

*T-Clinic: Providing Excellence in Multidisciplinary Care to Gender Diverse Youth and Their Families*

## **Feminizing Hormones : Brief Description**

**Estrogen:** Typically given in a patch form, applied 2x a week

- Estrogen *may* increase risk of
  - blood clots (pulmonary embolism, stroke, heart attack, leg vein pain)
    - WORSE IF YOU SMOKE: NO SMOKING
  - prolactin producing brain tumors
  - liver dysfunction
  - breast cancer
  - heart disease, cholesterol levels
  - increase in frequency of migraine headaches
  - increase blood pressure
  - increase gall stones

**Breasts** may take years to develop, and are a permanent change from taking estrogen

**Testicles:** will eventually produce less testosterone

- sperm may not mature, leading to reduced fertility
- ability to make sperm may or may not come back
- testicles may shrink by 25% (may be permanent, unknown)
- decrease in erections, wet dreams but still happen
- decrease in libido

**Non-permanent changes:** may reverse if stop taking estrogen

- softer skin, improved acne
- decreased muscle mass
- fat redistribution

Estrogen **will not change** hair growth, voice pitch, Adams apple once they have developed

### **Androgen receptor blockers: Block binding of testosterone to its' receptor**

**May eventually suppress testosterone production**

#### **Spironolactone**

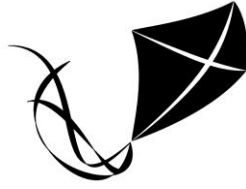
Affects balance of water and salt in the kidneys, diuretic (makes you pee more often). Side effect is blocking testosterone receptor.

- increase in amount of urine produced, increase frequency of urination
- reduces blood pressure
- increases thirst
- rarely, causes high levels of potassium which can change heart rhythm
- may have small amount of breast development
- levels of sodium and potassium are monitored regularly, as well as testosterone

#### **Biclutamide**

Strong anti-androgen used in prostate cancer

- Concern that it affects liver function, must have normal liver function to start
- Very little long-term data
- 85% develop breasts in 6 months on therapy



# RANDALL CHILDREN'S HOSPITAL

LEGACY EMANUEL

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## **Feminizing Hormones**

Hormone therapy can help transgender people feel more comfortable in their bodies, changing their bodies to align more with their gender identity. Like with other medical treatments, there are risks and benefits. This information is to help you and your doctor make the best decisions for what is right for you on your individual gender journey.

### **So, what is a hormone anyway?**

Hormones are chemical messengers that are made in one organ (a gland) and have an effect somewhere else. There are many different glands in the body (thyroid, pituitary, adrenal, testicles, pancreas and others) that produce many different hormones (thyroid, LH, FSH, growth hormone, cortisol, testosterone, insulin and others) that have a wide range of effects on the human body. Hormones are responsible for growth, puberty, overall metabolism, blood sugar regulation, hunger, thirst among other body functions. A hormone must bind to a receptor on a cell in order for specific actions to occur. All hormones are highly regulated by the body. An Endocrinologist specializes in the study of hormones, and thus helps in prescribing hormones to aid in transition.

### **And what about these Sex Hormones?**

Sex hormones regulate the development of puberty and the changes that result from it. They are mainly produced by a person's sex organ (ovary or testicle), although some are made in one's adrenal gland. These hormones produce the changes we associate with puberty such as facial and body hair, breast growth and bone strength, among others.

There are 3 categories of sex hormones:

1. **Androgens:** testosterone (produced in testicle), dihydrotestosterone (DHT, active form of testosterone, testosterone is converted to this near the organs it effects by an enzyme); other androgens that are produced in the adrenal gland
2. **Estrogens:** estradiol (produced in ovary)
3. **Progestin:** progesterone (produced in ovary)

### **What is Hormone (Replacement) Therapy (HRT)? Or Cross Hormone Therapy (CHT)?**

Both terms refer to taking medicine to change the level of sex hormones in your body. Changing these levels will affect features that are associated with sex and gender. ***Feminizing hormone therapy can help make the body look and feel less masculine and more feminine.***

### **What Medicines (or hormones) are Involved:**

#### **Estrogen**

Estrogen is the main hormone responsible for promoting “female” physical traits. It works directly on tissues in your body (for example, breasts will develop, fat will redistribute). Estrogen will eventually suppress testosterone production by the testicles. Most commonly we give estrogen by a patch (transdermally), as this way it is delivered thru the skin, and avoids passing through the liver. We can also administer it by taking a pill under the tongue (sublingually) or by injection. We do not prefer to have it taken by mouth and swallowing.

