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Project ECHO®

Pediatric TransECHO

Developmental Approaches to Caring for Transgender & Gender Diverse Pediatric & Adolescent Patients

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Why Talk About Gender with Kids?

- Professional responsibility
  - AMA, AAMC, AAFP, AAP, SAHM, APA
    - Recommend training on LGBTQIA health
  - Exclusion of coverage illegal in some states
  - Lack of formal medical training no longer "good excuse"
- Pediatric responsibility
  - Anticipatory guidance & prevention
  - Future planning
  - Models & promotes diversity, equity for all children

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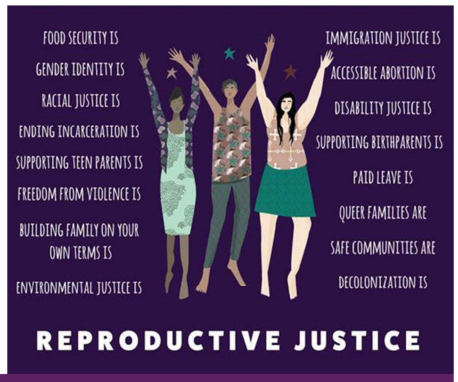
Several medical organizations, including the AAFP, recommend residents be trained to provide quality, culturally appropriate care to LGBTQ patients of all ages. AAFP and STFM went through a multi-year process to create detailed guidelines on this training, that will be discussed later.

Beyond professional organizations, as family physicians you all have committed yourselves to providing patient-centered primary care. Gender is a part of every patient, and therefore providing care to help affirm and support patients in their gender is part of the spectrum and scope of practice for this specialty.

Reproductive Justice Framework: Intersectionality of Our Children's Health Care Rights

- Bodily autonomy
- Right to self determine
- Right for safe, healthy environment with opportunity to develop potential
- Responsibility for most marginalized



Especially fitting for children & adolescents

SisterSong 1997 …

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the right to have children and to decide how many and under what conditions you give birth.
the right to not have children.
the right to parent one's own children in safe & healthy environments

International Conference on Population and Development in Cairo (1994)

Recognized individual's right to plan family must be central to global development

SisterSong Critical Role (1997 …)

National multi-ethnic Reproductive Justice collective

Membership represents Indigenous, African American, Arab and Middle Eastern, Asian and Pacific Islander, and Latina women and LGBTQ people

Membership also includes white, male, and pro-life allies who support women's human right to lead fully self-determined lives

Sexual Orientation and Gender Identity Middle School Students

Transgender Gender Identity

1.3%

Non-Hetero Sexual Orientation

15.9%

Table 1
Sexual orientation and gender identity of middle school students: population statistics

Sexual orientation/ gender identity	Unweighted count	Population estimate	Standard error	95% Confidence interval	
				Lower	Upper
Sexual orientation					
Heterosexual	2,254	8,721.410	316.362	8,094.191	9,348.628
Gay or lesbian	48	172.724	26.727	119.734	225.713
Bisexual	59	217.362	37.171	143.667	291.057
Not sure	276	1,250.964	131.543	990.167	1511.761
Total	2,637	10,362.459	374.772	9,619.437	11,105.482
Heterosexual	2,254	84.2%	1.1%	81.9%	86.2%
Gay or lesbian	48	1.7%	0.3%	1.2%	2.3%
Bisexual	59	2.1%	0.3%	1.5%	2.9%
Not sure	276	12.1%	1.1%	10.0%	14.5%
Total	2,637	100.0%	0.0%	100.0%	100.0%
Gender identity					
Female	1,331	5,148.062	224.796	4,702.382	5,593.742
Male	1,337	5,381.086	231.687	4,921.744	5,840.429
Transgender	33	137.053	48.423	41.050	233.057
Total	2,701	10,666.201	398.453	9,876.230	11,456.173
Female	1,331	48.3%	1.2%	46.0%	50.5%
Male	1,337	50.4%	1.1%	48.2%	52.7%
Transgender	33	1.3%	0.4%	0.6%	2.5%
Total	2,701	100.0%	0.0%	100.0%	100.0%

Shields JP, et al. "Estimating population size and demographic characteristic of LGBT youth in middle schools." J Adol Hlth. 2013:248-50.

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Kidd 2021

- 2 step: gender assigned, gender identity
- Urban YRBS capturing 91% high school students
- 3168 usable surveys (67%)
  - 27% (1282) ineligible lacking race/ethnicity or ender data
  - 5.1% (243) “mischievous”
- 9.2% (1282) identified as GDY
- 38.8% feminine, 29.0% masculine, 31.3% nonbinary

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New important study

Developmental Paradigm

- Gender, sexuality are universal, normalized
- Variance expected in biology & human development
- Diversity not = deviance but celebrated

- Meet patient goals (nothing to “diagnose” or “treat”)
- Address, reduce minority stress

