Fertility in 2020: Undescended Testis

Kate H. Kraft, MD, FAAP, FACS
September 28, 2019
Overview

• AUA Guidelines
• Semen analysis and paternity data
• Hormonal therapy
• Cryopreservation and other future directions
Undescended Testis

- 1-3% full-term male neonates
- ~30% preterm male neonates
- Histopathology – Ad spermatogonia counts
AUA Guidelines – Cryptorchidism (2014)

• Diagnose at 6 months
• Orchiopexy within the next year

AUA Guidelines – Cryptorchidism (2014)

- Orchiopexy within first 18 months → preserve fertility
- 25% cryptorchid boys born with reduced GCs
- After 15-18 mos, some lack GCs
  - No GCs on biopsy increases to ~40% in BUDT at 8-11 years

AUA Guidelines – Cryptorchidism (2014)

- # GCs remains low, does not increase with age
- Testes that remain undescended → loss of GCs and Leydig cells
- After 2 years → thermal effects
AUA Guidelines – Cryptorchidism (2014)

226 boys (6 mos – 16 years)

- 184 UUDT
- 42 BUDT

Age-matched comparisons - normal testes

- No significant difference in fertility index of patients <1 year old
- Fertility index differences statistically significant in all other age groups

Systematic review and meta-analysis comparing outcomes following orchidopexy for cryptorchidism before or after 1 year of age

B. S. R. Allin, E. Dumann, D. Fawkner-Corbett, C. Kwok, C. Skerritt, on behalf of the Paediatric Surgery Trainees Research Network

- Systematic reviews/meta-analyses support orchidopexy at 6-12 months for improved fertility
Paternity

- BUDT <<<< UUDT
  - Controls – 94%
  - BUDT – 62%
  - UUDT – 89.5%

Time to pregnancy:

- BUDT → 33.9 mos
- UUDT/controls → 11.1 mos

Semen Analysis

- 91 UUDT, 19 BUDT
- Bilateral testis biopsy in childhood → TGC/T and Ad/T
- SA parameters and hormonal evaluation in adulthood
- Total GC count at orchiopexy is not associated with significant changes in hormones or semen analysis in adulthood (UUDT or BUDT)

Semen Analysis

- In **UUDT**, low Ad count is associated with lower sperm count and sperm density, but even the lower sperm counts are above WHO standard.
- In **BUDT**, low Ad count at orchiopexy is associated with abnormal FSH and SA results in adulthood.
- Testis biopsy at orchidopexy may have limited use in UUDT and may be more clinically useful in BUDT.

Providers should counsel boys with a history of cryptorchidism and/or monorchidism and their parents regarding potential long-term risks and provide education on infertility and cancer risk. (Clinical Principle)
TESTICULAR SPERM EXTRACTION WITH INTRACYTOPLASMIC SPERM INJECTION IS SUCCESSFUL FOR THE TREATMENT OF NONOBSTRUCTIVE AZOOSPERMIA ASSOCIATED WITH CRYPTORCHIDISM

JAY D. RAMAN AND PETER N. SCHLEGEL*

From the James Buchanan Brady Urology Foundation, Department of Urology, Center for Male Reproductive Medicine and Microsurgery, New York Presbyterian Hospital, Weill Medical College of Cornell University (JDR, PNS) and The Population Council, Center for Biomedical Research (PNS), New York, New York
Hormonal Therapy after Orchiopexy

Meta-analysis: 10 studies

UDT + GnRH vs. UDT – no hormone

GC/T

RR 2.86

Hormonal Therapy after Orchiopexy

17 boys with BUDT (7 mos – 3 ½ years)

Normal FSH, decreased GC/T

5 had adjuvant LHRH, compared to controls

12 mos after o’pexy → repeat biopsy and cryopreservation
Hormonal Therapy after Orchiopexy

Cryopreservation

When to freeze?

How many samples?

Viability of sperm in the future?
SSC Transplantation

*Proc. Natl. Acad. Sci. USA*
Vol. 91, pp. 11303–11307, November 1994
Developmental Biology

Germline transmission of donor haplotype following spermatogonial transplantation

(testis/stem cells/spermatogenesis/transgenic mice/fertility)

Ralph L. Brinster* and Mary R. Avarbock

Laboratory of Reproductive Physiology, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA 19104

Contributed by Ralph L. Brinster, August 18, 1994
**Fig. 1. Human fetal testis (HFT) transplantation as a model of testicular development.** First trimester HFT (obtained from elective terminations) are cut into small pieces. A few fragments are fixed as reference histological samples (pre-graft control) to evaluate graft development at baseline (note: no seminiferous cord formation) and the remainder transplanted under the back skin of castrated immunodeficient mice. HFT grafts increase in volume and undergo subsequent development, including seminiferous cord formation.
## Cryopreservation

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**C.S. MOTT CHILDREN'S HOSPITAL**
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Retinoic acid: A potential therapeutic agent for cryptorchidism infertility based on investigation of flutamide-induced cryptorchid rats in vivo and in vitro

Zhou Yu\textsuperscript{a,b,d}, Zhang Deying\textsuperscript{a,b,c,d,*}, Hu Dong\textsuperscript{a,b}, Liu Bo\textsuperscript{a,b,d}, Peng Jinpu\textsuperscript{e}, Shen Lianju\textsuperscript{a,b,c}, Long Chunlan\textsuperscript{a,b,c}, Yu Yihang\textsuperscript{a,b}, Zhang Yuanyuan\textsuperscript{f}, Liu Xing\textsuperscript{a,b,c,d}, Tao Xu\textsuperscript{g}, Timashev Peter\textsuperscript{h}, Lin Tao\textsuperscript{a,b,c,d}, He Dawei\textsuperscript{a,b,c,d}, Wei Guanghui\textsuperscript{a,b,c,d,*}

- RA concentration lower in cryptorchid rat pups
- Histology approached normal in cryptorchid rats receiving RA
Summary

• Orchiopexy within first 18 months → preserve fertility
• Testes that remain undescended → loss of GCs and Leydig cells
• SA and paternity data are more favorable for UUDT but suggest reduced fertility in BUDT
• ART may need to be considered
• Role for cryopreservation in the future?
• Other therapies (e.g. hormonal tx, retinoic acid) need further investigation