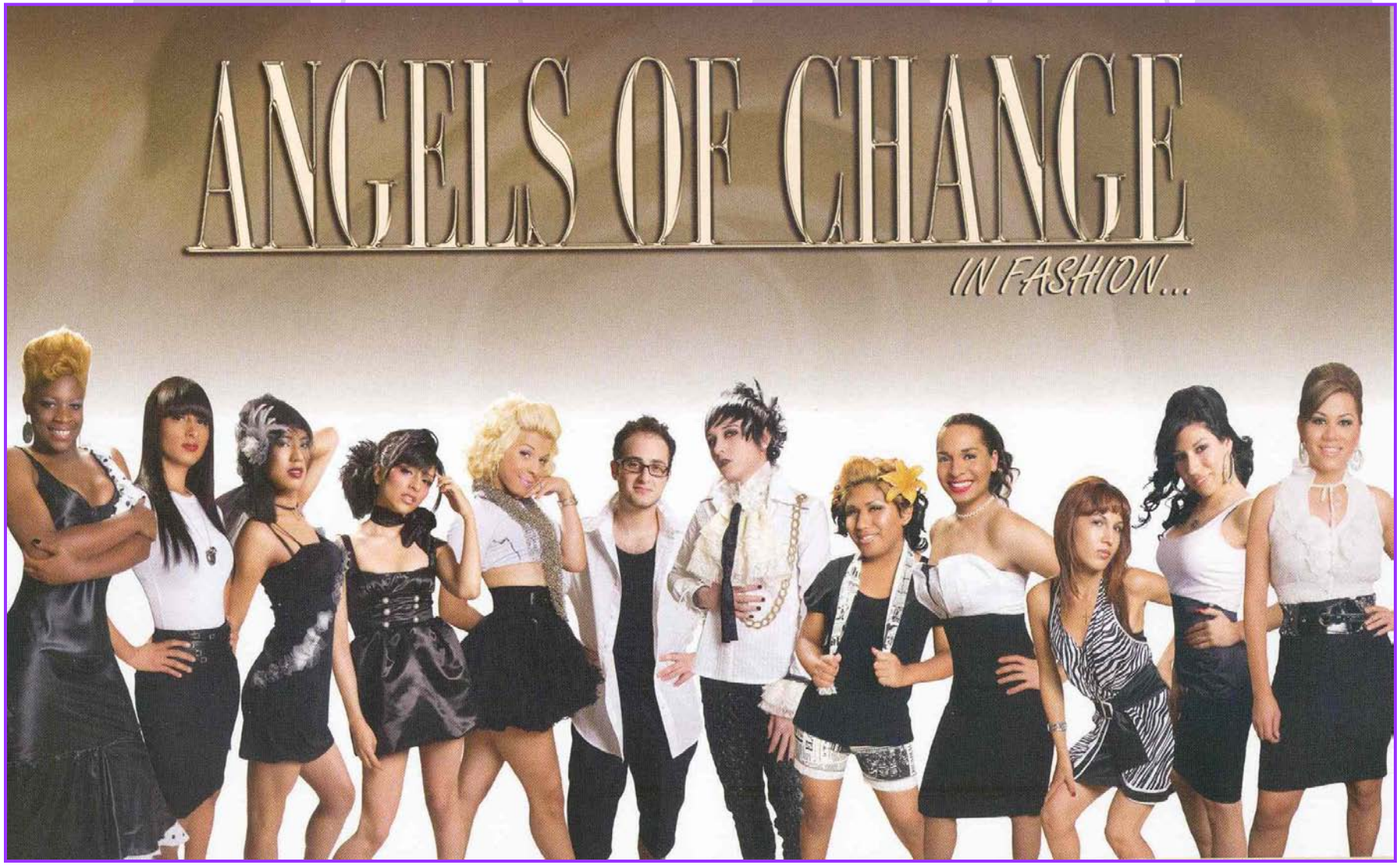
Endocrine Therapy for Transgender Youth

Daniel L. Metzger, MD



www.transyouthla.com

Normal puberty

- girls
  - breast development starts at 10 (8–12)
  - growth spurt peak at 11½ (9½–12½)
  - first period at 12½ (10½–14½)
- boys
  - testicular enlargement starts at 11 (9–13)
  - growth spurt peak at 13½ (11½–15½)
- considerable variability

The overarching treatment goal

"*The general goal of psychotherapeutic, endocrine, or surgical therapy for persons with gender identity disorders is lasting personal comfort with the gendered self in order to maximize overall psychological well-being and self-fulfillment*."

WPATH Standards of Care, 6th version

Why treat kids under age 18?

- studies show less post-operative function is related to the “ability to pass”
- physical outcomes much better if patient treated before breast development, beard growth, deepening of the voice
- prevent developmental problems related to ↑ discrepancy between body and mind
- patients are suffering!