- Advocate, empower ALL children
- Model, elevate cultural expectations

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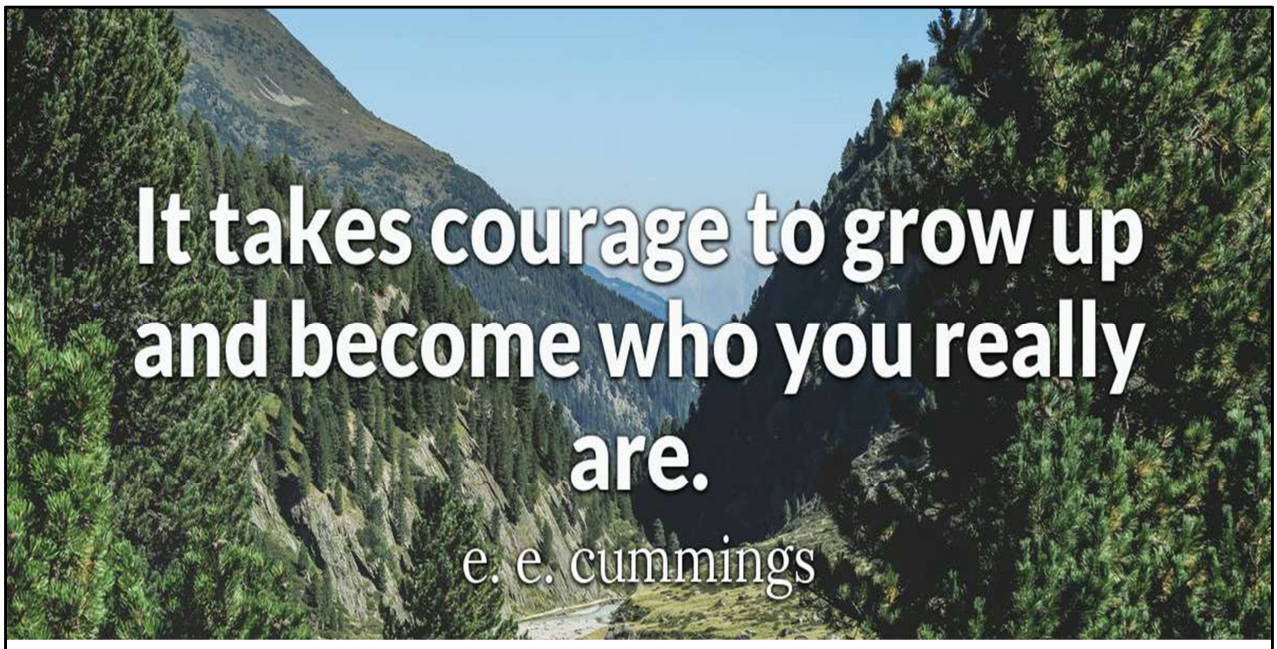
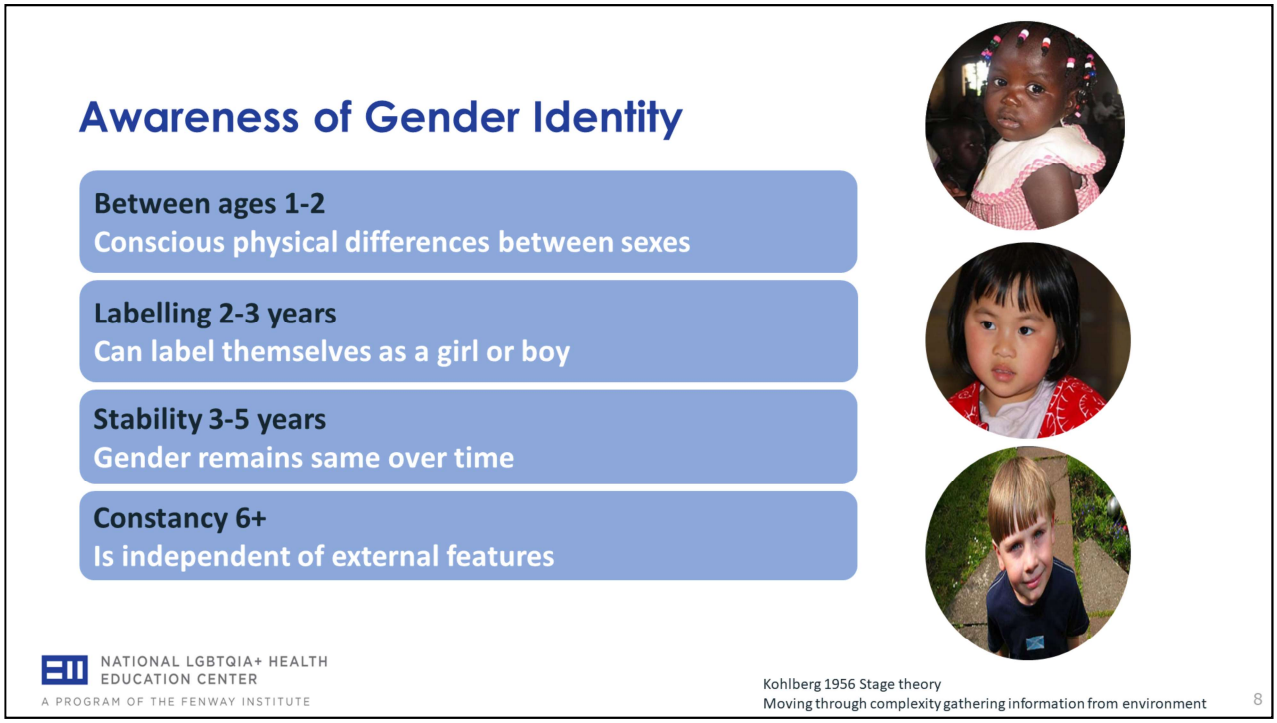

It takes courage to grow up and become who you really are.
e. e. cummings



Kolbery 1956

Awareness of being a boy or a girl begins during the first year of a child's life, when babies typically discover their genitals. Between the ages of 1 and 2, children become conscious of physical differences between genders. By the age of 3, children are easily able to label themselves as they acquire a strong concept of self. By age 4, a child's gender identity is stable.

During this same time of life, children learn gender role behavior—that is, doing things "that boys do" or "that girls do." Before the age of 3, children can differentiate sex-stereotyped toys. By 3 years of age, they have also become more aware of boy and girl activities, interests, and occupations. Many begin to play with youngsters of their own sex in activities identified with that sex. By the time they enter kindergarten, children's gender identities are well established.

Source: American Academy of Pediatrics. (1995). CARING FOR YOUR SCHOOL-AGE CHILD: AGES 5–12. New York: Bantam Books.

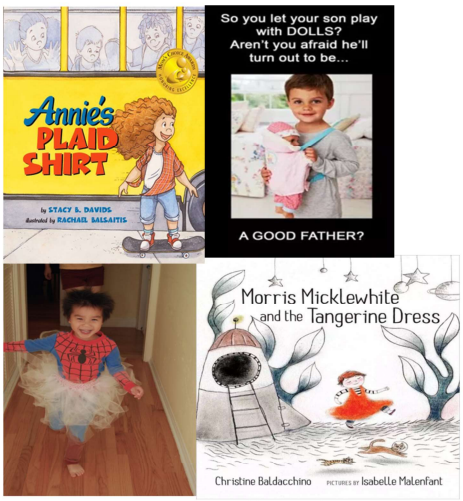
While most individuals will identify in binary "male or female," "boy or girl," or "man or woman" paradigms, it is important to note that some individuals' identities might

be in between these categories.

Gender Play

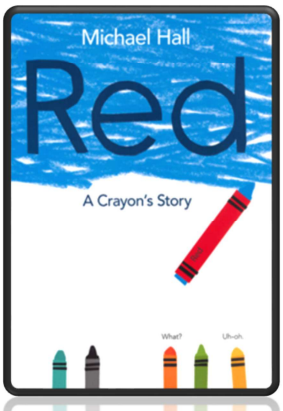
- All pre-pubertal children play with gender expression & roles
  - Passing interest or trying out gender-typical behaviors
  - Interests related to other/opposite sex
  - Few days, weeks, months, years

Behaviors and expression may be nonconforming, but children can still feel they are in right-gendered body!



Pediatric medical, mental health, social service, and school providers have many opportunities to explore with kids and parents what their children are interested in, behaviors that may be concerning, or general activities involved.

Gender Diversity



Persistent
Consistent
Insistent

- Cross gender expression, role playing
- Wanting other gender body/parts
- Not liking one's gender & body (gender dysphoria)

Non-Binary
Diverse
Fluid

- Agender
- Non-binary
- Refuses to ascribe to typical masculine or feminine assignments
- Can change, shift

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The overall idea is some people have discordance between gender assigned at birth and lived-gender identity which can include agender.

Where is Gender???

Increasing Evidence: Protective Effects, Short & Long-term

- Early identification, support, access to care benefits >> potential risks
  - Updates 2020 protective effects against suicidality
    - Russell 2018 -using asserted name, pronoun
    - Turban 2020 -access to blockers
- Parent & family acceptance
  - Ryan 2009
  - Olson K 2016,2017
- Role of professionals

POLICY STATEMENT Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of all Children

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Ensuring Comprehensive Care and Support for Transgender and Gender-Diverse Children and Adolescents

Jason Rafferty, MD, MPH, EdM, FAAP, COMMITTEE ON PSYCHOSOCIAL ASPECTS OF CHILD AND FAMILY HEALTH, COMMITTEE ON ADOLESCENCE, SECTION ON LESBIAN, GAY, BISEXUAL, AND TRANSGENDER HEALTH AND WELLNESS

abstract

As a traditionally underserved population that faces numerous health disparities, youth who identify as transgender and gender diverse (TGD) and their families are increasingly presenting to pediatric providers for education, care, and referrals. The need for more formal training, standardized treatment, and research on safety and medical outcomes often leaves providers feeling ill equipped to support and care for patients that identify as TGD and families. In this policy statement, we review relevant concepts and challenges and provide suggestions for pediatric providers that are focused on promoting the health and positive development of youth that identify as TGD while eliminating discrimination and stigma.

