeal knots (<p <.0001 for all comparisons). The magnitude of improvement was significantly higher for first year fellows as compared to their second and third year peers (60 sec vs 28 sec running suture improvement, p<.04). There were no strong associations observed between fellowship IVF case volume and the surgical skill of the fellow (all Spearman correlation coefficients <0.34). Interest in incorporating reproductive surgery into subsequent clinical practice was high when assessed immediately after the boot camp using a 5-point Likert scale and did not change when reassessed one month later (all p>0.36).

CONCLUSIONS: Given the heterogenous training in reproductive surgery among REI fellowship programs, a surgical boot camp may be useful in enhancing surgical skill among REI fellows. Improvements in laparoscopic suturing were most significant for first year fellows. Increasing IVF volume was not associated with less surgical skill.

P-756 Wednesday, October 16, 2019 6:30 AM
CLINICAL EXPOSURE IN OB/GYN RESIDENT TRAINING PROGRAMS IN THE UNITED STATES TO INFERTILITY CARE FOR LOW RESOURCE AND UNDERSERVED COMMUNITIES. Holly Mehr, MD MSEd.a Tia Jackson-Bey, MD MPH.a Jacqueline Ho, MD MS.c Lusine Aghajanova, MD PhD,c Molly M. Quinn, MD.a Jacquelyn Rose Hoffman, BA.e Christopher N. Herndon, MD.f aUniversity of California, Los Angeles, CA; bUniversity of Illinois at Chicago, College of Medicine, Chicago, IL; cUniversity of Southern California, Los Angeles, CA; dStanford University School of Medicine, Stanford, CA; eUniversity of Arizona College of Medicine - Tucson, Tucson, AZ; fUniversity of Washington, Seattle, WA.

OBJECTIVE: Assess exposure of US OB/GYN residents to the provision of clinical infertility care for low resource and underserved communities. DESIGN: Cross-sectional survey.

MATERIALS AND METHODS: An anonymous, self-administered 28 question survey was emailed to REI division directors or REI resident rotation directors affiliated with ACOG accredited OB/GYN residency programs. Respondents answered questions regarding REI practice and residency demographics, the presence of clinical programs designed to improve access to care, resident involvement in such programs, and perceived barriers to expanding access to care.Responses were analyzed descriptively and through logistic regression analysis using STATA software, with significance defined as p <0.05.

RESULTS: The response rate for the survey was 30% (80/270). Of respondents, average OB/GYN residency size was 6.1 graduating residents per year.
Residents spent an average of 7.2 weeks rotating through REI during a 4-year residency. 38% (n = 30) of practices had an affiliated REI fellowship. Less than half of OB/GYN residency programs (39%, n = 31) responded have an associated REI clinic in which OB/GYN residents provide direct infertility care to patients. Low resource populations in the United States for Obstetrics and Gynecology (Ob/Gyn), Internal Medicine, Emergency Medicine, Family Medicine, General Surgery, Pediatrics, and Psychiatry. They were asked to forward the survey link to their respective respondents. The survey consisted of three sections: 1) fertility knowledge, 2) oocyte cryopreservation knowledge, and 3) attitudes toward family building and fertility preservation. Outcomes were compared between Ob/Gyn residents and all other specialties, both combined and separately. Wilcoxon rank sum test or Chi-square test was used to compare variables, as appropriate. Multivariable logistic regression models were used to investigate the association between the number of correct answers and specialties with and without adjustment for age, gender, race/ethnicity, FGy year, marital status, preexisting children, and history of infertility.

RESULTS: Of the 2,828 completed surveys, 450 (15.9%) were by Ob/Gyn residents and 2,378 (84.1%) were by residents of other specialties. The median number of correct answers was 2 out of 5 on the fertility knowledge section and 1 out of 3 on the oocyte cryopreservation knowledge section among all survey participants. The adjusted and unadjusted models showed that specialties were not significantly associated with answering these questions correctly in either section. However, the majority of residents who had a child during residency or planned to have a child during residency was similar between Ob/Gyn and all other specialties, 33.9% vs. 35.5%, respectively, P = .50. Ob/Gyn residents were significantly more likely than residents of other specialties to feel “somewhat supported” or “very supported” by their program to pursue family building goals (83.5% vs. 75.8%, P = .0005).

CONCLUSIONS: Resident physicians have limited knowledge of natural fertility decline and the opportunity to cryopreserve oocytes. Knowledge of these topics is similar between Ob/Gyn residents and residents of other specialties. These data suggest a need for improved fertility education, particularly within Ob/Gyn residency programs. The majority of residents do feel supported to build their families during training, particularly Ob/Gyn residents. References: 1. Daniuk JC, Koert E. Childless women’s beliefs and knowledge about oocyte freezing for social and medical reasons. Hum Reprod. 2016;31(1):2313-2320.


P-759 Wednesday, October 16, 2019 6:30 AM
THE EFFECT OF RESIDENT PHYSICIAN INVOLVEMENT ON SURGICAL OUTCOMES AND COMPLICATIONS OF FERTILITY SURGICAL. Wesley Yip, MD; Sarah C. Yi, MD; Jinbo Li, PhD; Lauren Beeder, BS; Mary Katherine Sampslaski, MD. 1University of Southern California, Los Angeles, CA; 2Cleveland Clinic Foundation, Cleveland, OH; 3Keck School of Medicine, University of Southern California, Los Angeles, CA.
OBJECTIVE: We sought to determine the effect of resident physician involvement in fertility surgical procedures on patient surgical outcomes and complications.
DESIGN: A review of fertility-specific surgical procedures in the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) database was performed, followed by statistical analyses.
MATERIALS AND METHODS: The NSQIP database was reviewed for fertility surgical procedures from 2006 to 2012. The procedures included were: epididymectomy, spermatocelectomy, varicocelectomy +/- hernia repair, ejaculatory duct resection, vasovasostomy, vasoepididymostomy, and unilateral procedure male genital system (to capture sperm retrieval procedures).
Patient factors analyzed were: patient age, race, body mass index (BMI), morbidity probability, mortality probability, American Society of Anesthesiologists physical status classification (ASA), smoker status, alcohol usage status, history of diabetes, chronic obstructive pulmonary disease, congestive heart failure, peripheral vascular disease, cerebrovascular accident, and/or steroid usage. Outcomes examined included operative time, length of hospital stay, superficial infection, deep wound infection, wound dehiscence, urinary tract infection (UTI), and reoperation rate. Resident and non-resident groups were compared by Wilcoxon rank sum tests, followed by logistic regression, univariate, and multivariate analyses.
RESULTS: Of 924 cases were included: 309 with residents, and 615 without residents. The median post-graduate resident year was 3 (range: 0-10). There was no difference in baseline demographics between groups. On univariate analysis, mean operative time was longer with resident involvement, even after controlling for other covariates (76.2 vs 49.5 minutes, p = 0.00). Length of hospital stay was also longer in cases with resident involvement (0.41 vs 0.35 days, p = 0.02). There was no difference in superficial infections (p = 0.57) or UTIs (p = 1.00) with or without resident involvement.
CONCLUSIONS: While resident physician involvement in fertility surgical procedures may lengthen operative time, there were no significant differences in length of hospital stay, superficial infections, deep wound infections, wound dehiscence, UTIs, and reoperation rates. This data is reassuring for attending physicians operating with residents.

P-760 Wednesday, October 16, 2019 6:30 AM
INFERTILITY, FERTILITY PRESERVATION, AND ACCESS TO CARE DURING TRAINING: A NATIONAL-WIDE MULTI-SPECIALTY SURVEY OF UNITED STATES RESIDENTS AND FELLOWS. Ange Wang, MD; Christopher N. Herndon, MD; Evelyn Mok-Lin, MD; Lusine Aghajanova, MD PhD. 1Stanford University School of Medicine, Stanford, CA; 2University of Washington, Seattle, WA; 3REI UCSF, Center for Reproductive Health, San Francisco, CA.
OBJECTIVE: To investigate the prevalence of and experience related to infertility and utilization of fertility preservation during training for United States (US) medical residents and fellows.
DESIGN: Cross-sectional survey study.
MATERIALS AND METHODS: An online-based survey distributed to US postgraduate residents and fellows across medical specialties, via program directors and graduate medical offices of residency/fellowship programs.
RESULTS: Respondents included 732 residents and fellows, with the highest percentage in Obstetrics & Gynecology (26.0%), Pediatrics (14.1%), and Internal Medicine (13.9%). 75.5% of respondents were residents and 73.2% were PGY1-4. Respondents were 75.4% female and 18.4% male, with the most common ethnicities Caucasian (61.2%) and Asian/Pacific Islander (10.4%). 75.8% of respondents reported being married or partnered. In total, over half of respondents (56.6%) reported delaying childbearing plans due to medical training. 51 respondents (7.0%) reported infertility, while 11 (1.5%) reported recurrent pregnancy loss (RPL). For the infertility/RPL group, 19 respondents reported undergoing IVF. 11 reported undergoing IUI, and 14 reported using oral medications for fertility purposes. For the fertility preservation group, 18 respondents reported undergoing IVF for embryo or oocyte cryopreservation. Additionally, 208 respondents (28.4%) reported that they had considered oocyte or embryo cryopreservation, though only 46 respondents underwent a fertility consultation for this purpose. Of those seeking treatment, respondents most commonly reported their own insurance or partner’s insurance as the source of financial support, in addition to salary and parents/friends. Only 13.1% reported living in a state where fertility coverage is mandated by insurance. Respondents reported lack of time/flexibility (35.4%) and financial concerns (29.4%) as the top reasons for being unable to pursue either fertility consultation or treatment. The majority of respondents (65.5%) experiencing infertility/RPL or desire for fertility preservation reported that colleagues and program administration were unaware of treatments or struggles. However, of those whose challenges were known, the majority felt some degree of support by their program administrators (80.8%) and colleagues (84.4%).
CONCLUSIONS: The majority of residents and fellows delay childbearing due to medical training. The reported infertility rate in postgraduate medical trainees is comparable to general population, though may be under-estimated as individuals may further delay childbearing until established in practice. Time/flexibility and financial concerns were identified by residents and fellows as the greatest barriers to seeking and pursuing medical assistance with fertility training. Most trainees facing fertility-related challenges do not share their concerns with program administrators or colleagues, but most who did so felt supported. Specific measures and awareness are needed in order to increase access to fertility services for US medical trainees.

P-761 Wednesday, October 16, 2019 6:30 AM
UTILIZING A NOVEL RESIDENT EDUCATION INITIATIVE TO PROVIDE REPRODUCTIVE ENDOCRINOLOGY AND INFERTILITY CARE FOR UNDERINSURED WOMEN. Elizabeth S. Rubin, MD; Ana Chemerinski, MD; Samantha Butts, MD; Catherine R. Salva, MD. University of Pennsylvania, Philadelphia, PA.
OBJECTIVE: Few reports exist in the literature describing infertility evaluations or care in patients covered by Medicaid, but disparities in access are well documented. The objective of this study was to describe the health care received by a cohort of underinsured women with infertility after implementation of a novel quality improvement project designed to increase access to reproductive endocrinology and infertility (REI) specialists.
DESIGN: Retrospective observational study.
MATERIALS AND METHODS: We created a system for provision of infertility consultations from the REI division at an academic tertiary care institution. The Obstetrics and Gynecology (Ob/Gyn) resident clinic at our institution provides care for primarily African American and economically disadvantaged women. Patients are screened in by Ob/Gyn residents staffing routine gyn clinic when a patient presents with infertility. As part of their REI curriculum, Ob/Gyn residents reviewed patient charts in virtual visits under supervision of REI faculty. Patients were then provided diagnostic guidance, management recommendations and access to cost-saving research programs. Patients receive their individualized recommendations and associated costs to make informed healthcare decisions. Patient charts are maintained on a shared electronic medical record list for ongoing management. Charts from the first year of the service were reviewed for demographic and clinical information. This project was reviewed by the University of Pennsylvania Institutional Review Board and determined to be exempt as a Quality Improvement project.
RESULTS: Twenty-eight consultations were performed for underinsured women in the first year of service. Of these patients, 22 patients (78%) had Medicaid insurance. Two patients (7%) were seen in the REI office after initial consultation. Nine (22%) completed bloodwork and 10 patients (35%) underwent pelvic ultrasounds. Six evaluations of fallopian tube patency were completed via either imaging (hysterosalpingogram) or surgery (chromotubulation). Eight patients (28%) initiated ovulation induction. Five patients (17%) achieved pregnancy. Pelvic ultrasounds and blood work were fully covered by all insurance.
CONCLUSIONS: Though our resident clinic remains unable to provide standard infertility treatments like IUI and IVF to our Medicaid patients, patients were still take advantage of the robust REI division at our institution. Academic institutions may be able to connect uninsured and underinsured
patients with advice and diagnostics by utilizing resident educational opportunities to offset a portion of financial barriers.

P-762 Wednesday, October 16, 2019 9:30 AM
DOES LONGER EDUCATION MEAN POSTPONED PREGNANCY? Ecem Esercan, M.D.1, Burcin Simsek, Ph.D.1, Emre Selil, M.D.1 1Yale School of Medicine, New Haven, CT; 2University of Pittsburgh, Pittsburgh, PA.

OBJECTIVE: To delineate the continually increasing participation of women in education at bachelor’s, master’s, and doctoral degree levels and how it correlates with changes in age of marriage, pregnancy rate after age 35, and rates of diminished ovarian reserve (DOR) diagnosis and use of donor eggs, over time in the United States (US).

DESIGN: Population-based epidemiologic study.

MATERIALS AND METHODS: Education data (between 1970-2018) were collected from records and projections reported by National Center for Education Statistics, Institute of Education Sciences, and US Department of Education. Results on percent married and age at first marriage were gathered from Current Population Survey of US Census Bureau. Data on mean age of mother, mean age of mother at first birth, pregnancy and birth rates were gathered from annual National Vital Statistics Reports of Center for Disease Control and Prevention (CDC). Information on rates of DOR diagnosis and donor oocyte use among assisted reproduction technology (ART) cycles were collected from annual National Summary Reports on ART of CDC.

RESULTS: In 2018, prospected proportion women earning bachelor’s degrees (per 10,000 female citizens) almost doubled compared to 1970 (64.8 vs 32.6; p < .001). In the same time period, percentage of bachelor’s degrees awarded to females in a given year, increased significantly (57.5 vs 43.1; p < .001), surpassing males. Moreover, percentage of total US female population who completed four years of college raised significantly between 1970 to 2018 (8.2 to 35). This trend was followed in postgraduate education, with significant increase in the proportion of women earning master’s (27.3/10,000 vs 7.9/10,000; p < .001) and doctoral degrees (5.7/10,000 vs 0.54/10,000; p < .001) in 2018 compared to 1970. The percentages of master’s (from 38.8 to 61.0; p < .001) and doctoral degrees (from 9.6 to 52.7; p < .001) awarded to females also increased in the study period, both surpassing males. In the same time period the percentage of married women and median age at first marriage demonstrated an opposite trend. Less women were married (50.8% vs 61.9%) and marriages occurred at a more advanced age (27.8 vs 20.8). In parallel with this finding, an increase in mean age at first birth from 21.4 to 26.8 was observed between 1970 and 2017. Similarly, pregnancy rates of women in ages 35-39 and 40-44 more than doubled between 1980 and 2010 (0.036 to 0.077 and 0.009 to 0.019/1,000 respectively).

The rise in birth rates of 1st child in those age brackets was even more dramatic (0.002 to 0.01 and 0.0003 to 0.002/1,000 respectively). In parallel, rate of DOR diagnosis in women undergoing ART raised significantly from 12% to 31% in 2005 to 2016, and number of ART cycles using donor eggs increased from 16,161 to 24,300 in the same time period.

CONCLUSIONS: Since 1970, participation of women in education in the US has risen significantly. This trend is paralleled by decreased rates and later occurrence of marriage as well as increasing age for childbearing, which in turn are reflected in the dramatic increase in DOR diagnosis and utilization of donor eggs in ART.

P-763 Wednesday, October 16, 2019 6:30 AM
MEDICAL STUDENTS’ KNOWLEDGE ABOUT THIRD-PARTY REPRODUCTION. Kajal Khodamoradi, phd student,1 Fardin Amidi, phd,2 Zahra Khorasvazadeh, phd student,1 Ali Talebi, phd,2 Zahra Rashidi, phd student,1 Mohammad Hossein Ayati, MD, PhD,1 Parva Namiranian, MD.1 1School of Medicine, Tehran University of Medical Sciences, Tehran, Iran, miami, FL; 2School of Medicine, Tehran University of Medical Sciences, Tehran, Iran, Tehran, FL, Iran (Islamic Republic of); 3School of Medicine, Tehran University of Medical Sciences, Tehran, Iran, Tehran, FL, Iran (Islamic Republic of); 4School of Traditional Medicine, Tehran University of Medical Sciences, Tehran, Iran, Tehran, Iran (Islamic Republic of); 5Department of Persian Medicine, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran, tehran, FL, Iran (Islamic Republic of).

OBJECTIVE: to investigate obesity associated inflammatory factors in follicular fluid that may affect gene expression in cumulus cells of women undergoing IVF-ICSI.

DESIGN: Prospective cohort study.

MATERIALS AND METHODS: Follicular fluid and cumulus cells were collected during oocyte retrieval in women undergoing IVF-ICSI, and grouped based on body mass index (BMI). Cytokine levels were measured from the follicular fluid using enzyme-linked immunosorbent assay (ELISA). Expression of 4 genes (GREM1, IL-1β, IL-10, and VCAM1) which were positively correlated with oocyte maturity and/or pregnancy outcome in cumulus cells, was determined by quantitative reverse transcription polymerase chain reaction (RT-qPCR).

Mann Whitney tests were utilized to compare cohorts by BMI and reported as medians with interquartile ranges. Cumulus cells of normal BMI (21.1 kg/m2 to 23.6 kg/m2) were cultured with IL-1β to investigate its impact on gene expression. Change in gene
expression following IL-1β was analyzed by paired t test. P values <0.05 were considered significant.

RESULTS: A total of 68 women were included in the ELISA analysis. Women were grouped based on BMI with 57 women having BMI ≥35 kg/m² and 6 women with BMI ≥25 to <35 kg/m². Women with BMI ≥35 kg/m² had increased levels of IL-1β in the follicular fluid as compared to women with lower BMI (5.18 pg/mL vs 1.92 pg/mL, p = 0.02).

Gene expression from cumulus cells was measured from a representative cohort based on BMI, with 6 in the normal group (BMI 21.1 kg/m² to 23.6 kg/m²) and 6 in the obese group (35.6 kg/m² to 42.0 kg/m²). The obese group had a significantly lower relative expression of GREM1 compared to the normal group (0.51 [0.38, 0.74] vs 1.01 [0.66, 1.80], p = 0.03). No differences were seen with HAS2 (0.73 [0.49, 1.17] vs 1.06 [0.65, 1.78], p = 0.39), PTGS2 (1.54 [1.09, 3.11] vs 0.58 [0.47, 4.19], p = 0.22), or VCAN (0.88 [0.61, 1.56] vs 0.93 [0.63, 1.56], p = 0.82).

Given increased levels of IL-1β in follicular fluid of obese women, cumulus cells from women with normal BMI were cultured with IL-1β to investigate the impact on GREM1 expression. Following IL-1β incubation, GREM1 levels significantly decreased in cumulus cells of normal BMI women (p = 0.02) similar to the obese cohort.

CONCLUSIONS: Compared to women with normal BMI, obese women had higher levels of pro-inflammatory IL-1β in the follicular fluid and had lower cumulus cell expression of GREM1. Decreased expression of GREM1 in cumulus cells of normal BMI women following culture with IL-1β suggests that this pro-inflammatory cytokine may play a role in suppressing GREM1 levels in obese women. These molecular discrepancies may provide insights into physiological differences in oocyte development and cycle outcomes in obese women undergoing IVF-ICSI. Further studies are required to correlate these molecular findings to clinical outcomes.

P-765 Wednesday, October 16, 2019 6:30 AM

IMPACT OF YOGA BASED LIFESTYLE INTERVENTION ON QUALITY OF LIFE, DEPRESSION AND SPERM OXIDATIVE DNA DAMAGE: A RANDOMIZED CONTROLLED TRIAL ON INFERTILE MEN WITH RHEUMATOID ARTHRITIS

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OBJECTIVE: Rheumatoid arthritis (RA), an auto-immune disease, shows a consecutive stimulus of proinflammatory cytokines, following a wide range of pathophysiological reactions, leading to increased synthesis of acute phase proteins like C - reactive protein (CRP) and dysregulation in levels of immunomodulatory soluble Human Leukocyte Antigen-G (sHLA-G) molecule. Toxic effects of Methotrexate (MTX), a major component of disease-modifying anti-rheumatic drugs (DMARDs), can cross blood-tissue-barrier and can induce changes in sperm for men of reproductive age group like germ cell apoptosis, mitotic changes in germline cells, permanent gonadal failure and impaired spermatogenesis. Hence, it’s cytotoxic, mutagenic and teratogenic activities may have side-effects in various ways to reproductive health.

DESIGN: A randomized controlled trial to assess the impact of 8 weeks Yoga-based lifestyle intervention (YBLI) on quality of life (QoL), stress markers, immune and oxidative stress parameters of active RA infertile men group compared with usual-care control group.

MATERIALS AND METHODS: Forty six infertile males with RA were randomized into two groups: yoga (23): practicing Yoga based lifestyle intervention (YBLI) in addition to disease-modifying anti-rheumatic drugs (DMARDs) for 8 weeks; non-yoga (23): DMARDs only. All subjects were assessed pre and post intervention for erythrocyte sedimentation rate (ESR), C reactive protein (CRP), IL-6, IL-17a and soluble HLA-G levels for systemic inflammation as well as seminal reactive oxygen species (ROS), DNA fragmentation index (DFI) and 8-hydroxy-2-deoxyguanine (8-OHdG) levels.

RESULTS: The proportions of PD1+ Th17 cells (CD4+IL17+CD279+ cells out of total CD4+T cells) were significantly lower in the YBLI group than controls (P<0.05). However, there are no differences in PD1- Th1 (CD4+TNF-a+ CD279+ and CD4+IFN-g+CD279+) and Treg (CD4+CD25+CD127+CD279+) cells between the RPL group and controls. The proportions of PD1+ Th1 (CD4+IFN-g+CD274+ and CD4+TNF-a+CD274+), Th17 (CD4+IL17+CD274+), and Treg (CD4+CD25+CD127+CD279+) cells are not different between the RPL group and controls (P>0.05, respectively).

In Th1 and Th17 cells, the proportions of PD1+ (CD274+) cells were significantly higher than those of PD1+ (CD279+) cells in both the RPL group and controls (P<0.01 respectively). However, there were no differences in PD1+, and PD1+ Treg cells in both groups.

CONCLUSIONS: Reduced expression of PD1 on Th17 cells may lead to enhanced Th17 immunity and result in the imbalance between Treg and Th17 cells in women with RPL.

SUPPORT: This work was partially supported by grants from the National Natural Science Foundation of China (grant numbers 81741027, 81300533, 81601276), Chinese Medical Association Clinical Medicine Research Special Fund-2017, Reproductive Medicine Young Physicians Research and Development project (17020160685, 16020220638), and Yantai Key Research and development program (2017YT06000491).

P-766 Wednesday, October 16, 2019 6:30 AM

DECREASED EXPRESSION OF PD1 IN PERIPHERAL BLOOD TH17 CELLS IN WOMEN WITH UNEXPLAINED RECURRENT PREGNANCY LOSS

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OBJECTIVE: Programmed Death-1 (PD1) and PD-ligand (PDL-1) have been reported to participate in the regulation of T cells homeostasis and peripheral tolerance and have an important role in fetomaternal tolerance during pregnancy. PD1 blockade leads to CD4+ T (especially Th1, Th17 cells) activation and proliferation, which in turn increases embryo resorption and reduces litter size in a mouse model. The goal of this study was to investigate the expression of PD1/PDL1 on CD4+ T cells of peripheral blood in women with recurrent pregnancy loss (RPL).

DESIGN: A prospective cohort study.

MATERIALS AND METHODS: Forty-five women with RPL and 12 fertile women who had at least one or more live-born infants were enrolled in this pilot study. The expression of PD1/PDL1 on CD4+ T cells in the peripheral blood, including Th1, Th17, and Treg cells were analyzed by flow cytometry. The expression of PDL1 was tested using monoclonal antibodies (mAB) to CD279 (PD1) and CD274 (PDL1). The expression of Tregs was assessed using mAbs to CD245, CD3, CD4, CD25, and CD127. The expression of Th1 cells was assessed using mAB to CD45, CD3, CD8, IFN-g or TNF-a. The expression of Th17 cells was assessed using mAB to CD45, CD3, CD8, and IL-17.

RESULTS: The proportions of PD1+ Th17 cells (CD4+IL17+CD279+ cells out of total CD4+T cells) were significantly lower in the RPL group than controls (P<0.05). However, there are no differences in PD1+ Th1 (CD4+TNF-a+CD279+ and CD4+IFN-g+CD279+) and Treg (CD4+CD25+CD127+CD279+) cells between the RPL group and controls.

CONCLUSIONS: Decreased expression of PD1 on Th17 cells may lead to enhanced Th17 immunity and result in the imbalance between Treg and Th17 cells in women with RPL.

SUPPORT: This work was partially supported by grants from the National Natural Science Foundation of China (grant numbers 81741027, 81300533, 81601276), Chinese Medical Association Clinical Medicine Research Special Fund-2017, Reproductive Medicine Young Physicians Research and Development project (17020160685, 16020220638), and Yantai Key research and development program (2017YT06000491).
OBJECTIVE: The concept of immune-mediated Recurrent Pregnancy Loss (im-RPL) is gradually being accepted as a true clinical entity. However, there is no universally accepted screening test or a diagnostic test for this condition. Anti-nuclear antibody (ANA) screening is widely used for screening autoimmune diseases in clinical medicine. The objective of this study was to determine whether serum ANA would be a reliable marker to predict outcomes in women diagnosed with Recurrent Pregnancy Loss (RPL) without co-existing anti-phospholipid antibody syndrome (APS).

DESIGN: Systematic review and meta-analysis.

MATERIALS AND METHODS: This systematic review and meta-analysis was registered with PROSPERO. The search strategy was applied to Medline, EMBASE and Cochrane Central Register of Controlled Trials (from database inception to Oct 2018). Studies retrieved by the search and the reference lists of relevant studies were included in the review if: the study population was described as having a diagnosis of RPL; had serum ANA testing done; if there was a control group and if the outcomes of miscarriage (or live birth) were reported. Studies in women who had coexisting APS were excluded. There were no other restrictions, including ANA titer or co-interventions. The primary outcome was the miscarriage rate. Heterogeneity between studies was measured using I² statistics. Subgroup analyses included ANA titer levels, women who had two or more previous miscarriages, and those with three or more previous miscarriages. Data were extracted using a pilot data extraction proforma and meta-analysis was performed based on a random-effects model using R Version 3.5.2 (R Core Team, 2018) and the meta (Version. 4.9-5; Schwarzer, 2019) package. We also conducted a quality assessment of all included studies.

