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# Fertility in 2020: DSD

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# **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

<u>Cryopotential</u> = experimental gonadal tissue cryopreservation in hopes of future use



### **Fertility Potential in DSD**

- Impaired fertility is an important concern for families<sup>1</sup>
- Recent literature has noted germ cells in most patients with DSD<sup>2</sup>
  - Fertility potential may \u2275 over time



Germ cells present by patient's age<sup>2</sup>

<sup>1</sup>Johnson EK, *J Pediatr Urol*, 2017 <sup>2</sup> Finlayson C, *J Urol*, 2017 5



### **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?



#### All steps with patient input whenever feasible

specialist consult

![](_page_7_Picture_0.jpeg)

# Lurie Children's DSD FP IRB Protocol:

# A labor of love

![](_page_7_Picture_3.jpeg)

#### **Previous Approach: Planned Exceptions to Oncology IRB Protocols**

• Separate protocols for ovarian and testicular tissue

Cancer-specific language

 Binary gender- and sexspecific language
Informed updates to oncology protocols

![](_page_8_Picture_4.jpeg)

![](_page_8_Picture_5.jpeg)

https://mantasticpursuits.com/wpcontent/uploads/2015/12/loose.jpg

![](_page_9_Picture_0.jpeg)

| Торіс                  | Oncology Protocol | DSD Protocol | Implication |
|------------------------|-------------------|--------------|-------------|
| Tissue type            |                   |              |             |
| Condition              |                   |              |             |
| Gender/Sex<br>Language |                   |              |             |

![](_page_10_Picture_0.jpeg)

#### **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 clinicallyindicated and desired by patient/family
- Exclude 45 XO Turner (and other non-Y chromosome karyotypes)

#### **Original Paper**

HORMONE RESEARCH IN PÆDIATRICS

Horm Res Paediatr DOI: 10.1159/000502644 Received: May 20, 2019 Accepted: August 11, 2019 Published online: September 11, 2019

![](_page_11_Picture_4.jpeg)

#### Gonadal Tissue Cryopreservation for Children with Differences of Sex Development

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7/14 (50%) had germ cells

# 6/7 (86%) preserved tissue

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

1 patient chose not to preserve tissue discordant with gender identity

![](_page_12_Picture_0.jpeg)

#### **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

![](_page_13_Picture_0.jpeg)

#### **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

![](_page_13_Picture_6.jpeg)

![](_page_14_Picture_0.jpeg)

![](_page_14_Picture_1.jpeg)

4 months old

13 months old

Fig. 3. Right polar ovotestis at 2 different timepoints. 1, dysgenetic testis; 2, well-developed ovarian parenchyma.

![](_page_15_Picture_0.jpeg)

Gender Development Clinic: Transgender Sex Development Clinic: DSD

![](_page_16_Picture_0.jpeg)

#### **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 genderaffirming treatments includes fertility counseling
  - -Thus far, low uptake of fertility preservation<sup>1</sup>

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![](_page_17_Picture_0.jpeg)

#### 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

![](_page_17_Picture_5.jpeg)

![](_page_18_Picture_0.jpeg)

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