INTRODUCTION

In its dedication to the health of all children, the American Academy of Pediatrics (AAP) strives to improve health care access and eliminate disparities for children and teenagers who identify as lesbian, gay, bisexual, transgender, or questioning (LGBTQ) of their sexual or gender identity.[1,2] Despite some advances in public awareness and legal protections, youth who identify as LGBTQ continue to face disparities that stem from multiple sources, including inequitable laws and policies, societal discrimination, and a lack of access to quality health care, including mental health care. Such challenges are often more intense for youth who do not conform to social expectations and norms regarding gender. Pediatric providers are increasingly encountering such youth and their families, who seek medical advice and interventions, yet they may lack the formal training to care for youth that identify as transgender and gender diverse (TGD) and their families.[3]

This policy statement is focused specifically on children and youth that identify as TGD rather than the larger LGBTQ population, providing brief, relevant background on the basis of current available research

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Dr Rafferty conceptualized the statement, drafted the initial manuscript, reviewed and revised the manuscript, approved the final manuscript as submitted, and agrees to be accountable for all aspects of the work

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The guidance in this statement does not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

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FROM THE AMERICAN ACADEMY OF PEDIATRICS

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Who & When to "Screen"?

- All children!
  - Developmental stages
  - Opportunity for improving child/family communication & support
  - Teaches, models pro-diversity
- Diverse or nonconforming gender expression
- Concerns/problems with
  - Mood
  - Behavior
  - Social

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Who should be screened and what are you looking for in terms of gender nonconformity and patients struggling with their gender identities?

First, you should be screening all children to see if they are expressing gender as expected according to developmental stages.

Next, screen kids who present with gender nonconforming behaviors (dress, play choices, identifying as the opposite sex from their natal sex, choosing a gender nonconforming name, etc).

Also, screen kids who are expressing mood or behavior problems or may be struggling with a variety of issues, one of which is gender.

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Ask! Parent(s)

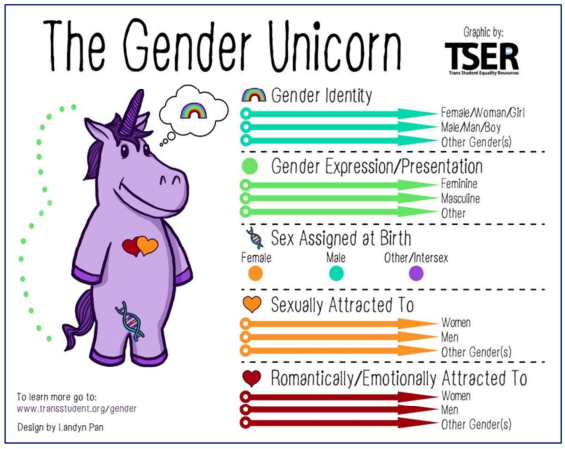
- Child play, peer, hair, dress preferences
- Concerns with these
- Concerns with behavior, friends, getting along at school, school failure, bullying, anger, sadness, isolation, other?

Ask! Patient

- Do you feel more like a girl, boy, neither, both?
- How would you like to play, cut your hair, dress?
- What name or pronoun fits you?
- What does it mean to be girl, boy, both, neither?

This is where clinicians can come in. What do you ask, and to whom?

Gender Screening "Tools"



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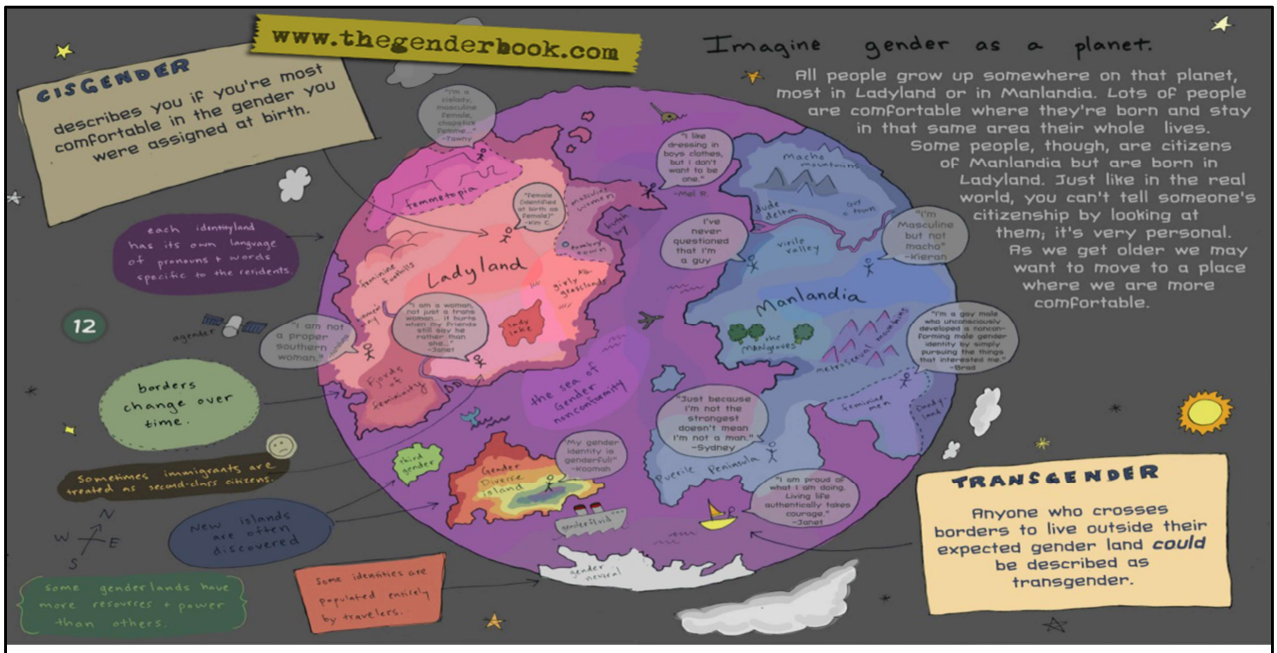
Four areas that we look at:
(1) sex—usually male or female;
(2) identity—how you do identify yourself?;
(3) attractions—whom you are attracted to; and
(4) expression, or sexual behavior.

It is NOT about the label, but we need to use labels for this talk, so we are all speaking the same language!

Source: http://itspronouncedmetrosexual.com



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Images taken from The Gender Book, are publically available on the book's website, www.thegenderbook.com

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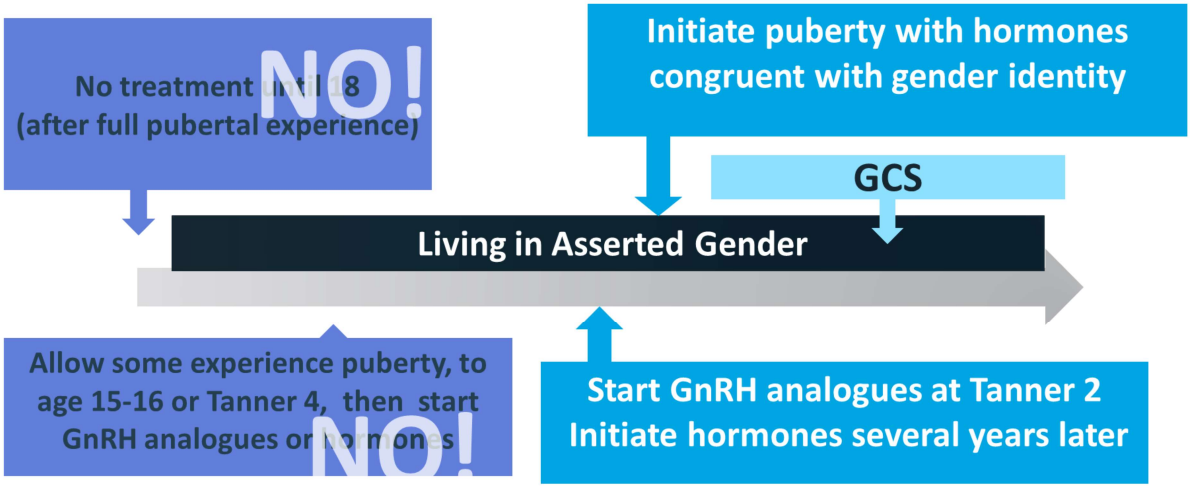
Lessons Learned: Historical Gatekeeping vs Explore/Affirm



