

The Fertility Counseling Challenges for Transgender Youth and Families





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WHITE PAPER

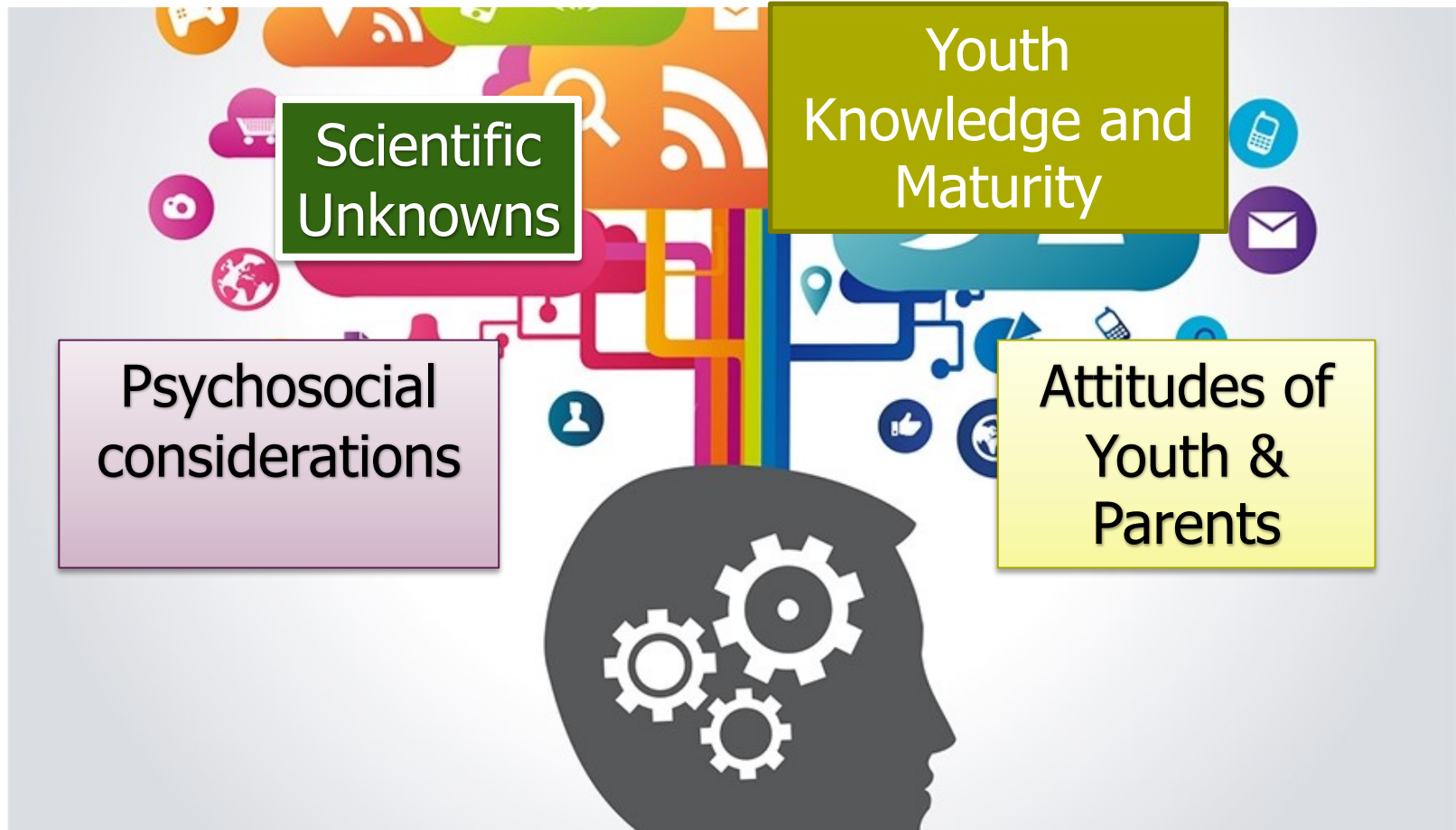
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Proceedings of the Working Group Session on Fertility Preservation for Individuals with Gender and Sex Diversity

