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**OBJECTIVE:** To develop the top 10 research priorities for female and unexplained infertility.

**DESIGN:** International consensus development study.

**MATERIALS AND METHODS:** Potential research questions were collated from an international survey, a systematic review of national and international fertility guidelines, and Cochrane systematic reviews. A rationalized list of confirmed research uncertainties were prioritized in an international survey. Prioritized research uncertainties were discussed during a consensus development meeting.

**RESULTS:** The initial survey was completed by 388 participants, from 40 countries, and 131 potential research questions were submitted. By reviewing nine clinical practice guidelines and 162 Cochrane systematic reviews, a further 136 potential research questions were identified. A rationalized list of 48 confirmed research uncertainties were entered into an interim prioritization survey completed by 317 respondents from 43 countries. The top 10 research priorities for female and unexplained infertility were identified during a consensus development meeting involving 41 participants from 11 countries (Table 1).

| **Table 1: Top 10 research priorities for female and unexplained infertility.** |
| --- |
| 1 | Can age-related infertility be prevented? |
| 2 | Can a predictive model be developed, tested, and validated to compare the outcomes of different management strategies for couples with unexplained infertility? |
| 3 | In couples with unexplained infertility, what is the optimal assisted reproductive technique? |
| 4 | Can a predictive model for fertility based upon ovarian reserve tests be developed, tested, and validated? |
| 5 | In women at risk of age-related infertility does standardized fertility assessment before attempting expectant management improve live birth rates? |
| 6 | What causes unexplained infertility? |
| 7 | In women with uterine fibroids what is the optimal management strategy to preserve fertility? |
| 8 | In women with otherwise unexplained infertility does hysteroscopic removal of an endometrial polyp increase live birth rates? |
| 9 | In women with mild intrauterine adhesions and otherwise unexplained infertility, does removal increase live birth rates? |
| 10 | In women with a uterine septum and otherwise unexplained infertility does hysteroscopic resection increase live birth rates? |

**CONCLUSIONS:** We anticipate these research priorities will help research funding organizations and researchers to develop their future research agenda. Healthcare professionals, professional organisations, and patient advocacy groups should champion the research priorities to highlight the many unanswered questions which need to be addressed in order to improve the outcomes of people with fertility problems.

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**P-288 4:30 PM Sunday, October 18, 2020**

**The use of virtual reality technology in Infertile Women undergoing in vitro fertilization-Embryo transfer: a randomized controlled trial.** Michal Dviri, MD, Lilach Marom Haham, MD, Jordana Beth Mashia Friedler, MD, Anjila Roumia, MD, Samantha Yee, Ph.D.1, Ari Y. Baratz, MD, Karen B. Glass, MD, Prati Sharma, MD, Clifford Lawrence Librach, MD, CRAreT fertility centre, Toronto, ON, Canada; CRAreT Fertility Centre, Toronto, ON, Canada; supported by the University of Toronto, Toronto, ON, Canada.

**Objective:** Embryo transfer (ET) is a crucial event in determining in vitro fertilization (IVF) outcome, perceived by many patients as the culmination of treatment. Therefore, it is often a stressful procedure for patients. We hypothesized that the stress accompanying this procedure may be inversely correlated with cycle outcome. The use of complementary therapies to reduce anxiety and improve IVF outcome is increasing. Various interventions...
have been studied, but their efficacy remains uncertain. Virtual reality (VR) technology, has been gaining attention over the past two decades, owing to evidence of it’s therapeutic potential for anxiety management and stress reduction. This study aimed to examine the possible effect of VR exposure on anxiety level and clinical pregnancy rate (CPR) in women undergoing IVF-ET.

**DESIGN:** A prospective randomized controlled trial (ClinicalTrials.gov Protocol Registration: NCT04394962).

**MATERIALS AND METHODS:** The study was conducted at the CReATe Fertility Centre (Toronto, Canada) after obtaining REB approval. Recruitment period was May 2019-March 2020 (suspended due to Covid-19). Infertile women aged 21-45-year-old using own ovum or older using the donor eggs, starting a frozen ET cycle, were recruited. All participants provided a written informed consent before study entry. Exclusion Criteria were contraindications to use VR technology, anxiety disorder and major uterine anomalies.

Participants were withdrawn if ET was cancelled. Patients were randomized (1:1) into two groups: A. Study group: 15-30 minutes of passive VR exposure (calming environment of choice) before ET; B. Control group: routine care only. Anxiety was assessed at 3 time points: T1—recruitment; T2—pre ET; T3=Post ET, using the validated “State-Trait Anxiety Inventory” questionnaire, heart rate (HR) and blood pressure (BP) measurements. The primary outcome was the CPR and the secondary outcomes were patients’ anxiety parameters, T-test or chi square were used as appropriate. P<0.05 was considered statistically significant.

**RESULTS:** Seventy six patients were included in the analysis, 38 in each study arm. Patient and cycle characteristics were comparable between the groups. The mean VR exposure time was 23.2 ±14.1 minutes, the majority chose a beach environment (78.9%) and stated they would recommend VR (75.3%). No serious adverse events were reported. HR was higher in T2 vs T1 and T3 (p=0.002), but the mean BP and HR did not differ between the groups. T1 and T2 ‘trait’ anxiety scores were comparable between the groups. No significant differences were found between the VR group to control in the ‘state’ anxiety scores during T2 (40.3 vs 39.3) and T3 (38 vs 38), respectively (P>0.05). CPR was comparable between the VR and the control group (50% vs 34.2%, respectively; p=0.42).