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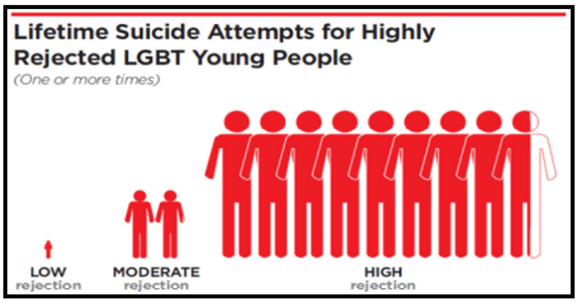
FAMILY ACCEPTANCE PROJECT
... building healthy futures for youth



Ryan CJ; 2010, 2009

N=245 LGBT Retrospective assess family accepting behaviors in response to gender & sexual minority status

Predicts improved

- Self-esteem
- Social support
- General health status

Protects against

- Depression
- Substance use
- Suicidality

TransYouth Project

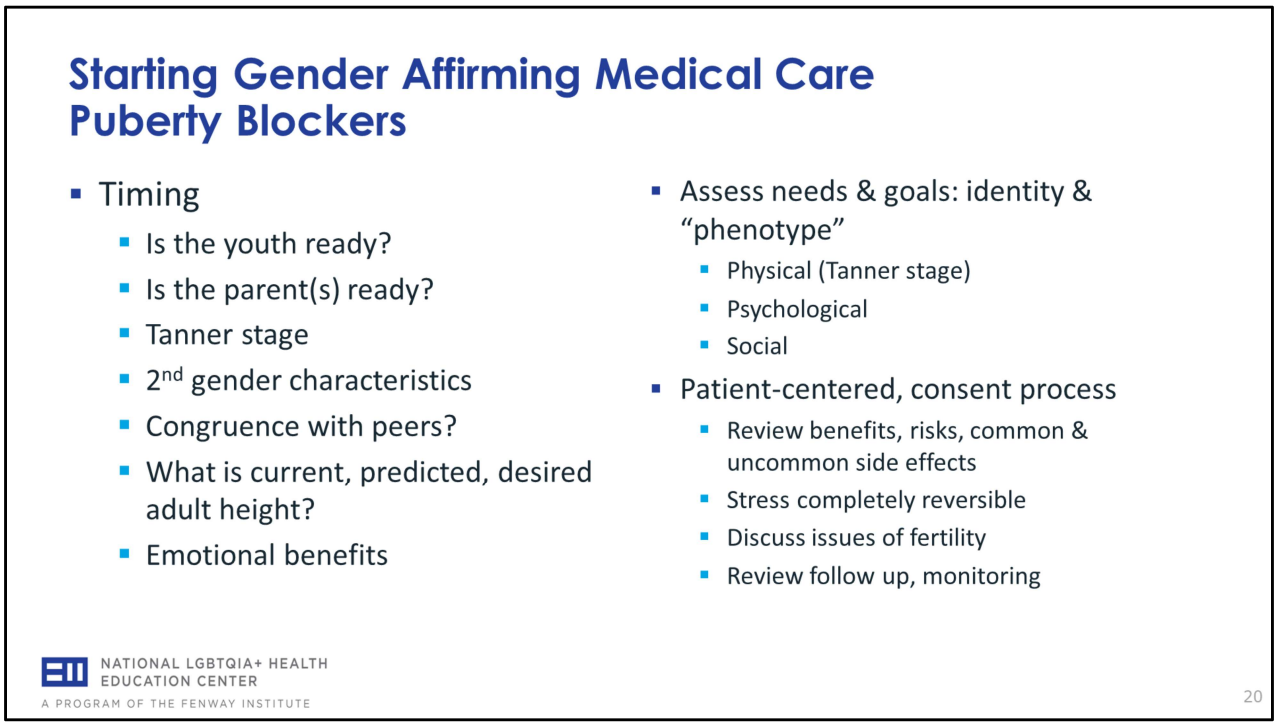
- NIH Patient Reported Outcome Measurement Information System
  - Large-scale (>150 children) longitudinal study
  - transgender children, 25 states
- (2016) 73 children, ages 3-12
  - Symptoms of depression, anxiety
  - Rates depression (50.1) and anxiety (54.2)
  - No higher than 2 control groups
    - Siblings & cis age- and gender-matched children

Significantly lower than TGD children in previous studies

- (2017) 116 trans, 122 controls, 72 sibs ages 6-14
  - Symptoms of depression, self worth same
  - Slightly higher anxiety

Olson KR, Durwood L, DeMeules M, et al. Mental Health of Transgender Children Who Are Supported in Their Identities. Pediatrics. 2016;137(3):e20153223

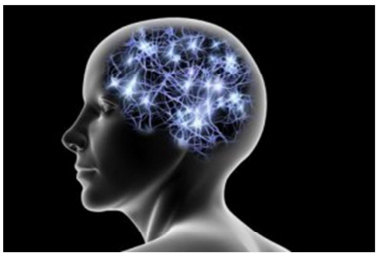
Dunwood L, McLaughlin KA, Oslon KR. Mental Health and Self-Worth in Socially Transitioned Transgender Youth. J Am Acad Child Adolesc Psych. 2017 Feb;56(2):116-123.

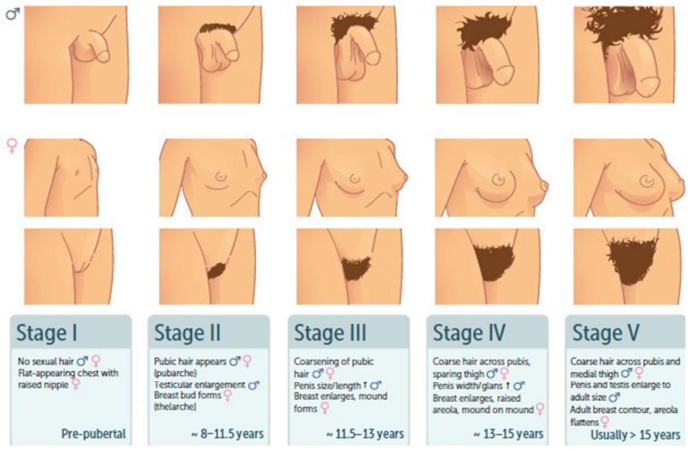


Before a specialist would begin K's transitioning, she would assess K's stage of development as this will determine whether pubertal suppression is an option. Working with a mental health professional, the provider will determine whether K is psychologically ready to transition. Additionally, the provider and patient must discuss how the transition will affect K's social interactions including school, family, and community life.