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Risk of Infertility
FP Options
Technical requirements
Ethical concerns
Barriers to Care

Challenges



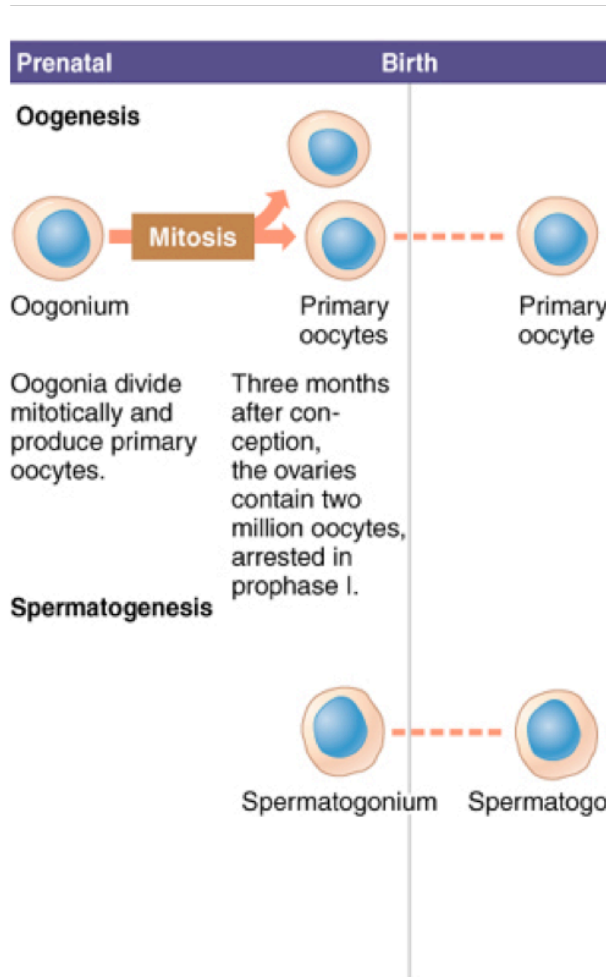
Basic Reproduction



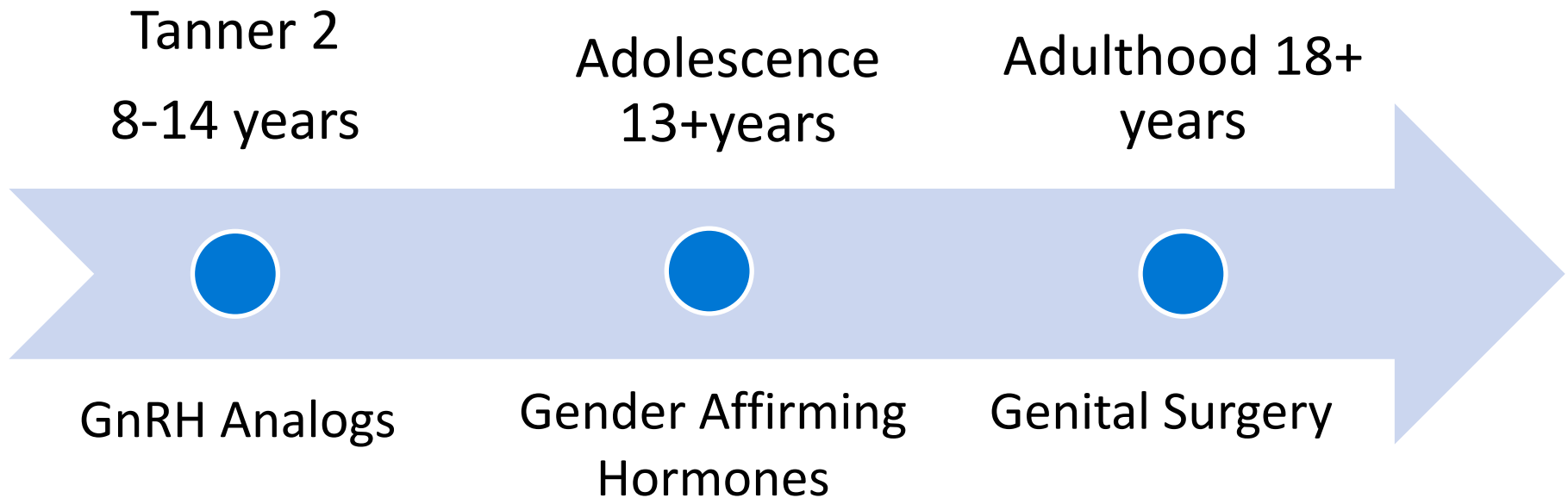
Fertility Potential



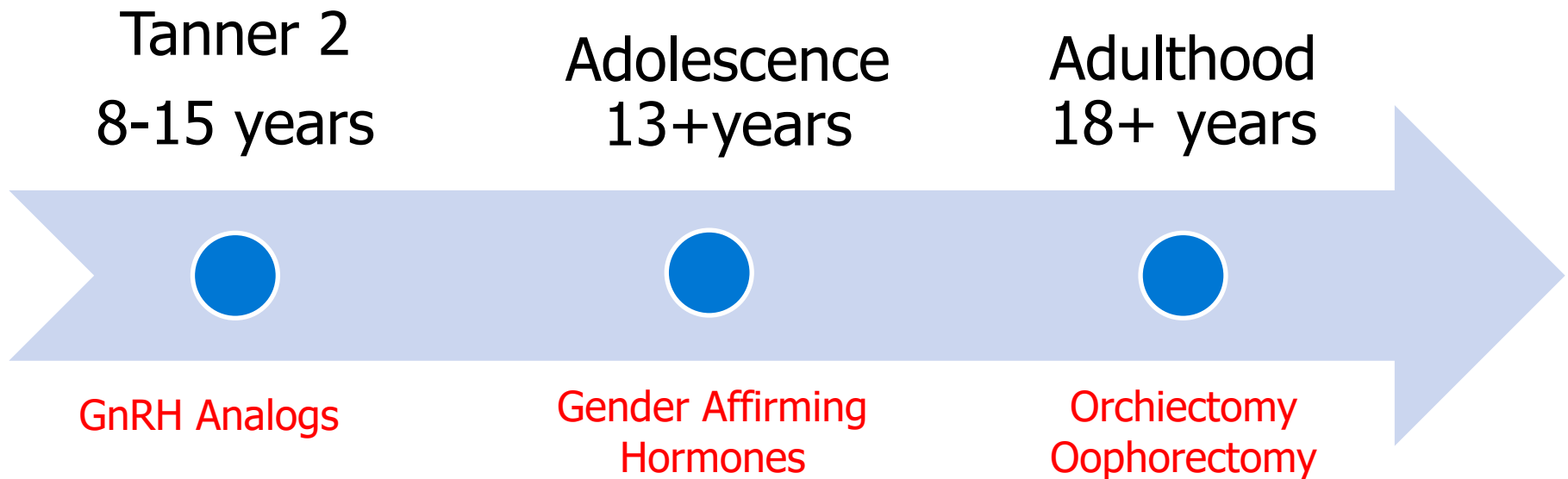