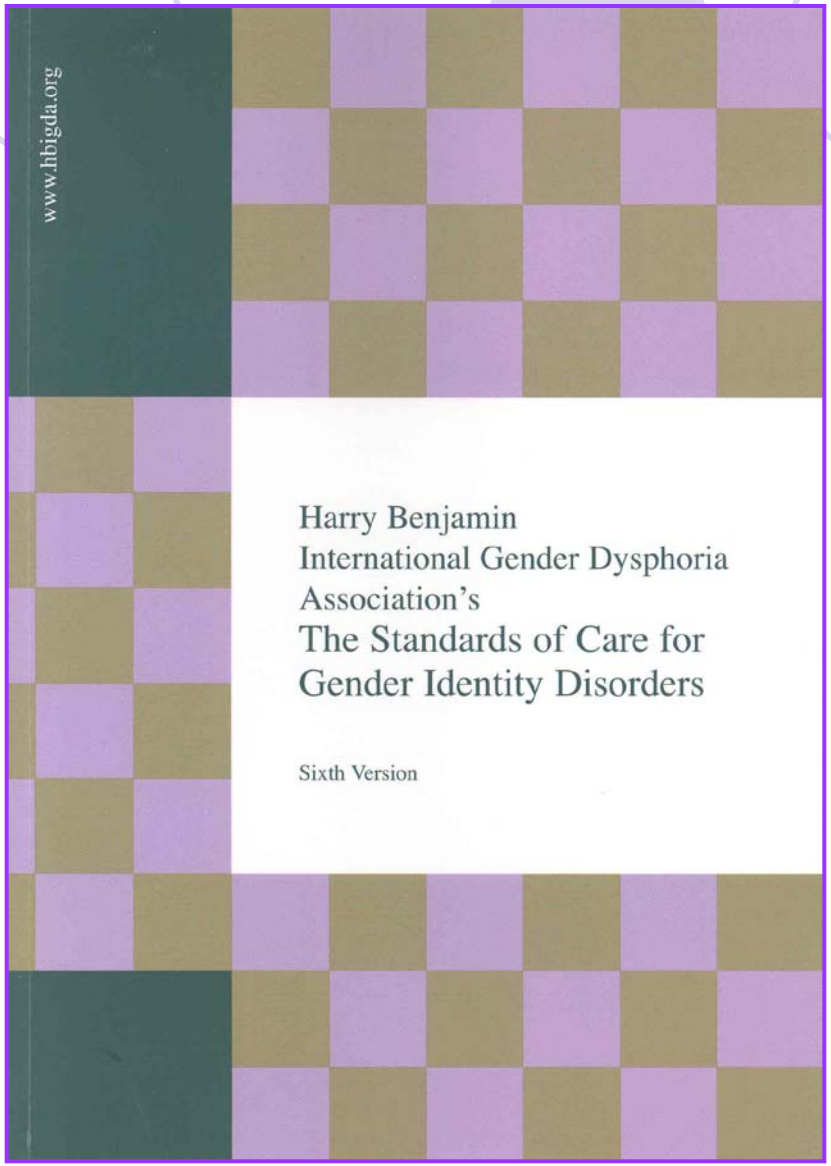
How are kids different?

- still growing
- still accruing bone-mineral content
- still going through the physical changes of puberty
- still going through the psychological and developmental changes of puberty
- their GID may not be as “solidified”
- they have to deal with the school system

Our approach to treating youth

- different from treating adults
- more of an attempt to mirror natural puberty
- therefore, end results appear more gradually

- use available guidelines and published experience (Netherlands!)



WPATH Standards of Care, 6th version

Caring for Transgender Adolescents in BC: Suggested Guidelines

Clinical Management of Gender Dysphoria in Adolescents

Annelou L.C. de Vries, M.D., Ph.D.[*]
Peggy T. Cohen-Kettenis, Ph.D.[†]
Henriette Delemarre-Van de Waal, M.D., Ph.D.[‡]

Ethical, Legal, and Psychosocial Issues in Care of Transgender Adolescents

Catherine White Holman[§]
Joshua Goldberg[**]

January 2006

a collaboration between Transcend Transgender Support & Education Society and Vancouver Coastal Health's Transgender Health Program, with funding from the Canadian Rainbow Health Coalition's Rainbow Health – Improving Access to Care *initiative*

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Endocrine Therapy for Transgender Adults in British Columbia: Suggested Guidelines

Physical Aspects of Transgender Endocrine Therapy

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Jamie L. Feldman, M.D., Ph.D.[†]
Joshua Goldberg[‡]
Afshin Jaberi, B.Sc.(Pharm), R.Ph.[§]

Assessment of Hormone Eligibility and Readiness

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January 2006

a collaboration between Transcend Transgender Support & Education Society and Vancouver Coastal Health's Transgender Health Program, with funding from the Canadian Rainbow Health Coalition's Rainbow Health – Improving Access to Care *initiative*