The provider will review all the benefits and risks associated with pubertal suppression and cross-hormone therapy.

Welcome to the Wonderful World of Puberty!!

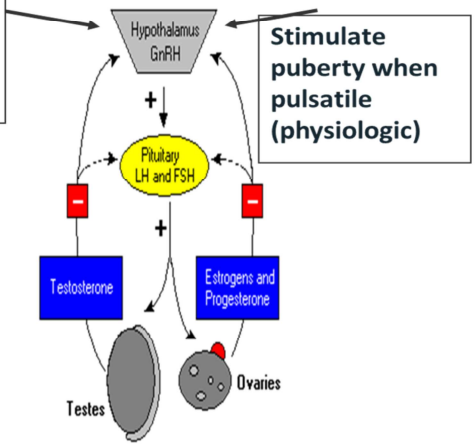




Gonadotropin-releasing Hormone (GnRH) Agonists

- Continuous GnRH secretion
  - Suppress follicle stimulating hormone (FSH) – plays role in hair growth, Luteinizing hormone (LH) – plays role in gonadal development
  - Initial ↑ LH, FSH followed by desensitized pituitary
  - LH, FSH secretion suppressed

Block hypothalamus when given continuously



Stimulate puberty when pulsatile (physiologic)

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Short-acting preparations that need to be delivered one- to three-times daily by nasal spray are also available but are not as efficient as sustained release preparations in suppressing gonadotropin secretion with prolonged non pulsatile GnRH-like hormone.

Gonadotropin-releasing Hormone (GnRH) Agonists

- Injectables
  - Leuprorelin (also Triptorelin, Goserelin)
  - Q 1,3,4,6 months
  - $500-3000

Table 1. ELIGARD® Recommended Dosing

Dosage	7.5 mg	22.5 mg	30 mg	45 mg
Recommended Dose	1 injection every month	1 injection every 3 months	1 injection every 4 months	1 injection every 6 months

- Long-acting Implant
  - Histrelin
  - 24 + month
  - $3500 (Vantas)
  - $20,000 +(Supprelin)

Implant drug delivery

2- Histrelin implants

Usual Adult Dose for Prostate Cancer:

- **Vantas®:** One 50 mg implant inserted subcutaneously in the inner aspect of the upper arm.
- Duration of therapy: The implant should be removed after 12 months.
- Palliative treatment of advanced prostate cancer

Usual Pediatric Dose for Precocious Puberty:

- **Supprelin LA®:** One 50 mg implant inserted subcutaneously in the inner aspect of the upper arm.
- Duration of therapy: The implant should be removed after 12 months.
- Discontinuation of therapy at the appropriate time point for the onset of puberty.

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Short-acting preparations that need to be delivered one- to three-times daily by nasal spray are also available but are not as efficient as sustained release preparations in suppressing gonadotropin secretion with prolonged non pulsatile GnRH-like hormone.

Benefits > Risks Puberty Blockers

Asserted Boys	Asserted Girls	Risks
▪ No female breast development ▪ Stop widening pelvis ▪ Block menses dysphoria ▪ Delay early epiphyseal closure, add height ▪ Low dose Testosterone for promoting height	▪ Avoid bigger, heavier skeletal changes ▪ Avoid Adam's apple ▪ Avoid male pattern face, body hair ▪ Still useful for some Tanner 4-5 with minimal external gender characteristics ▪ Estradiol earlier for earlier puberty & height reduction	▪ Perimenopause ▪ Hot flashes ▪ Initial mood, concentration ▪ Bone marrow density (BMD)? ▪ Psycho-cognitive? ▪ …RELIEF!

Puberty Blockers

Early Puberty	Middle Puberty	Late Puberty and Beyond
▪ Limited tissue for later gender affirming surgeries ▪ Sterility if gender affirming hormones (GAH) allowing for mature spermatogenesis or oogenesis ▪ Mature gamete production occurs late in puberty, associated with significant secondary sex characteristics	▪ Middle Puberty ▪ Won't take away characteristics already developed but can stop further development & distress ▪ Very effectively suppress menses ▪ Allows for lower estrogen/testosterone (E/T) doses, slower titration as no need to suppress ▪ Potential for fertility	▪ Phenotypic changes with lower GAH doses ▪ "…[In certain situations, such as above] continuation of GnRH analog treatment is advised until gonadectomy…" ▪ Implications for genderqueer & non-binary people

Height Considerations on Blockers

- Obtain each visit
- Calculate mid-parental heights Male & Female
- Patient goals
  - T Lower dose 10-20 mg SQ weekly
  - E supraphysiologic (16-24 mg SL daily)

Table 1. Formulas for Calculating Midparental Height in Children

Girls
[Paternal height (cm) – 13 cm + maternal height (cm)] ÷ 2
or
[Paternal height (in) – 5 in + maternal height (in)] ÷ 2
Boys
[Paternal height (cm) + 13 cm + maternal height (cm)] ÷ 2
or
[Paternal height (in) + 5 in + maternal height (in)] ÷ 2

Timing of Puberty

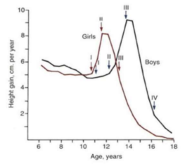
Puberty and the adolescent growth spurt occur on the average nearly 2 years earlier in girls than in boys

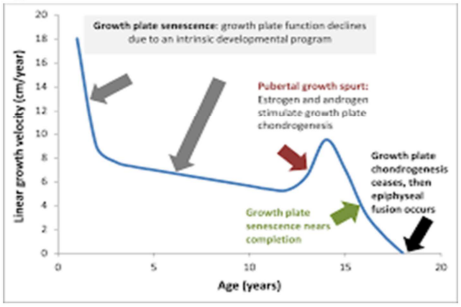
FEMALE:

Stage I : Physical growth spurt, appearance of breast buds and pubic hair.

Stage II: noticeable breast development, Pubic hair is darker and more widespread, axillary hair.

Stage III: onset of menstruation, noticeable broadening of the hips more adult fat distribution, development of the breasts





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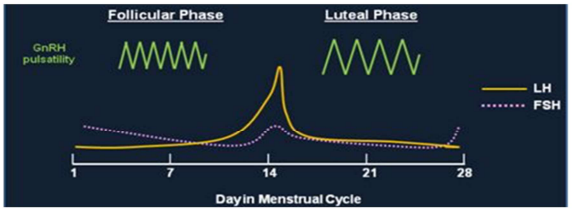
Progestin as Blockers

- Decreases GnRH pulse frequency
  - Antagonistic effect
- Decreases ant pituitary release LH, FSH
  - Low FSH = inhibit follicular development & estradiol production
  - P negative feedback, lack of estrogen positive feedback prevent LH surge



- Can be used an alternative to GnRH agonists
  - Payment Issues
  - Access
  - Patient or Parental Concerns
- Not as effective
  - Menses suppression for most
  - Not halt phenotype changes
  - Limited research in assigned males
  - ? BMD over years
- Use for genderqueer/non-binary patients

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decreases pulse frequency GnRH release by hypothalamus, which decreases release of FSH\LH by anterior pituitary
Decreased levels of FSH inhibit follicular development, preventing an increase in estradiol levels
Progestogen negative feedback and lack of estrogen positive feedback on LH release prevent a LH surge
Inhibition of follicular development and absence of a LH surge prevent ovulation.
-inhibition of sperm penetration by changes in the cervical mucus
-inibition of ovarian function during DMPA use causes endometrium to become thin and atrophic

