Fertility Preservation for Transgender Individuals

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Louise Brown
(Born July 25, 1978)

John, Lesley and Louise Brown
Impact

- IVF has now produced >6 million babies worldwide
- 2010 Nobel Prize in Physiology and Medicine for work done by Drs. Patrick Steptoe (Physician), Bob Edwards (Researcher) and Jean Purdy (Research Nurse)
How to make a baby
(what are the building blocks?)

=  +
**Intractable Infertility**

- 1% of women in the general population have premature ovarian insufficiency (no eggs)
- 1% of men in the general population have azoospermia (no sperm)
- These numbers correspond to 1.3 million people in the United States between the ages of 20 and 50
- It is impossible to have a biologically related child without sperm or eggs
- Infertility can be due to diseases, medical treatments, age, genetics, injury and other circumstances

**Medical Treatments Cause Infertility**

- Chemotherapy or radiation treatments for cancer, bone marrow transplantation, autoimmune diseases
- Removal of gonads (ovaries or testes)
  - Differences in sexual development
  - Ovarian cancer; testicular cancer
- Gender affirming hormone treatments for transgender individuals
- Gender affirming surgery (removal of gonads) for transgender individuals
Fertility Preservation

- Early intervention can preserve the fertility of individuals “at risk” for infertility due to their medical treatments
- Adolescents and adults can cryopreserve eggs, sperm or embryos, which can be used in the future to achieve pregnancy
- These options are not available to preadolescent children who are not producing mature eggs or sperm
- Centers worldwide are preserving immature testicular tissue and immature ovarian tissues for young patients in anticipation that new reproductive technologies will be available for them in the future

Fertility Preservation Program in Pittsburgh
(https://fertilitypreservationpittsburgh.org/)

Our Mission
- Educate Patients and Physicians
- Provide comprehensive menu of fertility preservation options
- Pioneer new reproductive technologies and responsibly translate them to the clinic
- Train the next generation of FP experts

Cryopreserved since 2011
- Testicular tissue: 462 boys
- Ovarian tissue: 148 girls/women
National/International Impact
Experimental fertility preservation protocols

- Male patients (462 total)
- Female patients (148 total)

- Pittsburgh Coordinating Center (145 patients)
- US Coordinated Centers (Research)
- US Coordinated Centers (Contracted Service)
- International Collaborators

Children's National Medical Center
Lurie Children's Hospital
Children's Hospital of Orange County
Medical College of Wisconsin
Cincinnati Children's Hospital Medical Center
Nationwide Children's Hospital
 Connecticut Children's Medical Center
Nemours Hospital for Children
University of Miami
Mayo Clinic
University of Chicago
Washington University in St. Louis
Cook Children's Medical Center
Riley Children's Hospital
Mississippi Children’s Hospital
Children's Hospital Colorado
Helen DeVos Childrens Hospital
Memorial Sloan Kettering Cancer Center
Phoenix Children's Hospital
Rush University Medical Hospital
Ben-Gurion University, Israel
Hadassah University Med Ctr, Israel
BabyCord, Jordan
King Hussein Cancer Center, Jordan

Our Team

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**FP Patients < 18**

- Testicular Involvement 0.9%
- Testicular cancer/mass 1.8%
- Rectal cancer 0.2%
- Pleuropulmonary blastoma 0.2%
- Ovarian cancer/mass 0.5%
- Other (non-cancer) 1.1%
- Transgender 2.7%
- Cancer Survivor 0.3%
- Carcinoma 0.3%
- Colon cancer 0.3%
- Cytoma 0.2%
- Genetic background 3.4%
- Gonadoblastoma 0.2%
- Head and neck cancer 0.7%
- Hodgkin’s Lymphoma 5.0%
- Kidney cancer/tumor 3.9%
- Leukemia 13.2%
- Non-cancer requiring BMT 21.1%
- NH Lymphoma 5.9%
- Melanoma 0.2%
Transgender and Gender Nonconforming Community

- Increasing numbers of transgender/gender nonconforming (TGNC) youth and adults seeking fertility care options

- Approximately 0.5 - 0.7% of US adults identify as TGNC

- Gender affirming treatments impact fertility
  - Male to Female (MTF) transgender (Lupron, Estrogen)
  - Female to Male (FTM) Transgender (Lupron, Testosterone)
TGNC and Fertility Preservation

- Transgender and gender nonconforming people desire to have children that are biologically related to them (20-50%)
- The Endocrine Society and the World Professional Association for Transgender Health advise health professionals to provide information about fertility risks and fertility preservation options before initiating gender affirming treatments
- TGNC people report a lack of information on fertility preservation options and many regret not preserving gametes (eggs or sperm)
- TGNC people agree that fertility preservation options should have been presented to them before medical transition
- Fertility preservation requires a multidisciplinary effort (gender support team, counselors, FP team)

Feigerlová et al., Clin Endocrinol 2019

Selma Witchel - Pediatric Endocrinologist
Children’s Hospital of Pittsburgh

“I have a patient......."
N=1 Case Study – IVF clinic MWH

- Male to Female (MTF) Transgender patient desires to freeze sperm prior to gender affirming surgery (removal of testes)
- Voluntarily discontinues gender affirming treatments to allow sperm production to occur
- Presents to Magee IVF clinic 5 months after discontinuation to bank a semen sample
- Diagnosis: no sperm
- Recommendation: return in 3 months and try again
- Selma calls: “Hey Kyle......”

