Hormonal Therapy of the Transgender

ALEJANDRO MARTINÓ, MD
ENDOCRINOLOGY

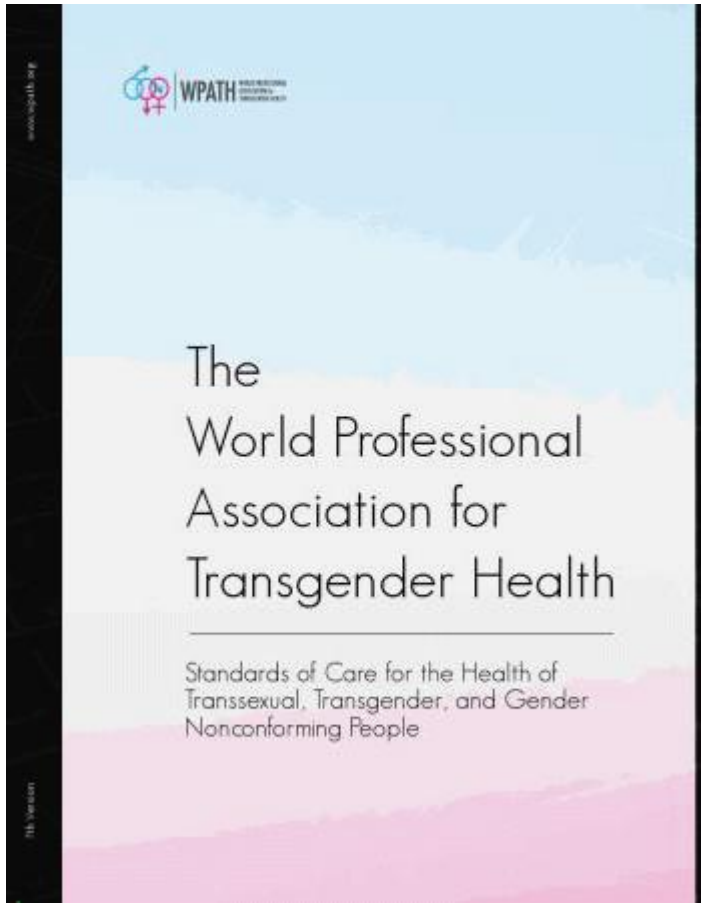
DISCLOSURES

- None

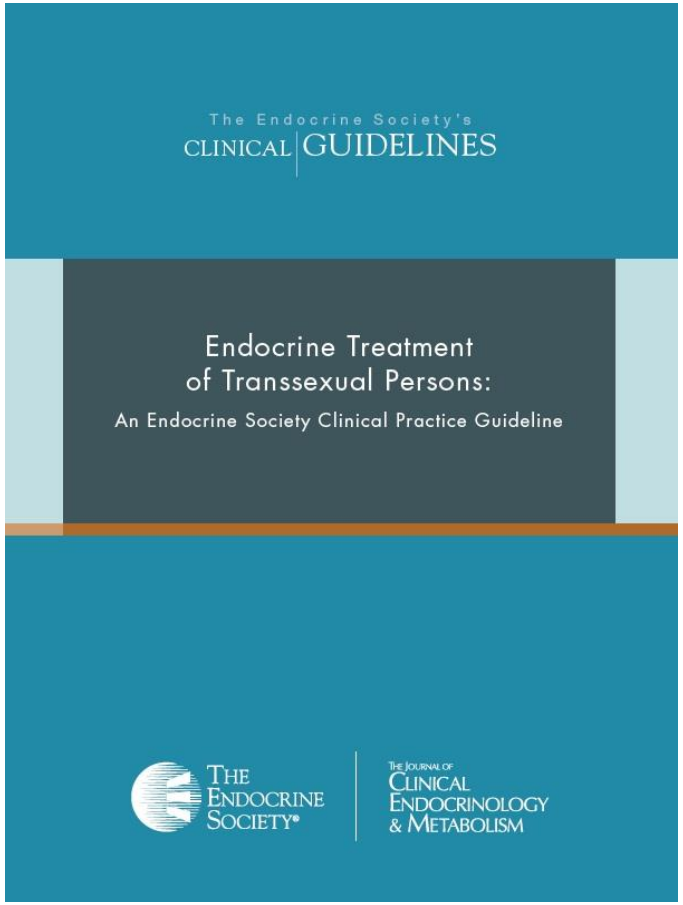
OBJECTIVES

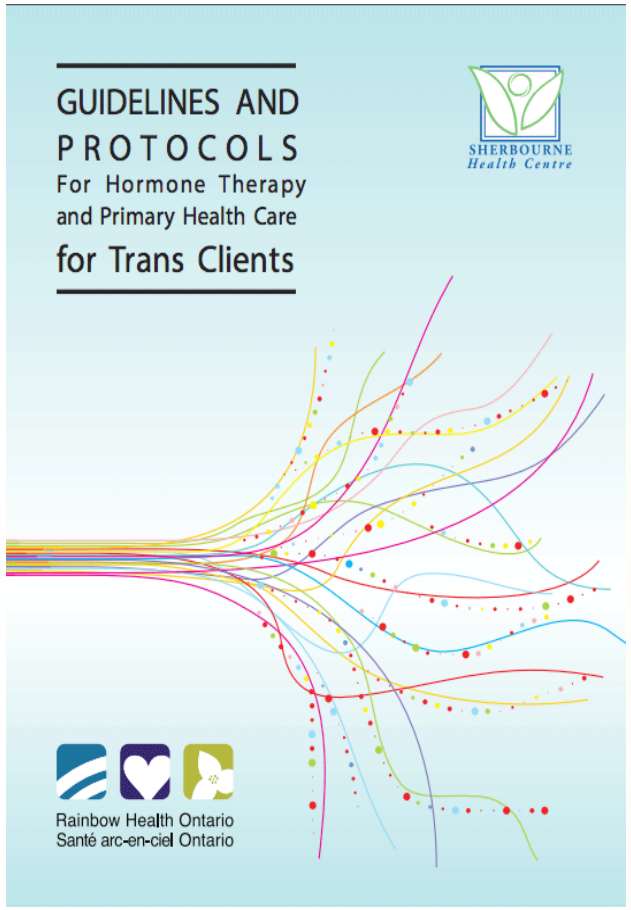
- Discuss the rationale of hormonal therapy in the transgender
- Discuss the hormonal regimen for Female-to-Male (FTM) transgender
- Discuss the hormonal regimen for Male-to-Female (MTF) transgender
- Discuss the hormonal regimen in the pediatric transgender
- General discussion of Gender Affirmation Surgery (GAS)/Sex Reassignment Surgery

REFERENCES



(Harry Benjamin International Gender Dysphoria Association)

