

ASRM Fertility Preservation Special Interest Group 2021 Newsletter

Greetings from the Chair

We had a delightful in-person meeting of the FPSIG members at ASRM in Baltimore on Monday, October 18th. The wine-and-cheese event was graciously sponsored by Joy Lewin from Ferring Pharmaceuticals. The meeting was held in a collegial and relaxed atmosphere and we are extremely grateful for Ferring's support.



I wanted to thank Lynn Davis for her outstanding leadership over the past year as Chair of the FPSIG and introduce myself, Rebecca Flyckt, as your incoming Chair. As we move into 2022, we look to a year of continued growth, educational opportunities, and advocacy from FPSIG.

The Mission of the FPSIG is to enhance knowledge among health care workers and the public on infertility induced by cancer therapy and other medical treatments through national and international collaboration among Reproductive Specialists, Oncologists, and allied health workers in order to promote research, education, and to develop new strategies of fertility preservation.

We are delighted to welcome Dr Gwendolyn Quinn as the incoming Vice Chair. Dr Quinn is a Professor in the Department of Obstetrics & Gynecology and a Professor in the Department of Population Health at NYU Langone Health. Dr Quinn completed her PhD from Florida State University, and she did her PostDoctoral training at the University of South Florida in the College of Public Health and in Medical Ethics.

The FPSIG Society membership now has 410 active member, ASRM's largest SIG. The officers serving on the FPSIG are:

Patient Representative: Joyce Reinecke, JD, Alliance for Fertility Preservation

Chair: Rebecca Flyckt, MD, University Hospitals Fertility Center

Chair Elect: Kara Goldman, MD, Northwestern Fertility and Reproductive Medicine

Vice Chair: Gwendolyn Quinn, PhD, NYU Langone Health

Immediate Past Chair: Lynn Bentley Davis, MD, MS, Seattle Reproductive Medicine

Past Chair: Pasquale Patrizio, MD, MBE, University of Miami, Miller School of Medicine

We bring you an update on the latest in Fertility Preservation including a summary of FP events at this year's virtual ASRM Scientific Congress & Expo 2021 in Baltimore, Maryland.

This year's FPSIG Prize Paper goes to O-217, ANTI-MÜLLERIAN HORMONE PROTECTS OVARIAN RESERVE FROM CYCLOPHOSPHAMIDE WHEN ADMINISTERED AS RECOMBINANT PROTEIN OR MODIFIED RNA. Authors: Limor Man, Nicole Lustgarten Guahmich, Eleni Kallinos, Lior Zangi, David Pepin, Zev Rosenwaks, and Daylon James. Dr. Man also won the FPSIG Prize Paper at ASRM in 2015.

Topics at the FPSIG Annual Meeting

1. Male Fertility Preservation Questionnaire.

You have received this questionnaire in your inbox. Please complete it and contribute if you have not already. The goal is to collect expert opinion, summarize guidance, and publish a reference regarding the optimal number of semen collections or sperm vials to freeze in different clinical situations of male fertility preservation.

2. National Fertility Preservation Bioethics Forum.

Fertility preservation is becoming increasingly complex, encompassing a broad range of patient populations including pediatric patients, oncology patients and those with hematologic or autoimmune diseases, transgender patients, and a growing list of additional populations for whom fertility preservation is indicated. As clinicians we are frequently faced with cases that are challenging from both a medical and ethical perspective, but the ethical complexities-- particularly when time is of the essence in urgent cases-- make these cases particularly challenging for clinicians. As the FPSIG we have a responsibility and opportunity to highlight some of these ethically challenging cases and to create a framework to think through these cases. Stakeholders include patients, parents, partners, reproductive medicine physicians and care teams, and the many specialists referring these patients for care (pediatric endocrinology/surgery/psychiatry/oncology

, adult oncology, mental health professionals, etc). Please contact Kara Goldman at kara.goldman@nm.org if you are interested in participation.