Decreases GnRH pulse frequency

- Antagonistic effect
  - Low frequency stimulates FSH synthesis – increasing follicular estradiol increase
  - Increased frequency stimulates LH Synthesis

& surge related to ovulation

Considerations: Fertility

- Discuss fertility as we approach/start totally reversible GnRH analogues
  - Knowing high % go to GAH
  - Developmentally appropriate language for youth ranging ages 8-14
- Genetic fertility (chromosomes, carrying pregnancy) does NOT equal parenting & having family
- Resources for fertility preservation, before GAH
  - Urology for sperm preservation
  - REI for oocyte preservation
- Issues
  - Cost, insurance coverage, time, future technologies
  - Risk self harm & suicide for trans and gender diverse (TGD) patients vs infertile persons

Starting Gender-affirming Hormones

- Timing
  - Is the youth ready?
  - Is the parent(s) ready?
  - Puberty congruent with peers?
    - Assigned females start 10-11 years
    - Assigned males 11-12 years
  - What is current, predicted, desired adult height?
    - Growth curve, percentile
    - Growth velocity
    - Mid-parental heights
- Assess needs & goals "phenotypic transition"
  - Physical (Tanner stage)
  - Psychological
  - Social
- Patient-centered consent process
  - Review benefits, risks, common & uncommon side effects
  - Differentiate reversible & irreversible changes
  - Determine if realistic sense of what can and can't be impacted by hormones
  - Review follow up, monitoring

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Before a specialist would begin K's transitioning, she would assess K's stage of development as this will determine whether pubertal suppression is an option. Working with a mental health professional, the provider will determine whether K is psychologically ready to transition. Additionally, the provider and patient must discuss how the transition will affect K's social interactions including school, family, and community life.

The provider will review all the benefits and risks associated with pubertal suppression and cross-hormone therapy.

Gender-affirming Hormones

- What are your *goals*?
  - Head to toe phenotype
  - Sexual function
  - Internal
  - Social
- What *problems* can we avoid?
  - Testosterone: acne, continued menses
  - Estradiol: sexual function +/-
- Physiologic *levels*
  - Testosterone 300-1000
  - Estradiol 100-350

subcutaneous

TABLE 2
Hormone Dosing for Transgender Patients

Male to female	
Hormone	**Initial dose/maximum dose***
Anti-androgen	
Spironolactone	100 mg/d; 200 mg/d
Finasteride (5-ARI)	1 mg/d; 5 mg/d
Estrogen	
Sublingual (estradiol)	1 mg/d; 6 mg/d
Transdermal (estradiol)	100 µg/d; 400 µg/d
IM (estradiol valerate)	2 mg weekly; 10 mg weekly
Female to male	
Testosterone	
IM (enanthate or cypionate)	100 mg q 2 wk; 200 mg q 2 wk
Transdermal gel (1%)	2.5 g/d; 10 g/d
Transdermal patch	2.5 mg/d; 7.5 mg/d

Abbreviations: 5-ARI, 5-alpha reductase inhibitor; IM, intramuscular.
*Hormone therapy should be titrated to achieve desired effects and blood levels.
Sources: Coleman et al. *Int J Transgender.* 2011[10]; Hembree et al. *J Clin Endocrinol Metab.* 2009[11]; University of California, San Francisco.[12]

Too low not good	Too high not good
Mood, energy, bmd, menses, other	Aromatize to estrogens
Mood, energy, sex function, bmd, other	VTE risk

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Initiating Puberty

Without Blockers	With Blockers

▪ Tanner 4-5
▪ Age appropriate
▪ Height considered
▪ If ready for GAH vs gender exploration
▪ If articulate present understanding of fertility & parenting goals
▪ If parent/s ready
▪ Estradiol 6 mg + sublingual
▪ Testosterone 60 mg + subcutaneous
	▪ Continue GnRh analogues to suppress gonads
	▪ Slow taper upward of puberty hormones to "mimic" endogenous puberty
	  ▪ Increase every 3-6 months
	▪ Estradiol
	  ▪ 0.5mg, 1mg, 1.5mg, 2mg….
	  ▪ Adult dosing 4-6 mg+
	▪ Testosterone
	  ▪ 10mg, 20mg, 40mg….
	  ▪ Adult dosing 60 mg +

Considerations: Non-binary, Agender

- What are issues for having no gender hormones?
  - Temporarily
  - Long term (age 18, over?)
  - Weight seriousness, magnitude

Benefit	Risks, known vs potential	
Alleviate anxiety	Fertility	
Alleviate dysphoria	BMD *	
Give youth more time	50 yro AMAB w bmd lowest 2.5% over 5-10 yrs risk of fractures 02.-0.3% hip 1-2% other	Compared to control NL BMD Same 5-10 yrs risk 0% hip 0.7-1%

* Based on adults gone through puberty (Pang KC 2020, Garvan 2019)

Fertility

- Some References:
  - AmSoc Reprod Med, resolve.org
  - Iris G. Insogna, Elizabeth Ginsburg, Serene Srouji. (2020) Fertility Preservation for Adolescent Transgender Male Patients: A Case Series. Journal of Adolescent Health.
  - Commentary N Engl J Med 2019; 380:886-887
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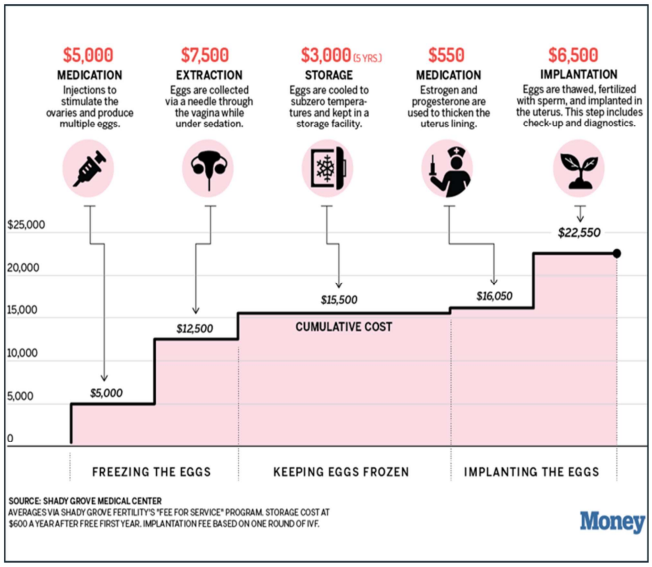
  - Noyes 2009, Chian 2009 Reprod Biomed



GAH & Fertility

- Puberty blockers
  - Tanner 2 gametes never exposed to T or E
  - Post GAH estradiol or testosterone gametes may never develop gonadal reproductive function
  - Tanner 3-4-5
    - Stop blockers = return to pre-existing fertility potentials
  - Fertility potential unpredictable
- Estrogen
  - Decrease testicular volume
  - Poor semen quality
  - Azoospermia with possible reversal
- Testosterone
  - Reversible amenorrhea without follicle depletion – pregnancies on or after T

De Roo et al. 2016, Wallace et al 2014

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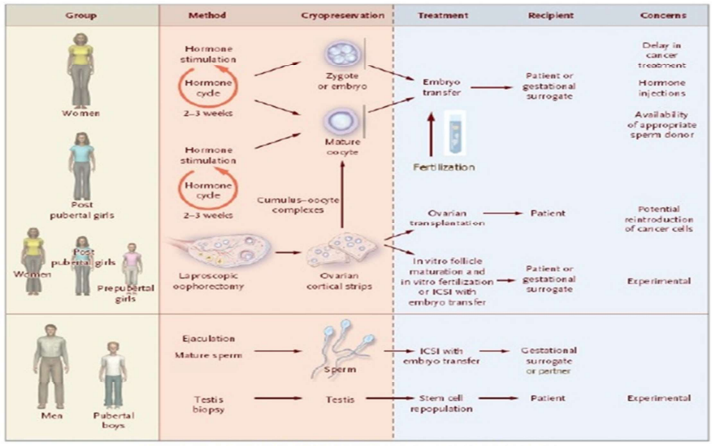
De Roo et al. 2016, Wallace et al 2014

GAH & Fertility



Jeruss and Woodruff (2009) New England Journal of Medicine.