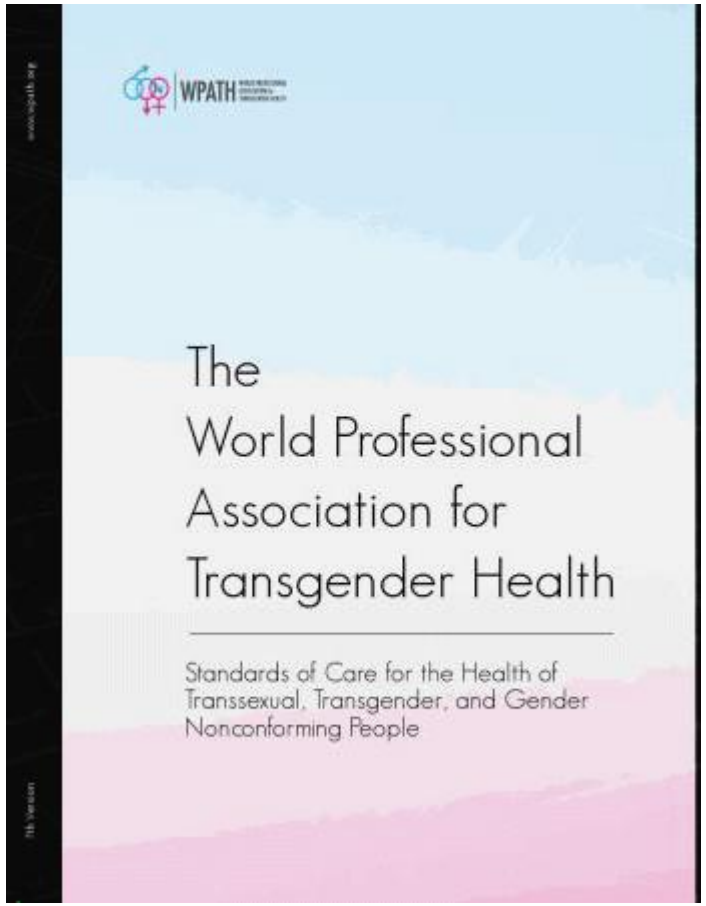




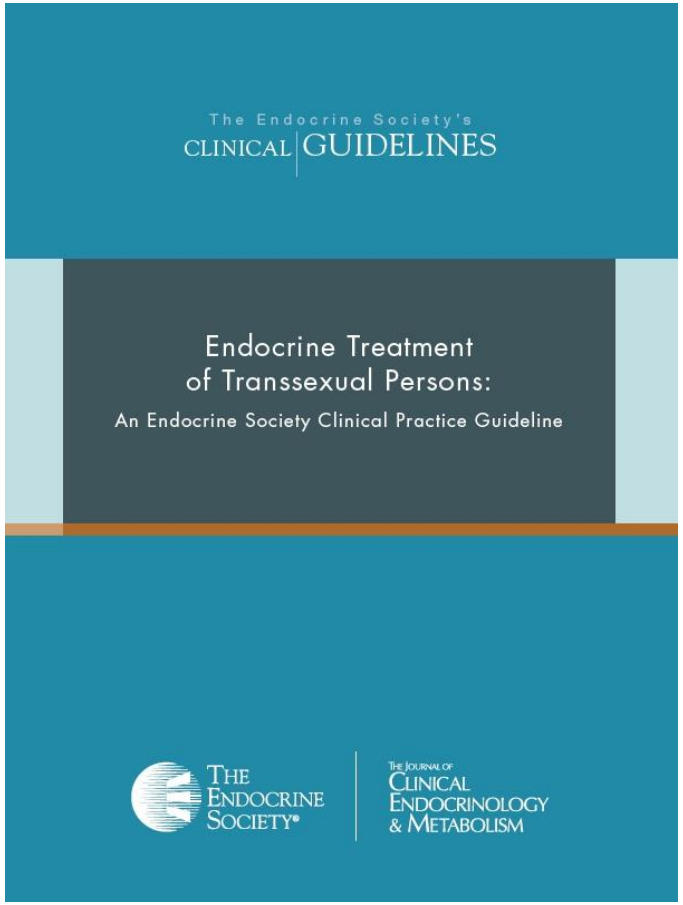
Dr. Harry Benjamin

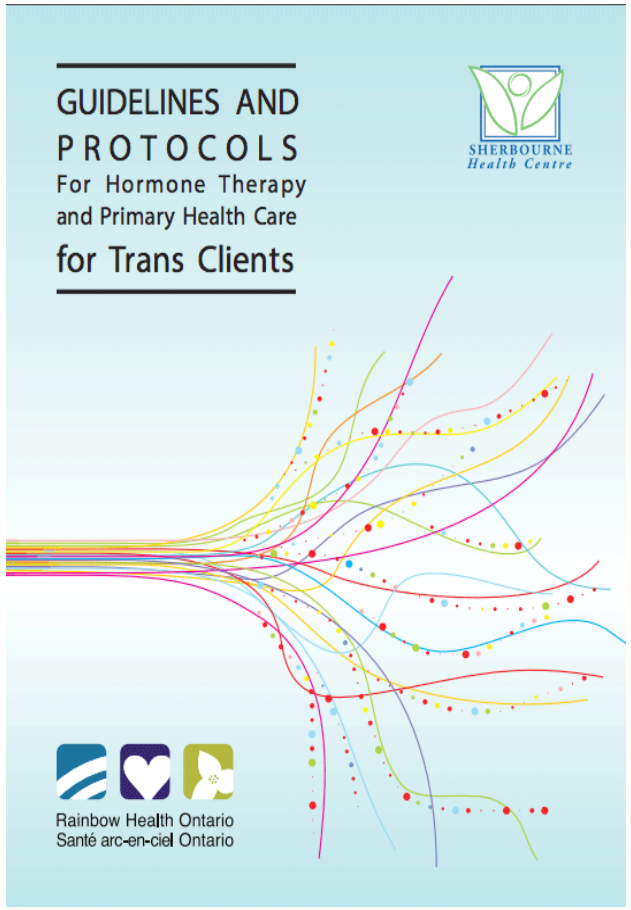
(January 12, 1885 – August 24, 1986)

REFERENCES



(Harry Benjamin International Gender Dysphoria Association)





RATIONAL OF HORMONE THERAPY IN TRANSGENDERS

- Medically necessary intervention for many transgender and gender nonconforming individuals with GENDER DYSPHORIA
- Hormone therapy can **provide significant comfort** to patients who do not wish to make a social gender role transition or undergo surgery, or who are unable to do so
- Some people seek **maximum feminization/masculinization**
- Others experience relief with an androgynous presentation resulting from **hormonal minimization of existing secondary sex characteristics**

Hormone Therapy of the Transgender

Eligibility and Readiness Criteria for Hormone Therapy

TABLE 4. Hormone therapy for adults

Adults are **eligible** for cross-sex hormone treatment if they (28):

1. Fulfill DSM IV-TR or ICD-10 criteria for GID or transsexualism (see Tables 2 and 3).
2. Do not suffer from psychiatric comorbidity that interferes with the diagnostic work-up or treatment.
3. Demonstrate knowledge and understanding of the expected outcomes of hormone treatment, as well as the medical and social risks and benefits; AND
4. Have experienced a documented RLE of at least 3-month duration OR had a period of psychotherapy (duration specified by the MHP after the initial evaluation, usually a minimum of 3 months).

Adults should fulfill the following **readiness criteria** before the cross-sex hormone treatment. The applicant:

1. Has had further consolidation of gender identity during a RLE or psychotherapy.
2. Has made some progress in mastering other identified problems leading to improvement or continuing stable mental health.
3. Is likely to take hormones in a responsible manner.

TABLE 5. Hormone therapy for adolescents

Adolescents are **eligible** and ready for GnRH treatment if they:

1. Fulfill DSM IV-TR or ICD-10 criteria for GID or transsexualism.
2. Have experienced puberty to at least Tanner stage 2.
3. Have (early) pubertal changes that have resulted in an increase of their gender dysphoria.
4. Do not suffer from psychiatric comorbidity that interferes with the diagnostic work-up or treatment.
5. Have adequate psychological and social support during treatment, AND
6. Demonstrate knowledge and understanding of the expected outcomes of GnRH analog treatment, cross-sex hormone treatment, and sex reassignment surgery, as well as the medical and the social risks and benefits of sex reassignment.

Adolescents are **eligible** for cross-sex hormone treatment if they:

1. Fulfill the criteria for GnRH treatment, AND
2. Are 16 yr or older.

Readiness criteria for adolescents eligible for cross-sex hormone treatment are the same as those for adults.