3. OTC Registry.

Ovarian tissue cryopreservation is no longer considered experimental by ASRM. Nonetheless, there is no formal system for tracking national or international outcomes. Clearly, outcomes data is necessary to be able to adequately counsel patients and families about their options and expectations. While it is outside the scope of the FPSIG as substantial resources would be required to establish and maintain a database, other organizations could take on a leadership role here. There is already a start and we may be able to work with SART. ASRM, NIH/NICHHD, or even pharma could possibly assist with funding.

4. OTC Media.

Ovarian tissue cryopreservation is no longer considered experimental by ASRM. However, there is no FDA-approved media for transportation or cryopreservation of ovarian tissue. The current manufacturer, Origio, intends to discontinue production of the current OTC media by the end of 2021, and no replacement media is available. Other manufacturers have been approached and now one has expressed interest. We owe a mountain of gratitude to Mary Zelinski, PhD, at Oregon Health Sciences University for her problem-solving endeavors.

Oral Abstracts

Fertility Preservation Oral Abstract Session, October 18, 2021

On Monday, October 18th, the FPSIG held an oral abstract session at ASRM's first in-person Congress since 2019. Six oral abstracts were selected for presentation based on scientific quality, and the live session was moderated by **Kara Goldman, MD** and **Mindy Christianson, MD**. The session was widely attended and audience engagement was excellent. Topics represented the full breadth of fertility preservation, including the use of oocyte and embryo cryopreservation for planned fertility preservation, ovarian tissue transplantation to mitigate reproductive aging, in vitro fertilization outcomes among women with BRCA1/2 mutations, and ultimately the impact of cancer and cancer treatment on ovarian reserve and semen parameters.

In abstract **O-19**, **Dr. Devora Aharon** from the Icahn School of Medicine at Mount Sinai in New York presented her group's work entitled, "The optimal number of euploid embryos needed to achieve a desired family size: a personalized predictive model." This study investigated the commonly encountered clinical question of how many euploid embryos are sufficient to achieve a patient's desired family size. The authors created two models to predict the likelihood of 1 and 2 live births based on a total of 7434 single euploid embryo transfer cycles in 4586 patients. They presented model-predicted probabilities of 1 and 2 live births after up to seven transfers, concluding that once a euploid embryo is obtained the variables predicting live birth are primarily embryo quality and

endometrial factors. They used patient and embryo-specific factors to generate individualized probabilities for 1 or 2 live births based on the number of euploid embryos cryopreserved, providing a useful counseling tool for patients seeking to optimize their likelihood of achieving their desired family size through embryo cryopreservation.

Patients pursuing planned oocyte cryopreservation often inquire whether the duration that their oocytes are cryopreserved will impact their likelihood of live birth with autologous warmed oocytes. In abstract **O-21** **Dr. Grace Whiteley** of the Eunice Kennedy Shriver National Institute of Child Health and Human Development presented her group's work entitled, "The impact of duration of oocyte cryopreservation on live birth outcomes in IVF cycles using autologous thawed oocytes." In this study, outcomes of 530 IVF cycles utilizing autologous vitrified/warmed oocytes were analyzed based on duration of vitrification. They utilized adjusted GEE analysis and found no impact of duration of oocyte vitrification on live birth rate. The authors urge continuous evaluation of oocyte vitrification/ warming outcomes to ensure patients are appropriately counseled.

Dr. Kutluk Oktay of Yale University presented **O-20** on behalf of first author **Boris Petrikovsky MD** of Nassau University Medical Center on their work "Does harvesting ovarian tissue to delay reproductive aging have a negative impact on the natural age of menopause in healthy women?" The authors had previously

harvested 1/5th of one ovarian cortex from 48 women under a prospective IRB-approved protocol investigating the use of ovarian tissue cryopreservation for fertility preservation/ reproductive longevity. To investigate whether these ovarian biopsies obtained for cryopreservation would impact patients' age at natural menopause, the authors contacted participants to assess their menstrual status. They reported no significant difference in the age of menopause between women who underwent ovarian biopsy for cryopreservation and controls who had declined ovarian biopsy but underwent similar benign surgeries. The authors conclude that this amount of tissue, if proven to be sufficient to extend ovarian function following auto-transplantation, would not negatively impact the age of natural menopause.