What Technique is Appropriate ?

De Roo et al. 2016, Wallace et al 2014

Fertility Preservation: Issues

- With Ovaries
  - Physical Barriers - vaginal examination & invasive procedures
  - Pre-pubertal ovarian and testicular cryopreservation more investigational
  - Immature ovaries loss, abnormal follicles and gain improved follicle competence with puberty
    - Presence of primordial follicles not guarantee cryopreserved ovarian tissue with sufficient ovarian potential for future function.
    - Human pre-pubertal ovaries contain high proportion abnormal non-growing follicles with reduced ability to grow in vitro
- With Testes
  - Physical Barriers - masturbation, semen production & storage; testicular sperm extraction/aspiration
  - Pre-pubertal testes stored as whole tissue or suspension
    - Cryopreserved as fragments maximize chances successful preservation spermatogonial stem cells; retain all potential clinical options for generating gametes3
    - Loss proportion spermatogonia is inevitable result of the freeze-thaw process2
    - Survival of spermatogonia has been described in cryopreserved prepubertal human testis (reviewed in Onofre 2016, Zarandi 2018)

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1de Roo, 2Onofre 2016, 3Zarani 2018

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spermatogonial stem cells (SSCs)
1de Roo et al., Inter Rev Psych2016; vol 28, no. 1, 112-119

Oktay al., JPAG. 2016 October ; 29(5): 409–416
Pre-pubertal girls
With sufficient ovarian reserve (AMH > 2 ng/ml)
serial serum AMH to delay intervention to post-puberty
ovarian tissue cryopreservation if AMH falls to < 2 ng/ml • oocyte cryopreservation post-pubertal age

With insufficient reserve (AMH ≤ 2 ng/ml)
ovarian tissue cryopreservation

2 Anderson et al. Hum Reprod. 2014 Jan;29(1):97-106.

All age pt ovarian cryo
10/24 underwent removal of cortical strips vs oophorectomy • Primordial and/or early-activated primary follicles in all samples • Small pre-antral follicles identified in patients

who had not received oncologic treatments Duncan et al. J Adolesc Young Adult Oncol. 2015 Dec 1; 4(4): 174–183

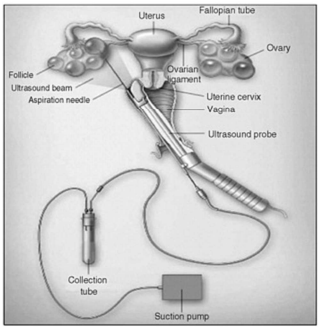
Overview Fertility Preservation

- Initial evaluation
  - Hysterosalpingogram, rubella varicella, STI, fragile x, CS FNA
  - d3 LMP- US, FSH, E2
  - Assess ovarian reserve
    - Antral follicle counts (>8)
    - Anti-müllerian hormone (AMH) >1 measures how many oocytes not marker of function
- IVF retrieval
  - D5, 8,9,10 E2 US
  - Trigger in pm, retrieval 72 hours
- GnRH antagonist protocol
  - 3-4 weeks/cycle for 3-4 cycles
  - D1 FSH
  - D6-7
    - FHS LH
    - Menotropin injections x 3 75IU FSH & LH each promotes multiple follicles & release of eggs
  - D10 hcg trigger
- Other protocols
  - Clomid 50 mg d3-7
  - Retrozole
  - Tamoxifen

Oocyte Harvest

- COC before treatment cycle or track ovulation
- After ovulation GnRH agonist or antagonist
- D1 =LMP1 baseline blood work estradiol TV ultrasound (?cysts)
- Ovarian stimulation w SQ injections gonadotropin
  - Q1-3 days E2 TVUS until E2 & follicle ready (>12mm)
  - Hcg trigger injection, the LH hcg 24 hrs before
  - Harvest 34-36 hrs post before ovulation

Age years	Likelihood Live Birth by egg (%)	For 75% Success
<30	7.4	Minimum 15-20 eggs
30-34	7.0	
35-37	6.5	
38-40	5.2	Minimum 25-30 eggs
41-42	6.8 small N	?



$15,000-18,000 per cycle

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Normally, your pituitary gland produces FSH and LH at the beginning of your menstrual cycle. The FSH is sent out into the body. LH is stored in the pituitary gland until just before ovulation.
FSH tells the follicles in your ovaries to wake up and grow.
FSH stands for "follicle stimulating hormone." Makes perfect sense, given it *stimulates* the *follicles*!
Gonadotropin fertility drugs, that are FSH or FSH along with LH, act similarly.
They tell the follicles on your ovaries to grow and develop.
LH typically peaks just before ovulation during a natural cycle and helps any mature eggs to go through one last growth spurt and release-ovulate
During treatment with gonadotropins, you may be given either an injection of rLH or, more commonly, hCG- acts like the natural LH spike and will trigger ovulation.

There are two basic types of gonadotropins: recombinant gonadotropins and urinary-extracted gonadotropins.[1]
Recombinant gonadotropins are created in a laboratory using recombinant DNA technology.
Recombinant FSH gonadotropins on the market include Gonal-F and Follistim.

Currently, Luveris is the only recombinant LH gonadotropin available.
Urinary-extracted gonadotropins are extracted and purified from the urine of postmenopausal women. (Their urine is naturally high in FSH.) They include human menopausal gonadotropins (hMG), purified FSH and highly purified FSH.
Purified urine-extracted FSH gonadotropins include Bravelle and Fertinex.
Human menopausal gonadotropins (hMG) contains FSH and LH. It includes medications like Humegon, Menogon, Pergonal and Repronex.
Menopur is a highly purified hMG.
A related drug, human chorionic gonadotropin (hCG) is often part of fertility treatment with gonadotropin injections.
You may know hCG as the pregnancy hormone, but it also happens to be molecularly similar to LH.
In a natural cycle, LH triggers ovulation.
As part of fertility treatment, an injection of hCG may be used to trigger ovulation.
Ovidrel, Novarel, Pregnyl and Profasi are brand names for hCG injectables.