#### **Androgen Blockers**

These medicines work by blocking testosterone from having its effect as they stop it from binding to it’s receptor. They result in slowing the growth of facial hair, and help stop spontaneous erections. They tend to have a mild feminizing effect when used alone. They are often used in conjunction with estrogen, as estrogen can work better when testosterone effect is blocked.

The most common form of androgen receptor blocker we use is called Spironolactone. This is actually a diuretic (makes you pee) that has a side effect of blocking testosterone. When on this medication you need to drink fluids, and we need to watch your electrolyte levels and blood pressure. Another androgen blocker is called Bicalutamide. With this medication, your liver needs to be healthy. There is little long-term information on Bicalutamide.

In addition to the changes mentioned above, some individuals will experience breast development while on an androgen receptor blocker. It is presumed, although not confirmed, that this breast development is permanent.

### **Progestins:**

There are mixed opinions about using progestins for feminizing hormone therapy. If used, they are introduced later in one's transition for final breast changes and nipple development. They have possible risks of depression and weight gain, so these must be discussed with your provider prior to starting.

### **What is a typical dose?**

Feminization therapy doses will differ from person to person as bodies respond to the hormones differently. Often this is because of genetics that are inherited from our families. Your doctor will prescribe what best fits your needs based on your medical history, and desired outcome. Our team will also investigate what your insurance will cover and decide with you the most appropriate path forward.

Everyone's journey is different. Each body absorbs, processes and responds to sex hormones differently. Some people show more changes than others on a similar dose. Changes may happen more quickly in some compared to others. There is no way to predict how your body will respond before starting the estrogen. Taking more hormone than your prescribed dose will not speed up your process. It can actually slow down changes as extra estrogen in the body can be converted to testosterone! Taking more than prescribed may increase health risks as well.

If you think your dose is too low, or you are not seeing the changes you would expect, please bring this up with your doctor. We may decide it is a good idea to try a different form or combination of medication(s) rather than empirically increasing the dose.

If you decide in the future to remove your testicles, you will need less estrogen to have the same effect, and you will no longer need androgen receptor blockers (or pubertal suppression if you are on that).

Because your body is unable to produce estrogen, you will need to take estrogen for the rest of your life to continually see the effects from it. This is also important for the health of your bones.

### **Changes and Timeline:**

#### ***Androgen Receptor Blockers without Estrogen***

Typically taking Spironolactone or Bicalutamide without estrogen has small effects. Most changes that happen from blocking testosterone are reversible and will go back to the way it was before if you stop taking the medication.

<b>Average Timeline</b>	<b>Effect</b>
After 1 to 3 months	<ul style="list-style-type: none"> <li>~ Decreased sex drive</li> <li>~ Fewer erections, or difficulty getting them</li> <li>~ Decreased ability to make sperm and ejaculatory fluid</li> </ul>
Gradual (usually takes at least 2 years)	<ul style="list-style-type: none"> <li>~ Slower growth of facial or body hair</li> <li>~ Slowed / stopped male patterned balding</li> <li>~ Variable breast growth (presumed permanent)</li> </ul>

### ***Estrogen***

Taking estrogen is stronger than an androgen receptor blocker alone. Estrogen works on cells in the body that have estrogen receptors. Eventually, taking estrogen will have an indirect effect of suppressing testosterone production.

