Fertility in 2020: DSD

Emilie K. Johnson, MD MPH

ekjohnson@luriechildrens.org
@eekayjay
Discussion Topics

1. Intro to fertility potential and preservation in DSD
2. Lurie Children’s experience offering experimental fertility preservation
3. Case example
4. Fertility considerations for transgender individuals
Many individuals with DSD at risk for impaired fertility

- Abnormal gonadal development
- Gonadectomy (traditional recommendation due to tumor risk)
- Anatomic barriers
- Abnormal hormone production/action
Fertility Preservation / “Cryopotential” Most Relevant to Certain DSD Conditions

- Many 46, XY DSDs
  - Androgen insensitivity syndrome
- Mixed gonadal dysgenesis
- 46 XY/45 XO Turner Mosaic
- Ovotesticular DSD

Cryopotential = experimental gonadal tissue cryopreservation in hopes of future use
Fertility Potential in DSD

- Impaired fertility is an important concern for families\(^1\)

- Recent literature has noted germ cells in most patients with DSD\(^2\)
  - Fertility potential may ↓ over time

\(^1\)Johnson EK, *J Pediatr Urol*, 2017
\(^2\)Finlayson C, *J Urol*, 2017
## Gonad Management is Changing

### Traditional Paradigm

- Infertility assumed
- Cancer risk thought to be high
- Early gonadectomy recommended

### Evolving Paradigm

- Expanded knowledge about possible fertility potential
- Individualized cancer risk assessment
- Gonadectomy with multidisciplinary eval, shared decision-making*

*with patient involved whenever possible
Fertility Preservation – A new possibility for individuals with DSD?

Multiple Multidisciplinary DSD Clinic Visits

Decision about gonadectomy

Experimental Gonadal Tissue Cryopreservation Discussed

Patient/Family Decide Whether to Attempt FP

Includes separate FP specialist consult

All steps with patient input whenever feasible
Lurie Children’s DSD FP IRB Protocol:

A labor of love
Previous Approach: Planned Exceptions to Oncology IRB Protocols

- Separate protocols for ovarian and testicular tissue
- Cancer-specific language
- Binary gender- and sex-specific language
  - Informed updates to oncology protocols

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Development of IRB Protocol: Lessons Learned

- Both DSD and Fertility Preservation Teams closely involved in protocol editing
- Opportunity to attend IRB meeting in person
- Assurances gonadectomy surgery otherwise clinically-indicated and desired by patient/family
- Exclude 45 XO Turner (and other non-Y chromosome karyotypes)
7/14 (50%) had germ cells

Diagnoses: Partial and mixed gonadal dysgenesis, complete and partial androgen insensitivity, ovotesticular DSD

6/7 (86%) preserved tissue

1 patient chose not to preserve tissue discordant with gender identity
Case Example: Infant with Ovotesticular DSD

- Atypical genitalia noted at birth
- Karyotype: 46, XX
- Ovotesticular DSD diagnosis made at 4 months based on diagnostic laparoscopy and biopsy
  - Mature ovarian and dysgenetic testicular tissue
- Female sex designation
Case Example: Infant with Ovotesticular DSD

- 13 months → unilateral gonadectomy to remove dysgenetic testicular tissue at risk for malignancy
  - Demarcation between dysgenetic testicular and ovarian portions of the gonad less distinct than prior
  - Pathology – mature ovary with oocytes, dysgenetic testis with gonocytes or spermatogonia

- Both ovarian and testicular components cryopreserved
Fig. 3. Right polar ovotestis at 2 different timepoints. 1, dysgenetic testis; 2, well-developed ovarian parenchyma.
Future Fertility for Transgender Individuals

- Inherent fertility potential normal
- Lack of interest in parenthood should not be assumed
- Gender dysphoria can complicate fertility preservation procedures
- Readiness Assessment before gender-affirming treatments includes fertility counseling
  - Thus far, low uptake of fertility preservation¹

¹Chen D, J Adolesc Health, 2017
Fertility in 2020: DSD – Looking Ahead

- Advances in prepubertal gonadal tissue maturation
- Gonadal tissue cryopreservation from biopsy or unilateral gonadectomy
- Biological fertility may be possible for expanded groups
Fertility Preservation Team

Erin Rowell, MD
Monica Laronda, PhD
Kristine Corkum, MD
Courtney Harris, MD
Barbara Lockart, DNP
Laura Erickson, MSN, CPNP
Shaina Goff
Molly Reimann

Gender and Sex Development Program

Earl Cheng, MD
Courtney Finlayson, MD
Elizabeth Yerkes, MD
Diane Chen, PhD
Mary Beth Madonna, MD
Julia Grabowski, MD
Robert Garofalo, MD
Danielle Lee, MSW

ekjohnson@luriechildrens.org
@eekayjay