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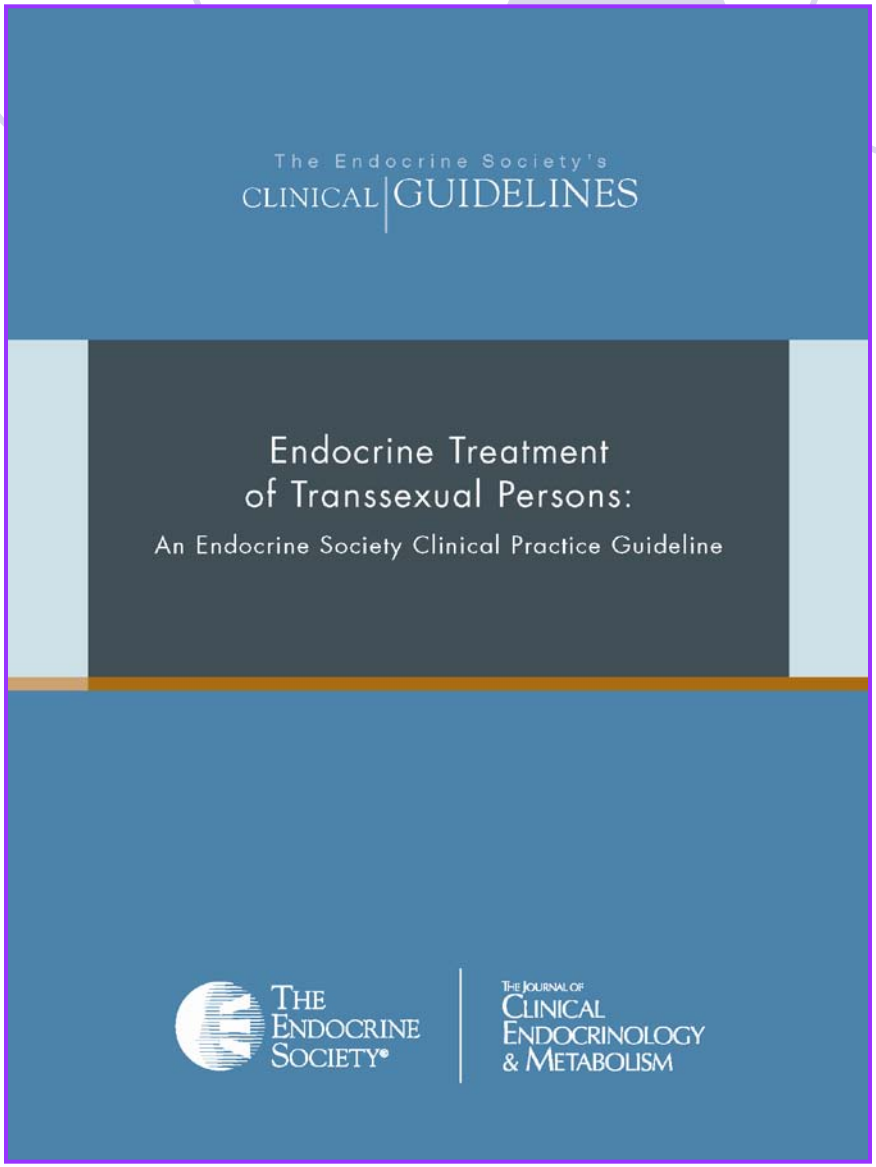
Vancouver Coastal Health, Transgender Health Program



Endocrine Society CPG: Endocrine Treatment of Transsexual Persons

ICD-10 criteria for GID in childhood

TABLE 3. ICD-10 criteria for transsexualism and GID of childhood (29)

TRANSSEXUALISM (F64.0) criteria:

1. The desire to live and be accepted as a member of the opposite sex, usually accompanied by the wish to make his or her body as congruent as possible with the preferred sex through surgery and hormone treatments.
2. The transsexual identity has been present persistently for at least 2 years.
3. The disorder is not a symptom of another mental disorder or a genetic, intersex, or chromosomal abnormality.

GID OF CHILDHOOD (F64.2) has separate criteria for girls and for boys.

FOR GIRLS:

1. The individual shows persistent and intense distress about being a girl and has a stated desire to be a boy (not merely a desire for any perceived cultural advantages of being a boy) or insists that she is a boy.
2. Either of the following must be present:
   a. Persistent marked aversion to normative feminine clothing and insistence on wearing stereotypical masculine clothing.
   b. Persistent repudiation of female anatomical structures, as evidenced by at least one of the following:
      i. An assertion that she has, or will grow, a penis.
      ii. Rejection of urination in a sitting position.
      iii. Assertion that she does not want to grow breasts or menstruate.
3. The girl has not yet reached puberty.
4. The disorder must have been present for at least 6 months.

FOR BOYS:

1. The individual shows persistent and intense distress about being a boy and has a desire to be a girl or, more rarely, insists that he is a girl.
2. Either of the following must be present:
   a. Preoccupation with stereotypic female activities, as shown by a preference for either cross-dressing or simulating female attire or by an intense desire to participate in the games and pastimes of girls and rejection of stereotypical male toys, games, and activities.
   b. Persistent repudiation of male anatomical structures, as evidenced by at least one of the following repeated assertions:
      i. That he will grow up to become a woman (not merely in the role).
      ii. That his penis or testes are disgusting or will disappear.
      iii. That it would be better not to have a penis or testes.
3. The boy has not reached puberty.
4. The disorder must have been present for at least 6 months.

www.who.int

Therapy for transgender youth

- fully reversible interventions
  - halting puberty, blocking androgens
- partially reversible interventions
  - masculinizing or feminizing hormones
- irreversible interventions
  - surgery

- all interventions are done in coordination with mental health professionals

WPATH Standards of Care, 6th version

Eligibility criteria for hormone treatment

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 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 analogue 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 years or older.