Early Development



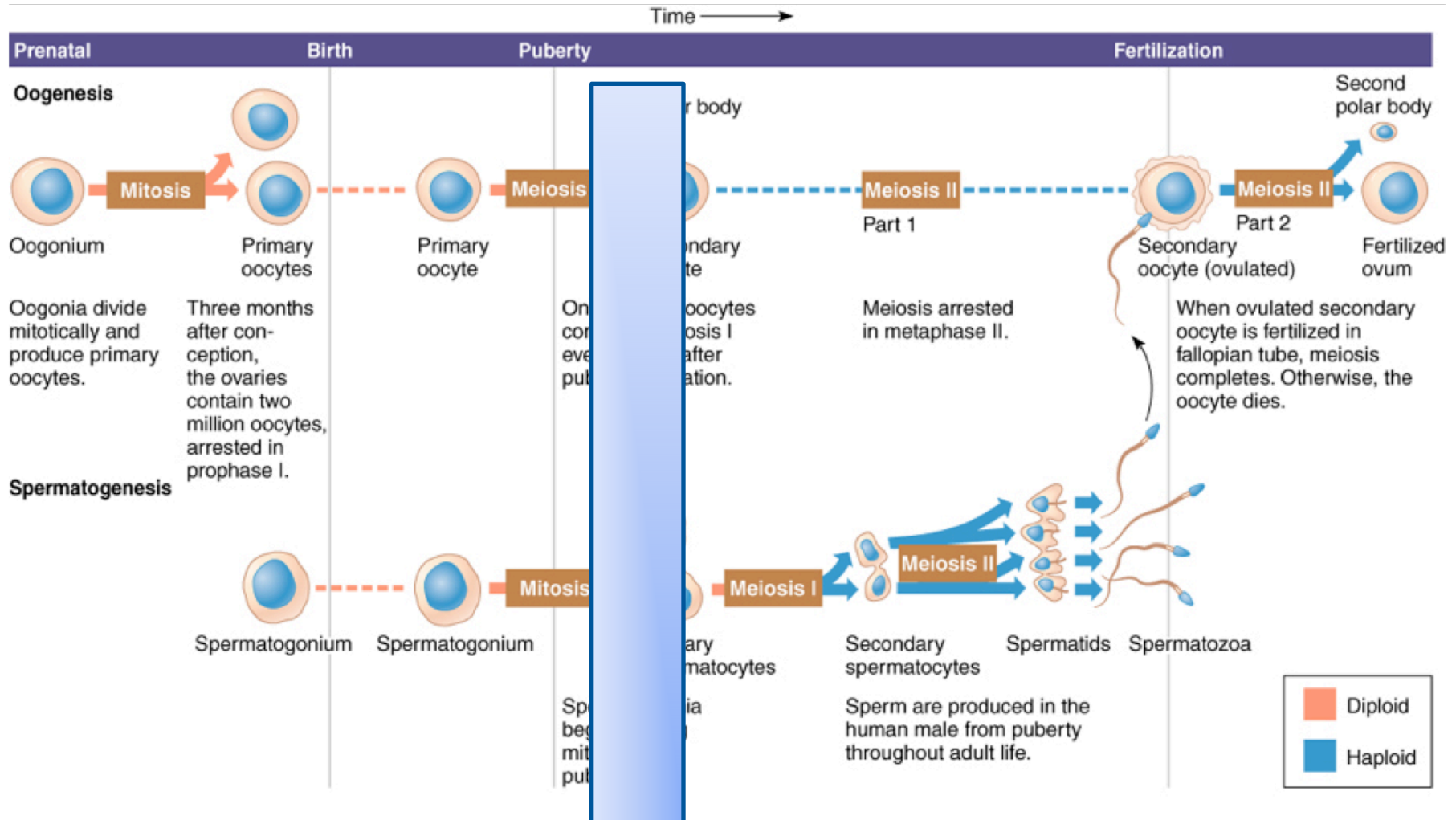
Timing of Potential Intervention



Which Treatments Affect Fertility?



GnRH analogs



Fertility?

