



A Transgender Therapy Primer

Basic information for hormonal treatment and drug interactions

by Enid Vázquez

Transgender individuals may use male or female hormones to make them more masculine or more feminine. Therapy is not just for physical changes. It has been found to greatly reduce psychological distress. Transgender hormonal therapy is taken for life.

Female-to-male transgender individuals, or FTMs, can take the male hormone testosterone. Male-to-female transgender individuals, or MTFs, can take the female hormones estrogen and progesterone (progesterone is not recommended). Everyone is born with both male and female hormones in their body, but the levels depend on the sex of the person.

Testosterone is an androgen, one of a number of steroid hormones in the body that stimulate the development of male sex organs and male secondary characteristics, such as beard growth or a deep voice. MTFs will therefore usually take an anti-androgen drug in addition to their female hormones. Estrogens alone do not lower testosterone levels and anti-androgens alone lead to serious bone density loss. One advantage of taking an anti-androgen is being able to reduce the estrogen dose taken. If they undergo transsexual surgery, they can drop the anti-androgen.

Hormones are available in pills, injections, and transdermal preparations (delivered through the skin in the form of creams, gels, and patches). Anti-androgen therapy includes anti-androgen drugs, GnRH ago-

nists (gonadotropin-releasing hormone), and bilateral orchiectomy (removal of the testicles).

Medical providers warn that “more is not better.” Premarin is removed in the urine—there is a limit to what the body can absorb. The side effects of the other hormones can become intolerable.

Also, hormones should be avoided in people with breast cancer, a history of blood clots, or active substance abuse. In addition, patients should be assessed for suicidal tendencies, before and during therapy, but especially if taking testosterone.

Hormonal therapy is highly individualized. It depends on the levels of the hormones already in the person’s body and then the individual’s response to therapy, which is affected by such things as age, weight, and genetics. There are other interactions as well. For example, when faced with an anti-androgen, the body may respond by increasing its production of testosterone, although eventually the testosterone will stay suppressed as the anti-androgen wins the battle. These are among the reasons that monitoring takes place, to make sure everything gets into the correct balance over time.

“With estrogen we’re worried about clotting and cardiovascular effect while with testosterone, we’re worried about the liver effect,” says pharmacist Andrew Halbur of Walgreens specialty pharmacy in Chicago.

“Most of the antivirals [but not all—see chart on page 48] cause an increase in estrogen,” says nurse practitioner Bethsheba Johnson of the Luck Care Center, also in Chicago. “We try to use the lowest dose of estrogen and then look at testosterone levels [in male-to-female patients, or MTFs].” She says estrogen therapy generally costs from \$25 to \$80 a month, plus the cost of lab monitoring, which can be costly. She finds that insurance companies will pay for the measurement of male hormones in men and female hormones in women, but not for a measure of both hormones in one person. She likes prescribing the patch, because of its lower risk of adverse events along with its efficacy.

She says her clinic, which focuses on HIV, looks at the effects on patients as well as their blood levels. Body hair, she says, is a big problem. An androgen antagonist suppresses male hormones in the body, which helps control male characteristics such as hair all over the body, she said. But, she points out that, “You can’t change bone with hormones—the strong jaw, the big hands.” Surgery on the jawline is available.

TESTOSTERONE THERAPY

A. Injection of testosterone cypionate (Depo-testosterone) and testosterone enanthate—every two to four weeks, and testosterone propionate—once or twice a week.

- B. Androderm patch—one or two patches a day.
- C. Androgel, rub directly on skin. May rub off on partner.
- D. Testosterone ointment (cream), applied to the face and clitoral area. Requires large areas of skin for application.
- E. Methyl/testosterone and oxandrolone pills are generally avoided due to their side effect profile (potential liver complications).

Permanent effects of testosterone include atrophy of the uterus and ovaries (resulting in sterility), baldness and hair loss (especially at temples and crown of head), beard and mustache growth, deepening of the voice, enlargement of the clitoris, increased growth of body hair, and sterility. Temporary testosterone effects, reversible upon discontinuation, include behavioral developments associated with production during puberty (aggression and increased libido), development of acne, increased muscle mass and strength, increase in number of red blood cells, and redistribution of fat from breast, hips and thighs to abdominal area. Other potential side effects include weight gain; larger feet; peripheral edema (swelling in the hands and feet); liver enzyme increases (a sign of liver damage); decreases in HDL (the “good” cholesterol); increased risk of cardiovascular disease and breast or endometrial cancer; headache; and high blood pressure. Caution should be used when taken with other liver-toxic drugs.