RESULTS: Thirty-two studies involving 4,375 women fulfilled the inclusion criteria and were subjected to quantitative and qualitative analysis. All studies included in this review were case-control studies. There was a statistically significant increase in risk of miscarriages in women with positive ANA (Odd's Ratio [OR] 2.99; 95% CI [2.22 – 4.04]; I² = 67%; P < 0.01). Subgroup analysis also confirmed a statistically significant association of an increase in the risk of miscarriage. In women with three or more previous miscarriages, analysis confirmed OR 2.47; 95% CI [1.66 – 3.65]; I² = 41%; P < 0.01. In women who had two or more previous miscarriages, analysis confirmed OR 3.47; 95% CI [2.24 – 5.39]; I² = 79%; P < 0.01. The total heterogeneity was high with I² = 67%, I² = 0.4, p < 0.01.

CONCLUSIONS: This systematic review postulates that positive ANA in women with RPL increases the risk of further miscarriage by three-fold. This finding underscores the importance of the immune system in RPL and suggests that ANA could be useful in outcome prediction for APS negative women with RPL. This study also opens a new direction for future research into disease mechanisms, and potential ‘personalized treatment option’ for women for this otherwise, difficult to treat clinical condition.

SUPPORT: Funding support: A Statistical analysis for this project was supported by the National Center for Advancing Translational Sciences at the National Institutes of Health (NIH).

P-768 Wednesday, October 16, 2019 6:30 AM
NATURAL KILLER CELL-BASED PREDICTIVE ASSAY FOR PREGNANCY OUTCOME IN FROZEN EMBRYO TRANSFER CYCLES. Warren J. Huber III, M.D., Ph.D.,a Paula M. Krueger, B.S.,b May-Tal Sauerbrun-Cutler, M.D.,b Geralyn Messerlian, Ph.D.,b Surendra Sharma, M.D. Ph.D.b Warren Alpert Medical School of Brown University; Women & Infants Hospital, Providence, RI; Warren Alpert Medical School of Brown University; Women & Infants Hospital; Department of Pediatrics, PROVIDENCE, RI; Warren Alpert Medical School of Brown University; Women & Infants Hospital, PROVIDENCE, RI.

OBJECTIVE: To characterize the pregnancy-compatible phenotypic and functional changes in peripheral blood natural killer (NK) cells during frozen embryo transfer (FET) cycles.

DESIGN: Prospective, investigator-cohort study.

MATERIALS AND METHODS: Peripheral blood was collected from patients undergoing FET cycles at three time points: 1) follicular phase, 2) day of the embryo transfer, and 3) day of quantitative serum β-hCG analysis. Serum progesterone, estradiol levels, and hCG were quantified. Peripheral blood NK cell phenotype and cytotoxicity were compared based on timing of the blood draw and then stratified by presence/absence of a clinical pregnancy as defined by fetal heartbeat at the time of ultrasound. For phenotypic analysis, frozen whole blood was stained for CD45, CD3, Nkp46, CD56, and CD16 and quantified by flow cytometry. Three-dimensional endothelial tube formation involving endothelial HUVECs and first trimester extravillous HTR8 cells and NK cell-specific K562 cell kill assay were used to compare NK cell cytotoxicity. ELISA assays were used to quantify VEGF-A and VEGF-C in sera from pregnant vs non-pregnant women. Continuous variables were compared by test or ANOVA if normally distributed and Mann-Whitney U or Kruskal-Wallis test if not normally distributed. Categorical variables were compared with Fisher’s exact or Chi-square test.

RESULTS: 35 patients were enrolled, 15 with clinical pregnancies and 20 with negative serum β-hCG levels. There were no differences in age, gravidity/parity, BMI, infertility diagnosis, endometrial preparation, mode of progesterone supplementation, embryo age, number of embryos transferred, serum progesterone and estradiol, or number of PGT-A cycles in the pregnant vs. non-pregnant patient groups. When all samples were analyzed together, CD45+CD3+CD56+ NK cell numbers did not change based on the timing of the FET cycle. When subjects were stratified by pregnancy status, there was an increase in CD45+CD3+CD56+ NK cell population in the pregnant group on the day of serum β-hCG. In the tube formation assay, NK cells from non-pregnant patients caused significant tube disruption when compared to NK cells from pregnant patients. When serum from pregnant patients was added to the tube, tube disruption by NK cells from non-pregnant patients was significantly reduced; whereas serum from non-pregnant women failed to protect tube formation. In the serum free K562 cell kill assay, NK cells from pregnant patients had significantly lower cytotoxicity potential compared to NK cells from non-pregnant patients. The addition of pregnancy serum decreased the cytotoxicity of non-pregnant NK cells. VEGF-A and VEGF-C levels were similar in pregnant vs non-pregnant serum; hCG was only found in serum from women who experienced clinical pregnancy.

CONCLUSIONS: Increase in CD45+CD3+CD56+ NK cells was observed in women with detected hCG. Pregnancy status and pregnancy serum have a significant impact on the cytotoxic potential of peripheral blood NK cells. In this regard, hCG, not VEGF-A or VEGF-C, may impart a non-cytotoxic phenotype on peripheral blood NK cells.

SUPPORT: Supported by NIH P20 GM121298.

REPRODUCTIVE SURGERY

P-769 Wednesday, October 16, 2019 6:30 AM
WEEKEND PRESENTATION IMPACTS TIMING OF ECTOPIG PREGNANCY SURGICAL MANAGEMENT AND OUTCOMES. Jessica Selter, M.D., Timothy Wen, M.D., MPH, Jenna M. Turocy, M.D., Eric J. Forman, M.D., Samuel Zev Williams, M.D., Ph.D., Alexander Friedman, M.D., MPH Columbia University Medical Center, New York, NY.

OBJECTIVE: To evaluate whether weekend presentation of ectopic pregnancy impacts admission from the emergency department (ED), surgical timing, and morbidity in a national sample.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: This study utilized the Nationwide Emergency Database Sample (NEDS, 2006-2011) and Nationwide Inpatient Sample (NIS, 2002-2011). Ectopic pregnancies and subsequent surgeries were identified utilizing ICD-9-CM codes stratified by day of admission (weekend vs. weekday). Time to surgery was calculated from time of admission, using variables provided by the NIS. Multivariable log-linear analyses adjusting for patient (age, race, payer status, comorbidities, income) and hospital (region, bed-size, teaching status, location) factors were utilized to determine the relationship between weekend presentation and surgery timing. Outcomes included admission from the emergency department, same-day surgery, surgery within one day, and the need for transfusion (adjusting additionally for time to surgery). Measures of association were reported as adjusted risk ratios (RR) with 95% confidence intervals (CI).

RESULTS: We analyzed 296,071 ED evaluations and 376,092 inpatient surgical admissions for ectopic pregnancy. Of ED evaluations, 25.4% were seen on the weekend, with an admission rate of 43.8% compared to 42.5% on a weekday. Once admitted, weekend admissions had lower same day surgery rates compared to weekday admissions (78.4% vs. 82.4%, p<0.05). Weekend admissions also had increased blood transfusion rates (15.1% vs. 9.2%, p<0.05). In multivariable analysis, patients seen on the weekend (RR 1.04, 95% CI: 1.03, 1.05 p<0.01), older patients (RR 1.07, 95% CI: 1.04, 1.10, p<0.01), and those with co-morbidities (RR 2.06, 95% CI: 1.98, 2.15

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p<0.01) were more likely to be admitted to the hospital. Of patients admitted, those on the weekend (RR 96 95% CI: 95, 97 p<0.01), black patients (RR 97 95% CI: 95, 98 <0.01), and those with co-morbidities (RR 86 95% CI: 84, 88 p<0.01) were less likely to undergo same-day surgery for ectopic pregnancy. Similarly, patients admitted on the weekend (RR 97 95% CI: 95, 97 p<0.01) and those with co-morbidities (RR 88 95% CI: 86, 89 p<0.01) were also less likely to receive surgery within one day. Furthermore, patients on the weekend (RR 1.49, 95% CI: 1.46, 1.53 p<0.01) and those with co-morbidities (RR 3.90, 95% CI: 3.73, 4.09, p<0.01) were more likely to have a blood transfusion during admission.

CONCLUSIONS: Ectopic pregnancies evaluated in the ED during the weekend are more likely to be admitted to the hospital, but less likely to undergo same day or surgery within one day of admission. Weekend admissions were independently at significantly higher risk for blood transfusions even after adjustment for timing of surgical management. Further studies are needed to understand factors such as provider staffing which may contribute to this weekend effect, and to work to mitigate this impact.

P-770 Wednesday, October 16, 2019 6:30 AM
NORMAL SALINE SOLUTION IS AS EFFECTIVE AS POVIDONE IODINE IN PREOPERATIVE VAGINAL CLEANSING BEFORE SHORT DURATION GYNECOLOGICAL LAPAROSCOPY. Ahmed M. Abbas, MD, Mohammed Khairy Ali, MD, Ahmed M. Abdelmagied, MD, Osama S. Abdalmageed, MD, Esraa Badran, MD Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt.

OBJECTIVE: Laparoscopy is a minimally invasive method used for diagnostic and therapeutic purposes. Our objective was to compare the postoperative vaginal irritation symptoms and infection rates after using povidone-iodine (PI) and normal saline (NS) solution in vaginal cleansing before short duration gynecological laparoscopy.

DESIGN: Randomized, single-blind clinical trial.

MATERIALS AND METHODS: All eligible patients who scheduled for short duration gynecologic laparoscopic procedures included diagnostic laparoscopy, bilateral ovarian drilling, and tubal sterilization were invited to participate in the study. Eligible participants were randomly allocated in a 1:1 ratio to two groups. Group I "PI group" where they subjected to PI for vaginal cleansing before laparoscopy and group II "NS group" where they subjected to the standard saline solution for vaginal cleansing. Two sponges of the same size and type were used for cleansing by both preparations. The primary outcome of the study was the difference in the rate of self-reported postoperative vaginal irritation symptoms and infection rates after using PI and NS for vaginal cleansing. The secondary outcomes included the rate of postoperative fever ≥ 38 °C during the first 24 hours, persistent vaginal irritation symptoms, urinary tract infection, candidal vaginitis and bacterial vaginosis and endometritis at one-week post-procedure. The outcome variables were calculated using an unpaired test and chi-square test.

RESULTS: Two-hundred forty-four women were analyzed in both groups (121 women in the arm). Both groups were similar regarding the mean age, residency, woman’s education, parity, BMI and operative time. Diagnostic laparoscopy was the most common laparoscopic procedure performed during the study period (84.29%), tubal sterilization (7.85%) then bilateral ovarian drilling (7.43%). The mean overall vaginal irritation symptoms in PI group were significantly more than that observed in the NS group (p=0.0001). The overall infection rates in the PI group were 15.9%, while in the NS group was 10.16% without a statistically significant difference in both groups (p=0.567). Both groups were quite similar in the rate of postoperative fever (p=0.505), urinary tract infection (p=0.654), vaginal candidiasis (p=0.254), bacterial vaginosis (p=0.366) and postoperative endometritis (p=0.749).

CONCLUSIONS: Being less irritant, normal saline can substitute iodide solution as a vaginal cleansing tool before short duration gynecologic laparoscopy without increasing the risk of postoperative infection.

SUPPORT: None.

FLUID DEFICIT CALCULATION AT HYSTEROSCOPY IN PATIENTS WITH AND WITHOUT TUBAL OCCLUSION: COULD CONSIDERATION OF TUBAL PASSAGE CHANGE SAFETY LIMITS? Irene Peregrín-Alvarez, MD, Robert Roman, MD, Mary Emily Christiansen, MD, Joshua Morris, MD, Laura Detti, MD. University of Tennessee Health Science Center, Memphis, TN.

OBJECTIVE: Hysterectomy (HSC) fluid management guidelines (1) are not well-defined regarding the contribution on the fallopian tube patency to the fluid deficit (FD) during HSC and most surgeons attribute the entire FD to intravasation (2). Women with patent tubes undergoing HSC have accumulation of distention media in the pelvis which can be seen during laparoscopy (LSC) and could be in part due to transtubal passage (3). We explored whether FD could be in part due to transtubal passage.

DESIGN: Prospective observational study.

MATERIALS AND METHODS: We studied 164 patients aged 20-45 years, who underwent HSC using normal saline as distention media between January 2014 and August 2017. Tubal patency was previously assessed at sonohysterogram. FD and, in LSC cases, the amount of fluid found in the pelvis, were prospectively recorded. Whitney U test was used to compare distributions with a p value <0.05 defining statistical significance (SPSS v25 for Windows; Chicago, Illinois).

RESULTS: 164 patients were included in the study. 77 underwent HSC prior to LSC and 87 patients underwent HSC only. In the LSC group, 69 had at least one patent tube with an average FD of 438.96 ml and a calculated FD due to extravasation of 175.61 ml; 8 patients had bilateral tubal occlusion and all were found to have 0 ml of peritoneal fluid with an average FD of 141. In the HSC only group, 83 had at least one patent tube with an average FD of 307.48 ml; 4 patients had bilateral tubal occlusion with an average FD of 375.75 ml. There was no correlation between intraperitoneal fluid pressure and the amount of FD, or the presence of peritoneal fluid.

CONCLUSIONS: Most women with patent tubes undergoing HSC have accumulation of distention media in the pelvis and transtubal passage was not correlated with the intraperitoneal fluid pressure. FD in patients with tubal occlusion appears to be entirely attributed to intravasation. These findings add new insight to our understanding of fluid dynamics during operative hysteroscopy that can help develop more accurate and patient-centered safety protocols.


P-771 Wednesday, October 16, 2019 6:30 AM
SEVERE HAEMATOMPERITONEUM AFTER TRANSVAGINAL OOCYTE RETREIVAL RELATED OVARIAN BLEEDING COULD BE MOSTLY MANAGED BY CONSERVATIVE TREATMENT: 8332 CASES OF ONE CLINICIAN’S EXPERIENCE IN 5 YEARS. Melih Aygun, M.D.,* Caroline Martinez, M.D.,* Serma Kahraman, Prof.,* In infertility specialist, ISTANBUL, Turkey;* Istanbul Memorial Hospital, Istanbul, Turkey.

OBJECTIVE: TVOR is the most common surgical procedure during in vitro fertilization (IVF) cycles. One of the most serious complications of the reference to the image.
PROCEDURE: The study was to compare single clinician’s complication rate for SHP caused by ovarian bleeding after TVOR with literature and to compare the outcome of treatment strategies.

DESIGN: This retrospective cohort study includes total of 8332 consecutive TVOR procedures performed by a single clinician (65.2%) among a total of 12776 TVORs, between June 2014 and March 2019 and in one IVF Center. All the suspected SHP cases who were hospitalized were enrolled in the study group. This “complication” group was categorized according to the need for a conservative or surgical treatment. General SHP rates and the treatment approaches were compared with the literature.

MATERIALS AND METHODS: The complications of SHP included in the study were grouped into two: Group I included patients in whom conservative treatment with or without red blood cell (RBC) transfusion was performed; Group II consisted of patients who were indicated for surgical treatment. Patients with non-ovarian bleedings were excluded. Number of RBC units for transfusion, duration of hospitalization of SHP patients, general body mass index (BMI) and women ages in TVOR were considered.

RESULTS: A total number of 79097 oocytes (8382 TVOR) were retrieved by the same clinician between June 2014 and March 2019. The mean female age was 35.04±5.67, the mean body mass index was 24.92±4.49, the mean number of retrieved oocytes and metaphase II oocytes was 9.50±8.35 and 7.92±6.97 respectively. The number of SHP related ovarian bleeding complications during TVOR was 17 out of 8332 (%0.2). The mean duration of hospitalization was 1.76 days/patient. The mean RBC units administered was 1.65 U/patient. Whereas 15 patients (88.23%) needed only conservative treatment, only two (11.77%) needed a laparoscopic intervention. None of the patients (17) had severe infections such as pelvic abscess or sepsis after the treatment.

CONCLUSIONS: The real complication rates of SHP after TVORand especially their treatment methods are variable in the literature. Differences of origin of intra-abdominal bleeding after TVOR and diagnosis of severity of haematometrium also make the therapeutic approaches more complicated in IVF patients. We report here a very low complication rate (0.2%) of SHP in a large series performed by a single clinician in nearly five years. Our data showed that most of the ovarian bleeding related SHP after TVOR could be managed without adverse outcome by conservative treatment (88.23%) not by surgery in contrast to the published data.

Reference: No.

Support: No.

P-773 Wednesday, October 16, 2019 6:30 AM
ANALYSIS OF THE PREGNANCY OUTCOMES OF HETEROTOPIC FALLOPIAN TUBAL PREGNANCY AND HETEROTOPIC INTERSTITIAL PREGNANCY AFTER IN VITRO FERTILIZATION - EMBRYO TRANSFER, Mingxiang Zheng, Bachelor’s degree, Xi Hong Li, MD, Ph.D, Yan Qian, MD, Ph.D, Qingqing Wu, Bachelor’s degree, Reproductive and Genetic hospital of CITIC-Xiangya, Changsha, China; Reproductive and Genetic hospital of CITIC-Xiangya, Changsha, China.

OBJECTIVE: To investigate the intraterine pregnancy (IUP) outcomes of heterotopic interstitial pregnancy and heterotopic fallopian tubal pregnancy after in vitro fertilization - embryo transfer (IVF-ET).

TABLE 1. Comparison of the IUP between the heterotopic fallopian tubal pregnancy and heterotopic interstitial pregnancy

<table>
<thead>
<tr>
<th>Pregnancy outcomes</th>
<th>Heterotopic fallopian tubal pregnancy (n=347)</th>
<th>Heterotopic interstitial pregnancy (n=160)</th>
<th>P-value</th>
<th>OR (95%-CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early pregnancy loss rate, % (n)</td>
<td>28.5% (99/347)</td>
<td>26.9% (43/160)</td>
<td>0.7</td>
<td>1.086 (0.714-1.653)</td>
</tr>
<tr>
<td>Late miscarriage rate, % (n)</td>
<td>0.6% (2/347)</td>
<td>0</td>
<td>1</td>
<td>1.464 (1.379-1.553)</td>
</tr>
<tr>
<td>Preterm delivery rate, % (n)</td>
<td>7.5% (26/347)</td>
<td>6.3% (10/160)</td>
<td>0.613</td>
<td>1.215 (0.571-2.584)</td>
</tr>
<tr>
<td>Term delivery rate, % (n)</td>
<td>62.8% (218/347)</td>
<td>66.9% (107/160)</td>
<td>0.377</td>
<td>0.837 (0.564-1.242)</td>
</tr>
<tr>
<td>Labor induction rate, % (n)</td>
<td>0.6% (2/347)</td>
<td>0</td>
<td>1</td>
<td>1.464 (1.379-1.553)</td>
</tr>
<tr>
<td>Babies born</td>
<td>255</td>
<td>119</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perinatal mortality rate, % (n)</td>
<td>1.6% (4/255)</td>
<td>0.8% (1/119)</td>
<td>1</td>
<td>1.880 (0.208-17.009)</td>
</tr>
<tr>
<td>Live birth rate, % (n)</td>
<td>69.2% (240/347)</td>
<td>72.5% (116/160)</td>
<td>0.345</td>
<td>0.851 (0.562-1.289)</td>
</tr>
<tr>
<td>Cesarean section rate, % (n)</td>
<td>77.1% (188/244)</td>
<td>86.3% (101/117)</td>
<td>0</td>
<td>0.334 (0.180-0.618)</td>
</tr>
<tr>
<td>Gestational age at delivery</td>
<td>38.345 ± 2.322</td>
<td>38.406 ± 2.271</td>
<td>0.818</td>
<td></td>
</tr>
<tr>
<td>Live birth weight (kg)</td>
<td>3.2 ± 0.6</td>
<td>3.2 ± 0.5</td>
<td>0.747</td>
<td></td>
</tr>
</tbody>
</table>

DESIGN: A retrospective study.
MATERIALS AND METHODS: Women who underwent IVF-ET and transvaginal sonography (TYS) in our reproductive center between January 2005 and December 2017 were included. All pregnancies were diagnosed by TYS and were confirmed by surgery and pathological analysis. The outcomes of IUP after surgical treatment of the ectopic pregnancies were compared between the heterotopic fallopian tubal pregnancy group (n=347) and the heterotopic interstitial pregnancy group (n=160).

RESULTS: The two groups were statistically similar with respect to maternal age, body mass index, cause of infertility, insemination methods, transfer cycle and endometrial thickness on transfer day (p > 0.05). The early pregnancy loss rate (28.5% vs. 26.9%, p=0.700), the late miscarriage rate (0.6% vs. 0.8%, p=0.613), preterm delivery rate (7.5% vs. 6.3%, p=0.613), perinatal mortality (1.6% vs. 0.8%, p=1.000), live birth rate (69.2% vs. 72.5%, p=0.445), live birth weight (3.2 ± 0.6 vs. 3.2 ± 0.5 kg, p=0.747) and the gestational age at delivery (38.3 ± 2.3 vs. 38.4 ± 2.3 weeks, p=0.818) were statistically similar. However, the cesarean section rate (77.1% vs. 86.3%, p < 0.001) in the heterotopic interstitial pregnancy group was significantly higher than that in the heterotopic fallopian tubal pregnancy group.

CONCLUSIONS: After surgical treatment of ectopic pregnancies, the IUP of both heterotopic fallopian tubal pregnancy and heterotopic interstitial pregnancy can achieve a good IUP outcome.

P-774 Wednesday, October 16, 2019 6:30 AM
THE IMPACT OF IPSILATERAL TESTICULAR ATROPHY ON SEMEN ANALYSIS AND DNA FRAGMENTATION RESPONSE TO VARICOCELE REPAIR, Natasha Abdulla, BA, Melissa S. Gilkey, M.S., Caitlin Hunn, M.S., Shu-Hung Chen, M.S., Keikhosrow M. Kavoussi, MD, Amy S. Esqueda, BSN, MSN, APRN, J. David Wineringer, PhD, HCLD, Shahryar K. Kavoussi, MD, MPH, Parviz K. Kavoussi, MD Austin Fertility & Reproductive Medicine/Westlake IVF, Austin, TX.

OBJECTIVE: The purpose of this study is to assess the response in semen parameters and sperm DNA fragmentation index (DFI) in men with ipsilateral testicular atrophy secondary to a varicocele in comparison to men without testicular atrophy.

DESIGN: A retrospective chart review was performed.
MATERIALS AND METHODS: Men who underwent varicocele repair for subfertility were categorized into 2 groups, those with testicular atrophy (TA) in the ipsilateral testicle and those with no testicular atrophy (NTA). Semen parameters and DFIs in both groups were compared preoperatively and 3 months postoperatively. Morphology was not included due to lack of standardization of criteria in different labs with some using WHO 4th edition criteria and others using strict Kruger morphology criteria. From 10/2010 and 1/2019, 359 varicocele repairs were performed by a single microsurgeon and 141 varicocele repairs met inclusion criteria. Exclusion criteria included men who underwent bilateral varicocele repairs, men with bilateral testicular atrophy, men with a history of cryptorchidism or testicular torsion, men who underwent varicocele repair for hypogonadism or orchialgia and not for fertility, men who were azoospermic preoperatively, and men who did not obtain a 3-month postoperative semen analysis because they achieved a pregnancy prior to then or who did not follow up. Student’s test was used with a p value of < 0.05 considered statistically significant. Results were expressed as mean ± standard deviations.
RESULTS: Of the 141 men who were included, 20 were in the TA group and 121 were in the NTA group. There was no statistically significant difference in age between the 2 groups, 34.3 (6.5) in TA group and 34.1 (5.8) in the NTA group. The grades of varicoceles were similar in both groups; TA group had 70% grade 1, 55% grade 2, 35% grade 3; while the NTA group had 6.7% grade 1, 58.7% grade 2, and 34.7% grade 3. There was no statistically significant difference in preoperative semen parameters between the two groups including semen volume, sperm concentration, motility, forward progressive motility (FP), and total motile count (TMC). The NTA group had a higher preoperative DFI than the TA group: 35.3% vs 29.7% respectively. Although both groups improved in semen parameters postoperatively, the TA group only showed a statistically significant improvement in DFI from 29.7% (5) to 22% (0), whereas the NTA group showed statistically significant improvements in concentration, motility, FP, TMC, and DFI. The mean change in preoperative to postoperative parameters when comparing groups only revealed a significant difference in TMC and DFI with a larger mean improvement in the NTA group than the TA group.

CONCLUSIONS: Men with ipsilateral testicular atrophy secondary to varicoceles have improved overall semen parameters and DFI after varicocele repair, but do not get as significant of an improvement as men without testicular atrophy. However, only TMC and DFI have a significantly greater mean change in preoperative to postoperative response in the NTA group compared to the TA group.

SUPPORT: None.

P-775 Wednesday, October 16, 2019 6:30 AM

Efficacy and Safety of Oral versus Vaginal Misoprostol in Cervical Priming Before Hysteroscopy: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.

Ahmed M. Abdelhamik, MBBCh,a Al-Hussein Gadallah, MBBCh,b Ahmed M. Abbas, MD,c Kasr Al-Ainy Faculty of Medicine, Cairo University, Cairo, Egypt; Faculty of Medicine, Assiut University, Assiut, Egypt; Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut University, Assiut, Egypt.

OBJECTIVE: Hysteroscopy is common to be used in the diagnosis and management of many problems related to gynecology. Most of the complications of hysteroscopy occur throughout the cervical entry including cervical lacerations, false tract and uterine rupture. Cervical priming can be used to decrease the incidence of these problems and hazards before performing hysteroscopy. Our objective is to evaluate the evidence from published randomized clinical trials (RCTs) about the efficacy and safety of oral versus vaginal misoprostol in cervical priming before hysteroscopy.

DESIGN: Systematic review and meta-analysis.

MATERIALS AND METHODS: We searched in different electronic data-bases including PubMed, Cochrane Library, Scopus, ClinicalTrials.gov and Web of Science using the relevant keywords ((misoprostol OR Cytotec) AND (hysteroscopy OR cervical)). All RCTs are assessing the effect of oral versus vaginal misoprostol before hysteroscopy were considered. The excluded outcomes were: width of the cervical canal, ease of dilatation, the time needed for cervical dilatation; adverse effects and any complications during the procedure. For continuous data, efficacy outcomes were pooled as weighted mean difference (MD) or Standardized mean difference (SMD). For dichotomous data of safety outcomes, we used pooled odds ratios (OR) using the Mantel-Hansel method with 95% confidence intervals (CI). All statistical analyses in this study were completed by the RevMan software package.