**CONCLUSIONS:** This is the first study to assess VR use in assisted reproduction. The preliminary findings suggest that VR exposure prior to ET does not reduce patients’ anxiety levels. Although non-significant, a higher CPR trend in the VR group suggests that this intervention may have a beneficial effect, but a larger sample size is needed to confirm this.

**SUPPORT:** CReATe Fertility Centre

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**P-289 4:30 PM Sunday, October 18, 2020**

**REGULATION OF OVUDICT HOMEOSTASIS AND FERTILITY BY PAX2 AND PAX8 GENES.** Abdul Soofi, PhD University of Michigan, Ann Arbor, MI.

**OBJECTIVE:** In mouse and humans, the development regulatory genes Pax2 and Pax8 are expressed in ovarian duct surface epithelia, yet the function of these genes and proteins in adult females remains unclear. By Generating double & single KO mouse modules of Pax2 and Pax8 we investigate their roles in maintaining the integrity of the oviductal cells. Our studies directly address aspects of oviduct epithelial homeostasis and fertility.

**DESIGN:** To create Pax2, Pax8, and Pax2/8 double mutants specifically in oviduct epithelium and characterize changes in gene expression, epithelial cell integrity, and fertility.

**MATERIALS AND METHODS:** We will implement detailed analyses of oviducts isolated at various times post tamoxifen administration from mice and Pax2 and Pax8 resulted in infertility (Table 1). To date, most of the preliminary data was obtained from Pax2/8 double mutants since we were concerned with redundancy and expected the most significant phenotypes in the double mutants. Analyses of histology, immunohistochemistry and changes in gene expression of total RNA from whole oviducts isolated after tamoxifen administration. For a rapid first pass screen, we compared controls (Pax2f/f;Pax8f/f) to single Pax mutants and Pax2/8 double mutants (Pax2f/f;Pax8f/f; Ovi-CreER) by Affymetrix microarrays. These data show hundreds of changes in gene expression levels upon Pax2 or Pax8 deletion, with significant overlap between the Pax2 and Pax8 mutants but also expression changes unique to each single mutant.

**CONCLUSIONS:** Little is known regarding the mechanisms underlying epithelial homeostasis, the proteins that determine cell fates, and epithelial integrity in the adult oviduct. Pax8 expressing secretory cells are thought to give rise to ciliated cells, which help move the oocyte down the duct and Pax2 is associated with cilia motility and physiology. Using a conditional KO model of Pax2 & Pax8 will allow us to understand those mechanisms and identify future novel therapeutic targets for diagnostics and treatments.

**TABLE 1. Fertility of Oviduct Specific Pax Mutants**

| Genotype | # females | Litter size | Pax2f/f | Pax8f/f | Ovi-Cre 5 15 0 0 | Pax2f/f, Pax8f/f, Ovi-Cre 5 12 6 9 | Pax8f/f, Ovi-Cre 3 6 2 6-7 |
|----------|-----------|-------------|---------|---------|-----------------|---------------------------------|----------------------|

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**P-290 4:30 PM Sunday, October 18, 2020**

**IUI AFTER LH SURGE: HOW SOON IS TOO SOON?** Samantha Simpson, MD, Lubna Pal, MBBS Yale University, Orange, CT.

**OBJECTIVE:** Intravenous insemination (IUI) following ovulation induction (OI) or in a natural cycle is a first line treatment for many etiologies of infertility. The timing of IUI in relation to ovulation trigger or spontaneous luteinizing hormone (LH) surge, as well as the number of IUI attempts that should be made remains a subject of debate. Many patients prefer a single IUI, whether due to expense of treatment or feasibility of making it to an office appointment on short notice. Sperm can theoretically survive in the female reproductive tract for up to 72 hours. The timing of oocyte(s) release is approximately 35-36 hours after the LH surge; following ovulation, the window of fertilization is restricted to approximately 24 hours. Therefore, it is logical to conclude that as long as the IUI is undertaken within two days of the LH surge, the actual timing of the procedure should not influence the probability of conception. Existing evidence on whether IUI cycle outcomes, such as ongoing pregnancy or live birth, differ following a single IUI timed at either 12 or 36 hours after LH surge is sparse.

**DESIGN:** Retrospective cohort study at a single academic fertility center.

**MATERIALS AND METHODS:** All patients presenting for a planned single IUI between January 2018 and December 2019 were eligible. Evidence of bilateral tubal patency, and yield of ≥ 15 maturing follicle(s) in the IUI sample were inclusion criteria. The IUI timing was specified based on timing of hCG induced ovulation (n=260) or by evidence of a positive urinary LH surge reading occurring 12 hours or less after a previous negative reading (n=16). OI treatments included clomiphene (n=152), letrozole (n=76), or injectable gonadotropins (n=35). Relationships between timing of IUI with ongoing pregnancy greater than 16 weeks (OP) and live birth (LB) were calculated.

**RESULTS:** 197 women undergoing 276 cycles with single IUI were included in the analyses. In 75 cycles, IUI was performed 12-16 hours following hCG trigger or LH-surge; IUI was performed 36-40 hours after trigger or LH-surge in 201 cycles. 32 cycles successfully lead to live birth or ongoing pregnancy >16 weeks gestation (11.6% of cycles). OP/LB following IUI differed based on timing of IUI. After adjusting for age, BMI, OI regimen, and endometrial thickness, the likelihood for OP/LB was threefold higher than the IUI was timed at 36-40 hours following trigger or LH surge, compared to 12-16 hours (14% v 5%, OR 3.0, 95% CI 1.00-9.81, p=0.047).

**CONCLUSIONS:** In women undergoing IUI for infertility management, the timing of IUI is an independent predictor of IUI cycle outcome.