J Clin Endocrinol Metab, September 2009, 94(9):3132–3154

Hormonal Regimen for Female-to-Male Transgender

Female-to-Male Hormonal Therapy

- Similar to TESTOSTERONE REPLACEMENT THERAPY in a *cis*-man(non-transsexual man)

Table 4. Testosterone Replacement Products

Formulation	Products Available	Dosing Ranges	Advantages	Disadvantages
Testosterone enanthate or cypionate	Delatestryl or Depo-Testosterone	100 mg/wk IM or 200 mg every 2 wk IM	Improves symptoms, inexpensive, longer intervals between dosing	Requires injection; fluctuations in serum testosterone levels
Topical gels	Testim and AndroGel	5-10 g (50-100 mg testosterone) applied daily	Corrects symptoms, flexible dosing, ease of application, good tolerability	Potential for secondary exposure
Transdermal patches[a]	Androderm	1-2 patches (5-10 mg) every 24 h	Ease of application, corrects symptoms, mimics diurnal rhythm, less erythrocytosis	Lower serum testosterone levels achieved, skin irritation likely
Buccal tablets	Striant	30-mg controlled-release tabs applied twice daily	Corrects symptoms	Gum and mouth irritation
Implantable pellets	Testopel	4-6 75-mg pellets implanted every 3-6 mo	Corrects symptoms, long duration of activity	Requires surgical implantation; pellet extrusions, infection

[a] *Patches available in 2.5 and 5 mg.*
Source: References 2, 7, 12.

Female-to-Male Hormonal Therapy

- Similar to TESTOSTERONE REPLACEMENT THERAPY in a cis-man
  - **Intramuscular** preparations induces **masculinizing changes faster**

TABLE 13. Masculinizing effects in FTM transsexual persons

Effect	Onset (months)[a]	Maximum (yr)[a]
Skin oiliness/acne	1–6	1–2
Facial/body hair growth	6–12	4–5
Scalp hair loss	6–12	[b]
Increased muscle mass/strength	6–12	2–5
Fat redistribution	1–6	2–5
Cessation of menses	2–6	[c]
Clitoral enlargement	3–6	1–2
Vaginal atrophy	3–6	1–2
Deepening of voice	6–12	1–2

[a] Estimates represent clinical observations. See Refs. 81, 92, and 93.

[b] Prevention and treatment as recommended for biological men.

[c] Menorrhagia requires diagnosis and treatment by a gynecologist.

J Clin Endocrinol Metab, September 2009, 94(9):3132–3154

TABLE 2: RISKS ASSOCIATED WITH HORMONE THERAPY. BOLDED ITEMS ARE CLINICALLY SIGNIFICANT

Risk Level	Feminizing hormones	Masculinizing hormones
Likely increased risk	Venous thromboembolic disease[A] Gallstones Elevated liver enzymes Weight gain **Hypertriglyceridemia**	**Polycythemia** Weight gain Acne Androgenic alopecia (balding) Sleep apnea
Likely increased risk with presence of additional risk factors[B]	Cardiovascular disease	
Possible increased risk	**Hypertension** Hyperprolactinemia or prolactinom[A]	Elevated liver enzymes **Hyperlipidemia**
Possible increased risk with presence of additional risk factors[B]	**Type 2 diabetes**[A]	**Destabilization of certain psychiatric disorders**[C] **Cardiovascular disease** **Hypertension** **Type 2 diabetes**
No increased risk or inconclusive	**Breast cancer**	Loss of bone density **Breast cancer** **Cervical cancer** **Ovarian cancer** **Uterine cancer**

[A] Risk is greater with oral estrogen administration than with transdermal estrogen administration.
[B] Additional risk factors include age.
[C] Includes bipolar, schizoaffective, and other disorders that may include manic or psychotic symptoms. This adverse event appears to be associated with higher doses or supraphysiologic blood levels of testosterone.