RESULTS: Our search found 110 studies from the electronic databases out of which, 35 were duplicates. Out of the remaining 75 studies, 65 studies were excluded based on the title, and abstract screening and ten studies were excluded during the full-text screening. About eight studies met our inclusion criteria. The quality of the included RCTs was from moderate to high quality according to the Cochrane risk of bias assessment tool. Both groups did not differ significantly in terms of cervical width diameter (MD= -0.25 mm, 95% CI [-0.92, 0.42], p=0.47). However, the vaginal route significantly superior to the oral route of misoprostol in reducing the time needed for cervical dilatation (SMD= -0.17, 95% CI [0.02, 0.32], P=0.03). We found no significant difference in any of the two routes regarding ease of dilatation (MD= 0.00, 95% CI [-0.15, 0.15], P=0.96). Regarding safety profile, no significant difference between oral and vaginal misoprostol groups except for diarrhea which favored vaginal more than oral misoprostol (RR= 2.48, 95% CI [1.17, 5.26], p=0.02). No significant difference was found in both oral and vaginal route of administration for increasing the risk of any other complications (RR= 1.7, 95% CI [0.74, 3.92], P=0.21).

CONCLUSIONS: Oral and vaginal misoprostol administration are similar regarding efficacy and safety in cervical priming before hysteroscopy, except that the vaginal route is associated with a lower incidence of diarrhea.

SUPPORT: None.

P-776 Wednesday, October 16, 2019 6:30 AM

Outcome of Laparoscopic Repair of Cesarean Scar Defect.

Hesham A. Salem, FA, M.D.,a M.D.,a Moustafa Z. Moustafa, M.D.,a, Diaa M. Aghan, M.D.,a, Emam A. Abdelnaby, M.B.D, Edel A. Elgergawy, M.D.,a, Ayman Shihata Dawood, M.D.,b Amro D. Aghan, MBBCCh,a Mohamed H. A. Salem, MBBCCh.a Professor at Faculty of Medicine, Tanta University, Tanta, Egypt; Consultant at Faculty of Medicine Tanta University Hospitals, Tanta, Egypt; Assistant Professor at Faculty of Medicine, Tanta University, Tanta, Egypt; Lecturer at Faculty of Medicine, Tanta University, Tanta, Egypt; House Officer at Tanta University Hospitals, Tanta, Egypt; Medical Student at Faculty of Medicine, Tanta University, Tanta, Egypt.

OBJECTIVE: To evaluate the gynecologic and obstetric outcomes of laparoscopic repair of symptomatic cesarean scar defect.

DESIGN: Prospective clinical study.

SETTING: University hospital and private gynecologic endoscopy center.

MATERIALS AND METHODS: Patients: A total of 52 women (age between 25 – 35 years) with symptomatic cesarean scar defect, who wish to conceive, and the remaining myometrial thickness at the site of defect is less than 3 mm. according to vaginal US examination and/or MRI.

Intervention: Laparoscopic excision and repair of the defective cesarean scar.

Main Outcome measures: Relief of relevant symptoms, restored myometrial thickness at the site of repair, achievement of pregnancy in infertile patients, obstetric outcome in those who become pregnant, and incidence of operative complications.

RESULTS: The mean thickness of the myometrium increased significantly from 1.62 ± 0.8 before surgery to 9.0 ± 2.1 mm after surgery. Among the 47 patients presented with menstrual abnormalities and/or pelvic pains, 34 patients (72.3%) demonstrated complete relief of symptoms, 8 patients (17.02%) demonstrated partial improvement, and 5 patients (10.64%) stated no improvement. Among the 25 patients who tried pregnancy 17 patients (68%) became pregnant. 12 patients demonstrated healthy pregnancy courses and delivered healthy babies by cesarean section at term (48%). There were no relevant major obstetric complications like scar dehiscence, placenta accreta, or cesarean scar ectopic pregnancy. The were no operative complications.

CONCLUSIONS: In women with symptomatic cesarean scar defect who wish to conceive, the laparoscopic approach for excision and repair of the defective scar is safe and efficient technique, ensures satisfactory symptoms relief, adequate restoration of sufficient myometrial thickness and strength, and results in good reproductive outcome.

P-777 Wednesday, October 16, 2019 6:30 AM


Kent Russell Edwards, Jr, MD, Nicholas Ross Major, BS, Kit N. Simpson, DrPh, Marc J. Rogers, MD Medical University of South Carolina, Charleston, SC.

OBJECTIVE: Non-obstructive azooejermpenia (NOA) causes male factor infertility in about 10% of cases. Multiple techniques have been described to obtain sperm from the testicle for use with assisted reproductive technologies. Conventional testicular sperm extraction (cTESE) is the most common but some argue that microdissection testicular sperm extraction (mTESE) is preferred for its superior sperm retrieval rates (SRR) and decreased microvascular damage to the testicle. However, mTESE is generally more expensive, time consuming, and requires more equipment. Previous work has attempted to identify variables that predict positive SRR with mTESE versus cTESE. The objective of this review was to create a model comparing the commonly evaluated variables; follicle stimulation hormone (FSH), testicular volume (TV), and testosterone (T), to better predict SRR.

DESIGN: The authors included 29 studies in the data analysis, with 9 studies including data on cTESE for a total of 1227 patients and 20 studies included data on mTESE for a total of 4760 patients. Not all studies included data for each variable.
RESULTS: Weighted-values means of SRR, FSH, testosterone, and volume were calculated and demonstrated mTESE to be superior to cTESE with a SRR of 51.9% versus 40.1% when there were no significant differences in FSH, T, or TV. Multiple weighted linear regressions were created to describe associations between SRR, procedure type, FSH, T, and TV. Model A demonstrated that one may expect an 11.8% increase in SRR when utilizing mTESE compared to cTESE. Model B showed that for every 1.19 IU/mL increase in FSH there will be a significant decrease in SRR by 1%. FSH values were then divided into low, medium, and high categories (FSH < 10, 10-19, and > 20 IU/mL respectively). The model demonstrated that for an index patient undergoing cTESE retrieval rates would be 57%, 44%, and 31% for values low, medium, and high respectively.

CONCLUSIONS: Based upon pooled available data, mTESE is more successful than cTESE for sperm retrievals in NOA patients. The models generated in this study demonstrated an ability for FSH to predict SRR using mTESE and cTESE however the models were not suggestive for a correlation regarding SRR and T and TV. FSH alone can be predictive of retrieval success and used to counsel patients. More standardized data collection and publication will be useful for future modeling to allow improved outcomes and counseling for patients.

SUPPORT: None.

P-779 Wednesday, October 16, 2019 6:30 AM
IMPACT OF SAFETY PROTOCOL IN AN AMBULATORY SURGICAL SETTING VS A HOSPITAL SETTING FOR LAPAROSCOPIC-ASSISTED MYOMECTOMY (LAM).
Mamta Mamik, MD,a Vanessa Sarfoh, MD MPH,b Nilofar Kazi, BS, Faraj Touchan, MD,c Leah Haworth, BS, Louise Van Der Does, PhD,d Natalya Danilyants, MD,e Paul Mackoul, MDf aCenter for Innovative GYN Care, Rockville, MD; bThe Center for Innovative GYN Care, Rockville, MD; cCenter for Innovative GYN Care, Rockville, MD; dCenter for Innovative GYN Care, Rockville, MD; eCenter for Innovative GYN Care, Rockville, MD.

OBJECTIVE: Ambulatory surgery center (ASC) for major gynecological surgery improves efficiency and decreases cost compared to a hospital setting. Protocols to ensure safety when performing major gynecological surgeries such as laparoscopic-assisted myomectomy (LAM) in a high-volume ASC and compare it with protocols and outcomes in a hospital setting. DESIGN: This is a descriptive / retrospective study.

MATERIALS AND METHODS: This paper descriptively outlines the similarities and differences of a surgical safety protocol in an ambulatory surgical center vs a hospital setting. Furthermore there is retrospective analysis of LAM outcomes that are commonly considered as safety standards in both settings including intraoperative and postoperative complications.

RESULTS: The protocols were similar with regards to preoperative patient selection and checklist, surgical precautions including prevention of retained surgical items, DVT prophylaxis, infection control, surgical wound classification, vaginal and genital antisepsis for the surgical patient, postoperative care in PACU and discharge criteria for surgical management.

The major preoperative differences from hospital protocol were transfusion criteria preoperatively. In the ASC, a cut-off of 9.0 g/dl was used, and a cut-off of < 7.5 g/dl was used in the hospital setting. LAM cases are only scheduled as morning cases. 23 hour observation is available at ASC. Additionally myomectomy patients at the ASC have ISTAT (blood analysis system to check Hemoglobin/Hematocrit) prior to procedure and at 1 and 2 hours after the procedure in the PACU to detect any signs of bleeding. Any patients that did require blood transfusion postoperatively were transferred to the local hospital from the ASC.

There were 588 patients that underwent LAM at the ASC compared to 228 patients at the hospital. There was no significant difference in case complexity factors between settings including BMI, number of previous abdominal and pelvic surgeries or other comorbidities. Intraoperative complication rate was 3.4% (95% CI 1.8-5.0) at the ASC compared to 4.9% (95% CI 1.7-8.1), p = 0.4430. There were no significant differences in postoperative complications between the ASC and the hospital setting including infections and thromboembolic events. Blood transfusion was required in 1.7% of the cases at ASC compared to 8.8% at the hospital setting. The estimated blood loss and average fibrinogen weight were not statistically different between the two groups.


SUPPORT: NONE.

TABLE 1

<table>
<thead>
<tr>
<th>Results</th>
<th>Yes</th>
<th>No</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ovulation prior to LOD</td>
<td>39.0%</td>
<td>58.1%</td>
<td>2.9%</td>
</tr>
<tr>
<td>Ovulation after LOD</td>
<td>77.2%</td>
<td>4.8%</td>
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<tr>
<td>Pregnancy rate prior to LOD</td>
<td>33.1%</td>
<td>66.9%</td>
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</tr>
<tr>
<td>Pregnancy rate after LOD</td>
<td>47.1%</td>
<td>25.7%</td>
<td>27.2%</td>
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</tbody>
</table>

MATERIALS AND METHODS: While not all studies included data for each variable, the authors were however able to create a weighted-means values of SRR, FSH, testosterone, and volume for the 29 studies. The authors then used weighted linear regression to describe associations between SRR, type of procedure, FSH, T, and volume.

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PREGNANCY RATES AFTER LAPAROSCOPIC OVARIAN DRILLING IN POLYCYSTIC OVARY SYNDROME PATIENTS FOLLOWING UNSUCCESSFUL OVULATION INDUCTION. Shruti Agarwal, DO,a Mark P. Trolice, MD,b¹ UCF College of Medicine/HCA Consortium of Greater Orlando, Kissimmee, FL;¹ Fertility CARE: The IVF Center; University of Central Florida College of Medicine – Associate Professor, Winter Park, FL.

OBJECTIVE: Polycystic ovary syndrome (PCOS) is one of the most common endocrine pathologies and is a frequent cause of anovulatory infertility affecting 5-20% of reproductive age women1. Medical induction of ovulation is considered the first-line treatment option for infertile PCOS women. Laparoscopic ovarian drilling (LOD) is currently accepted as a successful second-line treatment in drug-resistant PCOS2. Many authors have reported high (~80%) and pregnancy (~60%) rates following LOD3. The aim of this study was to evaluate the efficacy of laparoscopic ovarian drilling (LOD) on the reproductive outcome of anovulatory PCOS women. The results of our study were compared to historical controls from literature.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Women unable to achieve pregnancy with ovulation drugs who underwent LOD from 2013-2018 were included. One physician followed a standard technique for LOD and performed all surgeries. Age, BMI, years of infertility, tobacco or alcohol use, pre and post surgery ovulation rates, pre and post pregnancy rate, time until ovulation and pregnancy after surgery were documented.

RESULTS: 136 patients who underwent LOD were included in this study. Demographics were divided as follows: mean age 28.9; mean BMI 22.2 kg/m2, and mean duration of infertility 2.9 years. Race was divided as follows: 58.8% Caucasian, 22.8% Hispanic, 14% African American, 3.7% Asian, 0.7% other. Tobacco use was reported by 4.4% and social alcohol use was reported by 37.5%. 39% reported successful ovulation with drugs prior to surgery but were unable to achieve a pregnancy. Ovulation after LOD was reported by 77.2% with a live birth rate of 47.1% and mean time until ovulation of 79.0 days. Statistical analysis showed a woman was 2.27% (95% CI 1.83 - 2.82) more likely to ovulate following LOD. This was considered significant on a Chi Square test (X2 = 69.8, P<0.05). Furthermore, a patient was 1.95% (95% CI 1.48 - 2.58) more likely to achieve a live birth following LOD with a mean time of 241.1 days until pregnancy. This was also considered significant on a Chi Square test (X2 = 22.9, P<0.05) (Table 1).

CONCLUSIONS: Our study demonstrates significantly improved ovulation and pregnancy rates in drug resistant PCOS women after LOD. Although the rates are lower than those reported in previous published studies, this may be attributed to 37 out of 136 patients (27.2%) being lost to follow up. Some patients also did not achieve desirable results after the surgery due to other factors like male infertility, marital issues and diagnosis of cancer.
CONCLUSIONS: The LAM safety protocol at a free-standing ASC allows for patient complication outcomes that are comparable to an in-hospital setting with apparent limitations in patient complexity.

OVARIAN CYSTS REQUIRING SURGERY AND INFERTILITY. Lisa M. Shandley, MD, MSc, Jessica B. Spencer, MD, MSc,* Lauren M. Kipling, MPH,* Banna Hussain, MPH,* Ann C. Mertens, PhD,* Penelope P. Howards, PhD,* ‡ Emory University School of Medicine, Atlanta, GA; ‡Emory University Rollins School of Public Health, Atlanta, GA; †Aflac Cancer Center, Atlanta, GA.

OBJECTIVE: Benign ovarian cysts are a common condition in reproductive-aged women. The long-term effect of surgery for ovarian cysts on fertility remains unknown.

DESIGN: Women aged 22-45 years were interviewed about their reproductive histories (n = 2,219), including whether they ever had infertility (defined as 12 months of unprotected sex without getting pregnant) or surgery for ovarian cysts. Women who reported a hysterectomy prior to ovarian cyst surgery were excluded. A subset of women (n = 717) was invited to attend a clinic visit where markers of ovarian reserve (anti-Müllerian hormone [AMH], antral follicle count [AFC]) were measured. Women who reported surgery for benign ovarian cysts were compared with those who did not report ovarian cyst surgery.

MATERIALS AND METHODS: To account for age at surgery, each woman with a history of ovarian cyst surgery was randomly matched to a woman without such a history who was then assigned an artificial age at surgery equal to that of her match. This matching was repeated 1,000 times. For each matching iteration, adjusted Cox models were fit examining time to infertility after surgery; the median hazard ratio (HR) and 95% simulation intervals (SI) are reported. Log-transformed and negative log binomial models were fit for AMH and AFC, respectively, to examine the relationship between ovarian reserve and history of ovarian cyst surgery; AMH and AFC were predicted for a woman at the median age at clinic visit.

RESULTS: Approximately 6.6% of women reported ovarian cyst surgery. The median age at surgery was 26 years. Women with and without ovarian cysts requiring surgery were similar with regards to race, level of education, relationship status at the interview, income, health insurance status, and body mass index. Infertility after age at surgery was more common for women reporting ovarian cyst surgery than those without surgery after adjusting for age, history of cancer, race, body mass index, parity before surgery, and history of infertility before surgery age (median HR 1.74, 95% SI 1.06-2.94). This difference remained after also adjusting for history of endometriosis (median HR 1.79, 95% SI 1.02-3.23). The difference was more marked amongst those who reported attempting pregnancy (median HR 2.49, 95% SI 1.16-6.40). The model-based predicted mean level of AMH and AFC were predicted for a woman at the median age at clinic visit.

OBJECTIVE: To test the feasibility of rete tests ultrasound guided puncture in humans for either sperm retrieval or spermatogenic stem cell injection and colonization.

DESIGN: Tests ultrasound exploration first in rhesus monkeys, and later in humans undergoing vasectomy reversal or micro-surgical tests sperm retrieval (TESE).

MATERIALS AND METHODS: 7 Rhesus monkeys were anesthetized and subjected to ultrasound guided exploration of each testis. In one animal with large tests, it was difficult to visualize the rete. But in all animals, a 25 gauge needle was used to puncture the rete under ultrasound guidance. Then the same technique was applied to humans undergoing conventional micro-TESE or microsurgical vasectomy reversal.

RESULTS: Germ cells were successfully retrieved from all 6 Rhesus monkeys in which the rete could be visualized. Visualization depended on the proper settings (Musculo-Skeletal) not the factory settings. In smaller testes, the rete was easier to see. The rete was easiest to visualize in the smaller testes. The anatomy of the human and Rhesus rete was different from what is depicted in most textbooks, which base their description and drawings on rodent testes. Actually the rete of the human and Rhesus is a linear collecting system from top to bottom right in the center of the testis, similar to an apple core.

CONCLUSIONS: The rete testis is the perfect collecting point for TESE in non-obstructive azoospermia, because it will contain sperm from every single seminiferous tubule, and it is easy to visualize with the proper ultrasound settings, which makes it accessible to simple needle puncture.

OUTCOME OF HYSTEROSCOPIC REPAIR OF SYMPTOMATIC CESAREAN SCAR DEFECT. Diaa M. Aklan, M.D.* † Hesham A. Salem, M.D.,* ‡ Moustafa Z. Moustafa, M.D.* † Emam A. Abdelnaby, M.D.* † Amro D. Aklan, MBCHB,* † Mohamed H. A. Salem, MBCHB,* ‡Professor

FERTILITY & STERILITY
BACKGROUND: Cesarean section scar defect is currently a more frequently detected problem due to increased rate of cesarean section deliveries worldwide. Cesarean scar defect may be presented by: Post-menstrual uterine bleeding, chronic pelvic pain, dysmenorrhea and or dyspareunia.

OBJECTIVE: Evaluation of efficacy and safety of hysteroscopic treatment of symptomatic cesarean scar defect.

DESIGN: Prospective clinical observational study.

MATERIALS AND METHODS: • Setting: University hospital and private gynecologic endoscopy center.
• Patients: 40 patients with symptomatic cesarean scar defect who do not desire future pregnancy with myometrial thickness ≥ 3 mm at site of cesarean scar by transvaginal ultrasonography.
• Intervention: Hysteroscopic repair of cesarean scar defect.
• Main Outcome Measure: Relief of symptoms, occurrence of operative related complications and adequacy of repair of the defect evaluated by transvaginal ultrasonography.

RESULTS: Among 40 patients postmenstrual bleeding was completely resolved in 29 patients (72.5%) of patients and partially improved in 5 patients (12.5%). On the other hand, complete relief of chronic pelvic pain was reported in 23 patients (69.7%) out of 33 patients, while partial relief was recorded in 5 patients (15.2%). As regard dysmenorrhea, complete improvement was recognized in 15 patients (60.9%) out of 23 patients, and partial improvement in 4 patients (17.4%).

CONCLUSIONS: Hysteroscopic repair of symptomatic cesarean scar defect is an efficient minimally invasive safe procedure suggested for management of this lesion.

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POST-CESAREAN SECTION VENTRAL UTERINE ADHESIONS, CLINICAL AND LAPAROSCOPIC CHARACTERISTICS OF 167 CASES. A PRELIMINARY REPORT OF UTEROLYSIS. Mahmoud A. Abdel-Aleem, MD, Ahmed M. Abbas, MD. Department of Obstetrics and Gynecology, Faculty of Medicine, Assiut university, Assiut, Egypt.

OBJECTIVE: Rising cesarean section (CS) rate increase the possibility of pelvic adhesions. A recognized type is ventral adhesions between the anterior wall of the uterus and anterior abdominal wall. The current study aims to estimate the link between post CS ventral uterine adhesions and female fertility.

DESIGN: A case control study included patients undergoing laparoscopy for secondary infertility after previous CS.

MATERIALS AND METHODS: Patients were described as "cases" if there were abnormal adhesions between the uterus and anterior abdominal wall, while "control" patients had no such adhesions. Lysis of pelvic adhesions was done up to the maximum restoration of anatomical relations between different pelvic organs. Patients were followed for 6 months after the procedure waiting for pregnancy to occur. Quantitative variables were presented in terms of mean and standard deviation. They were compared using a Student’s t test. Qualitative variables were presented as frequency and percentage. Chi-square test was used for comparison between groups. For analysis, p <0.05 was considered to be significant.

RESULTS: The study included 167 cases (study group) and 40 patients in the control group. Adhesion between the uterus and anterior abdominal wall were mainly grade 2. Satisfactory uterolysis was achieved in 56% of cases. Pregnancy occurred in 71% of cases. Among a total of 134 patients who got pregnant over the 6 months follow up period, 88.1% were cases and only 12 % were control (P=0.000). The extent of uterine adhesions had a definite effect on the occurrence of pregnancy; most cases had either grade 1 or 2. Associated severe adnexal adhesions were commoner in patients who didn’t get pregnancy than pregnant ones (19 % vs. 0.2%).

CONCLUSIONS: Ventral adhesions between the uterus and anterior abdominal wall secondary to CS seem to have a significant impact on fertility and can be successfully treated by laparoscopic uterolysis.

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DETERMINING THE IMPACT OF SURGICALLY RETRIEVED SPERMATOZOA FROM AZOOSPERMIC MEN ON EMBRYONIC DEVELOPMENT BY GENOMIC PROFILING. Stephanie Cheung, B.S., Zev Rosenwaks, M.D., Gianpiero D. Palermo, M.D., Ph.D., The Ronald O. Perelman and Claudia Cohen Center for Reproductive Medicine, Weill Cornell Medicine, New York, NY.

OBJECTIVE: To assess the ability of surgically retrieved spermatozoa to support a viable pregnancy by whole-exome sequencing.

DESIGN: To determine the impact of surgically retrieved spermatozoa on embryonic development, we assessed gene mutations of epididymal and testicular spermatozoa from men with acquired azoospermia (OA) and non-obstructive azoospermia (NOA), respectively, as compared to ejaculated sperm from donors.

MATERIALS AND METHODS: DNA was extracted and amplified from at least 500 spermatozoa (DNA concentration, 741±519 ng/ul; quality, 1.7±0.1 nm) obtained through surgical retrieval. Following NGS, gene mutations, duplications, and deletions were detected using the CLC Genomic Server 9.0. Genes were considered duplicated or deleted when the read depth was >1.5 or <0.5 times the median read depth for at least 70% of the exons in the control. Gene mutation profiles of the OA and NOA men were then assessed in relation to their ability to generate a pregnancy.

RESULTS: Of the 23 couples (paternal age, 41.3±4.9yrs) included in this study, 14 OA men underwent surgical sperm retrieval with a concentration of 1.3±3.5x10⁹/ml and 7.1±14% motility. Nine NOA men yielded spermatozoa with a concentration of 0.02±0.1x10⁹/ml and 5.5±0.5% motility. NGS assessment did not show a significant difference in overall sperm aneuploidy between the two groups (OA, 1.6%; NOA, 1.8%).

In the OA group overall, 3 genes were mutated (ATP4A, SLC17A7, and OR1D4), which were classified as housekeeping genes unrelated to embryonic development. In the NOA patients, 5 genes were found to be mutated. These were involved in RNA transcription (POLR2L), apoptosis (AP5M1), and protein sorting (AP1S2, AP1G2, and APOE).

The OA patients were treated in 14 ICSI cycles (maternal age, 38.7±7.9yrs), resulting in a pregnancy and delivery rate of 50% (7/14). While no relevant mutations were identified in the male partners, the couples that failed to achieve a pregnancy were older (P<0.05).

When NOA men were treated in 9 ICSI cycles (maternal age, 32.9±7.3yrs), the pregnancy rate was 66.7% (6/9). While the fertile cohort displayed 1 mutated gene (MPIG6B), related to stem cell lineage differentiation, the infertile NOA cohort had 5 mutated genes involved in apoptosis and early embryonic development.

CONCLUSIONS: Compared to fertile donors, OA men did not have any meaningful gene mutations, as expected by their post-vasectomy status. The NOA men who were able to generate a pregnancy had only 1 affected gene, apparently responsible for the reduced number but albeit competent spermatozoa. Those men unable to procreate carried gene mutations responsible for apoptosis and impaired embryonic development. Although this study still contains a limited number of observations, screening men for gene mutations can help characterize the spermatogenic function and competence of their germinal epithelium.

STEM CELLS

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INDUCTION OF SPERMATOGENESIS UNDER 3-DIMENSIONAL TISSUE CULTURE CONDITIONS BY IN VITRO TRANPLANTATION OF SPERMATOGONIAL STEM CELLS ISOLATED FROM HUMAN FROZEN-THAWED TESTIS TISSUE. Mahdi Mohaqiq, PhD, Mansoureh Movahedin, PhD, Zohreh Mazaheri, PhD, Naser AmiriJannati, MD, Mansoura Mokhtari, PhD, Afshin Emami, PhD, Mansoureh Movahedin, PhD, Mansoura Mokhtari, PhD, Afshin Emami, PhD. 1Department of Urology and 2Department of Urology, Tanta University Hospitals, Tanta, Egypt; 3Medical Student at Faculty of Medicine, Tanta University, Tanta, Egypt.

BACKGROUND: In vitro production of sperm is one of the most important processes in the body. In vitro production of sperm is one of the most important goals of research in the field of male infertility treatment, which is very important in male cancer patients treated with gonadotoxic methods and drugs. In this study, we examine the progression of spermatogenesis after

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transplantation of spermatogonial stem cells under conditions of testicular tissue culture.

DESIGN: Testicular tissue samples from azoospermic patients were obtained and then these were freeze-thawed. Spermatogonial stem cells were isolated by digestion steps and the identification of these cells was confirmed by detecting the PLZF protein. These cells, after being labeled with Dil, were transplanted in azoospermia adult mice model. The host testes were placed on agarose gel as tissue culture system. After 8 weeks, histomorphometric, immunohistochemical, and molecular studies were performed.

MATERIALS AND METHODS: For each experimental group, 3 to 5 NMRI mouse were used at the age of 4 weeks. These mice are treated with Busulfan 40 mg/kg and after 4 weeks, the Azoospermia model is developed. This study is based on 5 biopsy samples taken from different obstructive azoospermic patients. SSCs were isolated by Mirzapour & et al. (2012) protocol under two steps of enzymatic digestion. SSCs were transplanted into the host testes below the stereo microscope then they were cut into small pieces and placed under 3-D tissue culture conditions on the agarose support layer.

RESULTS: The results of histomorphometric studies showed that the mean number of spermatogonial cells, spermatocytes and spermatids in the experimental group was significantly more than the control group (without transplantation) (P<0.05) and most of the cells responded positively to the detection of Dil. Immunohistochemical studies in host testes fragments in the experimental group express the PLZF, SCP3 and ACRBP proteins in spermatogonial cells, spermatocyte and spermatozoa, respectively, which confirmed the human nature of these cells. Also, in molecular studies of PLZF, SCP3 and ACRBP proteins in the experimental group was significantly more than the control group, while not in the control group.

CONCLUSIONS: These results suggest that the slow freezing of SSCs can support the induction of spermatogenesis to produce haploid cells under the 3-Dimensional testicular tissue culture.