From PLoS One. 2013; 8(2): e56189 2013 Feb
15. doi: 10.1371/journal.pone.0056189
PMCID: PMC3574022 Does the Number of Oocytes Retrieved Influence Pregnancy after Fresh Embryo Transfer?
Qianfang Cai, [1] Fei Wan, [2] Kai Huang, [3] and Hanwang Zhang [3,*]

relationship between the number of oocytes and pregnancy rates was hyperbolically distributed, based on the argument that ovarian stimulation and excessive response may have detrimental effects on oocyte and embryo quality, and that endometrial receptivity or supraphysiological estradiol levels could have deleterious effects on embryo implantation. These researchers then proposed the optimal number of oocytes for achieving the best pregnancy rates in IVF [6], [7]. Van der Gasst et al. found that the highest pregnancy rate was achieved with 13 oocytes, below and above which the outcomes were compromised [7]. Similarly, Sunkara et al. reported approximately 15 oocytes were required to maximize the live birth rate [6].
Ref
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7. Van der Gaast MH, Eijkemans MJ, van der Net JB, de Boer EJ, Burger CW, et al. (2006) Optimum number of oocytes for a successful first IVF treatment cycle. Reprod Biomed Online 13: 476–480. [PubMed] [Google Scholar]
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Bodri D, Colodrón M, García D, Obradors A, Vernaeve V, Coll O. Transvaginal versus transabdominal ultrasound guidance for embryo transfer in donor oocyte recipients: a randomized clinical trial. *Fertility and Sterility*. 2011;95(7). doi:10.1016/j.fertnstert.2011.03.028
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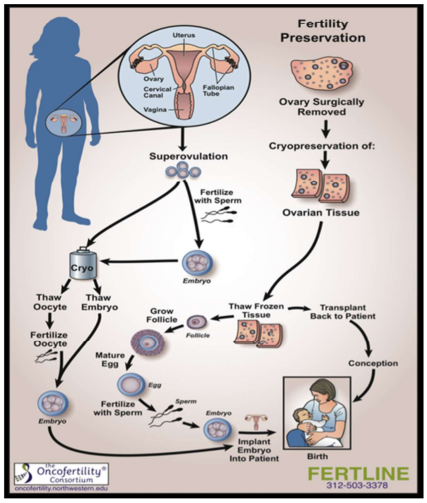
Lacamara C, Ortega C, Villa S, Pommer R, Schwarze JE. Are children born from singleton pregnancies conceived by ICSI at increased risk for congenital malformations when compared to children conceived naturally? A systematic review and meta-analysis. *JBRA Assist Reprod*. 2017;21(3):251–259. Published 2017 Sep 1. doi:10.5935/1518-0557.20170047

Fertility Preservation with Ovarian Tissues



- Jensen 2015 Denmark in 41 women
  - 53 transplantations to over 10 years
  - 32 women with a pregnancy-wish
    - 24 clinical pregnancies
    - 10 (31%) had a child/children
    - Transplanted ovarian tissue may last 10 years
- Meirow D 2016 in 20 patients
  - Ages 14-39 years at cryopreservation
  - 5.6 year time after cryopreservation
  - Mean age transplantation 34 years
  - 16 patients primary ovarian failure
  - 4 patients w ovarian function but infertile
    - 2 with lab work/ovarian insufficiency, 2/45y+
  - 93% endocrine recovery rate
  - 53% conception rate
  - 32% delivery rate

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Jensen et al. Hum. Reprod. 2015;0(0):1-8 • O

To Affirm or Not Affirm, There is No Question

Reconfirmed over time….

OlsonKR 2016, deVries AL 2014, Steensma TD 2013, deVries AL 2012, Spack NP 2012, deVries AL 2011, Steensma TD 2011, Steensma TD 2013, Malpas J 2011, Teurk CM 2012, Bussey K 2011, DeVries 2010, Wallien MS 2008, Drummon 2008, Zucker 2005, Green 1987, Davenport 1986

- Olsen 2016,17
  - TGDY supported early social affirmation depression = peers, lower anxiety rates
- Russell 2018
  - Benefit using asserted name, pronoun
- Turban 2020
  - Long term protective benefits want & have access to blockers for suicidal ideation

Social Gender Affirmation
- Preferred Name
- Preferred Pronoun

Psychological Gender Affirmation
- Felt Gender is Respected and Validated
- Resist Internalized Stigma and Transphobia

Medical Gender Affirmation
- Pubertal Blockers
- Hormone Therapy
- Gender Confirmation Surgery

Legal Gender Affirmation
- Legal Name Change
- Legal Gender Marker Change

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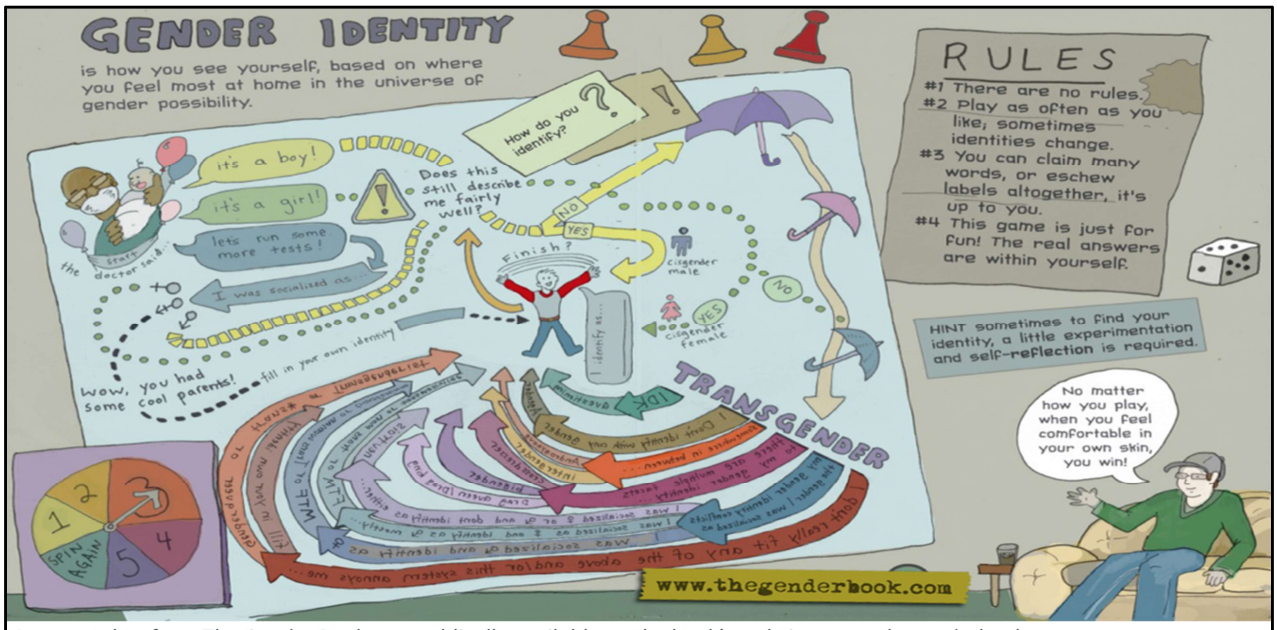

Images taken from The Gender Book, are publically available on the book's website, www.thegenderbook.com

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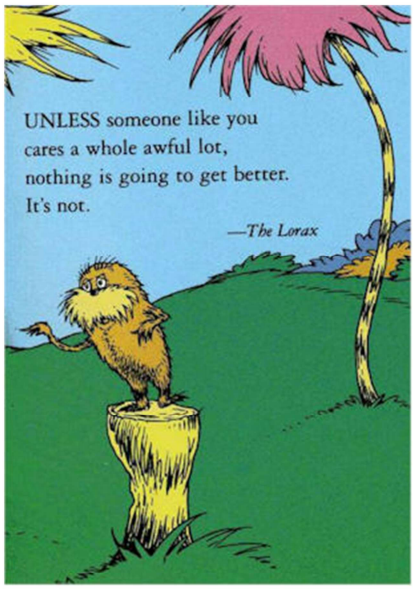
JASON


UNLESS someone like you
cares a whole awful lot,
nothing is going to get better.
It's not.
—The Lorax

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ECHO Training Model