

Fertility Preservation Special Interest Group Newsletter 2020

Greetings from the Chair:

2020 has been quite the year. Even in the midst of a world health crisis, fertility preservation endeavors have endured. We are delighted to welcome Dr Kara Goldman as the incoming Vice Chair. Dr Goldman is Assistant Professor of Reproductive Endocrinology and Infertility and Medical Director of Fertility Preservation at Northwestern University Feinberg School of Medicine. The FP SIG Society membership now has 406 active members. The officers serving on the FP SIG are:

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

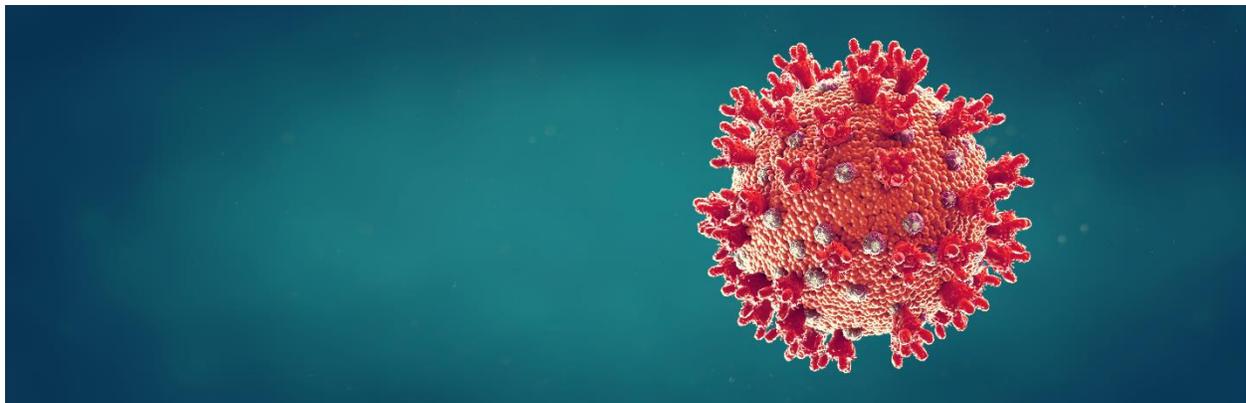
Chair: Lynn Bentley Davis, MD, MS, Seattle Reproductive Medicine

Chair Elect: Rebecca Flyckt, MD, University Hospitals Fertility Center

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

Immediate Past Chair: Pasquale Patrizio, MD, MBE, Yale Fertility Center

Past Chair: James Smith, MD, MS, University of California San Francisco



Fertility preservation in the time of COVID-19

Kara Goldman, MD

Fertility preservation is essential. These are words that we all understand to be true based on our daily clinical encounters, but which took on new meaning during the first peak of the COVID-19 pandemic in the spring of 2020. On March 17, 2020, the ASRM COVID-19 task force recommended suspending initiation of new treatment cycles and non-urgent gamete cryopreservation, but importantly emphasized that care should be continued for patients requiring urgent stimulation and cryopreservation. At face value this message is intuitive and not surprising, but the forced distinction of fertility preservation made clear by the pandemic

highlights the critical importance of access to this urgent and necessary care. Not even a pandemic should hinder access to urgent fertility preservation.

When speaking about access to care we are frequently referring to financial access and insurance coverage, and appropriately so given that cost has always been a primary barrier to fertility preservation. As discussed elsewhere in this newsletter we know that significant legislative gains have been made in recent years, but we anticipate that the ripple effects of the COVID-19 pandemic will only widen gaps in care and tremendous work lies ahead. Record unemployment and associated loss of employer-mandated insurance and loss of income means that need for dramatic legislative progress is urgent.

The less well-described side of the 'access coin' is geographic access to fertility preservation, as geographic access to a reproductive medicine physician and embryology lab varies widely throughout the United States. The COVID-19 pandemic has provided both geographic challenges and opportunities. Travel and mobility have been limited for those who may need to travel to seek fertility preservation care, and inter-state travel restrictions and quarantine mandates may affect ease of patients' clinic and procedural visits. Despite these limitations, the pandemic has highlighted tremendous opportunities to harness the power of telemedicine for our population. Oncology clinical trial sites are utilizing telemedicine to enroll patients who would otherwise not have access to a trial, and we similarly have opportunities to provide care to a far-broader patients base using telemedicine. Tremendous opportunities are unfolding to expand geographic access to care.