RESULTS: The dimensionality reduction tests PCA and DA showed a clear separation of PRE, ASCOT and POST samples (PC1: 38.9%, PC2 16.8% and D1 50%, D2 50%). Proteomic analysis identified a total of 296 proteins in our plasma samples. Elution of proteins (3.7%, PPI enrichment p = 1.56e−3) were found differentially expressed in apheresis when compared to previous samples, while increased to 70 (23.6%, PPI enrichment p < 1e−05) in samples collected 3 months after ASCOT. The differentially regulated proteins were common in the two comparisons highlighting the reliability of the stem cell effect and were mainly involved in vasculogenesis, stem cell regenerative effects, anti-apoptosis, anti-inflammation and niche protection. We found that Endothelial protein C Receptor (EPCR), Thrombospilon (1 (TSP-1), Vascular Cell Adhesion Molecule (VCAM1) and Serpin7 (THBG) were upregulated after ASCOT, being VCAM1 and THBG previously described as decreased with aging. Of the downregulated proteins, we identified the Apolipoprotein C5 and Vitamin D binding protein, which were previously described as increased with aging.

Presence of higher TSP-1 apheresis levels were found in patients whom AMH increased (p = 0.04).

CONCLUSIONS: Non-cellular components of apheresis could be crucial on the ovarian reserve observation observed after ASCOT in PR. These results allowed us the identification of specific proteins related to tissue regeneration and raised the possibility of long-term systemic effects induced by stem cell, according to several spontaneous pregnancies reported up to 6 months after ASCOT treatment. Nevertheless, this is a descriptive analysis of the proteomic modifications induced by stem cell ovarian transplant that should be confirmed in a larger population of patients with advanced maternal age or diminished ovarian reserve.

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AUTOLOGOUS PRP FOR THE MANAGEMENT OF THIN ENDOMETRIUM IN FROZEN EMBRYO TRANSFER CYCLES: WOULD IT IMPROVE THE OUTCOME? Siddhartha Nagireddy, MCh(Reproductive medicine and Surgery),1 N. Sanjeeva Reddy, MD (Obstetrics and Gynaecology), DGO,2 Monna Pandurangi, MD (Ob & Gynt),1 Radha Vembu, DGO, DNB (Obstetrics and Gynaecology), MNAMS, FICS, FIMG, PhD,1 Manjula Daniel G, PhD,2 Sindhuja Namboori Ninivasan, MBBS, M.Sc Clinical Embryology, PhD Research Scholar,1 Lahari Katneni, MS (Ob & Gynt),1 Assistant Professor, Sri Ramachandra Institute of Higher Education and Research, Chennai, India;3 Professor and Head, Department of Reproductive Medicine and Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, India;4 Associate Professor, Department of Reproductive Medicine and Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, India;5 Embryologist, Chennai, India;6 Bachelor of medicine, bachelor of surgery(MBBS), MSc Clinical Embryology, Chennai, India; Postgraduate in MCH Reproductive Medicine and Surgery, Sri Ramachandra Institute of Higher Education and Research, Chennai, India.

OBJECTIVE: Autologous platelet rich plasma (PRP) has emerged as a newer modality of treatment to improve endometrial thickness (ET) in cases of thin endometrium. Platelet activation would release growth factors from the alpha granules such as VEGF, EGF, PDGF, TGF and other cytokines, which may facilitate endometrial development. The present study was aimed to study the effect of autologous PRP on endometrial development in cases of thin endometrium in frozen embryo transfer cycles.

DESIGN: Non-randomized single arm trial.

MATERIALS AND METHODS: All women aged 20 - 40 years, presenting with thin endometrium (<7 mm) on day 11 of HRT (hormone replacement therapy) for FET (frozen embryo transfer) were included in the study. Patients with previous endometrial disease such as asherman syndrome, tubercular endometritis, mullerian anomalies, and premature ovarian failure were excluded. Endometrial preparation was performed by GnRHa down regulation and HRT by estradiol valerate at 6mg/day. PRP was prepared by two step centrifugation method, and administered intrauterine by IUI catheter. Repeat USG evaluation of endometrium was performed on Day 15 (4 days after PRP instillation). Statistical analysis was performed by Paired sample T test and Chi square test through SPSS version 17 software. P<0.05 was considered statistically significant.

Parameter | Result
--- | ---
Age | 32 ± 3.79
Male factor | 13 (46.4%)
PCOS | 03 (10.7%)
Tubal factor | 05 (17.9%)
Fibroid uterus | 01 (3.6%)
Endometriosis | 01 (3.6%)
Decreased ovarian reserve | 03 (10.7%)
Unexplained | 02 (7.1%)
Endometrial thickness (ET) before PRP | 6.3 ± 1.0
Endometrial thickness (ET) after PRP | 7.0 ± 1.1
No. of patients with good endometrial vascularity (Grade II & III) before PRP | 11 (39.3%)
No. of patients with good endometrial vascularity after PRP | 12 (42.8%)
No. of patients with improved ET (≥ 7 mm) | 20 (71.4%)
No. of patients with cycle cancellation | 08 (28.6%)
Preparation rate of transferred patients | 35% (7/20)
Implantation rate | 14.2%
Misscarriage rate | 14.2% (1/7)
Ongoing pregnancy | 02 (10.0%)
Live birth rate | 04 (20.0%)
RESULTS: Of the 28 women who presented with thin endometrium, 20 patients (71.4%) had increased ET to ≥ 7 mm, and underwent frozen embryo transfer. Eight patients (28.6%) had cycle cancellation due to persistent thin ET. There was a significant increase in the ET after PRP instillation: from 6.3 ± 1.0 to 7.0 ± 1.1 mm; P = 0.003. In transferred cycles, the pregnancy rate was 35% and implantation rate was 14.2%. The ongoing pregnancy and live birth rates were 14.2% and 20% respectively.

CONCLUSIONS: 1. Autologous PRP significantly improves endometrial thickness in cases of thin endometrium in FET cycles.
2. Intrauterine instillation of autologous PRP considerably reduces cycle cancellation in FET cycles.


EXOSOMAL MIR-664-5p DERIVED FROM HUMAN BONE MARROW MESENCHYMAL STEM CELLS IMPROVE OVARY FUNCTION OF PREMATURE OVARIAN FAILURE BY TARGETING p53 SIGNALING PATHWAY.

OBJECTIVE: Although many reports show that various kinds of stem cells have the ability to recover the function of premature ovarian failure(POF), few studies are associated with the mechanism of stem cell treatment of POF. We designed this experimental study to investigate whether human bone marrow stem cell-derived exosomes(hMSC-Exos) retain the ability to restore ovarian function and how hMSC-Exos work in this process. DESIGN: A POF mouse model was established and Cisplatin-damaged granulosa cells (GCs) were prepared to illuminate the mechanism of hMSCs in curing POF. MATERIALS AND METHODS: The hematopoietic and eosin assay method was employed to assess the number of follicles. Enzyme-linked immunosorbent assay (ELISA) was used to detect the serum levels of sex hormones. Cellular activity and apoptosis were measured by flow cytometry and CCK-8. Real-time PCR was used to determine the protein expression levels of p53 and exosomal miRNA secreted by hMSCs. Real-time PCR was used to detect the expression of p53 mRNA and the expression of in ovarian and granulosa cells. site-directed mutagenesis was used to establish p53 3'UTR mutant granulosa cells; miRNA mimics and miRNA inhibitor were used to target regulating the expression of hMSCs exosome-derived miR-664-5p. Western blot assays were used to test the protein expression levels of apoptosis genes (p53, Fas, FasL, caspase-3, and caspase-9). RESULTS: After the hMSC-Exos were transplanted into the POF mice model, they exerted better therapeutic activity on mouse ovarian function, improving follicle numbers during four stages. ELISA results showed that the expression of cell apoptosis genes was elevated in POF mice, and then decreased after hMSCs-Exos were cocultured with POFGCs, our results showed that hMSCs-Exos significantly promoted the proliferation rate and inhibited the apoptosis rate. Besides, miRNA and protein assays demonstrated that hMSCs-Exos downregulated the expression of p53 in vivo and in vitro. A series of microRNAs targeting p53 were screened by bioinformatics, and the expression of mir-664-5p was significantly increased in MSC exosomes. Western blot assay demonstrated that hMSCs-Exos inhibited expression of the apoptosis genes in POFGCs. CONCLUSIONS: These findings demonstrate for the first time the molecular cascade and related cell biology events involved in the mechanism by which exosomal mir-664-5p derived from hMSCs improved ovarian function of POF disease via regulation of the p53 signaling pathway. REFERENCE: 1. Joop S. E. Laven. Premature ovarian insufficiency. Semin Reprod Med 2016; 34(4): 230-234. 2. Jagarlamudi K, Reddy P, Adhikari D, Liu K. Genetically modified mouse models for premature ovarian failure (POF). Mol Cell Endocrinol. 2010; 315:1-10. 3. Torrealday S, Kodaman P, Pal L. Premature Ovarian Insufficiency- an update on recent advances in understanding and management. F1000Res, 2017; 6:2069-2083. 4. Kozub MM, Prokopiuik VY, Skibina KP. Comparison of various tissue and cell therapy approaches when restoring ovarian, hepatic and kidney’s function after chemotherapy-induced ovarian failure. Exp Oncol, 2017, 39(3): 181-185.


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SUPPORT: Henan Province Medical Science and Technology Research Project Joint Co-construction Project, 2018020116. The Chinese Medical Association clinical medical research special fund project, 17Z020190688.
embryo quality was understood as 1) no fertilized MII's; 2) deficient-quality embryos according to morphologic criteria; 3) arrested embryos. Patients with abnormal chromosome were excluded. BMSCs were isolated from 20ml bone marrow and cultured. Three days before oocyte retrieval, mitochondrial DNA transfer was performed differentially from BMSCs. The retrieved oocytes were randomly and averagely divided into two groups i.e. Mitochondria transfer (MT) groups and control group. In MT group, 4000-5000 copies mitochondria DNA were injected into each oocyte during intracytoplasmic sperm injection. By means of a time-lapse system (EmbryoScope; Unisense FertiliTech, Aarhus, Denmark), this study determined the timing of a number of developmental parameters including cleavage timing from a zygote to a 6-cell embryo (72 ± 7, 14 ± 5, 18 ± 5, 27 ± 6) and assessed fragmentation at each stage. The intervals between two consecutive cleavage stages were also analyzed. During the second cell cycle (c2 = t 1 – t 2) is the time from the division into a two-blastomere embryo until the time to the division into a three-blastomere embryo, and second synchrony (s2 = t 4 – t 3) is the time from this division into a four-blastomere embryo.

RESULTS: A total of 25 patients were included and we got 231 oocytes in total. Their average age was 33.00 years old. The average antinullerian hormone level and antral follicles was 3.86 ng/ml and 14.68 respectively. Most of patients was primary infertility(72.22%) and the major cause of infertility was tubar factor(64.00%). We observed that the timings of all embryo cleavage stages (from 2to 8) together with fragmentation values showed no significant differences between embryos deriving from oocyte with MT or without MT. It was noteworthy that s2 was shorter in MT group, although difference didn’t reach statistical significance (4.20 vs. 5.90), in addition, Oocytes of MT groups had lower fertilization rate (89.06% vs.88.35%; P=0.865).

CONCLUSIONS: This study demonstrated that BMSC-derived autologous mitochondria transfer didn’t alter embryonic development kinetics. It might help to improve embryo development synchrony and fertilization.

THE WEB

P-794 Wednesday, October 16, 2019 6:30 AM

HATETAGS AND HATCHING: AN ANALYSIS OF INFORMATION AND INFLUENCE IN FERTILITY-RELATED SOCIAL MEDIA. Arielle H. Bayer, MD, a Jennifer K. Blakemore, MD, b Meghan B. Smith, MD, b James A. Grifo, MD, PhD. a NYU Langone School of Medicine, New York, NY. a,bUniversity of Southern California, Los Angeles, CA. a,bNYU Langone Prelude Fertility Center, New York, NY.

OBJECTIVE: 79.9% of patients surveyed in a fertility clinic felt social media (SM), the use of electronic communication to share information, benefited the patient experience.1 Up to 40% of Americans doubt professional opinion when it conflicts with web-based findings.2 We examined 537 (278 TW, 259 IG) were included. There were 4 academic/professional societies used on 3/26/19 to generate a list of accounts with the terms: fertility, infertility, ttc, egg freezing, ivf, endometriosis and reproduction. The most frequent content by platform did not accurately classify INFs.

Platforms utilized included Facebook (91.4%), Instagram (85.2%), Snapchat (54.6%) and Twitter (41.9%). Instagram and Facebook were noted to have the highest daily engagement (46.4% and 43.6% respectively, vs 3.2% with Twitter). Instagram was cited as the most enjoyable to use social media (87.4%) and Twitter was the most engaged social media platform (54.6% and 41.6% respectively). Most content was tubar factor(64.00%). We observed that the timings of all embryo cleavage stages (from 2to 8) together with fragmentation values showed no significant differences between embryos deriving from oocyte with MT or without MT. It was noteworthy that s2 was shorter in MT group, although difference didn’t reach statistical significance (4.20 vs. 5.90), in addition, Oocytes of MT groups had lower fertilization rate (89.06% vs.88.35%; P=0.865).

CONCLUSIONS: As patients increasingly utilize SM to obtain and engage with health information, it is critical for REI physicians and clinicians to understand the fertility-related SM landscape in order to successfully enhance relationships with patients and ensure dissemination of accurate and evidence-based information.


SUPPORT: None.

P-795 Wednesday, October 16, 2019 6:30 AM

UNDERSTANDING THE ROLE OF SOCIAL MEDIA FOR PHYSICIANS. Natalie M. Crawford, MD, MSCR, a Emily Evans-Hoeker, MD. a,b Aspire Fertility Austin, Austin, TX. a,bVirginia Tech Carilion School of Medicine, Roanoke, VA.

OBJECTIVE: To evaluate current use and perceptions of physician usage of social media among users.

DESIGN: Survey study.

MATERIALS AND METHODS: Social media users, recruited via multiple social media platforms (blogs, Facebook, Instagram, Twitter), were asked to complete an electronic survey evaluating the role of social media in medicine.

RESULTS: A total of 3,080 people participated the survey. A majority of respondents were Caucasian (81%), highly educated (87.5% completion of 4 year degree or more), women (98.9%) of reproductive age (18-44 years, 92.8%). Platforms utilized included Facebook (91.4%), Instagram (85.2%), Snapchat (54.6%) and Twitter (41.9%). Instagram and Facebook were noted to have the highest daily engagement (46.4% and 43.6% respectively, vs 3.2% with Twitter). Instagram was cited as the most enjoyable platform for obtaining medical information (44% vs 18.1% for Facebook and 3.1% for Twitter). Most participants enjoyed learning about medical information on social media (84.8%), reported following at least one physician (75.3%), and indicated they would schedule an appointment with a physician they follow (74.6%), even if it required travel (54.4%). Of those who do not enjoy medical information on social media, 74.4% don’t trust the accuracy of the information, and 41.6% only want to use social media for fun.

Most consumers (59.8%) enjoy seeing their doctor on social media due to: finding medical information interesting (66.1%), understanding what their

TABLE 1. Interest in Topics Posted by Physicians

<table>
<thead>
<tr>
<th>Topic</th>
<th>Interest (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical facts</td>
<td>91.2%</td>
</tr>
<tr>
<td>Behind the scenes as a physician</td>
<td>88.1%</td>
</tr>
<tr>
<td>News-worthy research</td>
<td>87.6%</td>
</tr>
<tr>
<td>Work-life balance</td>
<td>86.6%</td>
</tr>
<tr>
<td>Clinical cases</td>
<td>84.6%</td>
</tr>
<tr>
<td>Behind the scenes personal</td>
<td>78.3%</td>
</tr>
<tr>
<td>Motivational posts</td>
<td>77.4%</td>
</tr>
<tr>
<td>Medical pictures</td>
<td>73.8%</td>
</tr>
<tr>
<td>Educational videos</td>
<td>73.7%</td>
</tr>
<tr>
<td>Local activities</td>
<td>68.7%</td>
</tr>
<tr>
<td>Live Q&amp;A</td>
<td>62.7%</td>
</tr>
<tr>
<td>Path to becoming a physician</td>
<td>62.6%</td>
</tr>
<tr>
<td>Giveaways</td>
<td>50.4%</td>
</tr>
</tbody>
</table>
there is opportunity to further increase public awareness of infertility through
urence this disparity, including duration of the campaign and resources
volume for the term ‘infertility,’ but this was substantially less than the in-
crease of 27.1% during the study period, not meeting the definition of sig-
ificant. In contrast, BCAM led to a significant increase in mean RSV for
NIAW and Breast Cancer Awareness Month (BCAM). Awareness
volumes (RSV) were determined for each year from 2010 – 2018 for ‘infertility’
trends.

OBJECTIVE: National Infertility Awareness Week (NIAW) aims to raise
awareness among the general public regarding infertility and ‘remove the
stigmas and barriers that stand in the way of building families.’ While the
success of other health awareness campaigns, most notably breast cancer,
have been well documented, the efficacy of infertility awareness campaigns
is less well characterized. Using internet search volume as a surrogate for
public interest, we sought to assess the efficacy of NIAW.

DESIGN: Retrospective, cross-sectional study examining internet search
trends.

MATERIALS AND METHODS: Using Google Trends, the relative search
volumes (RSV) were determined for each year from 2010 – 2018 for “infertility”
and “breast cancer,” the latter serving as a comparison campaign with well-
documented success. Baseline annual RSV was calculated by deter-
mining the median weekly RSV for each year. The RSV was then determined for
NIAW and Breast Cancer Awareness Month (BCAM). Awareness
campaign RSV was then compared with the yearly baseline RSV. Significant
increase was defined as a two-fold rise from baseline.

RESULTS: Search volumes for “infertility” increased from a mean RSV
of 77.5 at baseline to 97.98 during NIAW with a mean yearly search volume
increase of 27.1% during the study period, not meeting the definition of sig-
nificant. In contrast, BCAM led to a significant increase in mean RSV for
“breast cancer” from 28.1 at baseline to 100 during the awareness month
with a mean increase of 263.1%.

CONCLUSIONS: NIAW is associated with an increase in internet search
volume for the term “infertility,” but this was substantially less than the in-
crease for “breast cancer” seen during BCAM. Many parameters might influ-
ence this disparity, including duration of the campaign and resources
expended for campaign promotion. While additional metrics are needed to
evaluate the efficacy of public health campaigns, the current data suggest
there is opportunity to further increase public awareness of infertility through
the NIAW campaign.

SUPPORT: None.

TABLE 1. Percent rise in relative search volume (RSV) for the terms “breast
cancer” and “infertility” during Breast Cancer Awareness Month and National
Infertility Awareness Week from 2010 – 2018. *Denotes significant rise in RSV
from baseline.

<table>
<thead>
<tr>
<th>Year</th>
<th>NIAW (%)</th>
<th>BCAM (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>23.5</td>
<td>284.6*</td>
</tr>
<tr>
<td>2011</td>
<td>1.8</td>
<td>257.1*</td>
</tr>
<tr>
<td>2012</td>
<td>37.0</td>
<td>334.8*</td>
</tr>
<tr>
<td>2013</td>
<td>12.8</td>
<td>308.2*</td>
</tr>
<tr>
<td>2014</td>
<td>19.0</td>
<td>316.7*</td>
</tr>
<tr>
<td>2015</td>
<td>37.9</td>
<td>257.1*</td>
</tr>
<tr>
<td>2016</td>
<td>34.2</td>
<td>194.1*</td>
</tr>
<tr>
<td>2017</td>
<td>44.9</td>
<td>203.0*</td>
</tr>
<tr>
<td>2018</td>
<td>32.5</td>
<td>212.5*</td>
</tr>
</tbody>
</table>
ONLINE PATIENT EDUCATION INCREASES USE OF SINGLE EMBRYO TRANSFER. Deborah Anderson, JD FertilityIQ, San Francisco, CA.

OBJECTIVE: To ascertain to how online patient education impacts a US patient’s decision of whether to transfer one embryo per transfer (eSET).

DESIGN: 62 US patients were surveyed who met two strict criteria: #1 Would soon undergo a transfer whereby multiple embryos were available for transfer and B. Had completed a 10-minute online video course on the trade-offs of “Single or Multiple Embryo Transfer.”

MATERIALS AND METHODS: Surveys were sent to patients electronically following their date of expected embryo transfer. Results were compiled using Qualtrics Surveys & regression was run to account for patient age, embryo stage, PGT-A results or insurance coverage.

RESULTS: Of the 62 surveyed patients, 33 (79%) elected for a single-embryo transfer, of whom 72% believed the online course was “critically influential” in their decision of how many embryos to transfer. By contrast, less than 42% of those who did not complete the course believed the online course was “critically influential” in their decision making. Reassuringly, most of these websites were hospital based, and 72% provided unbiased information. Patients should be cautioned that incomplete and potentially biased information on male infertility is prevalent online.

CONCLUSIONS: Websites on “male infertility” are of low quality, and only 6.7% met JAMA benchmark criteria. Minimal information on treatments was present, with only 25% of websites describing treatment benefits, but only 5% describing treatment risks. Only 15% of websites described areas of clinical uncertainty. Despite that these websites were written at a college to graduate degree level of reading, only 27% encouraged shared decision making. Reassuringly, most of these websites were hospital based, and 72% provided unbiased information. Patients should be cautioned that incomplete and potentially biased information on male infertility is prevalent online.

P-799 Wednesday, October 16, 2019 6:30 AM

ONLINE PATIENT EDUCATION INCREASES USE OF SINGLE EMBRYO TRANSFER. Deborah Anderson, JD FertilityIQ, San Francisco, CA.

OBJECTIVE: To ascertain to how online patient education impacts a US patient’s decision of whether to transfer one embryo per transfer (eSET).

DESIGN: 62 US patients were surveyed who met two strict criteria: #1 Would soon undergo a transfer whereby multiple embryos were available for transfer and B. Had completed a 10-minute online video course on the trade-offs of “Single or Multiple Embryo Transfer.”

MATERIALS AND METHODS: Surveys were sent to patients electronically following their date of expected embryo transfer. Results were compiled using Qualtrics Surveys & regression was run to account for patient age, embryo stage, PGT-A results and insurance coverage.

RESULTS: Of the 62 surveyed patients, 33 (79%) elected for a single-embryo transfer, of whom 72% believed the online course was “critically influential” in their decision of how many embryos to transfer. By contrast, less than 42% of surveyed patients believe their doctor provided an “in-depth discussion” on the subject. Results persisted after accounting for potential confounders such as patient age, embryo stage, PGT-A results or insurance coverage.

CONCLUSIONS: Online patient education may compliment societal and clinical efforts to encourage patients to consider the benefits of elective single embryo transfer.

P-800 Wednesday, October 16, 2019 6:30 AM

UTILIZATION OF SOCIAL MEDIA FOR PERSONAL BRANDING BY PHYSICIANS. Natalie M. Crawford, MD, MSCR,a Emily Evans-Hoeker, MD,b sAspire Fertility Austin, Austin, TX; aVirginia Tech Carilion School of Medicine, Roanoke, VA.

OBJECTIVE: To evaluate the current usage of social media by physicians in medical practice.

DESIGN: Survey study.

MATERIALS AND METHODS: Physician users of social media, recruited via private physician Facebook groups and Instagram, completed an electronic survey evaluating the use of social media in medical practice and marketing.

RESULTS: 200 physicians participated in the survey. Most were Caucasian (81.9%) and of reproductive age (18-44 years, 80.4%). A majority of physicians (58.8%) were in private practice and had been out of training for 5 years or more (68%). Social media platforms most commonly utilized included Facebook (100%), Instagram (51.2%), Twitter (38.4%), and Snapchat (20%). Few physicians had a personal blog or website (8.8%).

CONCLUSIONS: Opportunities for personal branding and educating target populations via social media are likely underutilized by current physicians. Although the majority of physicians believe consumers enjoy medically related content on social media, there is a reluctance to posting medical content on a social platform. Efforts for personal branding and marketing could be improved by targeting popular platforms and topics preferred by the ideal audience.

IVF OUTCOME PREDICTORS

P-813 Wednesday, October 16, 2019 6:30 AM

PATERNAL FACTORS AND EMBRYO ANEUPLOIDY: IS SOMETHING RELATED?. Thiago F. Nunes, MD,a Andrea Belo, BSc,b Nathaly M. Menezes, BSc,b Thiago A. C. L. Lotti, BSc,b Nathalia Moreti, BSc,b Bruna Lima, BSc,b Isabela Mantelato, BSc,b Caroline Fauth, BSc,b Paulo Cesar Serafini, MD, PhDb, Thais S. Domingues, MD, PhDb, Aline R. Lorenzon, PhD,b Jose Roberto Alegetti, MSc,b Eduardo L. A. Motta, MD, PhD,b Guilherme J. A. Wood, MD, PhDa “Huntington Medicina Reprodutiva, Sao Paulo, Brazil; bHuntington Medicina Reprodutiva, Embryology Department, Sao Paulo, Brazil; bScientific Coordinator, Huntington Medicina Reprodutiva, Sao Paulo, Brazil.

OBJECTIVE: The high incidence of aneuploidy observed in preimplantation embryos is one of the most significant factors affecting the clinical outcomes in assisted reproduction treatments. We investigate the correlation between paternal factors that could have impact on embryo aneuploidy in an oocyte donation program, including male age, sperm concentration, morphology and DNA sperm fragmentation.

DESIGN: Retrospective analysis of Preimplantation Genetic Testing for Aneuploidy (PGT-A) data of biopsied embryos from an oocyte donation program in a private clinic in Sao Paulo, Brazil.

MATERIALS AND METHODS: The present study analyzed cycles from an oocyte donation program, which minimized the impact of anomalies arising from the female gamete. Between January 2017 and March 2019, a total of 229 biopsied embryos from 75 cycles have been analyzed by NGS (next generation sequencing) for numerical and structural abnormalities in chromosomes. Embryo biopsies were performed at blastocyst stage (day 5 or 6), and were allocated according to paternal age in two groups; <= 41 years (n = 26) and > 42 years (n = 49); sperm concentration in normozoospermic (n = 67) and oligozoospermic (n = 8); morphology according to Kruger’s strict criteria (> 4D, < 4D and < 4, respectively); and DNA sperm fragmentation has been assessed in 29 cases.

RESULTS: The results show a median paternal age of 44.7 years, with an average number of fertilized embryos of 6.2 and 1.9 of blastocysts at day 5 and 6. Of the 229 biopsied embryos, 143 were normal and 86 altered embryos
(37.55%), including 79 numerical and 7 structural abnormalities. Comparing the variables, the advanced paternal age was not related to an increase in the absolute number of embryo aneuploidy (p=0.15). The sperm concentration showed no statistical difference between normo and oligospermic males (p=0.70). According to strict morphology, Kruger < 4% had 36% of aneu-

ploidy comparing with 42.5% in Kruger > = 4 (p=0.38). Comparing sperm DNA fragmentation and aneuploidy, we did not observe difference between the groups using a cut-off of 15% in the fragmentation rate (p=0.08).