Tanner 2
8-15 years

Adolescence 13+ years



GnRH Analogs



Gender Affirming
Hormones

***Pause Gamete
Maturation***

***What happens if gender
affirming hormones are
started with no gamete
maturation? What is the
future fertility potential?***

CORRESPONDENCE



Oocyte Cryopreservation in a Transgender Male Adolescent

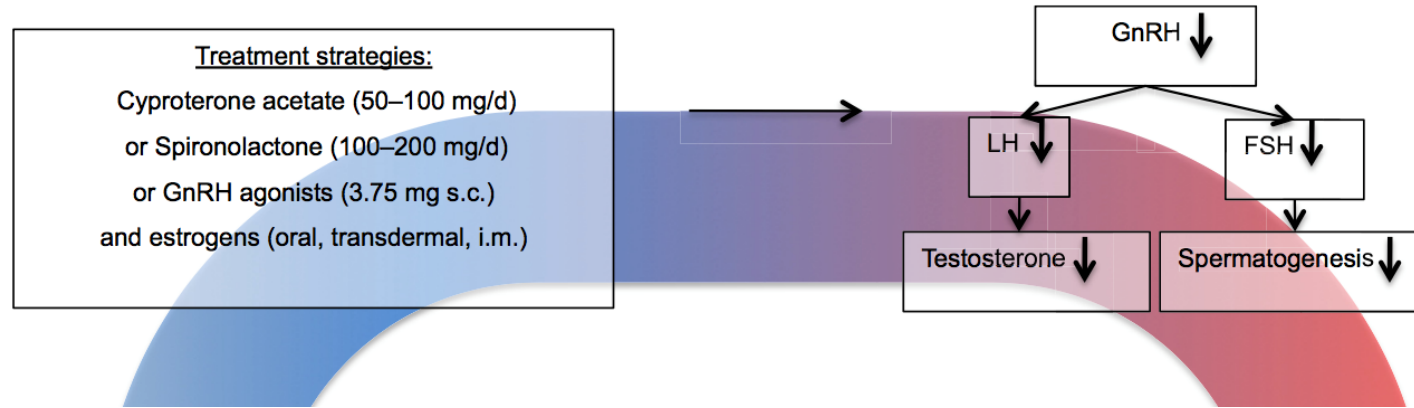
- Started GnRHa @ Tanner 2 (Age 14 years)
- Oocyte cryopreservation attempted @ Age 16 years
 - Remained on GnRHa
 - FSH & HCG given (monitoring via estradiol level, no transvaginal u/s)
 - 5 oocytes retrieved, 4 preserved
- Side effects
 - Distressing vaginal bleeding & breast development (regressed after 3 months)
 - Depressed mood and brief suicidal thoughts, resolved
- Testosterone started

- Successful oocyte harvesting, but guarded prognosis due to # of oocytes

Gender-Affirming Hormones & Fertility



For Transgender Women...



??? Short Term vs Long Term Effects ???

Some with severe involution of spermatogenesis & Leydig cells

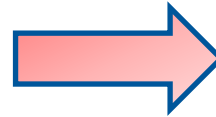
Others maintained spermatogenesis & normal Leydig cells

Table 1 Publications examining the influence of cross-sex hormone therapy on testicular morphology in gender dysphoria patients