Courtney Finlayson – Pediatric Endocrinologist
Lurie Children’s Hospital in Chicago

- Are gender affirming treatments reversible?
- If so, how long do you have to be off treatment?
- If you are able to recover eggs or sperm, can they fertilize or be fertilized?
- Are there long-term health implications for the development of offspring that result from using those eggs or sperm?
- What are the psychological impacts of discontinuing gender affirming treatments?
MTF Transgender Fertility

Xiang Yang
Medical Student
Visiting Scholar

FTM Transgender Fertility

Stephanie Rothenberg, MD
Outcome and Lessons Learned

▪ Patient returned after 3 months and was successful to produce a semen sample that was cryopreserved (frozen) for her future use.

▪ What did we learn from N=1 patient?
  ▪ It was possible to produce a semen sample with sperm after 8 months off gender affirming treatments
  ▪ This was psychologically difficult for the patient, but she was glad she did it
  ▪ We don’t know how long it is necessary to pause gender affirming treatments.....but we know that 8 months was enough
  ▪ We don’t know whether the sperm are functional but results from animal studies are encouraging

Selma and Courtney

“I have a patient....”

“Have you had any success gaining approval for gonadal tissue freezing for ovarian or testicular tissue freezing for transgender patients?”
Transgender OTC and TTC Approved!

- Approved to cryopreserve gonadal tissues for transgender patients who are not able or do not want to produce eggs or sperm
  - Gender dysphoria diagnosis from primary care team
  - ≥ 9 years old
  - Receiving or planning to start gender affirming treatments
  - Do not wish to delay or interrupt treatments to produce eggs or sperm

- Justification: The psychological risk of delaying or interrupting gender affirming treatments is greater than the surgical risk of removing ovarian tissue or testicular tissue

- We do not know whether transgender patients will return to use their tissues in the future, but we have preserved the option for them to do so

Testicular Tissue Freezing

- Controlled rate slow freezing
- 2-5 mm
- 0.5 cm x 2 cm strips

Controlled rate slow freezing
Testicular Tissue Cryopreservation for Transgender Female

- 13 yo transgender female with diagnosis of gender dysphoria
- On Lupron for 1 year and planning to start estrogen treatments
- Wants to pursue testicular tissue cryopreservation (TTC) prior initiation of estrogen

Testicular Tissue Cryopreservation for Transgender Female

- Pittsburgh TTC protocol for transgender females
  - Diagnosis of gender dysphoria from primary care team and referral for FP
  - >9 years old
  - Receiving or planning to start gender affirming treatments (hormone suppression or cross-sex hormones)
  - Do not wish to delay or interrupt gender affirming treatments to experience male puberty and produce sperm
- Patient is eligible
- 563 mg testicular tissue collected by wedge resection. 8 vials frozen for patient’s future use and 2 vials designated for research
Ovarian Tissue Cryopreservation for Transgender Male

- 18 yo transgender male on testosterone for 3 years
- Voluntarily stopped testosterone treatments to pursue ovarian tissue cryopreservation
- Patient eligible for Pittsburgh protocol
  - Diagnosis of gender dysphoria from primary care team and referral for FP
  - >9 years old
  - On gender dysphoria medication
- Declined controlled ovarian stimulation for oocyte collection and cryopreservation
- 9 strips of ovarian cortex (0.5cm x 2cm) were frozen for the patient; 2 strips were frozen for research

Ovarian Tissue Cryopreservation for Transgender Male

- What is the impact of long-term T treatment on ovarian function?
- Was it necessary to stop T treatment prior to OTC?
Germ Cells (sperm precursors) Confirmed in Testicular Tissue from Transgender Females on Hormone Suppression

Fertility Preservation/Restoration in People with Ovaries

Doungkamchan and Orwig, F1000 Faculty Reviews 2021
Acknowledgements

**Orwig Lab:**
Andre Caldeira-Brant, PhD
Mitch Harancher, BS
Sarah Munyoki, PhD
Brooke McClendon, PhD
Rachel Neelley, BS
Jennifer Orwig, BS
Zach Orwig
Yi Sheng, MD, PhD
Meena Suhkwani, PhD
Kien Tran, BS
Nagham Younis, PhD
Amanda Zielen, PhD

**Orwig lab alumni:**
Brian Hermann, PhD; Serena Dovey, MD; Adetunji Fayomi, PhD; Karen Peters, RN

**Pittsburgh Collaborators:**
Jerry Schatten, Aleks Rajkovic, Alex Yatsenko, Glenn Cannon, Kathleen Hwang, Serena Chan, Joe Sanfilippo, Mellissa Mann, Miguel Brietto-Enriquez, Selma Witchel, Miguel Reyes-Mugica

**National/International Collaborators:**
Teresa Woodruff and everyone associated with the Oncofertility Consortium
Amander Clark, Marv Meistrich, Gunapala Shetty, Charles Easley, Anthony Chan, Don Conrad, Jon Schimenti, Peter Schlegel, Courtney Finlayson

**Center for Reproduction and Transplantation**
Rachel Kelley-Lore, Gaby Navarro, Anna Wecht, Sarah Hughes, Danyale Brazos, Lauren Callewaert, Kayla Downs, Brooke McClendon, Rachel Neelley, Amanda Zielen, Jennifer Hamilton, Kathleen Hwang, Julie Rios

**Support:**
Eunice Kennedy Shriver NICHD
R01 HD055475; R21 HD061289; R01 HD076412; P01 HD075795;
R01 HD092084; P50 HD096723; R01 HD100197
US-Israel Binational Science Foundation
MWRIF, Richard King Mellon Foundation, Scaife Foundation, Depts Ob/Gyn/RS & Urology, UPMC, LucaBella Foundation

Patients