In many patients, changes in voice pitch, muscle mass, and hair growth become apparent after just a few months.

ANTI-ANDROGEN THERAPY

- A. Pills include spironolactone and finasteride. Spironolactone (brand names Aldactone, Novo-Spiroton, Spiractin, Spiroton, Verospiron, and Berlactone) is the treatment of choice due to safety and availability. It is a potassium-sparing diuretic. Finasteride (Propecia 1 mg or Proscar 5 mg) may be used alone or in combination with spironolactone. It reduces the size of the prostate and improves male pattern baldness. There are debates about its value and expense. Other anti-androgen drugs include Androcur (cyproterone acetate) and Eulexin (flutamide). They are unfa-

vorable because of their toxicity profile and lack of availability.

- B. GnRH agonists (gonadotropin-releasing hormone) include nafarelin acetate, goserelin acetate, and leuporelin acetate. They are generally fully reversible in adolescents and do not carry risk of thromboembolic disease (due to blood clots). They are available by pill, injection, or nasal spray.
- C. Bilateral orchiectomy is removal of the testicles. This eliminates 90% of testosterone production and helps reduce the estrogen dose used for therapy, but may shrink the amount of skin available to create a vagina, should that surgery be pursued.

ESTROGEN THERAPY

- A. Oral estrogens include the conjugated estrogen Premarin (purported to cause more mood swings); the synthetic, plant-based version of Premarin, Cenestin; and the estradiol valerate tablets Estradiol and Estrace. Oral estrogens stress the liver more than transdermal and injectable estrogens do. Sublingual forms of estrogen (dissolving under the tongue) absorb better and avoid passing through the liver, which reduces the risk of blood clots. Premarin is removed in urine and there is a limit to what can be absorbed, so taking more in one dose is not helpful.
- B. Transdermal estrogens include the skin patches Estroderm, Climara, Alora, and Vivelle, the creams Premarin and Estrace, and the gel Estrasorb. Patches may cause irritation and people could be allergic to the adhesion used. Creams require frequent use on large areas of skin.
- C. Estrogen injections include estradiol valerate (Delestrogen) and estradiol cypionate (Depo-Estradiol). One vial can last up to six months. The hormone preparation is thick and requires a 3 cc or 3 ml syringe, an 18 or 20 gauge needle to draw up, and a 21 or 22 gauge needle to inject. Length should be 1 to 1-½ inch. Because of the large sizes required, the puncture wound is bigger; watch for infection at the injection site. In Illinois, people over the age of 18 can buy up to 20 syringes without a prescription at a pharmacy (not always without a

hassle). Bulk purchases where available can save money; for example, a pack of 10 syringes may cost \$12 while 100 may cost \$25. Check also syringe exchanges, such as the one at TPAN, for free supplies.

Warning: Some medical providers believe only one form of estrogen should be used, not a combination of the different categories, although some doctors may disagree.

According to the Bantam Medical Dictionary, an estrogen is “one of a group of steroid hormones (including estriol, estrone, and estradiol) that control female sexual development, promoting the growth and function of the female sex organs (see menstrual cycle) and female secondary sexual characteristics (such as breast development).”

Permanent effects of estrogen include breast development, enlargement of the nipples, loss of ejaculation, loss of erection, shrinkage of the testicles, and sterility. Temporary effects reversible upon discontinuation include a decrease in acne, decrease in facial and body hair, decrease in muscle mass and strength, softening of the skin, slowing of balding pattern, decreased libido, suppression of testosterone production, and redistribution of fat from abdominal area to hips and buttocks.

Estrogen risks include benign (non-cancerous) pituitary tumors (see below for potential complications with this condition), gallbladder disease, high blood pressure (hypertension), hypothyroidism, liver disease, migraine headache, weight gain, worsening of depression (if present) and increased sensitivity to stress, melasma (skin darkening), acne, lipid abnormalities, nausea and vomiting, and tendency for blood to clot (which can be fatal)—aneurysm, deep vein thrombosis (DVT), and pulmonary embolism. Blood clots usually begin in the calf. If they break off and travel to an organ such as the heart, brain, or the lungs, they can cut off necessary blood flow carrying oxygen to vital organs, and so the organs can die. Oral estrogen has greater risk than transdermal formulations. Age over 40 also increases risk of clotting. Maintain weight control and watch for high blood sugar.

A prolactinoma is a benign (non-cancerous) tumor in the pituitary gland, located at the base of the brain, that may lead to excess levels of the hormone prolactin and

pressure on surrounding tissues, causing headaches and visual problems, including loss of vision, and may require surgical removal.