<b>Average Timeline</b>	<b>Effect</b>
After 1 to 3 months	<ul style="list-style-type: none"> <li>~ Softening of skin</li> <li>~ Less muscle mass, more body fat</li> <li>~ Redistribution of body fat to breasts and hips</li> <li>~ Possible decrease in sex drive</li> <li>~ Fewer erections, or difficulty getting them</li> <li>~ Decreased ability to make sperm and ejaculatory fluid</li> </ul>
Gradual changes (max effect in 2 years)	<ul style="list-style-type: none"> <li>~ Breast and nipple growth (quite gradual)</li> <li>~ Slower growth of facial and body hair</li> <li>~ Slowed or stopped male pattern baldness</li> <li>~ Smaller testicles</li> </ul>

A word on breast changes: It can take 2 years or more for breasts to reach their maximum size. As with all people, there is quite a range in how large breasts will grow. In many cases they will not get over an A or B cup size. If you are not happy with the size of your breasts after 24 months or more of estrogen, you can consider surgical augmentation. The implants look most natural if you have had as much growth as possible with hormone prior to placement.

**At your doctor visits:** As we are increasing and adjusting doses, your doctor will want to see you about every 3-4 months. They will ask about what changes you are noticing, how often you are shaving (if applicable) and ask about your sex drive. We obtain levels approximately 2 x a year to help adjust dosing and make sure we are getting to where we want to be.

## **What Changes are Permanent?**

### **Breast growth and Fertility**

Breast growth from estrogen (and if there is significant growth from an androgen receptor blocker) is permanent and will not go away after you stop taking it. Nipples will not shrink either. The only option for removal is surgery.

Both the androgen blockers and estrogen decrease sperm production. We do not fully understand the long term effects on fertility. If you stop taking the medications, your ability to make sperm may or may not come back. Again, given our uncertainty in this field, we strongly recommend that you use protection (condoms) if having sex with a person with a vagina/ovaries for birth control. In addition, your hormones will not protect you against any sexually transmitted infections, and proper protection is the only way to do so. If you have more questions about this topic, please ask your doctor.

We strongly recommend that you consider sperm banking before starting hormone therapy. Even if you are on hormones, you could take a break and donate sperm, and return to being on the hormones. We can refer you to our colleagues at OHSU to discuss these options and pricing.

## **What will not change?**

~ Penis    ~Pubic Hair    ~Testicle size    ~ Chromosomes

~ Adams' Apple: Once this is formed during puberty, it will not go away.

~ Bone Structure: If you have experienced a change in bone structure from puberty, taking estrogen will not change your bones. The distribution of the fatty tissue in your face may change altering the appearance to become more feminine but the bones themselves will not change.

~ Voice: Your pitch (how high or low your voice is) will not change. Speech or voice therapy can help train you to speak in a higher pitch. Some people have surgery on their vocal chords or surrounding cartilage to try to make their voices sound lighter.

### What won't change, cont'd:

~ Height: Once you are done growing, there is no way to affect your height with hormones.

~ When taking estrogen, the hair follicle does not produce hair as frequently as prior. However, the hair does not permanently go away unless you have either electrolysis or laser hair removal.

Other things that will not change:

Body image: often taking hormones significantly improves gender dysphoria as your body becomes more in line with your gender identity. However, if you are experiencing body dysphoria that is not improving with hormones, it may be beneficial to speak to a mental health therapist about these concerns.

Mental Health: as stated above, often taking hormones significantly improves gender dysphoria as your body becomes more in line with your gender identity. Life can still present with emotional and social challenges, stress and other factors can contribute to your mental health. Having an established mental health therapist that you feel comfortable talking to can really help work through these struggles.

## What are the risks of taking feminizing hormones?

As treating transfemale youth is such a new practice, we do not know the long-term effects of using estrogen and androgen receptor blockers. Our knowledge of using estrogen and these medications comes from use in older patients, as well as in individuals with different medical conditions requiring hormone therapy. Transmedicine is an ongoing field of study and we will know more the longer we are practicing it! And, there may be long term health risks we simply do not know about yet.

We try to create the safest hormone regimen for you by measuring levels and watching for the side effects we know about. The biggest thing you can do to prevent risks of feminizing hormone therapy is to **not smoke**. Smoking increases one's risk of blood clots and heart disease in and of itself. When estrogen is added to the mix, this risk increases several fold. Even the occasional smoker is at increased risk. If you do not smoke, it increases the amount of estrogen that we can prescribe safely.