The focus of the abstract session then shifted from research surrounding planned fertility preservation and reproductive longevity, to research focused on pathologic ovarian aging states. **Dr. Luwam Ghidei** from Baylor College of Medicine presented abstract **O-22** entitled, "Cycle characteristics and treatment outcomes among BRCA mutation carriers undergoing in vitro fertilization." Their group identified BRCA1/2 mutation carriers at their institution who presented for fertility preservation and/or preimplantation genetic testing over a 10-year period. BRCA mutation carriers who underwent IVF were compared to age- and BMI-matched controls. The authors report that among the 15 BRCA mutation carriers in their cohort who underwent IVF with PGT, IVF outcomes including fertilization, clinical pregnancy rate, and live birth rates were similar when compared to controls. Thoughtful audience

discussion followed regarding the small sample size despite 10 years of records being interrogated in a large urban center. The audience discussed the importance of considering opportunities to improve referral to reproductive medicine care among this population to ensure adequate counseling.

Dr. Beth Zhou of the University of California San Diego presented abstract **O-23** entitled, "Ripe for the taking - leveraging big data to estimate ovarian reserve." The objective of this work was to utilize administrative health claims data to assess the impact of cancer treatment on ovarian reserve. They describe the use of OptumLabs Data Warehouse to identify females aged 15-39 years with incident breast cancer during 2000-2019 with associated AMH levels. They matched females with breast cancer 10:1 to those without cancer by age at AMH, race, smoking, and obesity. The authors then modeled AMH patterns in females exposed to cyclophosphamide-based chemotherapy and platinum-based chemotherapy, showing long term impairment to ovarian reserve consistent with findings from prospective cohort studies. The authors concluded that administrative health data claims can be used to investigate the gonadotoxic effects of chemotherapy. Moderators and audience participants inquired about the information that can be obtained from administrative claims databases, recognizing the strengths of this data source to better understand the gonadotoxic effects of systemic therapies.

Shifting to a discussion of male reproductive function in the context of cancer, **Dr. Guy Shrem** of the Kaplan Medical Center in Montreal, Canada presented **O-24** entitled, "The effect of

malignant disease on semen parameters.” Dr. Shrem presented a retrospective study evaluating 12,188 sperm samples obtained from patients with cancer who cryopreserved semen before chemotherapy (n=265) and those without cancer who underwent semen analysis for infertility investigation (n=6283). They did not identify differences in semen parameters between tumor types, but they found that men pre-chemo had lower sperm concentrations and lower total motility when compared to healthy controls with semen parameters above the WHO 2010 reference limit. They conclude that a diagnosis of cancer significantly predicts impaired sperm concentration and total motility, consistent with prior studies and supporting the importance of careful counseling for men with cancer desiring future fertility.

Infertility and Cancer Oral Abstract Session, October 20, 2021

On Wednesday October 20th, the FPSIG held another oral abstract session. Five oral abstracts were presented and **Kathryn Coyne, MD**, a fellow from University Hospitals in Cleveland Ohio, moderated the live session. The session highlighted potential protective agents for patients undergoing gonadotoxic treatment, oocyte cryopreservation outcomes in cancer patients, the potential for in vitro maturation, and disposition of unused vitrified oocytes. These oral presentations sparked interesting discussion with the engaged audience and brought up ideas for further exploration and research.

