

Feminizing Gender-Affirming Hormone Care

The Michigan Medicine Approach

Our goal is to partner with you to provide the medical care you need in affirming your gender. Our focus is on your lifelong health, safety, and individual medical and transition-related needs. The Michigan Medicine approach is based on the limited but growing medical evidence surrounding gender-affirming hormone care. Based on the available science, we believe mimicking normal physiology will provide you with the best balance of physical and emotional changes and long-term health. This philosophy aligns with current national and international medical guidelines in the care of gender diverse people. We are committed to staying up-to-date with the latest research and medical evidence to ensure you are getting the highest quality care. We know that there are competing approaches to gender-affirming care that are not based on validated scientific evidence. These approaches make scientifically unsubstantiated claims and have unknown short and long-term risks. We are happy to discuss these with you.

Below are some answers to questions our patients have asked us about gender-affirming hormone care. We hope the Q&A will help you understand the medical evidence behind our approach to your gender-affirming hormone care, and how it may differ from other approaches, including the approach other well-known clinics in Southeast Michigan.

Is there a benefit for monitoring both estrone (E1) and estradiol (E2) levels and aiming for a particular ratio?

There are 3 naturally occurring human estrogens: estrone (E1), estradiol (E2), and estriol (E3). Your body naturally balances your estradiol and estrone ratio.

(this is called: bidirectional equilibrium). Both estrone and estradiol work on your body's estrogen receptors, but estradiol is a much stronger (more potent) estrogen. We follow estradiol laboratory levels, and not estrone levels, in our patients for 3 reasons:

1. Estradiol is a much stronger and meaningful estrogen in achieving feminization.
2. Estradiol and estrone can be converted by your body into one another.
3. Estrone assays are not reliable lab tests.

Our lab approach aligns with the recommendations of the national Endocrine Society (hormone specialists) which recommends monitoring total testosterone and estradiol.

The primary hormone we use for feminizing hormone therapy is estradiol. Estradiol is a human-made hormone that is very similar to the hormones produced by the human body (a bioidentical hormone). We do not use synthetic estrogens, such as ethinyl estradiol which is typically found in birth control pills, because they have an increased risk of blood clots in the lungs and legs.

Is a higher goal estradiol (E2) level safe and helpful in helping me achieve my goals for feminization? Why does Michigan Medicine aim for 100-200 pg/mL?

Our general approach is to gradually increase the estradiol level to be in the female physiologic range, with a goal of achieving this level within 6 months of starting estradiol. As suggested by the National Endocrine Society and World Professional Association of Transgender Health, we aim to achieve levels of estradiol in the blood which are equal to that of a cisgender woman in the middle of the menstrual cycle: 100-200 pg/mL. There is no evidence that higher estradiol levels in patients with adequate testosterone suppression result in additional feminization or breast development but there is evidence that higher levels may cause certain side effects like breast tenderness. There is also a

concern that having high levels of estradiol for an extended period increases the risk for serious complications, including blood clots in the lungs (pulmonary embolism) and legs (venous thromboembolism). These complications can be life-threatening.

What is the most effective way to take estrogen?

Estradiol can be taken in different forms including:

1. Oral - pills you swallow
2. Sublingually - placing the medication under the tongue to dissolve
3. Transdermally - patches on the skin
4. Injection, either intramuscular (in the muscle) or subcutaneous (under the skin)

The goal level of estradiol and testosterone is the same regardless of the form you take it.

The body processes different forms of estrogen differently. For example, oral estradiol is metabolized in the liver earlier than other forms of estradiol, which leads to an increased risk for blood clots. For this reason, different forms of estrogen are preferred for people who have risk factors for blood clots.

I have heard progesterone may be beneficial for its anti-androgenic effects and feminizing effects. Can I add progesterone to my regimen?

There have not been any well-designed studies on the role of progesterone in feminizing hormone regimens. We hope to see more research in this area soon. Some people who have used progesterone as part of their regimen feel it has improved their breast development and/or mood. However, progestones in combination with estrogen may also have negative side effects including depression, weight gain, negative changes related to cholesterol, and an increased risk for cardiovascular disease and breast cancer. There is also a

concern that early progesterone use may result in what is described as “tubular” breast shape.

Since the potential risk appears to be modest (not large), and the benefit is unclear, we think decisions about adding progestones to your regimen should be a shared decision between you and your doctor. It typically takes 2-3 years to reach the maximum effect of estrogen on breast growth, so we typically recommend waiting at least 2 years before considering adding progesterone to your regimen.

Why do Michigan providers typically use spironolactone for testosterone suppression? What other options are available?

Spironolactone is the most commonly used androgen (testosterone) blocker in the US. Spironolactone was developed as a blood pressure medication (you may hear it referred to as a “water pill” or “diuretic”) but also functions to block testosterone production and block testosterone receptors. Possible side effects can include increased thirst, increased urination, and dizziness when going from sitting to standing. These symptoms usually resolve after the first few weeks of taking spironolactone. Very rarely spironolactone increases potassium levels which is one of the reasons we recommend lab monitoring for all our patients. Most people take spironolactone with no significant problems but people with poor kidney function should avoid it.

Finasteride is often the next-best option for people who cannot use spironolactone. Finasteride blocks the action of an enzyme that converts one type of testosterone to a stronger, more potent type. Finasteride is often a good option for people who cannot take spironolactone due to kidney issues.

Possible side effects of finasteride include negative effects on sexual function.

Bicalutamide is an anti-testosterone blocker that was developed as a medication to treat prostate cancer. We try to avoid using bicalutamide because there is a concern that it may lead to severe liver failure that may be life-

threatening. Other side effects include swelling of the legs, pain, and constipation. While such risks are acceptable when considering the benefits of bicalutamide in the management of prostate cancer, they are less justified in gender-affirming treatment, especially since other therapies for blocking testosterone are available for gender-affirming care.

In summary,

We hope the Q&A was helpful to understand the science behind our approach to your gender-affirming hormone care. We aim to help you achieve your gender affirmation goals safely with minimal side effects. If you have more questions, please do not hesitate to ask.

References:

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