CONCLUSIONS: Therefore, these results suggested that the paternal factors, including age, sperm count, strict morphology and DNA sperm fragmentation were not related to the aneuploidy rate in preimplantation embryos in an oocyte donation program.

P-814 Wednesday, October 16, 2019 6:30 AM

OBJECTIVE: To evaluate whether the proportion of mature oocytes retrieved affects clinical intracytoplasmic sperm injection (ICSI) outcome.

DESIGN: Consenting couples with a female partner ≤35 years of age treated by ICSI at our center between 1993 and 2017 were included in this study. Cycles were allocated to four groups based on the proportion of meta-phase-II (MII) oocytes at the time of injection: optimal (70-100%), adequate (75-75%), partial (50-26%), and minimal (25-1%). Clinical outcome was compared among the four groups.

MATERIALS AND METHODS: Couple age, body mass index, smoking and drinking habits, and demographics were controlled for in our study. Oocyte retrieval and the ICSI procedure were performed in the standard fashion. Cycles without oocytes injected on the day of retrieval were excluded. Embryology and clinical outcome were recorded.

RESULTS: In total, there were 7,672 ICSI cycles included: 4,838 in the optimal group, 2,252 in the adequate group, 518 in the partial group, and 64 in the minimal group. There was no difference in the average number of oocytes retrieved per cycle.

Among the four groups, a decreasing proportion of MII oocytes lowered the fertilization rate from 78% to 71% (P < 0.0001) while raising the rate of 3PN embryos from 2% to 4% (P < 0.01). There was a concurrent reduced number of good-quality embryos (P < 0.0001) that resulted in a decreasing number of blastocysts cryopreserved (P < 0.0001).

The implantation rate fell from 33% in the optimal group to as low as 17% in the minimal group (P < 0.0001); thus, the clinical pregnancy rate dropped from 63.6% in the optimal group to 60.9% in the adequate, 52.1% in the partial, and 37.5% in the minimal groups (P < 0.0001). Consequently, the live birth rate decreased from 49.2% in the optimal group to 26.6% in the minimal group (P < 0.0001), whereas pregnancy loss rose inversely with oocyte maturity, from 22.6% in the optimal group to 29.1% in the minimal group (P = 0.001).

CONCLUSIONS: The different ICSI outcomes seen with the use of MII oocytes can only be explained by differences in ooplasmic maturity. Achieving an optimal proportion of mature oocytes may enhance fertilization and consequent embryo development and implantation.

P-815 Wednesday, October 16, 2019 6:30 AM
LONG-ANTAGONIST PROTOCOL: A NEW PROTOCOL WHERE A BOLUS LUTEAL DOSE OF LONG-ACTING GnRH-ANTAGONIST DEGARELIX CAN EFFICIENTLY DOWNREGULATE LH DURING OVARIAN STIMULATION FOR IVF ADDRESSING FLEXIBILITY IN AN ANTAGONIST PROTOCOL. Evangelos Papanikolaou, MD, PhD, Evangelia Timiothou, MSC, Carlo Aliviggi, MD, PhD, Petroula Tatsi, MSC, Tatiana Chortamatsidou, MSC, Eirini Asouchidou, MD, PhD, Dimitrios Petropiannis, Sr., MD, PhD, Robert Najdecki, MD, PhD, Apostolos Athanasiadis, MD, PhD, Assisting Nature, Center of Assisted Reproduction and Genetics, Thessaloniki, Greece; 2Fertility Unit, University of Naples Federico II, Naples, Italy; 3Medical Department, Aristotle University of Thessaloniki, Thessaloniki, Greece; 4PetropiannisNikolaos, Deputy Director of IVF Unit Naval and Vet-

ers Hospital of Athens, ATHENS, Greece; 53rd Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki, Thessaloniki, Greece. OBJECTIVE: The purpose of that study was to examine whether a bolus luteal dose of a new long-acting GnRH-antagonist can be compared with the classical short with follicular multiple doses antagonist protocol.

DESIGN: In this randomized control trial, did participate 129 infertile women aged 39 years of age prepared to undergo IVF treatment in Assisting Nature Centre. Trial registration number was NCT03684421 and performed between January 2017-January 2019. Two groups of patients were compared: Control-Group (Short Antagonist group) consisted of 69 women, who followed a classical fixed day-6 GnRH-antagonist protocol whereas, Study-Group (new Long Antagonist Group) involved 60 women undergoing the new long-antagonist protocol.

MATERIALS AND METHODS: The new protocol was as follows: in late luteal phase (day-24) a bolus injection of 0.5 mL Degarelix was administered subcutaneously. After menses, initiation of ovarian stimulation was flexible, with gonadotropins (200-300IU) could be initiated from cycle-day-2 to cycle-day-10 and no other dose of antagonists was allowed. In the classical short antagonist-group gonadotropins 200-300IU started on day-2 or 3 of the cycle and the 0.25 mg of antagonist (ganielex) was administered daily from stimulation day-6 in a fixed way. Ovulation triggering was administered when 3 follicles of 18mm were present and recHCG was used (unless more than 14 follicles were present then agonist triggering was proferred). Oocyte pick was performed 36h later. On day blastocyst transfer was decided upon response and progesterone rise.

RESULTS: No LH rise was noticed first of all in any patient. The mean age (33 ± 3, 33,0) and AMH (2.4 vs. 2.1) were not different among groups. Nevertheless, duration of stimulation ranged from 9-10 days in control group, whether in study-group ranged from 10-11 days. Similar number of oocytes retrieved (10.8 vs. 11.8) and similar mean number of blastocysts produced in both groups (5.0 vs. 5.5). No OHSS case was reported in both groups. Fresh embryo transfer was performed in 30/69 patients in control-group and the rest 39 patients underwent frozen embryo transfer in a Freeze-All strategy. Similarly, fresh embryo transfer was performed in 20/60 patients in study-group and the rest 40 patients underwent frozen embryo transfer in a Freeze-All strategy. Cumulative ongoing/delivery rate was 44.9% (n=31/69) in classic antagonist (Control-group) and 50.0% (30/60) in the new Long Antagonist (Study-group), p<0.05.

CONCLUSIONS: That new concept combines the II flexibility of the long agonist protocol, the security of the antagonist protocol, and eventually similar pregnancy efficacy as both of them used to. This new Long-Antagonist protocol addresses cycle programming that was missing with antagonist protocols and at the same time minimizes the risk for OHSS. It is for first time that a single dose of long-acting antagonist Degarelix, during luteal phase is described to efficiently down-regulate LH, produce mature eggs and implantable embryos. However, larger studies are required to confirm the success of this protocol.

P-816 Wednesday, October 16, 2019 6:30 AM
EUPLIOD EMBRYOS WHEREA ONLY 1PN OR NO PRONUCLEI (PN) WERE SEEN HAVE DELIVERY RATES COMPARABLE TO EUPLIOD 2PN EMBRYOS. Caroline McCaffrey, Ph.D., David H. Mc Culloh, Ph.D., b Hsiao-Ling Lee, BS, a Andrea G. Besser, MS, Xinjian He, MS, b Frederick L. Licciardi, M.D., b James A. Grifo, MD, PhD, c New York Langone Health, NYU Fertility Center, New York, NY; cNYU Langone Fertility Center, New York, NY; cNYU Langone Health, New York, NY. OBJECTIVE: To determine the incidence of euploid and implantation and delivery of Blastocysts derived from 0PN and 1PN compared with 2PN embryos.

DESIGN: Single center retrospective review of PGT-A cases over a 4 year period (2015-2018) where a biopsy and ploidy determination was performed on blastocysts (blasts) derived from zygotes where pronuclei (PNs) were either not evident (0 PN) or only 1 pronucleus (1 PN) were evident at the time of fertilization check.

MATERIALS AND METHODS: At our center fertilization checks are routinely conducted ~18 hours post insemination or ICSI. The number of PN in each egg is recorded and zygotes cultured individually. Cases where < 50% of the mature eggs exhibit 2PN are routinely rechecked later on Day 1 and omitted from this study if additional PNs seen. In cases for PGT-A, all viable inseminated eggs excluding those with > 3 PN remain in culture to Day 6/7. Good quality blastocysts with a distinct Inner cell mass and cohesive trophoderm are considered for PGT-A regardless of
whether they were 0PN, 1PN or 2PN at fertilization check. PGT-A results are shown in Table 1 along with PGT-A sex of blast derived from each group.

RESULTS: Prior to utilization of PGT-A and/or time-lapse zygotes not exhibiting 2PN at fertilization check were routinely discarded. However, it is now obvious that a percentage of these, albeit small, are fertilized normally and euploid. Though they account for only a small percentage, they may be the only euploid blast available. Implantation rates and LR rates following transfer of these blast are similar to those for 2PN blastocysts. Of interest, ratios of XX:XY blast derived from 1PN and 0PN zygotes were skewed towards female while those from 2PN zygotes were ~:1:1. It should be noted that NGS cannot detect pure haploidy (X, 2X) or triploidy (69, XXX) thereby possibly misdiagnosing these as euploid although our IR and LR results indicate otherwise.

SUPPORT: None

References: None

P-817 Wednesday, October 16, 2019 6:30 AM

SPERM MOTILITY IS ASSOCIATED WITH THE NUMBER OF GOOD QUALITY EMBRYOS PRODUCED IN WOMEN WITH DIMINISHED OVARIAN RESERVE. Amanda Adelye,Y MD, Z Liza Jalalian, BS, CLS,‡ Teresa Leung, B.S.,‡ Fleurdeliza Rabara, BS, CLS,* Marcelle I. Cedars, MD,⁎ Mitchell P. Rosen, MD, HCLD,⁎ UCSF REI fellow, San Francisco, CA; ‡University of California San Francisco, San Francisco, CA; *University of California San Francisco, Department of Obstetrics and Gynecology, San Francisco, CA; ⁎UCSF, San Francisco, CA.

BACKGROUND: Previous data suggests that semen parameters do not predict pregnancy rates after in vitro fertilization (IVF) in egg donation (OD) cycles. Less is known about the impact of semen parameters on IVF laboratory outcomes with good quality eggs and among women with diminished ovarian reserve (DOR) for whom may be more sensitive to subtle differences in semen parameters.

OBJECTIVE: To determine if semen parameters are associated with (1) IVF laboratory outcomes among egg donors with multiple cycles (2) IVF outcomes among women with DOR.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: We performed a chart review of all repeated egg donation cycles with different sperm sources and for women with DOR (<9 eggs collected) between January 1, 2010 and March 31st, 2019. The impact of semen parameters (volume, motility, and concentration) on the IVF laboratory outcomes including the number of normally fertilized eggs, good quality embryos (embryo(s) transferred + cryopreserved) and euploid rate were assessed in donor cycles and DOR with a mixed effects Poisson regression adjusting for age, eggs collected and repeated cycles.

RESULTS: 465 egg donation cycles and 2,456 DOR cycles were reviewed. The number of normally fertilized eggs differed in egg donation cycles in a univariate and multivariate model but these were not explained by semen parameters or male or female age (p<0.01 for both) There were no difference in the number of good quality embryos produced (p= 0.700). Among women with DOR, in a bivariate model adjusting for the number of eggs inseminated, sperm concentration was predictive of the number of normally fertilized embryos (p=0.037). After adjusting for male and female age and the method of sperm production (ejaculation vs surgical), concentration was not predictive of the number of normally fertilized eggs (p=0.082).

In a bivariate model, adjusting for the number of normally fertilized eggs, motility was predictive of the number of good quality embryos (p=0.042). Adjusting for male and female age and the method of sperm production, motility continued to be marginally predictive of the number of good quality embryos produced (p=0.046). A 10% increase in motility was associated with a predicted 0.012 increase in the number of good quality embryos.

CONCLUSIONS: When adjusting for within patient and between patient differences, semen parameters do not impact donor egg cycles but other male related predictors yet to be elucidated that impact fertilization. Among women with DOR, increased sperm motility is marginally associated with an increasing number of good quality embryos. Eggs from women with DOR may be less able to compensate for abnormal sperm function.

SUPPORT: None

P-818 Wednesday, October 16, 2019 6:30 AM

EVIDENCE-BASED EVALUATION OF REPEATED CYCLES OF OOCYTE DONATION BY THE SAME WOMAN: TREATMENT OUTCOMES ARE NOT ADVERSELY AFFECTED BY MULTIPLE PRIOR DONATIONS. Carol Lynn Curchoch, PhD, TS (ABB), Ashley Geka, BS, Heather Coulier, B.S. M.A., Rebecca Gu, BS, V. Julie Collier, TS, Sara Berkshire, BA, Lindsay Gates, BS, L.Ianda Anderson, BA, TS (ABB), Sigourney Anne Francisco, BS, Vanessa Julaton, PhD, TS (ABB), Jennifer Collins, MS, William Venier, MSc, ELD (ABB), Susanna Park, MD, Brooke Friedman, MD, Said Daneshmand, MD, Sandy Chuan, MD, L. Michael Kettel, MD San Diego Fertility Center, San Diego, CA.

OBJECTIVE: To evaluate the quality of oocyte cohorts retrieved from healthy young women undergoing repeated cycles of oocyte donation.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: Records of oocyte donation cycles performed at a single ART center from November 2011 through April 2019 were reviewed. The associations between oocyte donation cycle number and pre-treatment antral follicle count (AFC), total dosage of follicle-stimulating hormone (FSH) administered during ovarian stimulation, days of ovarian stimulation, follicles > 14 mm at trigger, retrieved oocyte number, mature (MII) oocyte number, the number of good quality blastocysts, and the percentage of euploid blastocysts among cycles undergoing PGT-A analysis by NGS were evaluated by linear regression analysis.

RESULTS: A total of 91 oocyte donation cycles among 18 oocyte donors (3 to 6 cycles each) were available for analysis. The total dosage of FSH administered per cycle remained constant across treatment cycle numbers. However, a higher number of prior oocyte donation cycles was associated with significantly increasing numbers of antral follicles, mature follicles (>14mm) at trigger, and mature (MII) oocytes retrieved.

CONCLUSIONS: Our investigative efforts focus on providing more couples the opportunity to have healthy children. One such group is egg donor recipients. There are limited available data on repeated ovulation stimulation cycles. It has been suggested that FSH stimulation may hasten ovarian aging by increasing recruitment of small growing follicles, thereby accelerating the depletion of follicle reserve. It has not been reported if repetitive oocyte donation affects average follicles recruited, oocyte maturity, blastocyst rate or ploidy status.

Increasing numbers of prior oocyte donation cycles are associated with a better response to ovarian stimulation, rather than adversely affecting treatment outcomes. Egg donation cycles 3-6 are associated with higher AFC;
more follicles > 14 mm at trigger, and retrieval of approximately one third more mature (MII) oocytes, relative to cycle 1. A reevaluation of the ASRM guidelines regarding numbers of oocyte donation cycles per woman may be warranted.

References: Repetitive oocyte donation does not decrease serum anti-Müllerian hormone levels. Bukulmez, Orhan et al. Fertility and Sterility, Volume 94, Issue 3, 905 - 912


P-819 Wednesday, October 16, 2019 6:30 AM

DOES LH SUPPLEMENTATION IN POOR RESPONDERS AFFECT GRANULOSA CELL APOTOPSIS RATE IN ART? Sebnem alanya Tosun, MD, a Enis Ozkaya, MD, a Basak Aru, PhD, b Gulderen Yanik, MD, PhD, c Ebru Cogendez, Jr., MD, c Mehmet Sipahi, MD d Giresun University School of Medicine, Department of Obstetrics and Gynecology, Giresun, Turkey; f Zeynep Kami Women and Children Diseases Education and Research Hospital, Istanbul, Turkey; y Yeditepe University, School of Medicine, Istanbul, Turkey; g Yeditepe University, Faculty of Medicine, Istanbul, Turkey; h Zeynep Kami Women and Children Education and Research Hospital, Istanbul, Turkey.

OBJECTIVE: To compare the granulosa cells apoptosis rate with or without luteinizing hormone (LH) supplementation in poor ovarian responders during controlled ovarian stimulation(COS) for assisted reproductive technologies (ART).

DESIGN: Prospective randomized controlled clinical trial comparing LH supplementation versus FSH only in poor ovarian response patients.

MATERIALS AND METHODS: A total of 40 women with poor ovarian response according to Bologna criteria enrolled. Patients were randomly separated into two clinical trial groups: 20 patients were in group A, in which ovarian stimulation included rFSH and LH, and group B, in which 20 patients received rFSH without further LH addition. After oocyte retrieval, the oocytes were extracted with hyaluronidase treatment for ART procedure by the embryologist. The rest of follicular fluid was transferred to the HLA Typing Laboratory within the same day. To eliminate the effect of hyaluronidase treatment on granulosa cell viability and apoptosis, the validation of the cytometry protocol has been performed initially.

The verified flow cytometry protocol analyzing with Annexin V-FITC/Propidium Iodide has been applied to all 40 women to determine the apoptosis rate of granulosa cells. A sufficient number of cells required for evaluation could not be obtained from 5 samples of study group, 4 samples of control group and were excluded from the study.

Primary outcome measure was granulosa cells apoptosis rate in terms of viability, early apoptosis, late apoptosis and necrosis. Secondary outcomes were total r-FSH dose, metaphase II oocytes retrieved, clinical pregnancy rate.

RESULTS: No statistically significant differences were determined in mean age, BMI, duration of infertility, FSH level, AMH level and AFC between the groups. Mean values of viability were 93.30 and 74.74 for groups A and B respectively (p<0.001). The granulosa cells apoptosis rates were compared as early apoptosis, late apoptosis and necrosis. Late apoptosis rates were significantly lower in group A (mean value = 4.2975) than group B (mean value =17.3473)(p<0.001). Interestingly, although early apoptosis rates were 3.0656 and 6.8267 for group A and B respectively, these differences did not reach statistical significance (p=0.04). Similarly, when clinical pregnancy rates were analyzed, no significant difference were observed; the rate of clinical pregnancy was %25 for group A whereas %20 for group B.

CONCLUSIONS: The results of this prospective and randomized trial show that the supplementation of LH in COS for ART decreases the late granulosa cell apoptosis rate in poor ovarian responder patients. Although LH supplementation seems necessary in poor responders to decrease the late granulosa apoptosis rates, this does not improve clinical pregnancy rates.

SUPPORT: This study was supported by grants from Giresun University Scientific Research Projects Department (SAG-BAP-A-2302)

P-820 Wednesday, October 16, 2019 6:30 AM

EFFICACY OF A MODIFIED MICROSECURE VITRIFICATION (MS-VTF) PROCEDURE WITH DMISO-FREE SOLUTIONS APPLIED TO A DEDICATED BLASTOCYST BIOSPY/VTTF-ALL PROTOCOL: OPTIMIZING SINGLE HEALTHY TERM LIVE BIRTHS. Mitchel C. Schiewe, MS, PhD.a John B. Whitney, BS.a Shane Zozula, B.S., T.S. (ABB), b Nancy L. Nugent, MS, c C Terence Lee, MD, d Ilene Hatch, MD, e Robert E. Anderson, MD f Oviation Fertility, Newport Beach, CA; g Ovation Fertility, Brea, CA; h FCSC, Irvine, CA; i SCCRM, Newport Beach, CA.

OBJECTIVE: Micro-Secure vitrification (µS-VTF) evolved as a non-commercial, FDA compliant device integrating sterile flexipettes (300μmID; Cook Medical) into CBSTM embryo straws. The mean cooling rate (1391°C/min) and warming rate (6233°C/min) of this closed, aseptic VTF system were verified by Dr. Greg Fahy (Schiewe et al., 2015). In 2014, CBS removed traditional hydrophobic plugged embryo straws from the worldwide marketplace, being replaced by 0.3ml semen straws. In turn, a modification of our µS-VTF procedure (Schiewe et al., 2017) was necessary to prevent wicking of flexipette contents. The goal of this study was to clinically validate the overall performance of our µS-VTF technique for human blastocysts over a 4-year duration.

DESIGN: Retrospective analysis of µS-VTF application with an a priori arrangement of FET cycle year (2015-2018) and number of euploid embryos transferred (1 or 2) were statistically analyzed by Chi-square analysis (p<0.05).

MATERIALS AND METHODS: The µS technique modification of semen straws involved creating a mid-straw weld seal in front of the inner PVA plug, thus eliminating any contact with the fluid-embryo filled flexipette tip once loaded prior to sealing the ends closed and LN2 immersion. Human blastocysts (>3CC grade) subject to trophectoderm biopsy on Day 5–7 were vitrified by µS-VTF using a Glycolerol/EG-based solution (≥7.9M; Innovative CryoEnterprises, NJ). Straw enclosed, individual embryos contained in an open flexipette (3ul volume) were warmed in a 37°C 0.5M Sucrose media bath (60μm dish, >15ml). Following a 4-step dilution and 1-4h of tri-gas in vitro culture (37°C), ET was performed by transvaginal ultrasound guidance.

RESULTS: Between 2015-2018, 12,583 blastocysts were vitrified in 2,139 patient cycles (94.2%; mean R2 euploid embryos transferred (1 or 2) were vitrified and warmed in a 37°C 0.5M Sucrose media bath (60μm dish, >15ml). Following a 4-step dilution and 1-4h of tri-gas in vitro culture (37°C), ET was performed by transvaginal ultrasound guidance.

RESULTS: Between 2015-2018, 12,583 blastocysts were vitrified in 2,139 patient cycles (94.2%; mean 2.13) blastocyst transfers were analyzed and vitrified by 0.3ml semen straws. In turn, a modification of our µS-VTF procedure (Schiewe et al., 2017) was necessary to prevent wicking of flexipette contents. The goal of this study was to clinically validate the overall performance of our µS-VTF technique for human blastocysts over a 4-year duration.

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P-821 Wednesday, October 16, 2019 6:30 AM

CAN THE MOST FREQUENT IMBALANCE SEGREGATION MODE FOR RECIPROCAL TRANSLLOCATION CARRIERS BE PREDICTED BY THE STENGEL-RUTKOWSKI METHOD OR HC-FORUM WEB SITE IN PRE-IMPLANTATION GENETIC TESTING FOR STRUCTURAL REARRANGEMENT?: Toshiaki Endo, M.D.; Tsuyoshi Baba, M.D.; Takema Kato, Ph.D.; Hiroki Kurahashi, M.D. Assistant Professor, Sapporo, Japan; Sapporo Medical University, Sapporo, Japan; Japan; Research assistant, Nagoya, Japan; Div. Molecular Genetics, ICMS, Fujita Health University, Nagoya, Japan.

OBJECTIVE: Thus far, predicting segregant outcomes has been done using a diagram of the presumed pachytene configuration of the quadrivalent to deduce which modes of segregation are likely to lead the formation of embryos in reciprocal translocation carriers. However, it is very difficult to predict segregation outcomes precisely. As the Stengel-Rutkowski method (S-R method) (1998) and HC-Forum web site (HC-F site) (Cohen et al. 2001) are well known to predict risks of having “a liveborn aneuploid child” due to imbalance from 3 modes (adjacent-1 segregation(ADJ-1), adjacent-2 segregation(ADJ-2) and 3:1 segregation(3:1)), these methods have not been utilized for predicting segregation outcomes of embryos of IVF by preimplantation genetic testing for structural rearrangement(PGT-SR). It is important to know if the most frequent imbalance segregation mode for reciprocal translocation carriers can be predicted by the S-R method or HC-F site in PGT-SR.

DESIGN: Chromosome segregations in embryos of 33 female and 20 male reciprocal translocation heterozygotes were studied by PGT-SR as reported in Table 5-3 in the 5th edition of Gardner and Southerland’s “Chromosome Abnormalities and genetic counseling.” Although Table 5-3 indicates that, in 53 cases, alternate segregation, ADJ-1, ADJ-2, and 3:1, each carrier had different mode patterns of segregation due to their different breakpoints. We tried to predict most frequent imbalance mode in embryos.

MATERIALS AND METHODS: We predicted “the most frequent imbalance mode” instead of risks of having “a liveborn aneuploid child” due to imbalance from 3 modes (adjacent-1 segregation(ADJ-1), adjacent-2 segregation(ADJ-2) and 3:1 segregation(3:1)), these methods have not been utilized for predicting segregation outcomes of embryos of IVF by preimplantation genetic testing for structural rearrangement(PGT-SR). It is important to know if the most frequent imbalance segregation mode for reciprocal translocation carriers can be predicted by the S-R method or HC-F site in PGT-SR.

RESULTS: There were multiple modes of segregation in embryos in 61% of female and in 55% male carriers. The S-R method predicted that the risk of having a liveborn aneuploid child was $1.81 \pm 0.60$% (mean±SE) and the HC-F site predicted $18.8 \pm 1.82$% in female carriers. In male carriers the risks were $3.35 \pm 1.70$, and $17.60 \pm 3.82$ by 2 methods. Thus, these risk figures were quite different. However, the most frequent segregation mode determined by the 2 methods was the same in 82% of the subjects in female carriers and 90% in male carriers. The most frequent segregation modes predicted by the S-R method and by HC-F site were the same in 85% and 86%, respectively, as those of the actual most frequent mode determined by PGT-SR. On the contrary, those modes by S-R method and by HC-F site were the same as 55% and 60%, respectively, as that by PGT-SR. Unfortunately, the HC-F site has been closed since December 31, 2000.

CONCLUSIONS: In PGT-SR for reciprocal translocation carriers, prediction of the most frequent imbalance segregation mode is quite important for genetic counseling. In this study, it is proposed that the S-R method and HC-F site are both good tools to predict the most frequent segregation mode of embryos for reciprocal translocation female carriers, not for male carriers.

SUPPORT: no support

References: no references

P-822 Wednesday, October 16, 2019 6:30 AM

THE MORPHOKINETIC EFFECTS OF CULTURE MEDIA WITH LOW LACTATE DURING EARLY EMBRYONIC DEVELOPMENT. Sule Dogan, PhD,* Mike Urich, BSc,* Fang Li, MD* PhD, Ahmed Hammoud, MD,* Hanh N. Cottrell, MD, Iqbal Khan, PhD,* Nicholas Shamma, MD* IVF Michigan Fertility Clinics, Bloomfield Hills, MI; IVF Michigan Fertility Centers, Bloomfield Hills, MI.

OBJECTIVE: To investigate the morphokinetic effects of culture media in early embryonic development.

DESIGN: Retrospective randomized study.

MATERIALS AND METHODS: Data used in this study were collected from our routine IVF-PGT patients who used either autologous and/or donor oocytes between February and December 2018. All cases whose embryos were incubated in conventional incubators were excluded. EmbryoScope slides were prepared using two different media where well 1-6 contained one media vs. well 7-12 had the second media and equilibrated overnight. On the day of retrieval, patients with at least 10 MII oocytes were randomly selected for this study. After ICSI, MII oocytes (n=35 patients, n=406 MII oocytes) were divided into two groups, and cultured in the same embryoScope (Vitrolife) slides including two different media; Group #1 (Global total by Life global) vs Group #2 (Low lactate: 1mM, CSCM-NX by Irvine). The embryos were hatched on Day 3 and trophectoderm biopsies (n=212) were performed accordingly. The biopsyed materials were sent to CooperGenomics for Next Generation Sequencing (NGS) testing. There was no bias between two groups in this study because, the sibling oocytes were incubated under the same condition. Morphokinetic parameters were analysed using t-test, Fertilization, Irregular division, Blastulation and Euploidy rates were analysed using χ²-test among the groups.