Female-to-Male Hormonal Therapy

- Monitoring
  - Every 2-3 months in the 1st year, then 1-2 times per year
    - Serum testosterone (initially the Total Testosterone can be high→SHBG)
    - CBC
    - LFT

Hormonal Regimen for Male-to-Female Transgender

Male-to-Female Hormonal Therapy

- Is more complex than the Female-to-Male regimen
- A **combination of estrogen and "anti-androgens"** is the most commonly studied regimen for feminization
- "Anti-androgens" **minimize the dosage of estrogen needed** to suppress testosterone
  - Thereby **reducing the risks associated with high-dose exogenous estrogen**

Anti-androgen Therapy

Spironolactone/aldactone	100-300mg/day
Finasteride/Proscar	1-5mg/day
Dutasteride/Avodart	0.5mg/day
Cyproterone acetate/Androcur (not in U.S.)	50-100mg/day
Depo-provera	150mg IM q2-3 mos
Prometrium or Provera	100-200mg/day, 5-30mg/day
GnRH analogs	

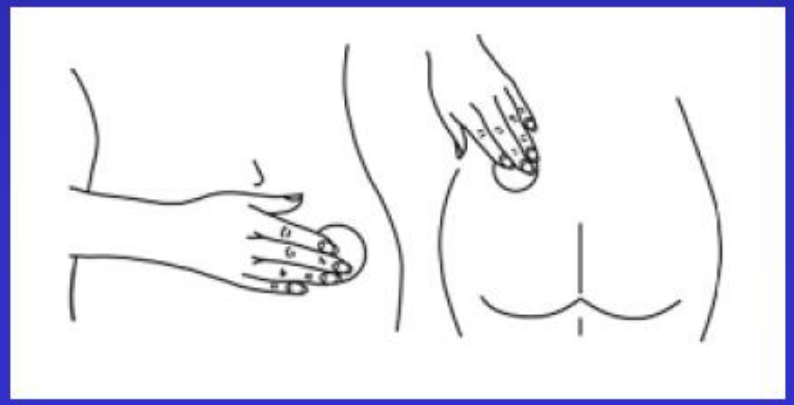
GnRH Agonists

- Histrelin Acetate SC Implant
  - Supprelin LA 50 mg SC
  - Duration: 1-2 years

- Leuprolide Acetate IM Injections
  - 1-month
  - 3-month
  - 6-month

Estrogen: 17 β estradiol

Transdermal



Oral or sublingual

Also: Parenteral estradiol (valerate or cypionate)

	Dosage
MTF transsexual persons[a]	
Estrogen	
Oral: estradiol	2.0–6.0 mg/d
Transdermal: estradiol patch	0.1–0.4 mg twice weekly
Parenteral: estradiol valerate or cypionate	5–20 mg im every 2 wk 2–10 mg im every week

TABLE 14. Feminizing effects in MTF transsexual persons

Effect	Onset[a]	Maximum[a]
Redistribution of body fat	3–6 months	2–3 yr
Decrease in muscle mass and strength	3–6 months	1–2 yr
Softening of skin/decreased oiliness	3–6 months	Unknown
Decreased libido	1–3 months	3–6 months
Decreased spontaneous erections	1–3 months	3–6 months
Male sexual dysfunction	Variable	Variable
Breast growth	3–6 months	2–3 yr
Decreased testicular volume	3–6 months	2–3 yr
Decreased sperm production	Unknown	>3 yr
Decreased terminal hair growth	6–12 months	>3 yr[b]
Scalp hair	No regrowth	[c]
Voice changes	None	[d]

[a] Estimates represent clinical observations. See Refs. 81, 92, and 93.

[b] Complete removal of male sexual hair requires electrolysis, or laser treatment, or both.

[c] Familial scalp hair loss may occur if estrogens are stopped.

[d] Treatment by speech pathologists for voice training is most effective.

