Everything You Want to Know About Hormone Replacement Therapy (HRT) in Women

What are the female sex hormones and what are their roles?

Estrogen

Estrogens are a group of hormones that play an important role in growth and reproductive development in a woman (estrone, estradiol, estriol). Estrone (E1) is the main form of estrogen that the body produces after menopause. Estradiol (E2) is the main form of estrogen in the body during the time a woman is able to reproduce, and is the strongest form of estrogen. Estriol (E3) is the main form of estrogen present during pregnancy.¹ The ovaries, which also produce a woman's eggs (ova), are the main source of estrogen from the body. Fat tissue and the adrenal glands, located at the top of each kidney, make small amounts of estrogen as well.

The most common reasons for low estrogen in women are menopause or surgical removal of the ovaries. Men also produce estrogen but in much smaller amounts.

Progesterone

Progesterone is a type of steroid hormone present in both men and women. Like estrogen, progesterone is produced by the ovaries and adrenal glands. It is also produced by the placenta during pregnancy.

The primary function of progesterone in women is to help regulate the menstrual cycle and prepare the body to accept a fertilized egg after ovulation. In pregnancy, progesterone supports the fetus, prepares the breast tissue for breast feeding, and helps to strengthen muscles in the pelvic wall ahead of labor. Progesterone also protects the uterus by balancing the effects of estrogen.

As women age, progesterone, along with estrogen, decreases dramatically.

Testosterone

Testosterone is one of the most abundant hormones in women and is essential to female health. In fact, a woman's body actually produces higher levels of testosterone than estrogen! A drop in testosterone can occur in many women starting as early as 20, with a significant reduction in testosterone production starting around age 35.

Testosterone, along with other "male hormones" (androgens), have an essential role in:

- Libido (interest in sex)
- Vaginal health
- Maintaining muscle mass and an ideal weight
- Regulation of menses
- Fertility
- Strength of bones
- Protection of the breasts

Balancing testosterone can have wide-ranging benefits to a woman's overall health and can be an essential component of preventative medicine. Restoring testosterone to optimal levels can help elevate mood, increase energy levels, improve muscle mass and help manage weight.

How do estrogen levels change throughout life and what are the symptoms of low estrogen?

In women, estrogen levels decrease with age. Hormone levels go down the most in the period just before menopause and during menopause. Menopause typically occurs between the ages of 45 to 55. If a woman has had a radical hysterectomy, in which both ovaries are removed, estrogen levels will decrease significantly. While the adrenal glands and fat tissue produce some estrogen, the amount is usually not sufficient to maintain adequate levels.

Ask any woman who has been through menopause, and you'll quickly recognize the symptoms of low estrogen. These include:

- Menstrual periods that are less frequent or that stop
- Hot flashes (suddenly feeling very warm) and/or night sweats
- Worsening of premenstrual syndrome
- Trouble sleeping
- Fatigue
- Dryness, thinning, and possible irritation of the vaginal walls
- Increased risk of vaginal yeast infections
- Low sexual desire
- Mood swings/ irritability
- Dry skin
- Brain fog
- Weight gain, mainly in the waist, hips, and thighs
- Feeling depressed or anxious

What are the "normal" ranges for sex hormones in women?

Estradiol:

- 30 to 400 pg/mL for premenopausal women
- 0 to 30 pg/mL for postmenopausal women

Testosterone:

• 15 to 70 ng/dL or 0.5 to 2.4 nmol/L

Progesterone:

In women, blood serum progesterone levels can range from as low as <= 0.20 ng/mL to as high as 200+ ng/mL. However, what is considered "normal" can depend on a number of factors including:

- Menstrual cycle phase
- Stage of pregnancy
- Stage of menopause

What are optimal levels of hormones for women?

Let's be honest. You're not interested in normal. You want **optimal hormone levels.** Optimal means the levels of hormones where you feel best, without having any unintended side effects. Although every woman is different, here are some general ranges for where our female patients feel best:

- Optimal estrogen levels: 50 100 pg/mL
- Optimal testosterone levels: 100-300 ng/dL

Typically we don't "optimize" progesterone levels as women feel better with estrogen and testosterone optimization alone. However, if you are post-menopausal and on estrogen replacement, then we may prescribe progesterone to protect your uterus (more to come on that subject).

Wait a minute! Those hormone levels are higher than the lab's normal range. Isn't that dangerous?