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

Endocrine Society CPG: Endocrine Treatment of Transsexual Persons

GnRH analogs: eligibility

- Dx of gender disorder, preferably by a psychologist/psychiatrist trained in child and adolescent psychopathology
- psychologically stable
- living in a supportive environment
- have begun pubertal development
- increased dysphoria with puberty

GnRH analog: Lupron Depot®

- monthly injection in the thigh
- dose: 7.5 mg IM every 4 weeks
- cost: $388/dose ($5044/year)
- covered by BC PharmaCare Plan G
- requires blood testing to ensure correct dosage
- 5% risk of local reaction, sometimes severe
- European alternative: Decapeptyl CR®
- ? use of 3- and 4-monthly formulations
- can be stopped when on cross-hormones

GnRH analog: Lupron Depot®

GnRH analogs: what they do

- causes lessening/slowing/cessation of:
  - linear growth
  - pubertal development
  - androgen-dependent hair growth
  - deepening of the voice
  - breast or testicular size
  - menstruation, fertility (semen cryopreservation)
  - libido
  - “teenage behaviour”
  - accretion of bone-mineral content

GnRH analogs: what they may do

- provide relief of gender dysphoria
- improve psychological and physical outcomes
- increase adult height in FTM
- decrease adult height in MTF
- cause hot flashes and first period in FTM
- ? make for a less satisfactory surgical outcome in MTF

GnRH analogs: what they don’t do

- cause complete regression in adult-sized penis, beard, body hair in MTF
- cause complete regression in adult-sized breasts, hips in FTM

Monitoring of GnRH analog therapy

- height, weight, BMI
- pubertal development
- bone age in growing kids
- bone-mineral density
- baseline and/or stimulated LH, FSH
- testosterone/estradiol
- urea/creatinine, LFTs, lipids, glucose, A1C

Anti-androgens

- block T action, synthesis, conversion to DHT
  - spironolactone (Aldactone®, generic)
  - cyproterone (Androcur®)
  - flutamide (Euflex®)
  - finasteride (Propecia®, Proscar®)
  - dutasteride (Avodart®)
- used to block the effect of androgens on the hair follicles
- used if not taking GnRH analog
- each has its own benefits and side-effects

Spironolactone

- fully reversible
- dose: 100 mg PO BID
- cost: $15/month
- “side-effect”: gynecomastia!
- can cause hyperkalemia:
  - check electrolytes and creatinine
- patients must be counselled about discontinuing with vomiting

What I do initially

- I offer Lupron Depot® to kids who haven't finished their pubertal development or started their periods
- I offer Lupron Depot® to kids who are distressed by libido, periods, erections
- I offer spironolactone for the other MTFs to prevent beard growth
- I broach topic of semen cryopreservation

Partially reversible interventions

- masculinizing hormones for FTM
  - testosterone
- feminizing hormones for MTF
  - estrogen
  - progesterone?
  - anti-androgens
- long-term effects not completely known
- both done with patient/parental consent

Cross-hormone therapy: age of treatment

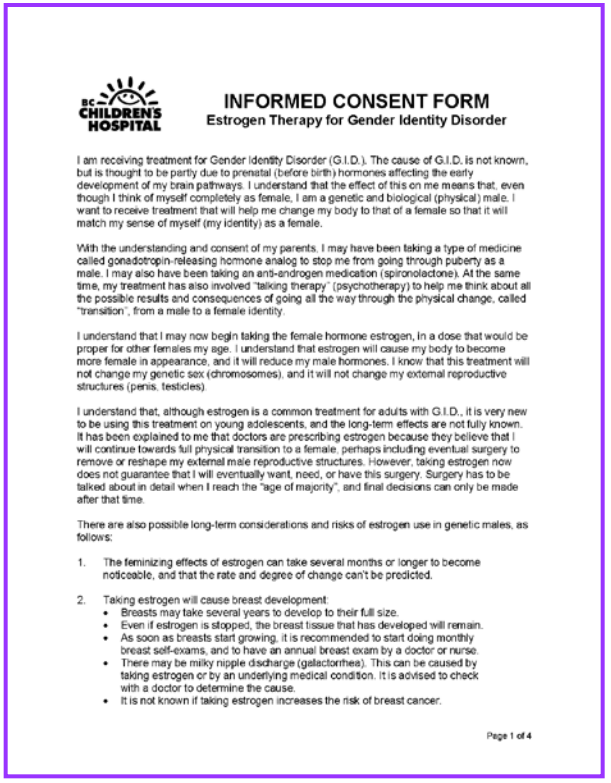
- "*Adolescents may be eligible to begin masculinizing or feminizing hormone therapy as early as age 16, preferably with parental consent*."
- "*In many countries 16-year olds are legal adults for medical decision-making, and do not require parental consent*."
- "*For the implementation of the real-life experience or hormone therapy, the mental health professional should be involved with the patient and family for a minimum of six months*."