Barriers related to infrastructure and operations are less prioritized, and we take for granted the seamless care that we can typically provide. The COVID-19 pandemic has spotlighted operational gaps that could result in devastating interruptions of care, and it has become acutely clear how fragile our operations are given reliance on technology, transportation, and significant manpower. It is not difficult to envision how quickly operations can be impacted in the event of manufacturing/production interruptions for embryology supplies, travel/transport restrictions in terms of distribution of liquid nitrogen and other laboratory needs, and staff/physician/embryologist illness. The ASRM committee opinion detailing development of an emergency plan for IVF programs provides a thorough outline for emergency preparation, but few clinics are prepared for the need to completely shutter their doors. In these cases, it's imperative to rely on a local network. In Chicago and the surrounding suburbs clinics collaborated to provide care when some centers were unable to remain open during the peak of the spring surge. Our center at Northwestern saw a high volume of patients during the peak of the surge as we absorbed patients from surrounding centers. This collaboration is necessary, and in preparation for future emergencies it would be prudent for centers to discuss in advance who they would rely on for reciprocal support in the event of clinic closures or significant disruptions. The many opportunities for infrastructure collapse highlighted by the pandemic suggest a need for protocols, preparation and safety nets to avoid gaps in care.

According to the National Association of Insurance Commissioners (NAIC) and the California Health Benefits Review Program (CHBRP), more than 30 million individuals in these states now have health insurance policies that must include fertility preservation coverage for those at risk for medically induced infertility. While the intent of these new state laws is the same, each one has important distinctions relating to coverage inclusions, limitations, and exemptions. Most importantly, the scope of policies affected in each state varies, so it is important to understand which types of insurance are subject to the law in your state. For example, the law in New York (which was enacted through the state budget process) requires all individual, small group, and large group policies to include this coverage, but the law in Maryland only extends coverage to large group policies. This means that passage in a state does not confer protection for all residents of that state. Perhaps the most significant gaps that remain are for large self-insured private companies which are regulated at the federal level, and for Medicaid (only the Illinois law includes Medicaid).

While much work remains to establish universal coverage for patients who need fertility preservation, the trend toward coverage is only accelerating. Despite the challenges – logistical and financial – posed by Covid-19 for upcoming legislative sessions, we expect to see coverage bills introduced in several states including Washington, Texas, Nevada, and Utah – with many others pending possible introduction. In addition to legislative efforts toward coverage, we have seen a growing interest in advancing coverage through extra-legislative means; for example, through private meetings with insurers and self-insured employers, including major hospital systems.

As fertility preservation laws are enacted across the United States, it is critically important to monitor their implementation and interpretation to ensure that qualified patients, in fact, gain access to this coverage. We are seeking to identify how insurers include this new coverage in their policies and how they communicate this new benefit to their insureds. In order to identify gaps in coverage and/or internal processes that might limit or frustrate the laws' purpose, gathering data about patterns of approvals and denials over time will help us measure the actual impact of these coverage laws.

If you live in a state without legislated fertility preservation coverage, consider mobilizing local advocacy efforts at the grass-roots level. Each one of these major achievements 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.

“intermediate risk” category. When asked “What resource did you find the most helpful regarding individual chemotherapy regimens?” Dr. Chung directed viewers to the Cyclophosphamide Equivalent Dose (CED) calculator (Green et al., 2014) which can be found online at <https://fertilitypreservationpittsburgh.org/fertility-resources/fertility-risk-calculator>).

Two studies from the University of California San Diego group focused on adverse pregnancy outcomes following cancer treatment. The first, abstract O-50, sought to estimate the association between cancer type and live birth, preterm birth, and severe maternal morbidity. Lead author and presenter **Dr. Beth Zhou**, an REI fellow at UCSD, used OptumLabs® Data Warehouse to identify women with pregnancies between 1/1/2001 and 6/30/2019 and history of AYA cancers. Over 2 million pregnancy episodes were evaluated and the authors found that brain, breast, renal, sarcoma and uterine cancers were associated with lower likelihood of live birth. They also focused on increased risk of preterm birth in survivors of GI cancers, leukemia and thyroid cancers, and increased severe maternal morbidity in leukemia, NHL, and sarcoma survivors. The second abstract regarding pregnancy outcomes after cancer treatment, O-54, focused on ART and adverse perinatal outcomes in survivors of AYA cancers. **Ms. Milli Desai**, a medical student at UCSD, presented her data also using OptumLabs® Data Warehouse to identify AYA cancer survivors with a live birth between 1/1/2001 and 6/30/2019 and use of ART. 3,708 singleton and 137 multiple live births were identified in 3,265 females with prior cancer. The most common cancer types were thyroid (22%), melanoma (21%), and breast (15%). In both singleton and multiple births, controlling for cancer and age, ART was associated with increased risk of preterm birth and increased risk of severe maternal morbidity. These risks appeared to be mediated through maternal comorbidities.