There were two abstracts that assessed potential protective agents for patients who undergo oncologic treatment with

alkylating agents. **Dr. Limor Man** from the Ronald O. Perleman and Claudia Cohen Center for Reproductive Medicine in New York presented abstract **O-217** on the role of AMH in protecting ovarian reserve from cyclophosphamide. This study investigated the potential of recombinant and modified RNA encoding for AMH to preserve ovarian reserve when administered before cyclophosphamide in both wild-type mice and xenografted human ovarian tissue. In both mice and human tissue, they found in the modified RNA encoding for AMH groups that there was retention of primordial follicles. This demonstrates that AMH renders a protective effect from cyclophosphamide in both murine and human xenograft models. Abstract **O-220** presented by **Dr. Oren Kashi** from Sheba Medical Center in Israel assessed combined suppression of follicle activation by both extrinsic and intrinsic pathways to protect ovarian reserve from cyclophosphamide in mice. Mature mice were treated with cyclophosphamide with or without mTOR inhibitor, Temsirolimus (TEM), and/or recombinant AMH (rAMH). They found that treatment of cyclophosphamide alone caused significant loss of primordial follicle reserve, and this was reduced when mice received cotreatment with either TEM or rAMH. Importantly, combined co-treatment of Tem + rAMH provided complete protection of the primordial follicle reserve, to the extent that the number of primordial follicles in this group was almost identical to untreated animals. This study advances our understanding of the pathways by which chemotherapy causes loss of the ovarian follicle reserve.

Abstract **O-218** presented by **Pe'era Wasserzug Pash, MSc**, from the Institute of Dental Sciences in Jerusalem, Israel, explored the therapeutic potential of immature oocytes from fertility preservation procedures and their in vitro maturation at various ages. Immature oocytes may be found in dissection medium during tissue handling of ovarian cortical tissue and the ability to mature them in vitro and cryopreserve them as mature oocytes would provide an additional option for fertility preservation. In this study, human oocytes collected from fertility preservation patients and evaluated for maturation in vitro. The results were compared at different age groups. As a complimentary model, mouse oocytes were matured in vitro as well. In both models, there was a gradual increase in maturation rates with onset of puberty and maturation potential was also tightly correlated with heterochromatin levels. These results represent promise in expanding the range of treatment options and success rates in oncofertility patients.

Oocyte cryopreservation cycle characteristics were compared in oncologic vs. non-oncologic patients in abstract **O-219**, presented by **Dr. Lisa M Shandley** from Emory University School of Medicine in Atlanta. In this study, patient demographics and cycle outcomes were compared between oocyte cryopreservation cycles for patients with and without a cancer diagnosis. Oncologic patients were younger at the time of the cycle, more likely to be at an academic center, and a greater

proportion identified as racial minorities, compared to patients undergoing oocyte cryopreservation for other indications. The major indication for patients undergoing oocyte cryopreservation for non-oncologic reasons was future family planning. Outcomes of cycles for both groups were similar in regards to cancellation rates, gonadotropin dose, and oocyte yield. These comparable short-term outcomes are reassuring for oncofertility patients.

Dr. Amalia Namath, a resident at Rush University Medical Center in Chicago, in collaboration with Shady Grove Fertility Center, examined the reasons behind discarding vitrified eggs in abstract **O-222**. This study included patients who underwent autologous egg vitrification and later requested to discard their eggs. Reasons for discard included: completed childbearing, worsening cancer, personal preference, storage costs, poor quality oocytes, and death. The average age at freezing and at discard, length of time and total number of eggs frozen varied significantly based on stated reason for discard. Cancer patients stored their eggs the longest and froze the most eggs overall. Interestingly, approximately one quarter of the discards over 2008-2021 were requested after the COVID-19 pandemic began.

Each of these oral abstracts add to the field of fertility preservation, either by providing more options and improved confidence in treatment of oncofertility patients, or by shedding light on the complex social and emotional aspects of infertility and cancer.

Stay Connected

You can easily connect with members of the FP community through the ASRM- message board: <https://connect.asrm.org/communities/community-home?CommunityKey=7a3a1916-8807-4526-abb-4a4795ec8a14>

Advocate

If you live in a state without legislated fertility preservation coverage, consider mobilizing local advocacy efforts at the grass-roots level. Each major achievement began as a thought, idea, or passion by a small group of people who brought it to fruition. If you believe all patients who need fertility preservation services should have access to it, then consider starting or joining an advocacy effort in your area.