Year	First author	Country	Patient number	Treatment	Results
1	1977 Rodriguez-Rigau <i>et al.</i>	Houston, USA	n = 1	Ethinylestradiol estradiol of 0.5–1 mg daily for 18 months	★ Germinal cells were absent, except very occasional spermatogonia, seminiferous tubules were reduced in diameter, heavy hyalinization and fibrosis. Atrophy of interstitial area with the absence of recognizable Leydig cells.
2	1978 Lu <i>et al.</i>	Houston, USA	n = 4	Long term treatment with ethinylestradiol (1–2 mg) daily	★ The estrogen-treated testicular tissue contained only Sertoli cells and very few spermatogonia within the seminiferous tubules.
3	1979 Payer <i>et al.</i>	Galveston, USA	n = 6	Steroid hormones ranging from 1.25 to 7 years	Inconsistent results: Reduced spermatogenesis and reduced numbers of Leydig cells to complete spermatogenesis with normal Leydig cell abundance.
4	1987 Thiagaraj <i>et al.</i>	Singapore	n = 10	Estrogen therapy (0.05–0.2 mg daily) for 6–13 years. Treatment was stopped 2 weeks before SRS	★ 3 cases of normal spermatogenic activity with normal Leydig cells and 7 cases of total absence of spermatogenic activity with reduced Leydig cells.
5	1988 Venizelos <i>et al.</i>	London, UK	n = 5	Estrogen treatment for periods ranging from 18 months till 5.5 years	★ Leydig cell population was reduced in all patients. Tubular hyalinization was present in all patients. Spermatogenic levels varied.
6	1987 Sapino <i>et al.</i>	Turin, Italy	n = 5	40–50 mg/week of polyestradiol phosphate treatment for varying periods. Withdrawal 10 days before SRS.	★ Atrophy of the seminiferous tubules was observed in all cases; its degree, and a marked decrease in Leydig cells, correlated with low plasma gonadotropin levels.
7	1988 Schulze <i>et al.</i>	Hamburg, Germany	n = 11	1–12 years of treatment with various amounts of estrogens, estradiol, or ethinylestradiol	Narrow seminiferous cords surrounded by an extensively thickened lamina propria. They contain Sertoli cells and spermatogonia exclusively. There is no evidence of typical Leydig cells.
8	1990 Kisman <i>et al.</i>	Amsterdam, The Netherlands	n = 8	18 months with a combination of 100 g ethinylestradiol and 100 mg CPA daily	★ Increase of interstitial tissue, decrease in number and in volume of Leydig cells and spermatogenic arrest
9	1992 Lübbert <i>et al.</i>	Berlin, Germany	n = 1	20 ug and 60 ug of ethinylestradiol	The low dose had no negative effect on sperm motility? and density. High dose reduced motility after a few days and density after 2 weeks.
10	2004 Aschim <i>et al.</i>	Oslo, Norway	n = 3	100 ug ethinylestradiol for at least 1 year	★ Dramatic decrease of estrogen receptor beta transcripts.
11	2015 Schneider <i>et al.</i>	Münster, Germany	n = 108	Anti-androgens (10–100 mg) combined with different dosages of estrogens or only estrogens or a combination of Spironolactone and estrogens. Multicenter study: Patients either discontinued treatment 6 weeks (clinic A) or 2 weeks (clinic B) prior to SRS or not at all (clinic C).	★ Histology revealed a highly heterogeneous picture with 24% patients with normal spermatogenesis irrespective of the treatment strategy. Only patients that did not discontinue hormonal treatment showed feminized blood levels on the day of SRS and the lowest ITT levels.

For Transgender Men...

Testosterone



Effects of prolonged
anovulatory state?
Testosterone exposure?
Often reversible

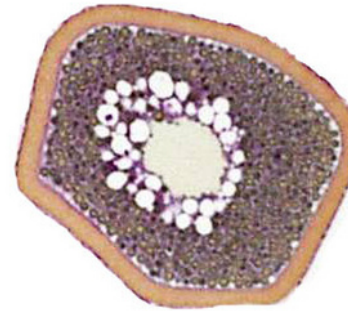
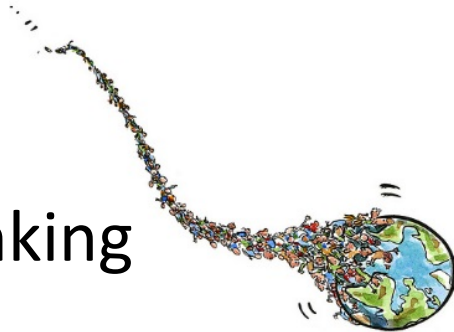
- Adeleye et al: 13 Transgender men
 - 6 before HRT and 7 after HRT
 - Mean length of HRT 46 months
 - Transgender men who used HRT had lower peak estradiol (1175 pg/mL vs. 2713 pg/mL) and oocytes retrieved (12 vs. 25.5)
 - No difference in other factors
 - 3 successful pregnancies from those with HRT
- Leung et al:
 - 26 Transgender patients (2/3 after HRT)
 - Mean length of HRT 44 months
 - Mean oocyte retrieval was higher in the transgender cohort and estradiol levels were similar
 - 16 banked oocytes
 - 7 achieved pregnancy

