

The Hormone Foundation's Patient Guide to the Endocrine Treatment of Transsexual Persons

Why were the guidelines written?

In 1923, the term transsexual was first used to describe persons who felt profound discomfort with their biological sex. Today, medical treatment, sometimes together with surgery, allows transsexual persons to make a male-to-female (MTF) or female-to-male (FTM) transition and to live a gender-appropriate life.

Sex reassignment involves a team of doctors in which the endocrinologist plays an important role, along with mental health professionals and surgeons. This patient guide is based on clinical guidelines for physicians on the endocrine (hormone-based) treatment of persons who have *gender identity disorder (GID)* diagnosed by a mental health professional. GID is also known as transsexualism.

The clinical guidelines were written to help endocrinologists provide appropriate hormone therapy for transsexual persons who want to develop the physical characteristics of their desired gender. In general, the aims of therapy are:

- To suppress the production of hormones that are determined by the person's genetic/biologic sex
- To maintain "cross-sex" hormone levels within the normal range for the person's desired, opposite gender

How were the guidelines developed?

The clinical guidelines were developed after an extensive review of the best human research studies related to the endocrine treatment of transsexual persons. An expert panel of The Endocrine Society examined evidence from studies published in quality medical journals. The panelists drew on their own extensive experience and observations in treating transsexual persons as a basis for the recommendations in the guidelines. The guidelines were reviewed and approved by several committees and the general membership of The Endocrine Society. No funding for the guidelines came from any pharmaceutical company.

When should endocrine treatment of transsexual persons begin?

Individuals seeking endocrine treatment must first be diagnosed with GID by a mental health professional, and undergo psychotherapy or counseling and a "real-life experience." The real-life experience is a year-long period during which the person lives full-time in the desired gender role before starting irreversible physical treatment. The real-life experience is recommended for adolescents and encouraged when possible in adults. Sometimes the real life experience runs parallel with medical treatment rather than preceding it. Neither a complete social role change nor hormone treatment is recommended before the onset of puberty, since GID in children often does not continue into adolescence.

How do hormones affect sex characteristics?

Before puberty, the major visible body differences between boys and girls are their external genitals—the male penis and the female vulva. Puberty brings increases in levels of *estrogens* and *androgens*, the two main classes of "female" and "male" sex hormones. Within these two classes, *estradiol* and *testosterone* are the sex hormones responsible for the development of secondary sex characteristics—the physical features of males and females that are not part of the reproductive system. In girls, this means growth of breasts, underarm hair, and pubic hair; widened hips; and fat deposits around the thighs and buttocks. In boys, puberty brings growth of the testicles and penis, heavier bones, increased muscle mass, a deepening voice, a prominent Adam's apple, and growth of facial and body hair.



Estradiol and *testosterone* are the sex hormones responsible for the development of secondary sex characteristics.

How is hormone therapy used to treat transsexual adolescents?

Preventing undesired sexual characteristics

A young adolescent with GID often considers the physical changes of puberty to be unbearable. Treating such adolescents with a medication that suppresses puberty may prevent this psychological harm. The medication, called a GnRH (gonadotropin-releasing hormone) analogue, stops the release of LH (luteinizing hormone) and FSH (follicle-stimulating hormone). These two hormones, which are produced by the pituitary gland located at the base of the brain, cause the male testicles (or the female ovaries) to produce male (or female) sex hormones that control sexual development and maturity.



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If GnRH-analogue treatment begins very early in puberty, the adolescent's slightly developed sex characteristics will go away. To prevent irreversible development of sex characteristics, the guidelines recommend starting GnRH-analogue treatment before there is much testicular or breast growth. With treatment, slight breast enlargement will disappear and menstruation will stop in girls. In boys, development of a masculine body appearance will stop and the testicles will get smaller. An advantage of using GnRH analogues is that their effect is reversible. If the medication is discontinued, puberty resumes immediately.