J Clin Endocrinol Metab, September 2009, 94(9):3132–3154

TABLE 2: RISKS ASSOCIATED WITH HORMONE THERAPY. BOLDED ITEMS ARE CLINICALLY SIGNIFICANT

Risk Level	Feminizing hormones	Masculinizing hormones
Likely increased risk	Venous thromboembolic disease[A] Gallstones Elevated liver enzymes Weight gain Hypertriglyceridemia	Polycythemia Weight gain Acne Androgenic alopecia (balding) Sleep apnea
Likely increased risk with presence of additional risk factors[B]	Cardiovascular disease	
Possible increased risk	Hypertension Hyperprolactinemia or prolactinom[A]	Elevated liver enzymes Hyperlipidemia
Possible increased risk with presence of additional risk factors[B]	Type 2 diabetes[A]	Destabilization of certain psychiatric disorders[C] Cardiovascular disease Hypertension Type 2 diabetes
No increased risk or inconclusive	Breast cancer	Loss of bone density Breast cancer Cervical cancer Ovarian cancer Uterine cancer

[A] Risk is greater with oral estrogen administration than with transdermal estrogen administration.
[B] Additional risk factors include age.
[C] Includes bipolar, schizoaffective, and other disorders that may include manic or psychotic symptoms. This adverse event appears to be associated with higher doses or supraphysiologic blood levels of testosterone.

Male-to-Female Hormonal Therapy

- Monitoring
  - Measure **serum testosterone and estradiol** every 3 months
    - Serum testosterone levels: < 55 ng/dL
    - Serum estradiol levels: < 200 pg/mL
  - For individuals on **spironolactone**
    - Serum potassium every 3 months, during the 1st year

Hormonal Regimen in the Pediatric Transgender

Gender Identity Disorder in Pediatric Population

- The **large majority (75–80%) of prepubertal children** with a diagnosis of gender identity disorder (GID) in childhood **do not turn out to be transsexual in adolescence**

- Clinical experience suggests that GID can be reliably **assessed only after the first signs of puberty**

Pediatric Transgender Hormonal Regimen

- **Suppress** pubertal hormones **not earlier than Tanner 2**
  - **GnRH analogs**

GnRH Agonists

- Histrelin Acetate SC Implant
  - Supprelin LA 50 mg SC
  - Duration: 1-2 years

- Leuprolide Acetate IM Injections
  - 1-month
  - 3-month
  - 6-month

Pediatric Transgender Hormonal Regimen

- **Suppress** pubertal hormones **not earlier than Tanner 2**
  - **GnRH analogs**

- **Pubertal development** of the desired, opposite sex **be initiated** at the **age of 16 y/o**, using a gradually increasing dose schedule of cross-sex steroids.

Pediatric Transgender Hormonal Regimen

TABLE 9. Protocol induction of puberty

Induction of female puberty with oral 17-β estradiol, increasing the dose every 6 months:
- 5 μg/kg/d
- 10 μg/kg/d
- 15 μg/kg/d
- 20 μg/kg/d
- Adult dose = 2 mg/d

Induction of male puberty with intramuscular testosterone esters, increasing the dose every 6 months:
- 25 mg/m^2 per 2 wk im
- 50 mg/m^2 per 2 wk im
- 75 mg/m^2 per 2 wk im
- 100 mg/m^2 per 2 wk im

J Clin Endocrinol Metab, September 2009, 94(9):3132–3154

Pediatric Transgender Hormonal Regimen

- **Suppress** pubertal hormones **not earlier than Tanner 2**
  - **GnRH analogs**

- **Pubertal development** of the desired, opposite sex **be initiated** at the **age of 16 y/o**, using a gradually increasing dose schedule of cross-sex steroids.

- **Defer** gender affirming **surgery** until the individual is **at least 18 y/o.**

Potential Adverse Effects

- Bone mass
- Growth
- Fertility

Gender Affirmation Surgery/ Sex Reassignment Surgery

Gender Affirmation Surgery/ Sex Reassignment Surgery

- **Many transgender** find **comfort** with their gender identity, role, and expression **without surgery.**

- **For many others**, **surgery** is **essential and medically necessary** to alleviate their **gender dysphoria**

Gender Affirmation Surgery/ Sex Reassignment Surgery

- Overview of Surgical Procedures
  - **Breast/Chest surgery**
  - **Genital surgery**
  - **Non-genital, non-breast surgical interventions**

Thank You