Fertility Preservation Options



Post-Pubertal FP Options

Sperm or
Embryo Banking



Oocyte or Embryo
Banking

Peri-Pubertal FP Options

- Testicular or ovarian tissue cryopreservation
 - *Experimental*
 - *Testicular protocols at UCSF and Pittsburgh (and others?)*
 - *Ovarian protocol at Pittsburgh (and others?)*
- Forgo GnRHa to allow in vivo germ cell maturation
 - *Worsening dysphoria, self harm, permanent 2° sex characteristics*
- Remain on GnRHa with hormone stimulation
 - *Experimental*
 - *Development of secondary sex characteristics, dysphoria, depression*

Psychosocial Considerations



Desire for Parenthood/Fertility in Adults

- Many desire parenthood (biological, adoption, sperm bank, fostering)
- Believe fertility preservation should be offered although desire to pursue varies
- Many have regret about not having fertility options

Desire for Parenthood/Fertility in Youth

- Future parenthood desires vary
- Family values around biological parenthood
- Gender dysphoria
- Financial considerations (high costs)
- Fertility Information: lack of awareness of FP options, procedures
- Invasiveness of the available procedures and the potential psychological impact of the FP process.

Factors to consider

- Gametes do not match gender identity
- Procedural Complexities
 - Trigger gender dysphoria
 - Exams and Body dysphoria
 - Hormonal stimulation with hormones that do not match gender identity
 - Procedures like transvaginal ultrasound
- Coping Strategies
 - Focus on reasons for undergoing procedures
 - Support from family and friends
 - Cognitive approaches for body dysphoria
 - Using non-gendered names for body parts

Original article

Low Fertility Preservation Utilization Among Transgender Youth

Leena Nahata, M.D.^{a,b,*}, Amy C. Tishelman, Ph.D.^{c,d}, Nicole M. Caltabellotta, B.A.^b,
and Gwendolyn P. Quinn, Ph.D.^{e,f}

2 of 72 adolescents (MtF) counseled within medical visit pursued FP

Adolescent health brief

Fertility Preservation for Transgender Adolescents

Diane Chen, Ph.D.^{a,b,c,d,*}, Lisa Simons, M.D.^{a,d}, Emilie K. Johnson, M.D., M.P.H.^{e,f},
Barbara A. Lockart, D.N.P., A.P.N./C.N.P.-A.C. & P.C., C.P.O.N.^{g,h}, and Courtney Finlayson, M.D.^{d,i}

13/105 adolescents counseled within medical visit did formal FP consultation
5/13 preserved (4 sperm, 1 oocyte)