This is where traditional medicine fails women unfortunately. We scare women with false information such as:

- Hormone replacement therapy (HRT) after menopause is always dangerous. You need to just live with your hot flashes, weak bones, irritability and weight gain.
- HRT definitely causes strokes, heart attacks, blood clots and cancer.
- Testosterone is a "male hormone" and should never be given to a woman.

False, false and false. Every medical intervention has risks. In the wrong person, aspirin or vitamins can cause significant harm or even death. We think it's important for each of our patients to have an informed, individualized discussion about the benefits and risks of HRT.

In our experience, when we help women optimize their hormone levels, they feel better. If they don't, or have side effects, then we can stop the therapy. If a woman has significant risk factors for serious medical illnesses (e.g. heart disease, breast cancer), then we may opt to hold on HRT and discuss other options.

Telling ALL women that they cannot be on HRT is the real danger.

Well that sounds reasonable. But I'm still scared about HRT. Doesn't HRT cause breast cancer?

That's OK to feel scared. Let's ease your concern about breast cancer. In 2020, the prestigious journal JAMA published an article which reviewed 2 placebo-controlled trials (the best kind of study to answer medical questions because it compares taking a sugar pill or placebo to taking an actual medication) examining this very question: what's the association of estrogen and/or estrogen + progesterone replacement and the frequency of/death from breast cancer?

After following almost 30,000 women for 20 years, the study concluded that **estrogen replacement alone causes a DECREASE IN BREAST CANCER RISK AND MORTALITY.** Read that again if necessary. A DECREASE risk in breast cancer. Not increased risk.

Even in women who were prescribed synthetic progestins (which we never prescribe), there was no difference in the likelihood of death from breast cancer.

Despite this data, our male-centric medical community still wants to rely on misinformation and scare women. We are typically not conspiracy theorists, but this false information is a disservice to women across the world.

Now all that being said, if you have a history of breast cancer, either yourself or within your family, then you may want to avoid estrogen replacement therapy. Don't worry, we can consider other safe options to treat your symptoms.

The use of hormone replacement therapy (HRT) after breast cancer survival remains controversial. No observational or retrospective study of breast cancer survivors has demonstrated an elevated risk of tumor recurrence or increase in mortality associated with use of HRT. However, because each study is retrospective and varies in terms of lymph node involvement, estrogen receptor status of the cancer, and the type of HRT used, a solid judgment on the use of HRT in breast cancer cannot be made.²

Well that makes me feel better. But what role does testosterone replacement have in breast cancer?

Testosterone therapy has been shown to be breast protective in both pre-and post-menopausal women. A study found that testosterone and/or testosterone/estrogen pellet implants significantly reduced the incidence of breast cancer in pre- and post-menopausal women.³

I'm actually not scared of breast cancer. What's the risk of having a heart attack, stroke or blood clots with hormone replacement therapy?

This question is a little bit more difficult to answer due to conflicting "science." One recent <u>randomized study from Denmark</u> followed 1000 women for 10 years who were randomized to HRT or placebo. They concluded that there was **NO INCREASED RISK OF HEART DISEASE, STOKE, BLOOD CLOTS OR DEATH FROM HRT.**

Now there are certainly plenty of studies also showing the opposite results with an increased risk of heart attacks, blood clots or strokes. It's important to point out however that most of these studies only showed an increased risk on women who took **SYNTHETIC PROGESTINS**. At Pazona MD, we NEVER prescribe synthetic progestins (a type of progesterone).

I think the best approach to assessing the cardiovascular risk of HRT is taken by the heart experts, the cardiologists. In 2019 the American College of Cardiology published an expert analysis that makes the following points with which we agree 100%:

- 1. The best approach to HRT is individualized.
- 2. For women with a history of heart attacks, strokes, or blood clots, HRT should be avoided if at all possible.
- 3. For most healthy, active women with a low risk of a cardiovascular event, HRT is an acceptable treatment.

What hormone replacement options do you offer for women?

We offer bioidentical hormone replacement pellet therapy, which is a personalized approach to hormone replacement. It allows the body to absorb the right level of hormones at the right time using a delivery method the body can process efficiently.

Pellets are small capsules (about the size of a grain of rice) that contain bioidentical

hormones, specifically testosterone or estrogen. A bioidentical hormone is the exact molecular structure of hormones the body produces naturally.