1. Liver Health

Typically, estrogens are processed by the liver, especially if taken orally. There is a chance that taking hormones over a long period of time can put a strain on the liver, leading to liver disease. Thus, we will be checking your liver function tests at the initiation of therapy and at regular intervals afterward.

2. Blood Clots, Changes in Fat Storage

Taking estrogen increases the risk of blood clots. Blood clots can cause death, lung damage (clot in the lungs), brain damage (stroke), heart attack, or chronic problems with your veins in your legs. The risk of blood clots is MUCH higher if you smoke.

The risk of clots is lowered by

Taking Estrogen by skin patch or under the tongue

Using lower doses of estrogen



Estrogen changes the way your body uses and stores fat. Taking estrogen can increase deposits of fat around your internal organs. This type of fat is associated with an increase risk for diabetes and heart disease. It can also increase your risk of gallstones, which can block your gallbladder. You need to see a medical professional right away if you:

- Have pain in your chest, leg or abdomen
- Have swelling in your legs
- Have a headache with vomiting

3. High Blood Pressure

Estrogen can also cause high blood pressure. We will watch your blood pressure at every visit. Watching your diet, being active and not smoking will all help your blood pressure.

4. Galactorrhea and Prolactinoma

Often, when breasts grow there can be a milky discharge from the nipples. This is called galactorrhea. This is caused by estrogen stimulating the production of the hormone prolactin, which stimulates the breast ducts to make milk. We check levels of prolactin regularly, and especially if you are experiencing galactorrhea, to monitor for very high levels that may indicate a small tumor on the pituitary gland that produces prolactin. This is called a prolactinoma. These lesions are not usually life threatening, but they can cause visual disturbances and headaches. They can be treated medically or, rarely, surgically.

5. Breast Cancer:

It is not known if taking estrogen causes an increased risk of breast cancer. There have been cases of people who have developed breast cancer after hormone therapy for gender affirming care. Your risk of breast cancer is higher if you:

- Have a family history of breast cancer
- Have been taking estrogen or progestin for more than 5 years
- Are 50 years or older
- Are over weight

6. Kidney Health (Spironolactone only)

Spironolactone affects the balance of water and salt in the kidneys. If the amount of water and salt gets out of balance, you can have issues with low blood pressure. Rarely this imbalance can lead to high levels of potassium in the blood, causing changes in heart rhythm that can be life threatening. We will check your blood for potassium levels and kidney function on a regular basis when on Spironolactone.

7. Skin rash

Occasionally the patches for estrogen can be irritating and cause a rash. If this happens, let us know and we can try a different preparation. Spironolactone rarely can cause a rash, and if this happens, we want to hear about it.

**Ok, I want these Hormones. What needs to happen?**

As per the World Professional Association for Transgender Health (WPATH) and Endocrine Society Guidelines, a mental health professional needs to write a letter of readiness for anyone wanting to start HRT. Once we have that letter, here is the typical sequence of events:

1. If you are new to T Clinic, you will have an intake visit with Clancy, our Behavioral Health Clinician. During this visit, Clancy will learn about where you are in your gender journey, and what your goals for treatment are. Once you sign an ROI (Release of Information) she can contact your mental health provider to obtain the letter of readiness. If you have been established with our clinic, and we have the letter of readiness, move on to #2.
2. Appointment with Medical Provider: review of treatment, side effects and timelines, physical exam if indicated
3. Labs will be obtained at first MD visit, a bone age x-ray may be obtained. If the doctor is concerned about your bones, a dexa scan for bone health may be ordered.
4. Once labs come back, and if all looks normal, our RN will call in a prescription for the patch and you can start placing it at home.
5. You will come back to clinic to see the doctor approximately every 3-4 months in the first year, and then every 6 months, at which time we will:
  - a. Ask questions about your overall health
  - b. Check your vital signs (pulse, blood pressure, weight, height)
  - c. Ask about what you are seeing in terms of physical and emotional changes on your treatment
  - d. Ask about signs and symptoms of the side effects mentioned above
  - e. Recommend timing of blood tests and dose adjustments

Resources:

Excellence for Transgender Health

[www.transhealth.ucsf.edu](http://www.transhealth.ucsf.edu)