Abstract O-51, presented by **Dr. Jennifer Chae-Kim**, a resident at East Carolina University, shared data from a systematic review comparing reproductive outcomes in women treated with progestin versus progestin plus metformin for endometrial hyperplasias and cancers. Reproductive-aged women with these conditions were found to have similar clinical pregnancy rates and lower cancer relapse with combined therapy compared to progestin therapy alone, although combination therapy was associated with a lower live birth rate. When asked “If the relapse rate was lower and the clinical pregnancy rates were similar, why do you think the live birth rate was lower?” she noted the possibility of confounding factors that could not be accounted for in the data available as well as heterogeneity in the medication types, dose, and duration of treatment. Dr. Chae-Kim suggested that additional research is needed to explore the potential benefits of progestin plus metformin therapy on hyperplasia/cancer relapse, especially with regard to duration of metformin treatment and/or other potential confounders such as infertility or other underlying pathologies.

Dr. Devora Aharon, a fellow at Icahn School of Medicine at Mount Sinai/Reproductive Medicine Associates of New York, presented abstract O-52 comparing ovarian reserve and ovarian stimulation in oncofertility patients versus patients without a cancer diagnosis over a 14 year period. Linear regressions were performed to assess cycle outcomes and control for

confounders. The authors found similar baseline ovarian reserve testing in cancer and non-cancer diagnoses. The ratio of mature oocytes to total oocytes retrieved was lower in cancer patients; Dr. Aharon suggested that this finding could be due to effects of the underlying disease process on oocyte maturation or a shorter timeframe to starting a cycle or physician biases. Overall, however, cancer patients can be reassured regarding the study findings of satisfactory numbers of mature oocytes for future use in cancer patients undergoing fertility preservation. Dr. Aharon noted additional research is needed to better understand the reproductive outcomes that can be achieved when cancer patients actually return to use their cryopreserved oocytes.

Abstract O-53 was presented by **Adriana Nicholson Vest, PhD**, a medical student at Emory University. Dr. Vest presented her cross-sectional review regarding the quality and quantity of website content at NCI-designated cancer centers regarding fertility preservation. She found that >25% of cancer center websites lacked patient-directed information regarding oncofertility and fertility preservation. This gap is an inadequacy that is particularly relevant for patients, such as AYA patients, who rely primarily on internet-based information for education during the critical window between diagnosis and cancer treatment.

[Fertility Preservation SIG Oral Abstract Session October 20, 2020](#)

On Tuesday, October 20th, the FP SIG held another oral abstract session of high quality submissions with Lynn Davis, MD, MS, moderating the live session. This session was also widely attended with active audience participation and question/answer sessions, allowing for stimulating discussion with the presenters regarding the data.

Abstract O-199, “Majority of Women Undergoing Elective Oocyte Cryopreservation Do Not Attain Optimal Number of Oocytes Cryopreserved for Reasonable Likelihood of Future Live Birth” was presented by **Dr. Amy Wijekoon**, an REI fellow at UCSF. This retrospective cohort study of 415 women (January 2012 to February 2020) showed that 58% of women do not bank sufficient eggs to yield an 80% chance of future livebirth. While 63% of women <35 achieved an optimal number of oocytes cryopreserved (OOC), few women ages 39-40 years, and no women >=41 years achieved OOC. AMH, AFC and age predicted failure to achieve OOC and should be utilized for patient counseling.

Dr. Jennifer Blakemore from NYU presented abstract O-200, “Planned Oocyte Cryopreservation – 10-15 Year Follow Up – Return Rates and Cycle Outcomes.” This retrospective cohort study of 231 patients (mean age 38.2 years) who planned oocyte cryopreservation between 1/2005 and 12/2009 showed that so far 88 patients (38.1%) have thawed their oocytes, at a mean age of 43.9 years. Eight PGT-A patients had a euploid embryo but no ET yet. Of the 80 thaw patients with a final outcome, 20 had nothing for ET, 60 had a least one ET, 27 had a total of 32 babies,

for a LB rate of 33.8%. The utilization rate of 38.1% and “no use” rate of 58.9% was similar across age groups. Whether more recent patients are demographically similar to this cohort is not yet known.