The pellets are inserted under the skin of the upper glutes, where hormones enter the bloodstream as they dissolve over several months. Studies show that patients may see the effects of hormone optimization within four weeks after a pellet insertion. Everyone is unique and some people may feel the effects immediately, while others may take up to two or more pellet insertions before they feel full effects.

Hormones delivered by pellet therapy bypass the liver, do not affect clotting factors, do not increase the risk of thrombosis, and avoid the fluctuations of hormone levels some patients may experience.

BioTe bioidentical hormone pellets are made from soy or the yam plant to create estradiol and/or testosterone molecules, unlike synthetic hormones, which are made from animal parts or urine and have a different molecular structure than what the body produces.

What is involved in the pellet insertion process?

First we gather a thorough medical history, including medical conditions, symptoms, and current medications. You will then go to the lab to have blood drawn to measure your hormone levels. Pellet dosage is patient specific and will be calculated based on a number of factors, including age, hormone levels, associated medical conditions, and menstrual status.

During a follow-up visit, you are brought into the exam room, and the insertion site, usually somewhere around the upper buttocks, is numbed and cleaned. A small incision is made, and the hormone pellets are inserted. Afterward, the insertion site is covered with a small bandage. The pellets dissolve over time, and the body absorbs the contents, leaving nothing behind. We will have you go to the lab for another blood draw 5-6 weeks following your first pellet insertion to measure your hormone levels again. We will then have a follow-up appointment to assess how you are feeling 6 weeks following pellet insertion.

Every patient's symptoms are unique, so each journey is customized to fit individual needs. Some patients report seeing improvement in as little as four weeks, but full optimization can take up to six months. Many patients report feeling the benefits after the second insertion.

Is BioTE pellet therapy covered by insurance? What's the cost?

Unfortunately BioTE pellet therapy is not covered by insurance. Pellet insertion costs \$450 per insertion for females.

What happens to the BioTE pellets? Do they need to be removed?

BioTE pellets are slowly absorbed by the body over time and do not need to be removed.

How often do I need to have the BioTE pellets reinserted?

BioTE pellets are inserted on average every 3-4 months for females. The length of time that pellets last depends on a number of factors, such as weight, absorption rates, and the degree of deficiency of the individual at time of insertion.

Do the pellets hurt? What's the recovery from the insertion procedure?

The pellet procedure is not typically painful. The insertion site is numbed using a numbing spray as well as a local anesthetic. It is recommended not to do lower body exercises or other strenuous activity for at least three days following pellet insertion. Walking should not be a problem, but more vigorous activity is not recommended. Hot tubs, bath tubs, and pools should be avoided; but showers are allowed.

You may remove the outer bandage of tegaderm and gauze after 48 hours, and the inner layer of steri strips may fall off on their own or can be removed after 3 days. You may resume normal activity once the bandage is removed.

What are the benefits from testosterone replacement therapy in women?

Testosterone can be a "wonder drug" that no one talks about for women. We have women report the following benefits from testosterone replacement:

Improved libido

• Improves bone health- 3x as powerful at creating new bone than estrogen • Increases lean body mass by improving insulin sensitivity and decreasing visceral body fat, which in turn helps to prevent diabetes and metabolic syndrome

- Improves skin health by increasing collagen and elasticity of skin and improving fullness and structure of skin
- Increases energy, strength, endurance
- Reduces cardiovascular risk—when combined with estradiol or estrogen replacement, lowers cardiovascular risk by reducing LDL and increasing HDL

Is testosterone exclusively a male hormone?

No, men's and women's bodies naturally produce testosterone, and it plays an essential role in women's health similarly to the better-known hormones like estrogen. Balancing testosterone can have the greatest overall effect on a woman's health.

Will testosterone make me more masculine?

No, testosterone does not masculinize women. The doses required to make you "manly" are 10-20x what would normally be given with BioTE pellets. While some women also worry if testosterone will deepen their voice, testosterone administered in the doses recommended in the BioTE method will not deepen or change a woman's voice.

Will I grow a beard on testosterone replacement therapy?

The reality is a tiny percentage (about 2%) of women will experience an increase in midline hair growth (lip, chin, happy trail, etc.) when raising testosterone levels, but it can be rectified with intervention. Laser hair removal or decreasing testosterone dose can decrease unwanted hair growth.

Are the main functions of testosterone in women libido and sex drive?