Cross-hormone therapy

- eligibility:
  - same for GnRH analogs
- readiness (same as for adults):
  - has had further consolidation of gender identity during a RLE or psychotherapy
  - has made some progress in mastering other identified problems leading to improvement or continuing stable mental health
  - is likely to take hormones in a responsible manner.

Informed consent

- know your local laws (BC Infants Act)



BC CHILDREN'S HOSPITAL

INFORMED CONSENT FORM
Estrogen Therapy for Gender Identity Disorder

I am receiving treatment for Gender Identity Disorder (G.I.D.). The cause of G.I.D. is not known, but is thought to be partly due to prenatal (before birth) hormones affecting the early development of my brain pathways. I understand that the effect of this on me means that, even though I think of myself completely as female, I am a genetic and biological (physical) male. I want to receive treatment that will help me change my body to that of a female so that it will match my sense of myself (my identity) as a female.

With the understanding and consent of my parents, I may have been taking a type of medicine called gonadotropin-releasing hormone analog to stop me from going through puberty as a male. I may also have been taking an anti-androgen medication (spironolactone). At the same time, my treatment has also involved "talking therapy" (psychotherapy) to help me think about all the possible results and consequences of going all the way through the physical change, called "transition", from a male to a female identity.

I understand that I may now begin taking the female hormone estrogen, in a dose that would be proper for other females my age. I understand that estrogen will cause my body to become more female in appearance, and it will reduce my male hormones. I know that this treatment will not change my genetic sex (chromosomes), and it will not change my external reproductive structures (penis, testicles).

I understand that, although estrogen is a common treatment for adults with G.I.D., it is very new to be using this treatment on young adolescents, and the long-term effects are not fully known. It has been explained to me that doctors are prescribing estrogen because they believe that I will continue towards full physical transition to a female, perhaps including eventual surgery to remove or reshape my external male reproductive structures. However, taking estrogen now does not guarantee that I will eventually want, need, or have this surgery. Surgery has to be talked about in detail when I reach the "age of majority", and final decisions can only be made after that time.

There are also possible long-term considerations and risks of estrogen use in genetic males, as follows:

1. The feminizing effects of estrogen can take several months or longer to become noticeable, and that the rate and degree of change can't be predicted.

2. Taking estrogen will cause breast development:
   - Breasts may take several years to develop to their full size.
   - Even if estrogen is stopped, the breast tissue that has developed will remain.
   - As soon as breasts start growing, it is recommended to start doing monthly breast self-exams, and to have an annual breast exam by a doctor or nurse.
   - There may be milky nipple discharge (galactorrhea). This can be caused by taking estrogen or by an underlying medical condition. It is advised to check with a doctor to determine the cause.
   - It is not known if taking estrogen increases the risk of breast cancer.

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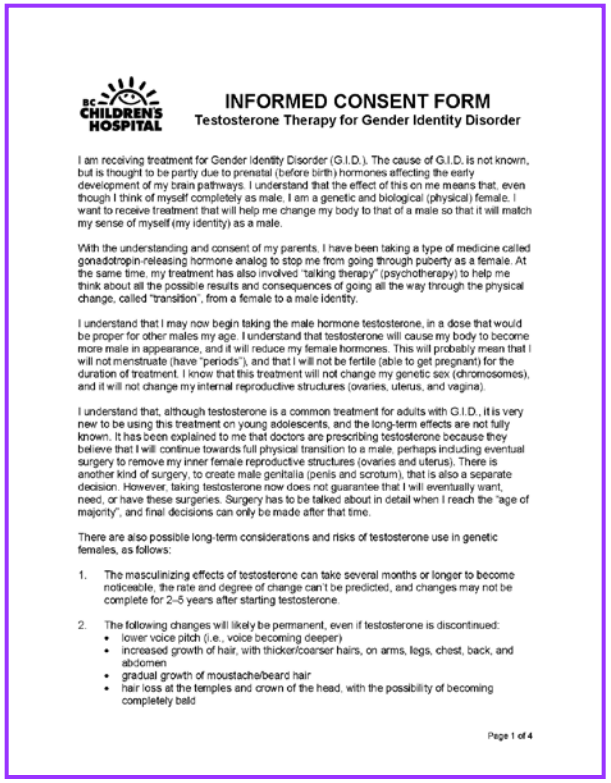

BC CHILDREN'S HOSPITAL

INFORMED CONSENT FORM
Testosterone Therapy for Gender Identity Disorder

I am receiving treatment for Gender Identity Disorder (G.I.D.). The cause of G.I.D. is not known, but is thought to be partly due to prenatal (before birth) hormones affecting the early development of my brain pathways. I understand that the effect of this on me means that, even though I think of myself completely as male, I am a genetic and biological (physical) female. I want to receive treatment that will help me change my body to that of a male so that it will match my sense of myself (my identity) as a male.