An aneurysm is a swelling in the wall of an artery. DVT is a blood clot, usually occurring in the lower legs. It may break off and travel to an organ. This can be fatal. Symptoms include swelling and a sharp, localized pain, often with redness. Lack of mobility, as with a hospital stay or a trans-

continental flight, increases the risk of DVT. There are other risk factors as well, such as obesity and varicose veins, and the biggie—smoking. Hormones should be stopped if experiencing trauma that leads to immobilization and weeks before undergoing surgery. If you suspect DVT or any other blood clot, go immediately to the emergency room, where an IV-drip medication can slowly work on dissolving the clot. If it's broken up quickly, it can burst, and be fatal. A pulmo-

nary embolism is a blood clot that traveled to the lungs. Again, this is often fatal.

People with a history or a family history of heart attack, coronary artery disease, or stroke should be supervised with a stress test and be treated with blood thinners as well as treated for high blood pressure and high lipid levels. To reduce the odds of a cardiac complication, estradiol (Estrace 1 or 2 mg), a naturally occurring estrogen, is preferred to Premarin. Cigarette smokers and people who are over 40 years old, obese, or have cardiac risk factors may take a daily aspirin to help reduce risks. Others may also consider taking aspirin. Also, try to control other conditions that may increase the risk of adverse events, such as cigarette smoking, diabetes, hepatitis, and alcoholic liver disease.

PROGESTERONE THERAPY

A. Provera (medroxyprogesterone) is usually avoided. There is no clinical evidence suggesting that it helps feminization, and it may cause a higher incidence of breast cancer, cardiovascular disease, high blood pressure, cholesterol increase, weight gain, depression, and varicose veins. Natural progesterone (Prometrium) does not have the adverse effects of Provera on blood cholesterol or blood pressure. ☞

Sources of information: the Tom Waddell Health Center Protocols for Hormonal Reassignment of Gender (www.dph.sf.ca.us/chn/HlthCtrs/transgender.htm); The Harry Benjamin International Gender Dysphoria Association's Standards Of Care For Gender Identity Disorders, Sixth Version February, 2001 (www.wpath.org/Documents2/socv6.pdf); Hormone Replacement Therapy for Transgenders: Do's and Don'ts, a PowerPoint presentation by Dr. Steven M. Brown, M.D., step-by-step information from "what is a hormone?" on up (from Trans-Health.com, <http://www.trans-health.com/displayarticle.php?aid=127>); and Transgender Pharmacopoeia, a PowerPoint presentation by Drew Halbur, BSPHarm, Walgreens Specialty Pharmacy at Howard Brown Health Center in Chicago.

DRUG INTERACTION CHART

Note: this is not a comprehensive list.

Hormones used for transgender therapy have not been tested in the lab for interactions with other drugs. Instead, the much lower dose of ethinyl estradiol (a form of estrogen) in birth control pills is used as a guide. Transgender therapy requires a much higher dose of estrogen than that used in the Pill. An increase in blood levels of a drug generally increases the risk of a side effect or adverse event. A decrease in blood levels generally decreases the efficacy of a drug.

	HIV DRUGS	OTHERS
Levels of estradiol, ethinyl estradiol, and testosterone are increased by	Sustiva (efavirenz) Crixivan (indinavir) Invirase (saquinavir) Reyataz (atazanavir) Intelence (etravirine)	Tagamet (cimetidine) Biaxin (clarithromycin) diltiazem erythromycin Diflucan (fluconazole) grapefruit isoniazid Sporonox (itraconazole) Nizoral (ketoconazole) verpamil vitamin C
Levels of estradiol, ethinyl estradiol, and testosterone are decreased by	Kaletra (lopinavir/ ritonavir) Norvir (ritonavir) Aptivus (tipranavir) Prezista (darunavir) Viracept (nelfinavir) Viramune (nevirapine)	Tegretol (carbamazepine) dexamethasone phenobarbital Dilantin (phenytoin) rifampin Topamax (topiramate)

1. According to the Tom Waddell Health Center in San Francisco, Lexiva (fosamprenavir) is the only HIV medication whose concentration decreases in the presence of ethinyl estradiol. The clinic recommends caution when using Lexiva.
2. In diabetic patients on testosterone, blood sugar decreases, requiring adjustments in dose of their diabetic medication.
3. Testosterone may also potentiate (increase blood levels of) the blood thinner warfarin (Coumadin).

Special thanks to Drew Halbur, BSPHarm, of Walgreens Specialty Pharmacy, for reviewing this drug chart.