While many women report a return of libido after optimizing hormones, testosterone is essential for much more than sex drive. Testosterone helps regulate several vital systems that influence mood, energy levels, physical fitness and overall physical and mental health as women age.

Does testosterone cause hair loss?

Less than 1% of women experience hair loss while following BioTE protocols. One study suggests that subcutaneous testosterone therapy, as in pellet treatment, actually positively affects scalp hair growth in females who are treated for low testosterone.⁷ The most common cause of hair loss in women is thyroid deficiency. Fortunately, the BioTE method also optimizes thyroid health to help ensure a whole-body approach to better health. Other medical conditions, medications, and physical and emotional stress can all cause hair loss in women.

If I experience hair loss due to testosterone, what can be done about it?

Topical minoxidil has been found to be the most commonly used treatment in combating hair loss due to hormones. Minoxidil was originally introduced as a medication to treat hypertension, but one of the effects observed was regrowth of hair and excessive hair growth in balding patients. Although it has been used for over thirty years, its effect on hair growth is not fully understood.⁸

Minoxidil is available in 2% and 5% concentration, both of which are available as over-the-counter medications without a prescription required. Minoxidil can have some side effects, such as itching or skin rash, which are uncommon. Other side effects, which are more

rare, include acne at application site, burning feeling of the scalp, growth of facial hair, worsening hair loss, reddened skin, facial swelling, and soreness at the root of the hair follicle.⁹

I know some women on estrogen and testosterone patches, creams, injections, pills, and injections. Do you offer any of those?

Similar to options for males, there are three different options for testosterone therapy in females:

- Injections
- Topical therapies
- Pellets

More so in women than in men, pellet therapy is the preferred option for a number of reasons:

- Consistent testosterone levels
- Safety
- Fewer side effects
- Convenience

What other forms of estrogen do you offer?

We offer a prescription for vaginal estrogen cream in addition to testosterone and estradiol pellets. As women age and their estrogen level decreases, the skin around the vaginal opening can become thinner, which causes dryness, itching, discomfort, and sometimes painful intercourse. Women may also experience urinary urgency, frequency, painful urination, and frequent urinary tract symptoms. Vaginal estrogen cream can help relieve such symptoms.⁴ What about progesterone replacement?

If you still have your uterus, progesterone **MUST BE USED** along with estrogen replacement. Taking estrogen without progesterone can increase the risk for cancer of the endometrium (the lining of the uterus). Cells from the endometrium are shed during menstruation, and if you are no longer having a period, estrogen can lead to an overabundance

of cells in the uterus, which may result in cancer.⁵

Progesterone replacement is typically taken orally, while there are some combination patches that include estrogen and progesterone. The recommended type of progesterone treatment is oral micronized progesterone at a dosage of 200mg/12 days of the month for a cyclic regimen (mimics the normal luteal phase for women who have not gone through menopause yet), or 100mg daily. It is recommended to take progesterone at bedtime, as it can cause drowsiness. Women taking a very low dose of estrogen only need a very small amount of progestin, such as a 12-day course every 6-12 months.⁶

What are some natural ways to support female sex hormone health?

- Protein, zinc, magnesium, B vitamins
- Foods rich in these nutrients:
 - Eggs (protein, vitamin B6, omega-3)
 - Almonds, pumpkin seeds (zinc, magnesium, protein)
 - Leafy green vegetables such as spinach, kale (magnesium, B6, iron)
 - Wild oily fish such as salmon and mackerel (omega-3, protein)
 - Beans such as black, kidney, pinto (protein, zinc, B vitamins, magnesium)

Lifestyle habits play a role in healthy hormone levels as well.¹

- Getting enough uninterrupted SLEEP each night helps the body to produce sufficient levels of hormones for bodily functions.
- Managing STRESS levels also helps to balance hormone levels, as excess stress produces too much of the stress hormones, adrenaline and cortisol. When these levels are too high, estrogen levels can be negatively impacted.
- Getting enough EXERCISE, preferably daily, also helps regulate body fat and sleep habits, which influence estrogen levels.
- Drinking too much ALCOHOL can lead to excess estrogen levels, which can cause cancer over time. Limiting alcohol consumption helps keep estrogen levels in a healthy range.
- Consuming adequate FIBER and healthy fats, such as in nuts, seeds, fish, and olives, and limiting sugar consumption also helps support healthy hormone levels.

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