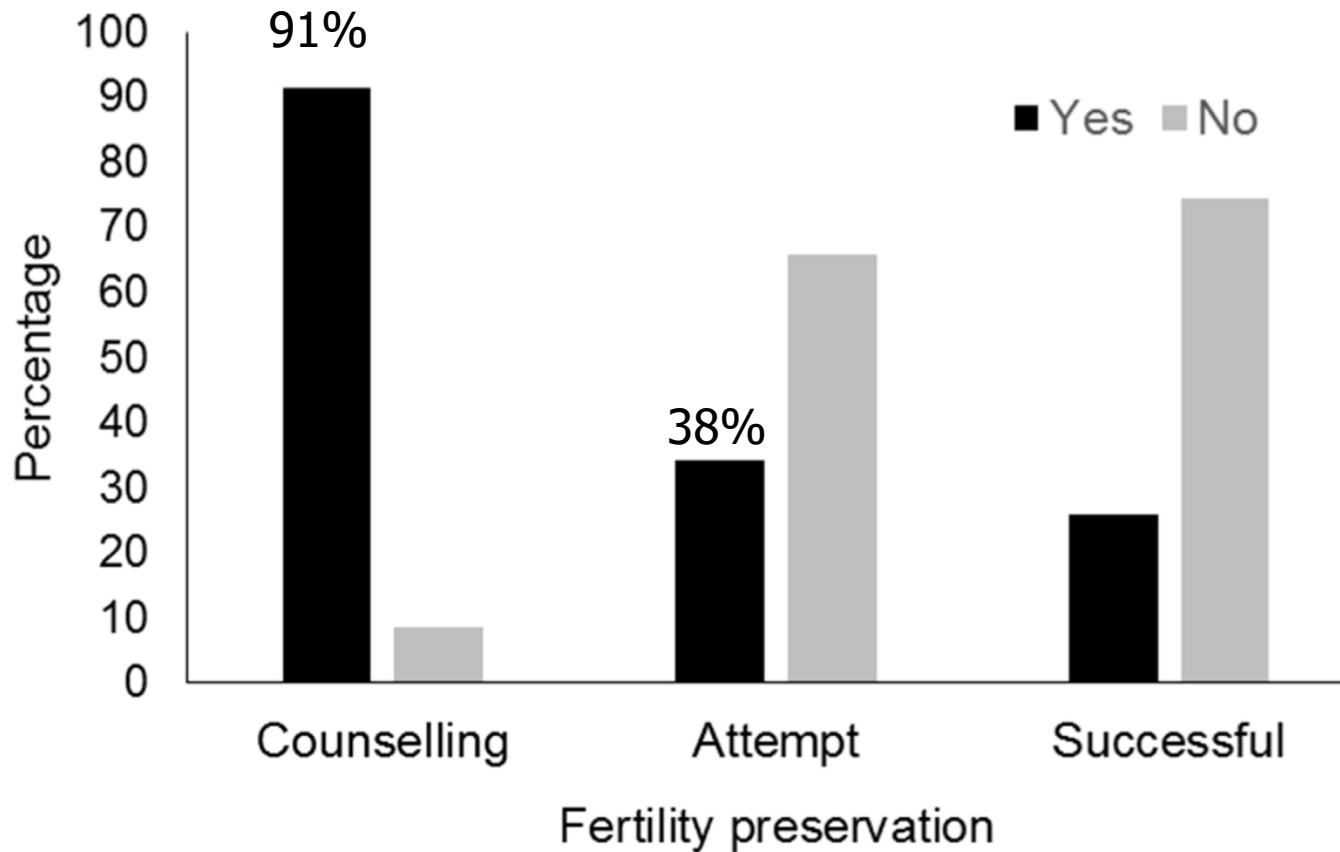
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Patterns of Fertility Discussions and Referrals for Youth at an Interdisciplinary Gender Clinic

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and Julia F. Taylor, MD, MA^{2,3}

66 adolescents, 52/66 counseled within medical visit
11/52 formal FP consultation, 3/11 attempted preservation, 2/3 preserved

35 Transgirls



Ultimately
9/12 preserved

Reasons FP
unsuccessful:
1 unable to
ejaculate, 1
azoospermia, 1
oligospermia
and poor
quality

Reasons for no FP: 17% did not want children,
13% wanted to adopt, body/process 17%, idea of
being "father" 4%

I understand
how it works, I
know what I
think....

I want to....



**Needed:
Standardized counseling protocols and patient
decision aids**



**Northwestern's
campus when it
isn't 9 degrees!**