RESULTS: According to our findings, all results were shown in Table 1. The differences were considered statistically significant once p-values are < 0.05.

CONCLUSIONS: In this study, we only demonstrated that the t2 and t3 divisions were earlier, and blastulation was later in Group #1 than Group #2. Although the euploidy rate was higher in media with low lactate (Group #2), this difference was not statistically significant. In conclusion, a larger sample size is needed to conclude the positive effects of culture media with low lactate.

SUPPORT: None


REPRODUCTIVE GENETICS

P-824 Wednesday, October 16, 2019 6:30 AM

REDUCING THE FREQUENCY OF EMBRYO MOSAICISM THROUGH ARTIFICIAL INTELLIGENCE. Annemieke Wilcox, MD, a Jeffrey Thorne, MD, b John Nulsen, MD, c Claudio Benadiva, MD, d Daniel R. Grow, MD e Center for Advanced Reproductive Services, University of Connecticut School of Medicine, Farmington, CT; e Center for Advanced Reproductive Services, Farmington, CT; f Center for Advanced Reproductive Services, University of Connecticut, Farmington, CT; g University of Connecticut Health Center, Center for Assisted Reproductive Services, Farmington, CT.

OBJECTIVE: With the advent of Next Generation Sequencing (NGS) used in Preimplantation genetic testing (PGT), identifying mosaicism within a sample biopsy of trophectoderm has become increasingly common. While reports show that transfer of these embryos can result in live births, the implantation of mosaic embryos remains controversial. With advancement in artificial intelligence (AI) algorithms, it may be possible to detect embryo mosaicism with higher efficiency and accuracy. This study seeks to determine the difference in identification of embryo mosaicism between subjective calling (SC) by trained technicians and the use of AI algorithms at a single academic center.

DESIGN: Retrospective cohort study

MATERIALS AND METHODS: PGT data of 1,090 blastocysts from 351 patients at our center was obtained through CooperGenomics. 522 embryos evaluated using PGT with SC (4/2018 to 11/2018) were compared to 568 embryos evaluated using PGT with AI (11/2018 to 4/2019). PGT results were reported as euploid, low level mosaic (20-40% mosaicism), high level mosaic (40-80% mosaicism) and abnormal or complex abnormal (containing 3 or more aneuploid or mosaic chromosomes).

RESULTS: AI technology identified a higher number of euploid embryos and fewer low level mosaic embryos, leading to the identification of more embryos suitable for transfer. Further analysis of pregnancy outcomes is needed to determine if this translates into a clinically significant increase in livebirths.


Embryo Results Stratified by Age

<table>
<thead>
<tr>
<th>Embryo Classification</th>
<th>Age (yrs)</th>
<th>PGT w/SC (N=522)</th>
<th>PGT w/AI (N=568)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Euploid</td>
<td>≤ 35</td>
<td>42.7% (94)</td>
<td>56.3% (130)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td></td>
<td>&gt; 35</td>
<td>26.2% (79)</td>
<td>38.6% (130)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Low Level Mosaic</td>
<td>≤ 35</td>
<td>18.2% (40)</td>
<td>6.5% (15)</td>
<td>&lt; 0.01</td>
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<tr>
<td></td>
<td>&gt; 35</td>
<td>8.6% (26)</td>
<td>4.2% (14)</td>
<td>0.02</td>
</tr>
<tr>
<td>High Level Mosaic</td>
<td>≤ 35</td>
<td>8.2% (18)</td>
<td>8.2% (19)</td>
<td>0.99</td>
</tr>
<tr>
<td></td>
<td>&gt; 35</td>
<td>7.9% (24)</td>
<td>5.6% (19)</td>
<td>0.24</td>
</tr>
<tr>
<td>Abnormal/ Complex Abnormal</td>
<td>≤ 35</td>
<td>24.5% (54)</td>
<td>23.4% (54)</td>
<td>0.86</td>
</tr>
<tr>
<td></td>
<td>&gt; 35</td>
<td>55.0% (166)</td>
<td>46.6% (157)</td>
<td>0.03</td>
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<tr>
<td>Other</td>
<td>≤ 35</td>
<td>6.4% (14)</td>
<td>5.6% (13)</td>
<td>0.74</td>
</tr>
<tr>
<td></td>
<td>&gt; 35</td>
<td>2.3% (7)</td>
<td>5.0% (17)</td>
<td>0.07</td>
</tr>
</tbody>
</table>
VIDEO PROGRAM PRIZE SESSION

V-1 Monday, October 14, 2019 4:30 PM

TECHNIQUES FOR SUCCESSFUL VAGINAL ANASTOMOSIS IN THE UTERINE TRANSPLANT

PATIENT: Jenna M. Rehmer, MD; Elliott G. Richards, MD; Cecile A. Ferrando, MD, MPH; Rebecca Flyckt, MD. Cleveland Clinic Foundation, Cleveland, OH.

OBJECTIVE: To demonstrate our techniques for successful vaginal anastomosis in the uterine transplant patient.

METHODOLOGY: We report the case of a recent uterine transplant from a deceased multi-organ donor and highlight the vaginal anastomosis portion of this multi-step surgery. This video uses live action footage from surgery and detailed descriptions review our techniques for successful vaginal anastomosis in the uterine transplant patient.

CONCLUSIONS: Following uterine transplantation, access to the donor allograft cervix is important for many reasons. Vaginal strictures pose a unique problem in this surgical population. We believe strictures result from difficult in approximating donor vaginal mucosa to recipient vaginal mucosa, and that this is paramount in reducing this untoward postop complication. Given the difficulty of surgery and tendency for the recipient vaginal mucosa to retract, our teams has employed techniques from vaginal reconstructive surgery to reduce the occurrence of postoperative vaginal strictures.

Reference: None.

SUPPORT: No financial support to disclose.

V-2 Monday, October 14, 2019 4:42 PM

SURGICAL MANAGEMENT OF DEEP INFILTRATING ENDOMETRIOSIS INVOLVING THE RECTOSIGMOID COLON

Natalia C. Llarena, MD; Anup B. Shah, MD, MS; Hermann Kessler, MD, PhD; Tommaso Falcone, M.D.; Rebecca Flyckt, MD. Cleveland Clinic Foundation, Cleveland, OH; Cleveland Clinic, Cleveland, OH; Cleveland Clinic, Cleveland, OH.

OBJECTIVE: To discuss the surgical management of deep infiltrating endometriosis involving the rectosigmoid colon.

METHODOLOGY: Here we demonstrate a case of a 34-year-old female with chronic pelvic pain, infertility, and a 1-cm rectosigmoid endometrioid implant noted on preoperative MRI. She underwent segmental bowel resection of the involved rectosigmoid colon with colorectal anastomosis.

CONCLUSIONS: There are several surgical approaches to managing endometriosis involving the rectosigmoid colon, including rectal shaving, disc resection, and segmental resection. Segmental resection allows for complete resection of endometriotic lesions and histologic analysis of the specimen.

Reference: None.

SUPPORT: None.

V-3 Monday, October 14, 2019 4:53 PM

NO-SCALPEL VASECTOMY: PUNCTURE-FIRST WITH MULTI-OCCCLUSION TECHNIQUE

Khushabu Kasahwala, MD; Helen Levey Bernie, DO MPH; Soo Jeong Kim, MD; Vanessa L. Dudley, MS SH; Michael Bernard, MD; Marc Goldstein, MD New York Presbyterian - Weill Cornell Medical Center, New York, NY; Memorial Sloan Kettering Cancer Center, New York, NY; Weill Cornell Medicine, New York, NY; Weill Cornell Medicine, New York Presbyterian Hospital, New York, NY.

OBJECTIVE: Vasectomy is a widely utilized, permanent contraceptive method. Vasectomy failure may occur secondary to recanalization (1-10%) and is a major cause of malpractice suits and pregnancy. The no-scalpel vasectomy (NSV) is a minimally invasive technique where failure rates depend on occlusion techniques. We describe a puncture-first NSV with four occlusion techniques to optimize outcomes and minimize technical difficulty.

METHODOLOGY: Men who had a puncture-first NSV by a single surgeon (MG) over 25 years (1993 - 2018) were included in this study. The procedure begins administering local anesthesia to the skin overlying the vas. The vas, excluding vasal vessels and nerves, is then delivered through a single midline puncture hole. After securing two ends of the vas and hemi-transecting them, the first occlusive step, intraluminal cautery, is performed on the testicular end of the vas by rotating the cautery for 10 seconds to ensure a 360-degree burn. A hemoclip is lightly placed on the testicular end to prevent sperm leakage until cautery causes a permanent seal. The abdominal end of the vas is cauterized intraluminally, completely transected, and allowed to retract into the vasal sheath. The sheath is grasped and sealed over the abdominal end with a hemoclip, accomplishing fascial interposition. A 5mm vas segment is excised. The ends are dabbed with betadine before retraction into the scrotum. The contralateral vas is accessed through the same puncture hole and occluded identically. No antibiotics are administered before or after the procedure. Post-vasectomy semen analysis (PVSAs) is performed 6-8 weeks or 15 ejaculations after the procedure. Complications were graded using the Clavien-Dindo classification scale.

Over 25 years, 819 vasectomies were performed. The mean age of the patient and partner was 41.6 years (+/- 5.8 years) and 38.6 years (+/- 3.8 years), respectively. At least one PWSA was performed in 484 (59%) of men, at a median of 53 days post-procedure. Nearly half of those, 222 men (45%) required a second PWSA to confirm vasal occlusion. No pregnancies were reported after vasectomy. Three complications occurred including one abscess requiring incision and drainage (Grade IIIa) and two hematomas managed conservatively (Grade I). No chronic pain or orchitis was reported.

CONCLUSIONS: Vasectomy failure and complications can be minimized by utilizing a combination of four occlusion techniques: 1) intraluminal cautery for 10 seconds; 2) testicular end occluding clip; 3) fascial interposition and 4) removal of 1/2 to 1 cm segment of vas. Additionally, the puncture-first technique eliminates the need to grasp the scrotal skin with the vas in the ring clamp, decreasing technical difficulty. This technique has minimal complications and a 100% success rate in our patient cohort.

Reference: None.

SUPPORT: No financial support to disclose.

V-4 Monday, October 14, 2019 5:06 PM

DEVELOPMENT OF AN AUTOMATIC PRONUCLEAR DETECTION SYSTEM FOR HUMAN EMBRYOS USING DEEP LEARNING TECHNOLOGY

Hirokatsu Watanabe, M.S.; Noritaka Fukunaga, Ph.D.; Sho Sanami, Ph.D.; Hiroya Kitasaka, Ph.D.; Yuji Tsuzuki, M.S.; Yuta Kida, M.S.; Seiji Takeda, M.S.; Yoshimasa Asada, M.D., Ph.D.; Asada Ladies Clinic, Nagoya, Aichi, Japan; Research & Development Center, Dai Nippon Printing Co., Ltd., Kita-ku, Tokyo, Japan.

OBJECTIVE: Fertilization is generally evaluated by pronuclear number. Correct judgment may sometimes be difficult due to morphology and number of pronuclei of pronuclear embryos.

Correct evaluation of the pronuclear number is important in order to reduce the possibility of transferring abnormal embryo.

Therefore, in this study, we aimed to develop an automatic pronuclear detection system by deep learning technology using time lapse embryo images.

Deep Learning technology is an information processing system using Deep Learning Neural Networks (DLNN). DLNN is a multi-layered combination of neural networks that mimics a cranial nerve network. This technology has several important features such as a) high-precision learning is possible, b) currently it is the highest performance image recognition method, and c) it makes effective use of all time-lapse embryo images.

METHODOLOGY: 70-80 images before and after pronuclear formation of one embryo were extracted from the time-lapse incubator. Using these 70-80 images as one set, each 400 sets of 2PN, 1PN and 0PN images that were evaluated by an embryologist were prepared in order to construct the automatic pronuclei detection system.

The automatic pronuclear detection system used DLNN which outputs the number of pronuclei to the inputted embryo image. The 400 sets of images, 300 sets of each were input to the DLNN with labels of 2 PN, 1 PN and 0 PN, and the DLNN learned from these images by Deep Learning.

The remaining 100 sets of images that were not used for learning were entered without labels to the DLNN which completed the learning, and the DLNN detected the number of pronuclei from these images.

CONCLUSIONS: In 2PN embryos, the rate of correctly detected 2PN was 97% and the rate of incorrectly detected 1PN, 0PN was 3%, 0% respectively, with respect to the input of 100 unlabeled time-lapse images.

In 1PN embryos, the rate of correctly detected 1PN was 68%, and the rate of incorrectly detected 2PN, 0PN was 29%, 12% respectively, with respect to the input of 100 unlabeled time-lapse images.

In 0PN embryo, the rate of correctly detected 0PN was 78%, and the rate of incorrectly detected 2PN, 1PN was 4%, 18% respectively, with respect to the input of 100 unlabeled time-lapse images.
As a result of this study, we succeeded in constructing a system for automatic detection of pronuclear number from embryo images using Deep Learning technology.

The correct answer rate was 97% in 2PN embryos, but the rate was lower in 1PN and 0PN embryos compared to 2PN embryos.

These results are very promising, but it is necessary to improve the detection system further and apply this technology to embryos with 3 or more PN number.

Reference: None.
SUPPORT: None.

V-5 Monday, October 14, 2019 5:18 PM

TRANSGENDER YOUTH: EXPLAINING HORMONAL AFFIRMATION TREATMENT VIA POWTOON FORMAT (MTF). Gloria Bachmann, md. mms, Ian Marshall, MD. Rutgers Wood Johnson Medical School, New Brunswick, NJ.

OBJECTIVE: To explain to transgender youth in an animated format containing auditory, visual and written explanations, the pros and cons of hormone use that may be prescribed to them in order to achieve their desired gender changes.

METHODOLOGY: Written materials on hormonal therapy used for affirmation of gender may not be comprehensively read by young individuals seeking this intervention. To address this issue, an animated presentation was developed that addresses the pros and cons of hormonal use for gender affirmation. The script was developed by clinicians who care for transgender individuals with the input of learner and community groups. The Powtoon format was utilized for creating the animated presentations.

CONCLUSIONS: The appropriate Powtoon is being shown to transgender individuals being cared for by a pediatric endocrinologist, who has over 200 transgender youth in his practice. Parents and guardians are also encouraged to watch them. Comments have been overall positive both from the individuals being managed with hormonal therapy and the parents/guardians.

Reference: None.
SUPPORT: None.

V-6 Tuesday, October 15, 2019 4:15 PM

CONTINUOUS MONITORING OF THE EMBRYO DEVELOPMENT: A LEAP TOWARDS AUTOMATED SYSTEMS. Lorena Bori, PhD.1 Raquel Del Gallego, PhD.1 Lucia Alegre, PhD.2 Antonio Pelllicer, MD.3 Marcos Meseguer, PhD.3 IVIRMA Global, Valencia, Spain;3 IVD Foundation Innovation - Reproductive Medicine IIS La Fe, Valencia, Spain; 4 IVIRMA Global, Valencia, Spain, Tel Aviv, Israel.

OBJECTIVE: To illustrate the introduction of automated systems to assess the embryos in daily clinical practice in IVF laboratories.

METHODOLOGY: More than 80,000 embryos have been cultured in time-lapse incubators since 2009 at IVIRMA Valencia. Abnormal embryo development has been observed thanks to the high number of videos available. The best examples of zygotes with one or three pronuclei and embryos with irregular divisions that achieved good quality blastocysts were gathered. Blastocysts that changed their quality 24 hours before embryo selection were also selected for the project. Automated systems based on image analysis technology have been introduced in our laboratory to assess embryo development. A step by step video demonstration of the automatic annotations performed by EmbryoScope® and Geri Connect and Assess 2.0® was conducted. Additionally, a table of the comparison between the manual annotations performed by an embryologist team and the automated annotations performed by the software software Geri Assess 2.0a in 1,360 embryos (10,880 development events) at IVIRMA Valencia is shown. The parameters included were: pronuclear fading (tPNF), division time to 2 cells (t2), division time to 3 cells (t3), division time to four cells (t4), division time to five cells (t5), division time to six cells (t6), appearance of morula (tM) and expanded blastocyst (tEB). High accordance was found between both, showing a struggle in the detection of late parameters by the embryologist team. Finally, a demonstration of a method to measure novel embryo parameters, impossible to assess with automated systems, were performed by embryologists through the drawing tools provided by the EmbryoViewer®. The parameters included were: blastocyst expanded diameter, inner cell mass area and trophoderm cell cycle length. Additionally, the impact of these parameters over the implantation rate was analyzed and illustrated through graphs.

CONCLUSIONS: Time-lapse technology allows monitoring of unusual patterns of embryo development and makes it possible to progress towards automated and objective systems to assess the embryos. The use of big data technology as a tool to detect embryo development events combined with embryologist skills are a promising approach towards the improvement of IVF treatments.

V-7 Tuesday, October 15, 2019 4:23 PM

COMPARISON OF SPERM RETRIEVAL TECHNIQUES FOR MEN WITH OBSTRUCTIVE AZOOSPERMIA. Joshua N. Bitran, BS.1 Premal Patel, MD.2 Ranjith Ramasamy, M.D.3 *University of Miami, Miami, FL;3 University of Miami Miller School of Medicine, Miami, FL; *University of Miami.

OBJECTIVE: To compare the Percutaneous Epididymal Sperm Aspiration (PESA) and Microsurgical Epididymal Sperm Aspiration (MESA) techniques, requirements, and outcomes for men with obstructive azoospermia.

METHODOLOGY: Intra-operative video highlights the main steps for performing PESA and MESA, along with their complications and sperm retrieval outcomes. Intra-operative table microscope was used to visualize sperm from PESA and MESA.

CONCLUSIONS: PESA and MESA are both effective means for obtaining sperm for in-vitro fertilization with differences in technique, equipment required, complications, and sperm quality outcomes.

V-8 Tuesday, October 15, 2019 4:28 PM

POST-ABLATION RESIDUAL DISEASE: HISTOLOGICAL ASSESSMENT OF EXCISED PERITONEAL ENDOMETRIOSIS. Christine Hur, MD.1 Tommaso Falcone, M.D.2 Rebecca Flyckt, MD.3 *Cleveland Clinic, Cleveland, OH; *cleveland Clinic, cleveland, OH; *Cleveland Clinic Foundation, Cleveland, OH.

OBJECTIVE: The objective of this video is to present a case of post ablation residual peritoneal endometriosis while also highlighting surgical techniques of excision of endometriosis.

METHODOLOGY: This video presents a case of a 25 year old para 2 who had a history of a prior diagnostic laparoscopy with ablation of peritoneal endometriosis two months prior. The surgical case presented is her second laparoscopy, which was performed with the intention of excision of endometriosis per patient preference. Surgical findings were significant for remaining endometriosis in areas of previous ablation. The histological findings included residual endometriosis deep to prior superficial ablation.

CONCLUSIONS: Superficial ablation may not treat deeper forms of endometriosis. Ablation without appropriate dissection and mobilization risks injury to the bowel, ureters and bladder. For these reasons, excision of endometriosis may be a superior form of treatment for deep peritoneal endometriosis.


V-9 Tuesday, October 15, 2019 4:34 PM

TEACHING SURGERY FOR MASSIVE ADENOMYOSIS WHICH PRESERVES THE UTERUS. Sherman Silber, MD.1 Yuting Fan, M.D.1 Sierra Goldsmith, B.S.1 *Infertility Center of St. Louis, Chesterfield, MO;1University of Michigan, Ann Arbor, MI.

OBJECTIVE: To determine the feasibility of teaching massive adenomyectomy surgery with favorable results.
METHODOLOGY: 4 patients with massive adenomyosis in China who wished to get pregnant and have a baby were enlisted for the teaching the Chinese surgical team. Subsequently 20 more such patients were operated on in China by the surgical team we taught. For the first two teaching cases, we did the surgery, and the Chinese team assisted. For the next two cases, the Chinese team did the surgery, and we assisted. We described the quintuple flap reconstruction with no overlapping suture lines to prevent uterine rupture. Video documentation was performed.

CONCLUSIONS: Following this intense two day training in China, the Chinese team did 20 more cases on their own over the next six months, with a live birth rate of 55%, and uneventful pregnancies with no uterine rupture.

V-10 Tuesday, October 15, 2019 4:53 PM

LAPAROSCOPIC RELOCATION OF THE OVARIAS AFTER PRIOR TRANSPOSITION. Jessica Traylor, M.D., Jaclyn Friedman, M.D., Magdy P. Milad, M.D., MS. Northwestern University Feinberg School of Medicine, Chicago, IL.

OBJECTIVE: To describe the indications, surgical approaches and expected outcomes for ovarian transposition and highlight a case of ovarian relocation to the pelvis in a patient who underwent prior transposition.

METHODOLOGY: A 34 year old patient with a history of metastatic spinal ependymoma underwent laparoscopic ovarian transposition prior to craniospinal radiation. Eleven years after her transposition, she was seen by reproductive endocrinology and infertility for preconception counseling and evaluation. Her follicle stimulating hormone levels were within normal limits, but her hysterosalpingogram demonstrated bilateral tubal isthmic occlusion. She was referred to minimally invasive gynecologic surgery for surgical consultation.

The patient was taken to the operating room for operative laparoscopy, ovarian relocation to the pelvis and evaluation of her fallopian tubes. Intraoperative findings were notable for transposition of the bilateral ovaries and fallopian tubes to the lateral abdominal peritoneum. Adhesiolysis was performed to mobilize each ovary on its vascular pedicle. Without compromise to the ovarian blood supply, and in a tension-free manner, each ovary was sutured to the ipsilateral round ligament.

CONCLUSIONS: Laparoscopic ovarian transposition is an important surgical technique to aid preservation of ovarian function in reproductive aged women undergoing pelvic radiation. Gynecologic surgeons should be aware of the techniques to perform ovarian transposition, as well as relocation of the ovaries to the pelvis for future spontaneous or assisted reproduction. Knowledge of abdominal and pelvic anatomy, as well as proficiency in laparoscopic suturing are essential to perform ovarian transposition and relocation in a minimally invasive fashion.


SUPPORT: None.

V-11 Tuesday, October 15, 2019 5:01 PM

OPTIMIZING FERTILITY PRESERVATION USING MULTIPLE MODALITIES IN A YOUNG PATIENT WITH CERVICAL CANCER. Natalia C. Llarena, MD, Bouran Kilany, MD, Mariam Alhilli, MD, Rebecca Flyckt, MD. Cleveland Clinic, Cleveland, OH.

OBJECTIVE: Oocyte cryopreservation is the mainstay of fertility preservation in patients with malignancy; however, live birth rates after oocyte cryopreservation are lower in cancer patients than in healthy patients. Multiple modalities of fertility preservation can be combined to optimize success rates.

METHODOLOGY: We demonstrate a case of a 24-year-old female who was diagnosed with cervical clear cell adenocarcinoma and was advised to undergo treatment with cisplatin and radiation therapy. She strongly desired fertility preservation and opted to proceed with oocyte cryopreservation, ovarian tissue cryopreservation, and ovarian transposition.

CONCLUSIONS: Ovarian transposition is a surgical approach to fertility preservation that preserves both fertility and gonadal function. Different modes of fertility preservation may be combined to optimize live birth rates in patients with malignancy.

SUPPORT: None.

V-12 Tuesday, October 15, 2019 5:09 PM

LEFT OVARIAN TRANSPOSITION OF UNDESCENDED OVARY WITH UNICORNATE UTERUS. Kirsten Sasaki, M.D., Charles E. Miller, M.D.a,b "Advocate Lutheran General Hospital, Naperville, IL;" The Advanced Gynecologic Surgery Institute/The Advanced IVF Institute, Charles E. Miller, MD & Associates, Naperville, IL.

OBJECTIVE: To review the presentation, symptoms, diagnosis and treatment of an undescended ovary, and to demonstrate a laparoscopic technique for ovarian transposition to facilitate trans-vaginal oocyte monitoring and retrieval.

METHODOLOGY: Left ovarian transposition and ovarian drilling. CONCLUSIONS: Laparoscopic ovarian transposition is a feasible, safe option to facilitate oocyte retrieval in cases of undescended ovaries.


SUPPORT: None.

V-13 Tuesday, October 15, 2019 5:15 PM

EXCISION OF A PELVIC SIDE-WALL FIBROID. Alexander Koltay, MD, a Pinar Kodaman, MD/PhD, b "Yale University, New Haven, CT;" "Yale School of Medicine, New Haven, CT.

OBJECTIVE: To share our experience in excising a retroperitoneal pelvic fibroid.
METHODOLOGY: This video describes the essential steps for resecting a retroperitoneal pelvic fibroid. These fibroids are rare and do not typically arise from the uterus or cervix and carry a higher risk of sarcoma compared to typical uterine fibroids. In this video, we review a case presentation including preoperative MRI imaging, and outline the key steps in retroperitoneal fibroid excision. These steps include proceeding with lateral to medial excision, systematic identification of the retroperitoneal structures and use of bipolar electrocautery to transect key vascular connections to the fibroid. Once this has been completed, the fibroid is then removed and linearized within a surgical containment system.

CONCLUSIONS: Retroperitoneal fibroids are a rare type of pelvic tumor that carry an increased risk of sarcoma. The resection of these tumors requires pre-operative imaging to assess their relationship to adjacent pelvic structures and judicious dissection of the retroperitoneum.


VIDEO SESSION 3

V-14 Wednesday, October 16, 2019 3:45 PM

2-PORT MYOMECTOMY TECHNIQUE FOR UTERUS ADHERENT TO THE ANTERIOR ABDOMINAL WALL. Hadi Ramadan, M.D., Jerri A. Waller, M.D., Traci E. Ito, M.D., Joseph L. Hudgens, M.D., Eastern Virginia Medical School, Norfolk, VA.

OBJECTIVE: To describe a 2 port myomectomy technique in the setting of extensive adhesions aiming for fertility preservation.

METHODOLOGY: Our patient is a 40 year old female G3P2012 presenting with symptomatic fibroids with a history of prior C-section. Her MRI showed extensive adhesions requiring specific surgical techniques. Using a 2 port method and gel point mini, lysis of adhesions was performed. Enucleation of fibroids followed. This multistep process ensures hemostatic and efficient myomectomies without jeopardizing the integrity of the endometrium.

CONCLUSIONS: This case is an example of how reduced port technique can be utilized in complex fertility preserving techniques.

SUPPORT: None.