Puberty can also be halted in adolescents who are in later stages of puberty. However, physical sex characteristics such as breast development in girls and lowering of the voice and outgrowth of the jaw and brow in boys cannot be completely undone. Hormones started during adolescence can decrease full development of the genitals, but only surgery can change the appearance of the genitals to the desired gender.

used to stop it. GnRH analogues or progesterone may also be used to stop menstruation before testosterone treatment and to reduce estrogens to the levels found in biological males.

Male-to-female transsexual (MTF) persons

Cross-sex hormone therapy for MTF transsexual adults requires the use of an anti-androgen along with an estrogen. For estrogen therapy to have its fullest effect, the MTF person's testosterone levels need to be reduced to levels found in biological women. Both the anti-androgen spironolactone and GnRH agonists are effective in reducing testosterone levels. Estrogen is available as a pill, a skin gel, a patch, or an injection. The MTF person's blood level of estrogen should be maintained at the average level for premenopausal women, and the testosterone level should be in the female range.

What are the risks of hormone therapy and how can they be avoided?

Cross-sex hormone therapy has the same risks as sex hormone replacement therapy in biological males and females. Pretreatment screening and regular medical monitoring are recommended for both FTM and MTF transsexual persons. The guidelines recommend monitoring every 3 months during the first year of hormone therapy and then once or twice yearly.

Female-to-male transsexual persons

Problems that might occur with long-term testosterone therapy include excessive or cystic acne, excessive weight gain, salt retention, increases in red blood cells (which can increase the "thickness of blood" in the circulation), and negative psychological changes. The guidelines suggest that FTM transsexual persons consider surgical removal of the uterus, cervix, and ovaries to prevent the risk of cancer of the reproductive tract.

Male-to-female transsexual persons

For individuals on estrogens, a key issue is avoiding very high doses or high blood levels of estrogen, which may increase risk for blood clots, liver problems, and high blood pressure. The guidelines suggest that MTF transsexual persons, who have no known increased risk of breast cancer, follow breast screening guidelines recommended for biological women, and also follow the screening guidelines for prostate cancer recommended for biological men.

What can you do to help your endocrine treatment process?

You, your endocrinologist, and your referring mental health professional should be partners in your medical care. Ask about the possibilities and limitations of sex reassignment so that you can make informed decisions. Be sure that you understand the effects of hormone suppression and cross-sex hormone treatment before you start endocrine therapy. In particular, ask about its effects on fertility and about available options that may improve the chances of future fertility, if that is a concern for you. Follow your doctor's advice for treatment and see him or her regularly for testing and monitoring of your condition. It is important to make needed changes before serious complications develop.

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and your referring mental
health professional should
be partners in your
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Developing desired sexual characteristics

The guidelines suggest that treatment to develop secondary sex characteristics of the desired, opposite sex start at age 16 years. They suggest using a gradually increasing dose (increased every 6 months) of cross-sex hormones until the adult dose is reached. To induce feminization, estrogen must be taken daily, usually as a pill. To induce masculinization, testosterone is injected directly into a muscle every one to two weeks. During treatment to bring about the desired secondary sex characteristics, the guidelines suggest that treatment with GnRH analogues be continued to prevent development of undesired sex characteristics.

The time to begin cross-sex hormone treatment is arbitrary, but the goal is to start when the adolescent is able to make informed, mature decisions and take part in the treatment. It is also preferable that the transsexual adolescent develop along with his or her peers.

How is hormone therapy used in transsexual adults?

Female-to-male (FTM) transsexual persons

Several different androgen preparations can be used to develop masculine characteristics in FTM transsexual adults. Injections, skin gels, or patches can be used to bring testosterone levels in the body into the normal male range. Testosterone treatment results in increased muscle mass, decreased fat mass, increased facial hair and acne, and increased libido (sex drive).

Testosterone treatment may also result in enlargement of the clitoris, decreased fertility, deepening voice, and, usually, the end of menstruation. Menstruation may stop within a few months with testosterone treatment alone, although high doses may be needed. If menstrual bleeding continues, addition of another hormone (progesterone) or endometrial ablation (an outpatient surgical procedure that destroys the lining of the uterus) may be