With the understanding and consent of my parents, I have been taking a type of medicine called gonadotropin-releasing hormone analog to stop me from going through puberty as a female. At the same time, my treatment has also involved "talking therapy" (psychotherapy) to help me think about all the possible results and consequences of going all the way through the physical change, called "transition", from a female to a male identity.

I understand that I may now begin taking the male hormone testosterone, in a dose that would be proper for other males my age. I understand that testosterone will cause my body to become more male in appearance, and it will reduce my female hormones. This will probably mean that I will not menstruate (have "periods"), and that I will not be fertile (able to get pregnant) for the duration of treatment. I know that this treatment will not change my genetic sex (chromosomes), and it will not change my internal reproductive structures (ovaries, uterus, and vagina).

I understand that, although testosterone is a common treatment for adults with G.I.D., it is very new to be using this treatment on young adolescents, and the long-term effects are not fully known. It has been explained to me that doctors are prescribing testosterone because they believe that I will continue towards full physical transition to a male, perhaps including eventual surgery to remove my inner female reproductive structures (ovaries and uterus). There is another kind of surgery, to create male genitalia (penis and scrotum), that is also a separate decision. However, taking testosterone now does not guarantee that I will eventually want, need, or have these surgeries. Surgery has to be talked about in detail when I reach the "age of majority", and final decisions can only be made after that time.

There are also possible long-term considerations and risks of testosterone use in genetic females, as follows:

1. The masculinizing effects of testosterone can take several months or longer to become noticeable, the rate and degree of change can't be predicted, and changes may not be complete for 2–5 years after starting testosterone.

2. The following changes will likely be permanent, even if testosterone is discontinued:
   - lower voice pitch (i.e., voice becoming deeper)
   - increased growth of hair, with thicker/coarser hairs, on arms, legs, chest, back, and abdomen
   - gradual growth of moustache/beard hair
   - hair loss at the temples and crown of the head, with the possibility of becoming completely bald

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based on: Vancouver Coastal Health, Transgender Health Program

Virilizing therapy: route and cost

- testosterone
  - route:
    - shot (Delatestryl®) every 2–4 weeks
    - patch (Androderm®) daily
    - gel (Androgel®) daily
  - cost:
    - shots: $12/month
    - patch: $125/month
    - gel: $125/month

Virilizing therapy: formulations

Virilizing therapy: what I do

- I use Delatestryl® (testosterone enanthate)
- I get informed consent from patient
- I increase dosage every 6 months over 2 years:
  - start: 50 mg IM every 2 weeks × 6 months
  - then: 100 mg IM every 2 weeks × 6 months
  - then: 150 mg IM every 2 weeks × 6 months
  - then: ~200 mg IM every 2 weeks (adult dose)
- Endo Soc: 25–50–75–100 mg/m²/2 weeks

Virilizing therapy: benefits

- permanent:
  - growth of pubic, axillary, body hair and beard
  - increased height (if epiphyses are not fused)
  - accretion of bone-mineral content
  - deepening of voice, Adam’s apple
  - enlargement of the clitoris, vaginal dryness
- not permanent:
  - increased muscle mass, male fat distribution
  - increased libido
  - cessation of periods

Virilizing therapy: risks

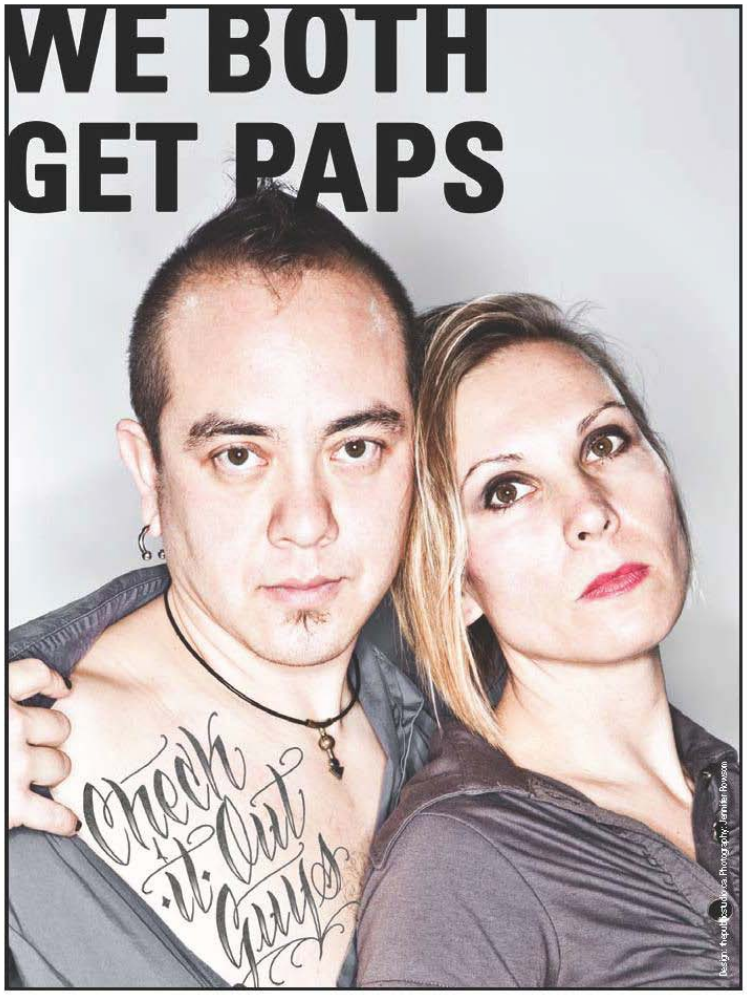
- permanent:
  - male-pattern balding
- not permanent:
  - acne
  - increased risk of heart disease
  - behavior changes
- unknown:
  - fertility
  - effect on uterus, breasts, ovaries