V-15 Wednesday, October 16, 2019 3:53 PM

PROOF OF CONCEPT FOR AN AUTOMATED TANK STORING FROZEN EMBRYOS AND GAMETES IN AN ART LABORATORY. Timothy Allen Sharp, B.S., William N. Garbarini Jr., MBA,

vette 18, Chad A. Johnson, PhD,

ette 18, Ann Watson, B.A.,

ette 18, Kathy H. Go, Ph.D. TMWR Life Sciences, New York, NY; TMWR Life Sciences, Inc., New York, NY.

OBJECTIVE: We explored proof of concept for an automated, cryogenic robot for the storage of human embryos and gametes.

METHODOLOGY: Adapt an automated, electronically-monitored storage system to ART.

CONCLUSIONS: Proof of concept was obtained to apply a robotic, electronically-monitored automated tank for ART.

SUPPORT: Financial support was provided by TMWR Life Sciences, Inc.

V-16 Wednesday, October 16, 2019 3:56 PM

LAPAROSCOPIC RESECTION OF FUNCTIONAL, NON-COMMUNICATING UTERINE HORN. Rachel M. Whynott, M.D.,* Rachel Mejia, D.O.,† University of Iowa Hospitals and Clinics, Iowa City, IA; †University of Iowa, Iowa City, IA.

OBJECTIVE: To review a common presentation of unicorionate uterus with a functional, non-communicating rudimentary uterine horn and a laparoscopic method of management, highlighting laparoscopic surgical techniques.

METHODOLOGY: A 13-year-old G0 was referred to the clinic for severe, cyclic right lower quadrant pain during menses. A transvaginal ultrasound revealed a left unicorionate uterus with a right-sided, non-communicating rudimentary horn measuring 4.8 x 4.7 x 4.6 cm, containing blood consistent with hematometra. Kidneys were bilaterally present and normal by ultrasound. Due to the patient’s worsening pain and presence of hematometra, decision was made to proceed with diagnostic laparoscopy and removal of the rudimentary uterine horn. The entire procedure was performed laparoscopically, with an estimated total blood loss of 20 cc. She had no complications or readmissions. Her severe menstrual pain was resolved at her follow up appointments.

CONCLUSIONS: In patients with severe menstrual pain from outflow obstruction from a non-communicating rudimentary uterine horn with functional endometrium, laparoscopic resection can be a safe and effective method of treatment.


SUPPORT: None.

V-17 Wednesday, October 16, 2019 4:03 PM

MEIOTIC SPINDLE AVOIDANCE USING A POLARIZING FILTER AT THE TIME OF ICSI, A STEP CLOSER TOWARDS INDIVIDUALIZED ICSI. Alejandro Chavez-Badiola, MD,* Rodolfo Garcia-Sánchez, MSc,* Erika L. Iniguez-Artega, Biol,* Dante José Sánchez González, Biol,* Carmen Ortega Madera, Biol,* Sarai Vazquez-Pacheco, Biol,* New Hope Fertility Center Mexico, Mexico City, EM, Mexico; †New Hope Fertility Center Mexico, Guadalajara, JA, Mexico.

OBJECTIVE: To assess the impact of routine meiotic spindle identification during intra-cytoplasmic sperm injection (SI-ICSI), on fertilization and blastocyst formation rates when compared against conventional intra-cytoplasmic sperm injection (ICSI).

METHODOLOGY: All ICSI cycles undertaken between February 2015 and December 2016 in two similarly run IVF centers were included. At February 2016, spindle identification was introduced into routine practice. ICSI was performed following standard protocols: polar body was positioned either at 6 or 12 o’clock and used as reference for sperm injection at 3 o’clock. SI-ICSI oocyte identification was performed just before ICSI under 40 times magnification and then rotated until polar body was positioned at 12 o’clock. At this point a polarizer filter (Olympus IX2), was inserted while light turned to maximum intensity. Oocytes were rotated until a birefringent spindle was identified. Spindle position and intensity was recorded by embryologist as 6+/+++ or 12+++/+++ by embryo with length assigned to spindle absence and +++ to maximum spindle intensity when compared against the most birefringent area in zona pellucida. Sperm injection was performed at 3 o’clock. Fertilization and blastocyst formation rates were recorded blind to spindle characteristics. Comparison was performed using Fisher’s Exact test.
CONCLUSIONS: With an increased 5% normal fertilization rate and 7% higher blastocyst rate, this study suggests that visualizing the oocyte meiotic spindle using an inexpensive polarizing filter at the time of ICSI can avoid inadvertent damage and leads to improved normal fertilization and blastocyst formation. Other potential benefits could include better timing for injection in accordance with cytoplasmic maturation. Prospective studies would be needed to validate this later concept.

V-20 Wednesday, October 16, 2019 4:35 PM

SPECIALIZED PIEZO-ICSI FOR LOW QUALITY OOCYTES. Atsushi Tanaka, M.D., Ph.D., Motoi Nagayoshi, M.D., Izumi Tanaka, Phar.B., Takashi Yamaguchi, M.D., Ph.D., Motoharu Ohno, M.D., Saint Mother Hospital, Kitakyushu, Japan.

OBJECTIVE: In 1995, Kimura and Yanagimachi reported the usefulness of ICSI using Piezo-micro manipulator by applying a Piezo pulse which produced ultra-fast sub-micron forward momentum using uniquely shaped flat-topped micropipettes with no bevel or spike (Piezo-ICSI).

Hirao et al reported that Piezo-ICSI has advantage of high fertilization rate, low damage rate of oocyte at ICSI and high clinical outcome in 2015. However, we have worried about one problem in Piezo-ICSI, that is the volume of injected medium at ICSI. So, we developed a newly specialized Piezo-ICSI with sperm with a shortened sperm tail after cutting the tails to lessen the damage to the cytoplasm of these low-quality oocytes. We then investigated the effect of the specialized Piezo-ICSI.

METHODOLOGY: Prospective study to improve clinical outcome of Specialized Piezo-ICSI for Low quality oocytes.

The sperm tail was cut with injection pipette a little below the mid piece then aspirate it injection pipette head first. The zona pellucida was penetrated using a weak piezo pulse (speed 1.5, intensity 1) and the tip of injection pipette was introduced forward to stretch the cytoplasmic membrane. A weaker pulse (speed 1.0, intensity 1) was added to break it and the sperm injected simultaneously. Pushing the sperm forward and aspiration of the medium injected at ICSI were unnecessary.

CONCLUSIONS: Oocytes that received ICSI, Oocytes that survived after ICSI (%), Oocytes fertilized (%), ood quality day-3 embryos (%), Blastocysts (%), Clinical pregnancies (%): Between conventional Piezo-ICSI and Specialized Piezo-ICSI were [512, 124] [435 (85), 112 (90)] [409 (80), 103 (83)] [266 (52), 69 (56)] [230 (45), 60 (48)] [27, 31] respectively.

This newly developed Piezo-ICSI, using tail-cut shortened sperm through tail first was successful in making the injection easier. The reduction in injected volume of medium resulted in production of high-quality embryos.

V-21 Wednesday, October 16, 2019 4:42 PM

NOVEL UTERINE CLOSURE TECHNIQUE TO PREVENT INTRAUTERINE ADHESIONS. Clarissa J. Lam, MD. Anthony N. Imudia, MD, University of South Florida, Tampa, FL.

OBJECTIVE: The purpose of this video is to describe a novel uterine closure technique to prevent intrauterine adhesions after myomectomy. This is an important topic in the field as intrauterine adhesions can result in infertility, recurrent pregnancy loss, and future pregnancy complications, such as morbidly adherent placenta.

METHODOLOGY: In this video, we first discussed the epidemiology and the existing techniques that have been studied regarding the prevention of intrauterine adhesions. We then used an illustration to describe the suturing technique. We concluded with video clips demonstrating the technique from three of our myomectomy cases.

CONCLUSIONS: This novel intraoperative uterine closure technique is one method that can potentially reduce the risk of intrauterine adhesion formation.


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LATE-BREAKING ABSTRACTS

O-265

TREATMENT OF SYMPTOMS OF UTERINE FIBROIDS WITH RELUGOLIX COMBINATION THERAPY: EFFICACY AND SAFETY RESULTS FROM THE PHASE 3 LIBERTY 1 CLINICAL TRIAL. Ayman Al-Hendy, MD PhD, Andrea S. Lukes, MD,1 Alfred Pinder, III, MD,2 Roberta Venturini, MD PhD,1 Claudio Valandro, MD,1 Yulan Li, PhD,1 Laura F. McKain, MD,1 Elizabeth A. Stewart, M.D,1 1University of Illinois College of Medicine, Chicago, IL; 2Carolina Women’s Research and Wellness Center, Durham, NC; 3Advances In Health, Houston, TX; 4Magna Graecia University of Catanzaro, Department of Obstetrics, Catanzaro, Italy; 5Institute for Mother and Child Research (IDIMI), Faculty of Medicine, Universidad de Chile, Santiago, Chile; 6Myovant Sciences, Inc., Brisbane, CA; 7Mayo Clinic, Rochester, MN.

OBJECTIVE: To evaluate the efficacy and safety of relugolix for 24 weeks of treatment with the oral GnRH receptor antagonist, relugolix, in combination with estradiol (E2) and norethindrone acetate (NETA) compared with placebo in women with uterine fibroid (UF)-associated heavy menstrual bleeding (HMB).

DESIGN: Multinational phase 3 randomized, double-blind, placebo-controlled trial

METHODS: Premenopausal women (18-50 years) with menstrual blood loss (MBL) volume ≥ 80 mL/cycle assessed by the alkaline heparin method and ultrasound-confirmed UF, were eligible to participate in the study. Women were randomized 1:1:1 to one of three arms: once daily treatment with relugolix 40 mg + E2 1 mg/NETA 0.5 mg for 24 weeks (Group A), relugolix 40 mg alone for 12 weeks followed by relugolix 40 mg + E2 1 mg/NETA 0.5 mg for 12 weeks (Group B), or placebo for 24 weeks (Group C). The primary efficacy endpoint was the proportion of women in Group A vs Group C who achieved an MBL of < 80 mL and ≥ 50% reduction from baseline MBL over the last 35 days of treatment. Secondary endpoints included mean % reduction in MBL, amenorrhea rate, improved anemia, and reduced UF-associated pain. Group B was included to explore the impact of E2/NETA on the anticipated hypoestrogenic effects of relugolix. Adverse events (AEs) and bone mineral density (BMD) changes by dual-energy X-ray absorptiometry were assessed.

RESULTS: In LIBERTY 1, 388 women were randomized and 308 (79%) completed the study. In Group A 73.4% met the primary endpoint vs 18.9% in Group C (p < 0.0001). Mean % reduction in MBL from baseline at Week 24 was 84.3% for the Group A and 23.2% for Group C (p < 0.0001). The proportion of women who achieved amenorrhea was 52.3% vs 5.5% in Groups A vs C, respectively (p < 0.0001). In women with anemia (hemoglobin ≤ 10.5 g/dL) at baseline who completed 24 weeks treatment, 50.0% experienced a ≥ 2 g/dL increase in hemoglobin in Group A vs 7.6% in Group C (p < 0.0001). A higher proportion of women reporting moderate/severe UF-associated pain (based on a maximum daily pain score of ≥ 4 at baseline where 0 = no pain, 10 = worst pain ever) 43.1% in Group A reported minimal/no pain (maximum pain score ≤ 1) in the last month of treatment vs. 10.1% in Group C (p<0.0001). Efficacy results in Group A were similar to those of Group A. Incidence of AEs was comparable between Groups A and C (62% vs 66%, respectively) and higher in Group B (73.5%), including the most common AE, hot flushes (11% and 8% in Groups A and C, respectively, vs 36% in B). The mean % change from baseline to Week 24 in lumbar spine BMD was -0.36%, -1.82%, and 0.05% in Groups A and C, respectively, vs 36% in B). The mean % change from baseline to Week 24 in lumbar spine BMD was -0.36%, -1.82%, and 0.05% in Groups A and C, respectively, vs 36% in B).

CONCLUSIONS: In this Phase 3 pivotal study, relugolix combination significantly reduced MBL in women with UF-associated HMB and was generally well tolerated. Additional benefits were observed including a clinically meaningful reduction of UF-related pain, a high rate of amenorrhea, and improved anemia. Coadministration of E2/NETA maintained BMD and mitigated vasomotor symptoms. Relugolix combination with E2/NETA represents a potential long-term treatment option for women with UF.

SUPPORT: The Phase 3 LIBERTY clinical trial was funded by Myovant Sciences, Inc.
hypogonadal symptoms and 2 semen analyses (SA) with total motile sperm counts (TMSC) > 5 million. Eligible men began Natesto TID for 3 months. T, LH, FSH, and 2 semen analyses were collected at baseline and after 3 months of therapy. Symptoms were evaluated using the international index of erectile function (IIEF-6) and the short form 36 (SF-36) questionnaires. The primary endpoints were change in T, LH, FSH, sperm motility and TMSC. Secondary end points were change of symptoms and adverse events (AEs). Data are presented as means (SD), students t-test was used to compare changes after 3 months, p<0.05 was considered significant. The study was adequately powered to detect a decline in 30% of gonadotropin levels at 80% with alpha set at 0.05.

RESULTS: In total, 55 men (age 19-55 years) were eligible and enrolled into the trial. Of the 55 who enrolled, 38 completed the trial and 17 dropped out (nasal irritation was a common cause of dropout). Among the men that completed the trial, mean T increased from 230(62) to 605(278) ng/dL (p=0.005), LH and FSH decreased but remained within the normal range (2-5 IU/mL). Most importantly, semen parameters remained unchanged; sperm concentration 26.6(15.2) vs 26.0(21.2) million/cc (p=0.6), sperm motility 49.6(12.4) vs 48.9(22.5)% (p=0.8), TMSC 40.8(36.7) vs 41.0(56.4) million p=0.9. There was improvement across all domains of the IIEF scores in erectile function, libido, intercourse satisfaction, orgasm, and overall sexual satisfaction as well as improvement in questions related to energy in the SF-36. Only 3 (7.9%) men developed severe oligospermia and one (2.6%) became azoospermic. All of these 4 men recovered spermatogenesis after discontinuation. The only adverse events were nasal irritation in 10 men.

CONCLUSIONS: This single center phase IV clinical trial demonstrated that Natesto increases serum T and improves hypogonadal symptoms while simultaneously maintaining gonadotropins and semen parameters. Natesto® appears to be a safe and effective treatment for men with hypogonadism who wish to preserve fertility.

SUPPORT: Ayut Biosciences provided drug free to patients.

O-267

DECREASED LIVE BIRTH RATE WITH LONGER OVARIAN STIMULATION IN FRESH BUT NOT FREEZE-ALL IN VITRO FERTILIZATION (IVF) CYCLES: ANALYSIS OF 17,830 CYCLES FROM THE SART REGISTRY. Rachel S. Gerber, MD,a Michelle Kappy, MD,a Melissa Fazzari, Ph.D.,a Sharon Galperin, BS,a Alexa Cohen, MD,a Harry Lieman, MD,a Sangita K. Jindal, Ph.D.,b Erkan Buyuk, MDc aAlbert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY; bMontefiore Institute for Reproductive Medicine and Health, Hartsdale, NY. OBJECTIVE: To evaluate the effect of controlled ovarian stimulation length on first transfer live birth rates in fresh and freeze-all antagonist IVF cycles. DESIGN: Historical cohort study of the SART CORS database. MATERIALS AND METHODS: Patient data was obtained for all gonadotropin antagonist IVF cycles (n=17,830) from 2014 to 2015 in which a single embryo transfer was completed as part of a fresh embryo transfer (n=14,866) or the first frozen embryo transfer in freeze-all non-preimplantation genetic testing-aneuploidy cycles (n=2964). Days of ovarian stimulation, patient and cycle characteristics, and pregnancy outcomes were extracted in both fresh and freeze-all cycles. Binomial regression models estimated the relative risk of live birth with respect to days of stimulation categorically, and after adjustment for a priori confounders.

RESULTS: In fresh cycles, days of ovarian stimulation ranged from 4 to 40 days, with 24% of patients having 4-8 days, 62% 9-11 days, 8% 12 days, and 6% with 13 or more days. In fresh transfer cycles, live birth rates decreased significantly with each additional day of stimulation from ≤ 8 days to 12 days by univariate analysis ranging from 47.36% to 41.49%, p-value (trend) =<0.0001. These findings were validated in a multivariable model controlling for age, gravidity, BMI, Max FSH, and etiology of infertility with a p-value (trend) = 0.005. In freeze-all cycles, a decline in the live birth rate with increasing days of stimulation was observed with p(trend)=0.01, however this trend was not statistically significant in the adjusted model p(trend) = 0.46. (Table 1)

CONCLUSIONS: Increasing length of ovarian stimulation negatively affects live birth rates in fresh but not freeze-all antagonist IVF cycles. In fresh transfer cycles, live birth rate is highest with stimulation of ≤ 8 days (47.4%), and was observed to decline with increasing days of stimulation (4.15%) with 13 or more stimulation days. This points to an endometrial cause for the adverse impact on live birth rates with longer stimulation in fresh transfer cycles that may not be relevant in freeze-all cycles.

<table>
<thead>
<tr>
<th>Days of Stimulation</th>
<th>Fresh (n=14,866)</th>
<th>Frozen (n=2,964)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-8</td>
<td>1716</td>
<td>308</td>
</tr>
<tr>
<td>9</td>
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<td></td>
<td>41.49%</td>
<td>45.28%</td>
</tr>
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<td>adjusted (trend)</td>
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<td>0.46</td>
</tr>
</tbody>
</table>

1 Corresponding to a non-zero estimate for linear trend across days of stimulation categories in a univariate binomial regression model
2 Corresponding to a non-zero estimate for linear trend across days of stimulation categories in a multivariable binomial regression model

O-268

IN VITRO MATURATION (IVM) VERSUS IN VITRO FERTILIZATION (IVF) IN WOMEN WITH HIGH ANTRAL FOLLICLE COUNT (AFC): A RANDOMIZED CONTROLLED TRIAL (NCT03405701). Lan N. Vuong, M.D.; Ph.D.,a Vu N. A. Ho, MD,a Tuong M. Ho, MD,a Vinh Q. Dang, MD,a Tu Anh V. Dinh, MD,a dToan D. Pham, BSc,a Rui Wang, MD,a Robert J. Norman, MD, PhD, Prof.a Robert B. Gilchrist, Ph.D., Prof.,a Johan Smitz, MD, PhD, Prof. aBen W. Mol, M.D., Ph.D. Prof.a 1University of Medicine and Pharmacy at Ho Chi Minh City, Ho Chi Minh, Viet Nam; 2HoPE Research Center, Ho Chi Minh, Viet Nam; 3The University of Adelaide, Robinson Research Institute, Adelaide, SA, Australia; 4School of Women’s and Children’s Health, University of New South Wales Sydney, Sydney, NSW, Australia; 5Follicle Biology Laboratory, Vrije Universiteit Brussel, Brussels, Belgium; 6Monash University, Monash Medical Centre, Department of Obstetrics and Gynaecology, Melbourne, VIC, Australia.

OBJECTIVE: IVM has been proposed as an alternative to IVF for women at increased risk of ovarian hyperstimulation syndrome (OHSS) due to a high antral follicle count (AFC) and/or polycystic ovary syndrome (PCOS). Here, we compare the effectiveness and safety of one IVM and one IVF cycle in women with infertility and high AFC.

DESIGN: A single-center noninferiority randomized controlled trial (NCT03405701) in Vietnam.

MATERIALS AND METHODS: Women scheduled for assisted reproductive technology (ART) with an AFC ≥ 24 were randomized (1:1 ratio) to IVM or IVF. In the IVM group, oocyte pick-up was performed 42 hours after the last injection of highly purified human menopausal gonadotropin (hp-hMG) 150 IU/day; all oocytes were cultured in capacitation pre-maturation medium for 24 h and then transferred to maturation culture for 30 h. Women allocated to IVF underwent ovarian stimulation using a hp-hMG/gonadotropin

<table>
<thead>
<tr>
<th>IVM (n=273)</th>
<th>IVF (n=273)</th>
<th>Rate difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Embryos transferred, n</td>
<td>1.9±0.3</td>
<td>2.0±0.2</td>
</tr>
<tr>
<td>Clinical pregnancy, n (%)</td>
<td>138 (51)</td>
<td>154 (56)</td>
</tr>
<tr>
<td>Ongoing pregnancy, n (%)</td>
<td>104 (38)</td>
<td>126 (46)</td>
</tr>
<tr>
<td>Twins</td>
<td>71/104 (68)</td>
<td>79/126 (63)</td>
</tr>
<tr>
<td>OHSS, n (%)</td>
<td>33/104 (32)</td>
<td>47/126 (37)</td>
</tr>
</tbody>
</table>

FERTILITY & STERILITY®
releasing hormone ( GnRH ) antagonist protocol and oocytes were retrieved 36 h after GnRH agonist trigger.

In both groups, mature oocytes were fertilized using intracytoplasmic sperm injection, and all embryos were frozen on day 3: ≤ 2 embryos were transferred in a subsequent frozen cycle. The primary outcome was live birth after first embryo transfer of the started treatment cycle. The planned sample size was 546, assuming an expected live birth rate of 45% in the IVF group, a noninferiority margin of −10%, 90% power and 15% loss to follow-up. While follow-up for live birth is ongoing, we report ongoing pregnancy in this abstract.

RESULTS: Between January 2018 and December 2018, we randomized 546 women (273 in each group). Baseline characteristics were comparable (mean age 30 years, BMI 22 kg/m²). The ongoing pregnancy rates after the first embryo transfer were 38% and 46%, respectively (difference −8.1% [-16.7%, 0.6%]). Other fertility outcomes after first embryo transfer were also not statistically significant between the groups (Table). All laboratory outcomes favoured IVF over IVM: oocytes retrieved (19.8 vs 14.1), MII oocytes (15.7 vs 8.9), maturation rate (79% vs 64%), fertilized oocytes (13.7 vs 7.3), top-quality embryos (7.9 vs 3.2), and freezeable embryos (7.6 vs 4.0) were significantly higher in the IVF vs IVM group (all p <0.001).

CONCLUSIONS: Among women undergoing ART with an AFC ≥24, IVM did not result in significantly lower ongoing pregnancy rates than IVF. Live birth data will be available by October 2019.

O-269

ANTI-MULLERIAN HORMONE (AMH) IN THE CALIPER COHORT OF HEALTHY COMMUNITY CHILDREN AND ADOLESCENTS: IMPROVING CARE IN ONCOFERTILITY.

Ruth Ronn, MD, a Mary Kathryn Bohn, BSc, b Khosrow Adeli, PhD, FCACB, DABCC, c Barry Hoffman, PhD, FCACB, d Ellen M. Greenblatt, MD e Mount Sinai Fertility, Sinai Health System, Toronto, ON, Canada; The Hospital for Sick Children/University of Toronto, Toronto, ON, Canada; The Hospital for Sick Children, Toronto, ON, Canada.

OBJECTIVE: Serum AMH is an excellent biomarker of ovarian reserve (1,2). The assessment of AMH pre- and post gonadotoxic treatment helps define reproductive potential in young adults facing cancer treatment. Normative childhood and adolescent AMH levels are not well defined despite the potential for high clinical utility (3). Most studies have been limited by sample size, varying and less sensitive manual assays, and with conflicting trends (4-12). Our objective is to establish accurate reference intervals (RIs) for AMH in the pediatric population that can be used to assess AMH in pediatric/adolescent survivors.

DESIGN: This cross-sectional study examined AMH in serum samples from healthy pediatric subjects in the Greater Toronto Area.

MATERIALS AND METHODS: 300 samples were collected from healthy females aged 6-19 years, which were previously drawn and stored as part of a collaboration with the Canadian Laboratory Initiative on Paediatric Reference Intervals (CALIPER), an internationally recognized initiative developing normative reference values for clinically important biomarkers of paediatric health and disease (13). Samples were analyzed using the automated Beckman DxI AMH assay in one batch. Basic demographics and menstrual data on sample subjects was also noted.

RESULTS: Divided into four predetermined age groups (6 to <9 years, 9 to <12, 12 to <15, 15 to <19). Statistical significance between each age group was determined by the Harris & Boyd method. Outliers were removed from each age partition separately using the Tukey method and the adjusted Tukey method. Mean ± SD, associated quartiles and reference intervals were calculated in alignment with CLSI guidelines. The effect of menstrual status and ethnicity on study cohort was assessed using a one-way analysis of variance. Outliers were removed by the Harris & Boyd method. Outliers were removed from each age partition separately using the Tukey method and the adjusted Tukey method. Mean ± SD, associated quartiles and reference intervals were calculated in alignment with CLSI guidelines.

CONCLUSIONS: Our results demonstrate comparable trends to other studies with respect to rising AMH in childhood. This contributes to the limited literature on normative AMH values throughout childhood and adolescence. This study presents reliable reference ranges, from a single batched assay on healthy children. This is also the largest series of its kind using an automated AMH assay. These normative values for AMH will be a major adjunct to counseling pediatric cancer patients and their families who require or have completed fertility damaging therapies.

SUPPORT: AMH assay kits were provided by Beckman Coulter (Lot 971017).


**O-270**

**DAMAGED SPERM PARAMETERS AND SPERMIA TION FAILURE IN VENLAFAXINE-TREATED RATS: A CORRELATION WITH HIGH TES TICULAR AROMATASE IMMUNOEXPRESSION AND REDUCED EPIDIDYMAL V-ATPASE.** Estela Sasso-Cerri, PhD, Fabiane de Santi, Master degree, André A. S. da Silva, Under graduate, student, Beatriz M. Rodrigues, Under graduate, student, Flávia L. Beltrame, PhD, Paulo S. Cerri, PhD, São Paulo State University - UNESP, Araraquara, Brazil; São Paulo Federal University - UNIFESP, Morphology and Genetics, São Paulo, Brazil.

OBJECTIVE: The antidepressant venlafaxine (Serotonin Norepinephrine Reuptake Inhibitor-SNRI) has impaired sexual function in male patients. We investigated the impact of this SNRI on sperm parameters, relating them to testicular and epididymal histopathological markers. The recovery of sperm and testicular changes was also evaluated following the interruption of treatment.

DESIGN: Adult male rats were grouped: Venlafaxine-35 days (VFG-35; n=6) and Venlafaxine-65 days (VFG-65; n=6) received venlafaxine (30mg/kg BW) by gavage for 35 days; Control-35 days (CG-35; n=6) and Control-65 days (CG-65; n=6) received saline. After treatment, the animals from CG-35 and VFG-35 were killed while the animals from CG-65 and VFG-65 were maintained without treatment for 30 days to evaluate reversibility of changes. In these groups, sperm parameters were evaluated in association to seminiferous epithelium integrity, steroidogenesis, testicular aromatase and epididymal V-ATPase immunoperoxidase.

MATERIALS AND METHODS: Rats received 30mg/kg (therapeutic dosage) of venlafaxine for 35 days (minimal period for the antidepressant effect). The concentration, morphology and mitochondrial cytochemical activity (MCA) of sperm from cauda epididymis were analyzed. In epididymal and testicular sections, the following parameters were evaluated: epididymal duct diameter, frequency of tubules with spermiogenesis failure, number of Sertoli cells (NSC), viability of germ cells by TUNEL, Leydig cells nuclear diameter (LCn), StAR immunopexpression (steroidogenesis), testicular diameter (LCd), mitochon
drial (MCO), and mitochondrial (MCA).