Abstract O-201 “Predicting the Probability of Having One Euploid Blastocyst in Elective Oocyte Cryopreservation Cycles: A Counseling Resource” was presented by **Ms. Patrizia Rubino**, an embryologist at HRC in Pasadena, CA. While patients may commonly request PGT for their egg thaw cycles, current predictive models do not take PGT into account when considering number of oocytes needed for a successful outcome. A predictive tool was developed from the retrospective analysis of 186 cycles to calculate the ideal number of frozen oocytes to have at least one euploid blastocyst. The number of thawed oocytes needed to obtain 90% probability of at least one euploid blastocyst for donors and women age <36 was 9 and 12, respectively. For other age groups, no number of thawed oocytes guaranteed a 90% probability. To achieve 80% probability of at least one euploid blastocyst, 5, 11, and 14 oocytes were needed, respectively, for the donor, <36, and 36-39 age groups. The group with age >39 did not reach 80% probability with any number of thawed oocytes. Data on PGT in frozen egg cycles are minimal and these results may be useful for patient counseling and oocyte thaw planning.

Ms. Paxton Voigt, a medical student at NYU presented abstract O-202, “Socio-Demographic Disparities in Utilization of Fertility Services Among Reproductive Age Women Diagnosed with Cancer in the US: A Secondary Analysis of the 2011-2017 National Survey for Family Growth (NSFG).” Women who sought fertility services (FS) any time after cancer diagnosis were compared with women who never sought FS after their diagnosis. Of 580 respondents with a history of cancer, 35 (6.03%) accessed FS before their cancer diagnosis and were excluded from analysis, leaving 545 women analyzed with a mean age of 35.1 years. 43 women (7.41%) accessed FS after their cancer diagnosis and 502 (86.6%) never accessed FS. Women of higher socioeconomic status and women who were married were more likely to pursue FS, whereas women who identified as Hispanic and Non-Hispanic Other were less likely to utilize FS. This study highlights the importance of addressing socioeconomic and racial differences in access to FS.

“The Use of Oocyte Cryopreservation (OC) for Fertility Preservation (FP) in Girls with Sex Chromosome Disorders (SCD): A Case Series Describing Outcomes,” abstract O-203, was presented by **Ms. Rachel Martel** from NYU. This retrospective case series of all adolescent or young adult (AYA) patients (<25 years) with SCD seen for OC consultation between 2011-2019. 16 patients with Turner Syndrome (TS), 5 with Turner Syndrome Mosaicism (TSM) and 1 with 47XXX were included for analysis. 14 patients (64%) elected OC for a total of 31 cycles. 10 underwent retrieval and 9 had oocytes successfully frozen. 3 out of 3 patients who pursued cycles after first cancellation never got to retrieval. Age, SCD type, and FSH at cycle start did not predict ability to freeze MIIs or cycle cancellation. AYA patients with SCD have a high risk of poor response and cycle cancellation, but the majority in this study froze MIIs. OC is an important option for patients with SCD, but setting expectations is important.

Dr. Esther Chung from Duke presented abstract O-204, “Oocyte Cryopreservation Versus Ovarian Tissue Cryopreservation as Fertility Preservation for Adult Women Undergoing Gonadotoxic Therapy: A Cost-Effectiveness Analysis.” Incremental cost-effectiveness ratios (ICERs) were determined to establish cost-effectiveness, and sensitivity analyses were run to assess variations in costs and clinical probabilities. The base case cost of each strategy was: OC \$16,588 and OTC \$10,032. OC had an effectiveness of 1.6% and OTC an effectiveness of 1.0% at achieving a live birth. OC was more costly but more effective than OTC, with an ICER of \$1,163,954 per additional live birth. OC is less expensive and more effective when the utilization rate is 63% or higher. OC is also less expensive and more effective when the cost is less than \$8,100. Lowering the cost of OC and increasing the utilization of OC can significantly increase its overall cost-effectiveness.

Don't Forget

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

More to Come

One silver lining of the pandemic has been the realization that national meetings can happen virtually without the need for travel. We are therefore planning more frequent Fertility Preservation SIG meetings. Look for an invitation for our upcoming January meeting soon.