Virilizing therapy: what it doesn't do

- shrink breast tissue completely
- make the clitoris grow to the size of a penis ("rule of thumb")
- make the uterus or ovaries regress

Virilizing therapy: monitoring FTMs

- testosterone level:
  - midway between injections or at any time on a patch/gel
  - maintain level ideally 12–24 nmol/L (adults)
- estradiol level: ideally <180 pmol/L
- weight, BP
- CBC, LFTs, fasting lipids, glucose
- Pap smear, mammograms PRN
- BMD at baseline, after age 60



checkitoutguys.ca

Feminizing therapy: route and cost

- estrogen
  - route:
    - pill (Estrace®, Premarin®, others) daily
    - patch (Estraderm®, Estradot®, Oesclim®) 2×/week
    - gel (Estrogel®) daily
    - shot (Delestrogen®) every 2–4 weeks
  - cost:
    - pills: $14/month
    - patch: $25–50/month
    - gel: $20/month
    - shot: not available

Feminizing therapy: formulations

Feminizing therapy: what I do

- I use Estrace® (micronized 17β-estradiol)
- I get informed consent from patient
- I increase dosage every 6 months over 2 years:
  - start: 0.5 mg PO daily × 6 months
  - then: 1 mg PO daily × 6 months
  - then: 1.5 mg PO daily × 6 months
  - then: 2 mg PO daily (adult dose)
- Endo Soc: 5–10–15–20 μg/kg/day PO

Feminizing therapy: what it doesn’t do

- raise the voice pitch
- shrink the Adam’s apple
- shrink the penis
- cause regression of the beard

Feminizing therapy: benefits

- permanent:
  - breast development (may take a few years)
  - accretion of bone-mineral content
- not permanent:
  - softer skin
  - decreased muscle mass
  - female fat distribution
  - less body hair (not complete)
  - slower balding

Feminizing therapy: risks

- permanent:
  - ? increased breast cancer risk
  - decreased adult height
- not permanent:
  - testicular shrinkage, infertility
  - decreased libido
  - ? increased risk of blood clots, gallstones
- unknown:
  - fertility
  - effect on testicles

Feminizing therapy: monitoring MTFs

- estradiol level (if on E_2):
  - keep <1600 pmol/L (normal peak in women)
  - ideally ~720 pmol/L (adults)
- testosterone level: ideally <2 nmol/L
- weight, BP
- CBC, LFTs, fasting lipids, glucose
- electrolytes if on spironolactone
- breast, colon, prostate screening PRN
- BMD at baseline, after age 60

Progestins

- felt by some to be beneficial for breast growth
- remains controversial
- Endocrine Society does not mention
- gives you PMS, feeling of “cycling”
- pills:
  - Prometrium® (micronized progesterone)
  - Provera® (medroxyprogesterone)

Monitoring of kids on cross-hormones

- height, weight, sitting height, BMI
- ? pubertal development
- bone age in growing kids
- bone-mineral density

- LH, FSH, testosterone/estradiol
- urea/creatinine, LFTs, lipids, glucose, A1C

Irreversible interventions: surgery

- "*Any surgical intervention should not be carried out prior to adulthood, or prior to a real-life experience of at least two years in the gender role of the sex with which the adolescent identifies*."
- "*The threshold of 18 should be seen as an eligibility criterion and not an indication in itself for active intervention*."

Irreversible interventions: surgery

TABLE 17. Sex reassignment surgery eligibility and readiness criteria

Individuals treated with cross-sex hormones are considered eligible for sex reassignment surgery if they:
1. Are of the legal age of majority in their nation.
2. Have used cross-sex hormones continuously and responsibly during 12 months (if they have no medical contraindication).
3. Had a successful continuous full-time RLE during 12 months.
4. Have (if required by the MHP) regularly participated in psychotherapy throughout the RLE at a frequency determined jointly by the patient and the MHP.
5. Have shown demonstrable knowledge of all practical aspects of surgery (e.g., cost, required lengths of hospitalizations, likely complications, postsurgical rehabilitation, etc.).
Individuals, treated with cross-sex hormones, should fulfill the following readiness criteria prior to sex reassignment surgery:
1. Demonstrable progress in consolidating one's gender identity.
2. Demonstrable progress in dealing with work, family, and interpersonal issues resulting in a significantly better state of mental health.