RESULTS: In VFG-35, the epididymal duct diameter, sperm concentration and MCA decreased, and a high frequency of sperm tail abnormalities was found. Changes in seminiferous epithelium and high frequency of post-spermiogenesis tubules with retained spermatids were found. The NSC decreased whereas the number of TUNEL-positive germ cells and Cyp19 immunoperoxidase increased in this group. In VFG-65, LCn was larger than CG; a high immunoexpression of StAR and elevated serum and testicular testosterone levels were observed. Venlafaxine also impaired the epididymal V-ATPase immunoperoxidase. Except for the tail changes and MCA, sperm concentration and testicular parameters were improved following the interruption of treatment.

CONCLUSIONS: Venlafaxine stimulates LC steroidogenesis and increases aromatase levels, impairing spermiation and sperm concentration and quality. Therefore, the evaluation of fertility together with a careful analysis of spermatogenesis and hormonal status of patients treated with SNRI is useful. The changes in sperm parameters may also be associated with disturbances in the acid/basic milieu of epididymal lumen due to reduction in V-ATPase. The improvement of sperm parameters following the interruption of treatment is, at least in part, due to recovery of aromatase/estrogen levels and the restoration of spermiogenesis process.

**SUPPORT:** FAPESP (2017/19829-6; 2018/13590-4; 2018/25353-7)

**O-271**

**THE AGE TAX: OOCYTE CRYOPRESERVATION (OC) AGE-BASED COST ANALYSIS.** Bat-Sheva L. Maslow, MD, MSCTR,a Kristen Mancinelli, MSPH,a Jennifer Nicole Lannon, BS,b Sidonia R. Swarn, BS,b Joshua U. Klein, MD °Extend Fertility, New York, NY; °FreezeHealth, Miami, FL.

OBJECTIVE: The degree to which OC costs increase with age is not known. Data regarding OC outcomes and associated costs are limited. With increasing demand for OC, there is a need for evidence-based counseling tools for age-related costs. The primary aim of this study is to quantify relative age-based increase in OC costs with an evidence-based cost evaluation model of OC cost, incorporating age, medication, oocyte yield, and potential for LB. DESIGN: Cost analysis. Nested retrospective cohort study.

MATERIALS AND METHODS: All women undergoing OC at Extend Fertility Medical Practice from 4/2016-12/2018 were included in the cohort. Demographic and cycle data were abstracted from the electronic medical record. Cycle and storage fees were calculated for 135 U.S. practices from FreezeHealth’s public dataset. Medication pricing was calculated using first 15 listings in a national online database (fertilitydrugcalculator.com).

Mathematical model for cost per cryopreserve MII oocyte and cost per potential LB were developed with age, MII oocyte per cycle, total cycles, total medication utilization, national cycle and medication fees, and per oocyte potential LB rates from Doyle et al. Using the <34 group as a reference, relative increase in median cost per MI and cost per potential LB were calculated as multiples of the median (MoM) and 25-75’tiles. Associations were analyzed using ANOVA and Kruskall-Wallis, where appropriate.

RESULTS: 1241 subjects with a total of 1791 cycles were included. Mean age =35.6±3.3, mean # cycles 1.45±0.79, mean MII cryopreserved oocytes = 16.19±9.34, median cost per MII oocyte cryopreserved = $1170.99 ($708.19-2051.69) and median cost per potential LB = $17,041.34 ($9589.29-33253.79).

CONCLUSIONS: The relative cost of OC significantly increases with age.

**TABLE 1.** demonstrates significant increase in relative costs per MII oocyte and potential LB with age. In our model, cost per potential LB at 30-32 is 2.18x less the cost at 37-39 and 1.28x less the cost at 34-36 (p<0.001). The difference equals 6-12 years of storage.

<table>
<thead>
<tr>
<th>≤34 N=415</th>
<th>35-37 N=524</th>
<th>38-40 N=234</th>
<th>41-42 N=51</th>
<th>&gt;42 N=17</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td># Cycles</td>
<td>1.28±0.60</td>
<td>1.46±0.77</td>
<td>1.60±0.93</td>
<td>1.76±0.97</td>
<td>2.29±1.49</td>
</tr>
<tr>
<td>MII</td>
<td>18.16±9.52</td>
<td>16.18±9.06</td>
<td>13.88±8.43</td>
<td>12.35±10.7</td>
<td>11.23±9.99</td>
</tr>
<tr>
<td>GND (IUs)</td>
<td>4254.22±3302.98</td>
<td>5473.56±3830.88</td>
<td>6239.31±4238.65</td>
<td>7703.92±5061.78</td>
<td>9798.53±6590.56</td>
</tr>
<tr>
<td>Relative increase: Cost per MII</td>
<td>Ref</td>
<td>1.34 (0.80-2.23)</td>
<td>1.78 (1.13-2.78)</td>
<td>2.71 (1.35-5.46)</td>
<td>3.70 (1.83-6.13)</td>
</tr>
<tr>
<td>Relative increase: Cost per potential LB</td>
<td>Ref</td>
<td>1.51 (0.90-2.50)</td>
<td>3.25 (2.01-5.07)</td>
<td>8.89 (4.36-17.91)</td>
<td>12.13 (6.01-20.12)</td>
</tr>
</tbody>
</table>

Women considering OC should be counseled about the drastic increase in cost with age. This study represents the most robust analysis to date of OC costs with data collected from OC cycles.

**CONCLUSIONS:** Successful elective and medically indicated oocyte vitrification and warming for autologous inA vitro fertilization, with predicted birth probabilities for fertility preservation according to number of cryopreserved oocytes and age at retrieval. Doyle, Joseph O. et al.Fertility and Sterility, Vol 105, Issue 2, 459 - 466.e2

**O-272**

**MENSTRUAL CYCLE REGULARITY AND LENGTH AND RISK OF MORTALITY: A PROSPECTIVE COHORT STUDY.** Yixin Wang, MD,a Mariel Arvizu, MD,a Janet Rich-Edwards, PhD,a JoAnn E. Manson, MD, DrPH,a Pan, PhD,b Jorge E. Chavarro, MD, Sc.D,a JoAnn E. Manson, MD, Sc.D,a An Pan, PhD,a OECD, DrPH,a Jennifer Stuart, Sc.D,b Janet Rich-Edwards, PhD,c Marilyn A. Trabert, MD,a,b° Massachusetts General Hospital, Boston, MA; °Brigham and Women’s Hospital and Harvard Medical School, Boston, MA; °Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China.

OBJECTIVE: To prospectively assess the impact of menstrual cycle characteristics in adolescence and adulthood with risk of all-cause and cause-specific mortality.

**MATERIALS AND METHODS:** Women from the Nurses’ Health Study II (NHS-II) were followed from 1991-2015. The NHS-II is a prospective study of 82,750 women age 30-55 years at baseline in the US. Participants report their menstrual cycle length and regularity at baseline and in each year of follow-up. Mortality data were collected through 2015. Women with >2 months of missing data were excluded from the analyses. The primary outcome was all-cause mortality. Causes of death were identified by a Committee of Expert Confidential Mortality Reviewers using a standardized dictionary to match death certificates to cause categories. For each woman, a variable was calculated based on her menstrual cycle length and regularity at age 16. Women with irregular cycles were excluded from this analysis.

**RESULTS:** From 1991-2015, 27,273 women had complete data on menstrual cycle regularity and length at age 16. Compared to women in each quintile of regularity (1-5), women in the highest quintile had a 9% lower risk of death during follow-up (HR 0.91; 95% CI 0.87-0.96). Women in the highest quintile of regularity and shortest length at age 16 had a 22% lower risk of death compared to women in the lowest quintile of regularity and longest length at age 16 (HR 0.78; 95% CI 0.72-0.85). The association between menstrual cycle characteristics and mortality was consistent across age groups, race/ethnicity, body mass index, and family history of cardiovascular disease.

**CONCLUSIONS:** Women with regular menstrual cycles and shorter cycle lengths at age 16 had a lower risk of death compared to women with irregular cycles and longer cycle lengths. These findings suggest that menstrual cycle characteristics may be markers of future health and should be assessed to identify women at risk for mortality.
Fertility Center, Dallas, TX; Dallas Fort Worth Fertility Associates, Dallas, associated with longer menstrual cycle lengths (respectively). Elevated HR for cardiovascular and cancer mortality was also associated with menstrual cycle length of 32-39 days [HRs > 32 days] than women whose current usual cycle length was 26-31 days [HRs > 32 days] respectively. Elevated HR for cardiovascular and cancer mortality was also associated with longer menstrual cycle lengths (>32 days) between the ages of 28-48 years. CONCLUSIONS: Irregular and long menstrual cycles are associated with an increased risk of mortality.

O-273
THE EFFECT OF EXTENDED BLASTOCYST EXPOSURE OF HYALURONAN ENRICHED TRANSFER MEDIA ON IMPLANTATION RATE IN FROZEN EMBRYO TRANSFERS. Oscar Perez, Ph.D.,* Hannalie Adriaanse, BS,† Breanna Tilley, MSc,‡ Gabriella Navarrete, BS,† Linda Lay, BS,§ Lucille M. Little, BS,|| Ravi Gada, MD,*, Laura Lawrence, MD,*, Karen Lee, MD,† Mika R. Thomas, MD,§ Samuel Chanttilis, MD,† Dallas Fertility Center, Dallas, TX, ‡Dallas Fort Worth Fertility Associates, Dallas, TX.

OBJECTIVE: Hyaluronan enriched transfer media (EmbryoGlue®, Vitrolife, Inc) published reports demonstrating conflicting results on improving clinical pregnancy and implantation rate outcomes in frozen embryo transfers (FET).

DESIGN: Prospective randomized study

MATERIALS AND METHODS: A total of one hundred nineteen FET patients were included in this study. Frozen blastocysts were thawed following the Dallas Fertility Center laboratory thaw protocol and randomly divided into four treatment groups. Blastocyst transfer dishes were prepared using 2 ml (1 ml in inner well and 1 ml in outer well) of EmbryoGlue® in organ well dishes for all experimental groups. These transfer dishes were equilibrated overnight. Embryos in the control group were transferred in embryo glue following the manufacture’s guidelines. Treatment groups consisted of one-hour, two-hour and three-hour post thaw exposure to EmbryoGlue® before blastocyst transfer. Clinical pregnancy, ongoing pregnancy, and implantation rate after embryo transfer were compared among the groups. Clinical pregnancies were confirmed by the presence of an intrauterine gestational sac. Chi square analysis was used to analyze data.

RESULTS: No statistical difference was seen between the control group and one-hour treatment group in terms of clinical pregnancy, ongoing pregnancy and implantation rate. In contrast, statistical difference was presented after exposure increment of blastocysts to EmbryoGlue®.

CONCLUSIONS: Blastocysts with extended exposure of hyaluronan enriched medium before embryo transfer showed an improved implantation rate in frozen embryo transfers. This procedure before embryo transfer provides better clinical outcomes when thawed blastocysts were exposure to embryo glue for more than 2 hours.

O-274
THE RATE OF TRUE RECURRENT IMPLANTATION FAILURE (RIF) IS LOW: RESULTS OF THREE SUCCESSIVE FROZEN EUPLOID SINGLE EMBRYO TRANSFERS (SET). Paul Pirtea, MD,† Dominique De Ziegler, MD,† Diego Marin, M.S.,§ Li Sun, Ph.D.,∥ Yiping Zhan, Ph.D.,∥ Jean Marc Ayoubi, MD PhD,∥ Emre Seli, MD,∥ Jason M. Franasiak, MD,∥ Richard Thomas Scott, Jr., MD,∥ IVI-RMA New Jersey, Basking Ridge, NJ, §Hospital FOCH, Paris, France; ∥Foundation for Embryonic Competence, Basking Ridge, NJ.

OBJECTIVE: RIF is one of the more challenging areas of reproductive medicine. Despite a significant interest in RIF, its definition has not yet been agreed upon, and etiologic factors responsible for RIF have not been fully characterized. One of the most common causes of pregnancy failure is chromosomal abnormality of the embryos. Therefore, it is likely that a number of RIF cases are due to aneuploidy. Other potential causes of RIF include immune and endometrial factors; however, the relative contribution of these factors to RIF have not yet been established. In this study, we aimed to determine the true prevalence of RIF in women undergoing successive SET.

DESIGN: Retrospective cohort study.

MATERIALS AND METHODS: To answer this question we analyzed all patients (n=4,515) with up to three consecutive euploid frozen SETs taking place from January 2012 to July 2018, excluding cycles with donor eggs or gestational carriers. We analysed the cumulative outcomes from these cycles in order to determine what percentage of them had causes of RIF that were not related to the ability to achieve a euploid blastocyst. All embryos underwent PGT-A at the blastocyst stage using qPCR or NGS-based platforms. All embryos were vitrified at the blastocyst stage after a trophectoderm (TE) biopsy was performed. Endometrial preparation was achieved with oral E2 and intramuscular progesterone supplementation with transfer of a single euploid blastocyst performed on the 6th day of progesterone exposure. The primary endpoint was implantation as determined by the presence of a gestational sac with fetal cardiac activity. A logistic regression model was employed to assess the differences of outcomes between first, second, and third euploid SET and a Kaplan-Meier curve as utilized to analyze cumulative implantation rate.

RESULTS: The mean age of the patients included in the study was of 35.4±4.2. The implantation rates of the first, second and third euploid SET were 69.4%, 59.3%, and 59.2% per transfer, respectively. Of those who failed to achieve implantation after the first euploid SET (n=1381), 799 (57.9%) underwent a second euploid SET and of those who failed to achieve implantation after the second euploid SET (n=325), 142 (43.7%) patients underwent a 3rd euploid SET. The second (OR=0.638, 95% CI 0.547-0.746) and third (OR=0.627, 95% CI 0.446-0.886) frozen euploid SET provided a slightly decreased implantation when compared to the first frozen euploid SET. The cumulative implantation rates after up to three consecutive frozen euploid SET was 94.9% (95% CI: 93.7%-95.9%).

CONCLUSIONS: Our findings suggest that true RIF is rare. For those patients with the ability to make euploid blastocysts, 94.9% would achieve clinical pregnancy with 3 embryos transferred. The implantation rates decline minimally with increasing transfers, but the fact that they remain high.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>n</th>
<th>Age (Average)</th>
<th>Exposure Time to Embryo Glue Hours (Average)</th>
<th>Embryos Transferred (Average)</th>
<th>Clinical Pregnancy Rate</th>
<th>Implantation Rate</th>
<th>Ongoing Pregnancy Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>26</td>
<td>33</td>
<td>0</td>
<td>1.2</td>
<td>46%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>47%&lt;sup&gt;a&lt;/sup&gt;</td>
<td>45%&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>One-hour</td>
<td>26</td>
<td>33</td>
<td>1.3</td>
<td>1.3</td>
<td>54%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>48%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>46%&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Two-hour</td>
<td>31</td>
<td>33</td>
<td>2.2</td>
<td>1.3</td>
<td>68%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>60%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>59%&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Three-</td>
<td>36</td>
<td>34</td>
<td>3.3</td>
<td>1.2</td>
<td>81%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>73%&lt;sup&gt;b&lt;/sup&gt;</td>
<td>75%&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a,b,c</sup> Different superscripts within columns indicate significant differences (P<0.05)
suggests that 5% who fail to implant after three attempts may largely be victims of simple probabilities/statistics and that additional transfers offer hope of a good outcome.

O-275

A SINGLE INJECTION OF LONG ACTING GNRH-ANTAGONIST -DEGARELIX- DOWNREGULATES HYPOPHYSIS DURING OVARIAN STIMULATION. A RANDOMIZED CONTROLLED TRIAL. Tatiana Chartomatsidou, MSc,a Robert Najdecki, MD, PhD,a Fotini Choulia-Li, MD,a,7 Evangelia Timotehou, MSc,a,7 Petroula Tatsi, MSc,a,7 Eirini Asouchidou, MD, PhD,a,7 Sofia Bouchlariotou, MD, PhD,a,7 Evangelos Mmbmas, MD, PhD,a Lazaros Konstantinios Karagiannidis, MD,a Nikolas Nikolaotoss, MD, PhD,a Evangelos Papapanoalaou, MD, PhD,a* Assisting Nature, Center of Assisted Reproduction and Genetics, Thessaloniki, Greece; aMedical Department, Aristotle University of Thessaloniki, Thessaloniki, Greece; aMedical Department, Democritus University of Thrace, Alexandroupolis, Greece.

OBJECTIVE: Study’s objective was to examine if the use of a novel long acting, single dose GnRH antagonist, Degarelix, can cause efficient pituitary downregulation during ovarian stimulation in oocyte donors.

DESIGN: This RCT (Trial Registration Number: NCT03861715) recruited healthy young oocyte donors (<35yrs) between January 2017-January 2019 in Assisting Nature, Centre of Assisted Reproduction and Genetics, Thessaloniki, Greece. Two groups of patients were examined; the first group (study group) received a single Day-6 follicular dose of degarelix (Firmagon, Ferring Pharmaceuticals); the second group (control group) received daily 0.25mg of ganirelix as is the standard antagonist protocol. Study Group (Degarelix group) consisted of 80 women, who followed the new protocol, whereas, 93 donors followed the classical fixed Day6 GnRH-antagonist protocol.

MATERIALS AND METHODS: Ovarian stimulation was initiated on cycle Day2 or 3 with gonadotropins 225 IU (200-300), daily, in both groups. In Control group 0.25 mg of antagonist ganirelix was administered daily from stimulation Day6 in a fixed manner. In the new study group, on the same day, day-6, a single bolus injection of 0.1 ml Degarelix was administered subcutaneously. agonist triggering (Triptorelin 0.3ml) was employed for all and OPU performed at 36h. Fresh or frozen blastocyst-only transfer was performed following recipient endometrial estrogen and progesterone priming.

RESULTS: No LH rise or any OHSS was noticed in any groups. Mean age (27.1 vs 27.9 years), mean AMH (4.1 vs. 3.6ng/ml) and total gonadotropin dose (2400 vs 2508 IU) of participants were not different among Control-group- and Study-group respectively. Similar number of oocytes retrieved (18.1 vs.17.1, p>0.05) with degarelix short antagonist group, and similar number of blastocysts produced in both groups (6.6 in Control-group-A vs. 6.9 in Study-group). All recipients underwent 2 blastocysts transfer. Pregnancy is expressed per donor. Initial positive HCG per donor was significantly higher (p<0.05) in the Degarelix Short Antagonist (Study-Group) 78.7% (63/80) as compared with 65.5% (n=61/93) in classic short antagonist (Control-Group). Cumulative delivery rate was higher 60.0% (48/80) in the new single shot Degarelix short antagonist group as compared to 50.5% (n=47/93) in classic antagonist group, however not significant (p>0.05).

CONCLUSIONS: The new long-acting GnRH antagonist in a single bolus dose of 0.1 mg carries no risk for LH, produce mature oocytes and achieve comparable pregnancy outcome to the classical short multiple dose antagonist protocol. This new protocol is first described by us, it is more patient friendly decreasing the number of injections that a patient receives. This is an ongoing study, dose of degarelix was arbitrarily chosen by our team, and more degarelix doses can be tested in future studies.

O-276

EFFICACY OF LF111 IN OBESE WOMEN, AN INVESTIGATIONAL PROGESTIN-ONLY ORAL CONTRACEPTIVE. Carolyn L. Westhoff, MD, MSc,a Kurt T. Barnhart, MD, MSCE,b Anne E. Burke, MD, MPH,c Thomas D. Kimble, MD,a David F. Archer, MD,a Enrico Colli, MD,d Columbia University, New York, NY; dUniversity of Pennsylvania, Division of Reproductive Endocrinology and Infertility, Philadelphia, PA; aJohns Hopkins School of Medicine, Baltimore, MD; eEastern Virginia Medical School, Norfolk, VA; eExeltis, Madrid, Spain.

OBJECTIVE: Obesity is common in North American women and may be associated with lower contraceptive efficacy. As a sub-analysis of a phase 3 safety and efficacy trial, we evaluated the efficacy, stratified by age and obesity status, of LF111, a progestin-only oral contraceptive regimen with drospirenone (dosage: 4.0 mg x 24 days and 4 placebo days).

DESIGN: An open-label trial in women ≥ 15 years desiring contraception to evaluate efficacy and safety during 13 consecutive 28-day cycles.

MATERIALS AND METHODS: We calculated the Pearl Index (PI) in non-breastfeeding women who received at least one dose of LF111 (modified Full Analysis Set [mFAS]). We defined obesity as body mass index (BMI) ≥ 30 kg/m2.

RESULTS: Among 1006 subjects, 354 (35.2%) were obese, a proportion similar to the overall US population (36.5%). This analysis included 352 obese subjects of all ages. Four confirmed pregnancies occurred among 352 obese subjects versus 8 among 641 non-obese subjects. The PI in 2283 exposure cycles in obese subjects was 2.3 (95% CI 0.6 - 5.8) versus 2.4 (95% CI 1.0 - 4.8) in 4283 exposure cycles in non-obese subjects. No women >35 years had a confirmed pregnancy; thus, the PI in women ≤ 35 age was 2.9 (95% CI 0.8 - 7.3) in 1817 evaluable cycles in obese participants versus 3.0 (95% CI 1.3 - 5.8) in 3520 evaluable cycles in 590 non-obese participants. No cases of venous or arterial thromboembolism, myocardial infarction, stroke, or pulmonary embolism were reported in the clinical trial.

CONCLUSIONS: Drospirenone 4.0 mg 24/4 provides effective contraceptive protection in obese women.

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AUTHOR AND SPOUSE/PARTNER DISCLOSURES INDEX: ORAL, POSTER, AND VIDEO SESSIONS

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<td>(travel expenses to attend conference covered by the company; IBSA (travel expenses to attend conference covered by the company)</td>
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<td>Edwards Life Sciences; Fertility Nutriceutical (Receive Royalty based on Patent); Merck Manual (Editorial)</td>
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1 Company Officer 2 Direct Stockholder 3 Full-Time Company Employee 4 Grant Recipient 5 Honoraria 6 Paid Consultant 7 Speaker’s Bureau 8 Other 9 Partner/Spouse 10 Both
Bustillo, M. Genetics&IVF Institute

Butler, S. A. MAP IP Holding

Calderón, G. Embryotools

Callum, P. California Cryobank; Tandem Genetics

Cantineau, A. E. Ferring BV (visiting ESHRE congress Barcelona); Thermamex (visiting a ESHRE congress Vienna)

Caplan, A. L. Eli lilly (lecture); Janssen (unpaid consultant); pfizer (lecture); WIRB/copernicus (advisory board)

Cardona, C. Androvia

Carrell, D. T. EMD Serono; Episona, Inc

Carrera, M. Ferring; MSD; Theramex

Casablanca, Y. Celsion

Casper, R. F. Abbvie; Circadian light; Inception Lifebank (Medical director); Reproductive Nutraceuticals; Teva (Royalties); UpToDate (Royalties)

Catherino, A. B. EMD Serono, Inc.

Catherino, W. Abbvie; Allergan; American Board of Obstetrics and Gynecology; American Society for Reproductive Medicine; Bayer; EMD Serono

Cedars, M. I. Ferring Pharmaceutical

Chan, C. EMD Serono; Merck

Chan, J. L. Binto (Scientific Advisor)

Chandarkar, S. Spovum technologies pvt. Ltd.

Chang, C. Prelude Fertility; Reproductive Biology Associates

Chavez-Badiola, A. Darwin Technologies LTD

Chen, S. Create Fertility Centre

Chen, S. H. Cooper Genomics; Hologic; MedAnswers; Ohana; Phosphorus

Cheng, D. Reproductive and Genetic Hospital of CITIC-Xiangya

Chettier, R. Rakesh N chettier

Chkonia, L. Ovamedi LTD

Cholkeri-Singh, A. Abbvie; American Regent, Inc; Bayer (Research); Boston Scientific; Caldera Medical; Channel Medsystems; ESP Linx; Spovum technologies pvt. Ltd.

Chorich, L. Augusta University

Chou, C. Natera Inc

Choudhary, K. Previso Genetics inc

Christ, M. Igenomix

Clemente-Ciscar, M. Celmatrix

Clementi, C. multiple pharma companies; Population Council; TherapeuticsMD

Cooper, A. Celmatrix (Scientific Advisory Board); Ferring

Copel, J. A. Jubel LLC

Copperman, A. B. Progyny; Sema
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Isley, L. California Cryobank
Jahangiri, S. CREAtE Fertility Centre
Jalalian, L. UCSF Center for Reproductive Health
Jalas, C. Foundation for Embryonic Competence
Jasper, M. J. PerkinElmer Health Sciences (Australia) Pty Ltd
Jasulaitis, S. EMD Serono
Jenkins, T. G. Nanonc
Jensen, J. T. AbbVie (research support to OHSU); Bayer (research support to OHSU); Cooper Surgical; Date (research support to OHSU); Estera SPRL (research support to OHSU); Medicines360 (research support to OHSU); Merck; Sebela (research support to OHSU)
Jian, L. DIAsource ImmunoAssays SA, Belgium
Jimenez-Almazán, J. Igenomix
Jobanputra, V. FEC
Johansen Taber, K. Myriad Women’s Health
Johnson, R. Progenity
Johnson, S. SPD Development Company Ltd
Jonker, D. M. Ferring Pharmaceuticals
Jukic, A. Theralogix (Vitamin D supplements from this company were donated for a clinical trial of which I am PI.)
Kadoch, I. Yadtech
Kalaghan, L. CCRM Boston
Kaneshiro, B. Gynuity Health Projects; Merck Sharpe Dohme; Mithra Pharmaceuticals; National Institutes of Health; Sebela Pharmaceuticals; Uptodate
Kaseniit, K. E. Myriad
Kashanian, J. A. Roman Health
Kavoussi, P. K. AYTU Biosciences
Kavoussi, S. K. AbbVie
Keeffe, D. L. Illumina; March of Dimes; Origo
Khair, A. F. Ferring Pharmaceuticals
Kielh, M. Natera, Inc
Kijacic, D. Natera; National Institute of Health
Kim, J. J. Abbie; Intuitive
Klein, B. M. Ferring Pharmaceuticals
Klein, J. rmaafy
Kloos, B. Androvia LifeSciences (Part Time Employee)
Knowles, T. G. Fertility Focus Ltd (Receive royalties from the Company, co-founded the Company.)
Knox, K. Coppe Healthcare Solutions
Knudtson, J. Bayer; Endometriosis Foundation of America; Merck
Kodaman, P. Ferring
Korevaar, T. Berlin Chemie, Goodlife Healthcare, Quidel
Kostaras, K. Idiotiko iatreio Konstantinos E Kostaras & SIA Iatrik E.E.
Kadesia, R. Progyny; Simple Health
Labarta, E. Ferring; FINOX; IBSA/ Angelin; MSD; OvaScience
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