Endocrine Society CPG: Endocrine Treatment of Transsexual Persons

BCCH Endocrinology Clinic

- access requires a referral
- Pediatric Endocrinologists
- Endocrine Nurse Clinician
- Social Worker/Counsellor
- liaison with Transgender Health Program
- liaison with mental health professionals

- http://endodiab.bcchildrens.ca

Before the appointment

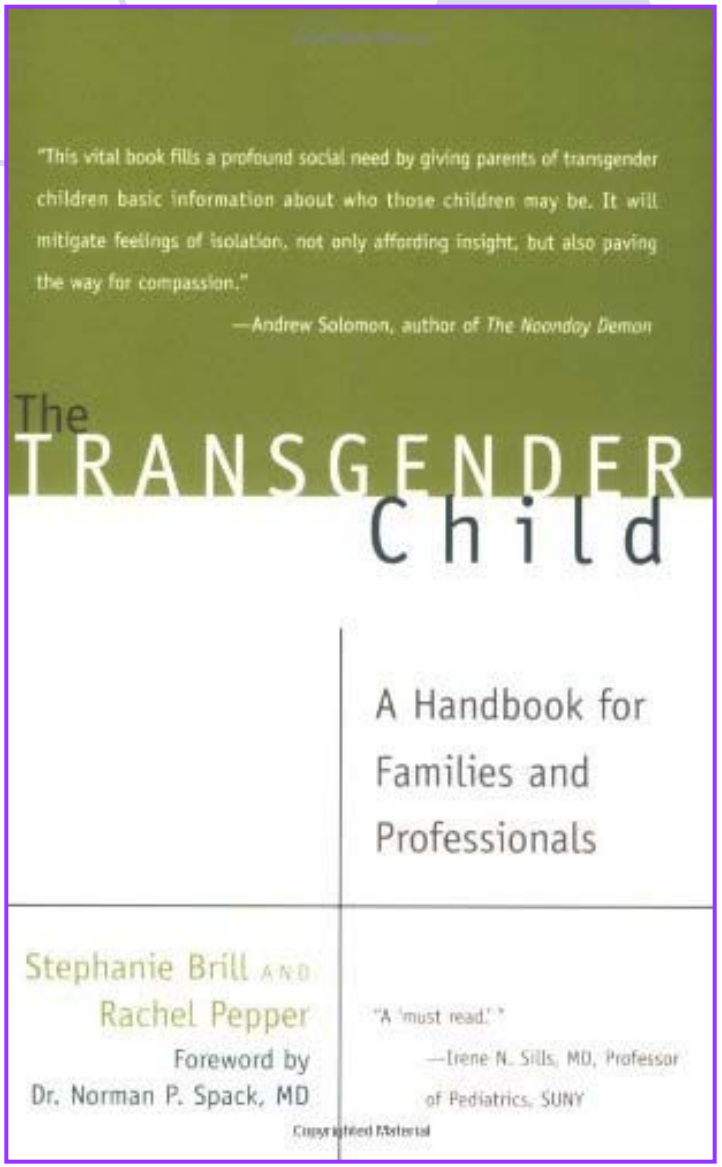
- prepare front-desk office staff
- use gray (photocopied) growth charts
- liberal use of nickname field in databases
- prepare any out-of-clinic services

Send in the scouts

- Our Nurse Clinician meets family first:
  - finds out desired name, pronouns
  - figures out who is who
  - assesses family dynamics, etc
  - describes in general how our clinic works
  - provides access to local resources, handouts, books, videos, etc.

Resources

- CPATH:
  - cpath.ca
- WPATH:
  - wpath.org
- Endocrine Society:
  - endo-society.org/guidelines/
- VCH Transgender Health Program
  - transhealth.vch.ca


"This vital book fills a profound social need by giving parents of transgender children basic information about who those children may be. It will mitigate feelings of isolation, not only affording insight, but also paving the way for compassion."
—Andrew Solomon, author of The Noonday Demon
The TRANSGENDER Child
A Handbook for Families and Professionals
Stephanie Brill AND Rachel Pepper
Foreword by Dr. Norman P. Spack, MD
"A 'must read.'"
—Irene N. Sills, MD, Professor of Pediatrics, SUNY
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Transgender children

Mourning a daughter, celebrating a son

More transgender teens are coming out than ever before – and at increasingly earlier ages. But even as resources for families grow, parents struggle with being supportive while coping with their own conflicting emotions

The Globe and Mail, August 30, 2009

Thanks!

- BC Children's Hospital
  - Sheila Kelton, RN
  - Mabel Tan, RN
- VCH Transgender Health Program
  - Lukas Walther, Coordinator
  - Gail Knudsen, MD and Oliver Robinow, MD
  - Melady Preece, PhD
  - Christopher Booth, MD
- All our patients and families!