



Women's Wellness Center  
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## Estrogen and Progesterone Hormone Therapy

- **What to expect when initiating Estrogen and Progesterone?**
- **What are the types of hormone products, and which ones are best?**
- **What is the proper use of hormone prescriptions?**
- **What follow up is necessary when using hormone therapy?**

### Symptom Relief

When you begin using hormone therapy (HT), some of your symptoms will resolve quickly, and some will take a few weeks to resolve. Hot flashes, night sweats, and sleep disturbance will improve within a few days. If these symptoms do not resolve within 2-3 weeks, you likely will need to increase your dose of estrogen. Mood disturbance, foggy thinking, forgetfulness, fatigue, and decreased libido may take a few weeks to improve. After 6-8 weeks, if you do not see improvement, you should be re-evaluated. Your hormone dose may need to be adjusted, or other hormones may need to be added. Vaginal dryness and discomfort can take up to 2-3 months to resolve.

### Side Effects: Usually Minor and Transient, if any.

Estrogen side effects: It is not uncommon to experience breast tenderness and/or mild vaginal bleeding upon initiation of HT. The breasts and uterus have estrogen receptors, so this is to be expected when estrogen is re-introduced after a period of depletion. These side effects might occur after a few days or weeks, and are usually limited to the first few weeks of treatment. If breast tenderness is severe or persistent, you should decrease your estrogen dose, at least for a while. You may cut your patch in half, or use less gel (partial pump instead of whole pump, for example). If bleeding occurs it's a good idea to examine the uterus with pelvic ultrasound to assure that no anatomical problem is present. Upon initiation of HT, some women will experience some fluid weight gain for a few weeks, this usually resolves. HT does *not* cause fatty weight gain.

Progesterone side effects: About 10% of women cannot tolerate oral progesterone. They may experience sleepiness, dizziness, mood depression, or abdominal bloating. The oral route of administration stimulates the liver to produce harmless metabolites, or byproducts, that act on the central nervous system (CNS) to cause sedation. This is a *benefit* for many women, helping them get a good night's sleep, or reducing anxiety. However, some will experience residual sleepiness the next day, or have depression from using oral progesterone. There are other ways to use progesterone (discussed later) that avoid the liver first-pass effect, and therefore do not cause these CNS side effects.

**Important:** Do not alter your dose of progesterone without discussing with your physician. Those who have a uterus must use a minimum amount of progesterone for uterine protection.

## How to Use Your Hormone Therapy (HT)

### ESTROGEN

My preference is to prescribe a transdermal formulation of estrogen, meaning it is absorbed through the skin. An advantage of this method is that the hormone is absorbed directly into the bloodstream, avoiding first-pass through the liver, thus avoiding the increase in blood clot risk and adverse effects on triglycerides known to be associated with oral administration of estrogen. Also, blood levels of the hormone are steady throughout the day and night, avoiding peaks and valleys associated with oral dosing. The following examples of estrogen products may be prescribed for you.

Estrogen patch: *Minivelle* and *Vivelle Dot* are two brand name bioidentical estradiol patches, available in a range of dosages. As of January 2015, there is a high quality generic patch almost identical to *Vivelle* that is more affordable for most insurance plans. The patch should be placed on the lower abdomen and changed twice weekly, providing steady levels of estrogen throughout the day and night. The patch sticks to the skin, even with showering, swimming, or sweating. Rarely, a woman will have skin irritation with the patch adhesive, or will find that it does not stick well on her skin. If this is the case, there are other products available.

**\*\*\* Tip for patch users \*\*\*** With use of the patch some will notice a build-up of adhesive around the edges of the patch, leaving an unsightly ring after removing the patch. This residual adhesive cannot be easily removed with soap and water but *can* be easily removed by rubbing with a cotton ball soaked in baby oil or olive oil. Rub for 30 to 60 seconds to remove all residual adhesive without abrading the skin.

Estrogen Gel: *EstroGel*, *Elestrin*, and *Divigel* are brand names of bioidentical estradiol gels to be used topically. The gel is supplied in a pump dispenser or in foil packets, and should be rubbed into the skin of the inner arm daily. Your dose may be one, two, or three pumps gel per day (or the contents of one foil packet per day).

Estrogen Spray: *Evamist* is the brand name of a bioidentical estradiol spray. It is sprayed onto the soft skin of the inner forearm and dries quickly – no rubbing-in is required. Your dose may be one, two, or three sprays daily.

Estrogen Cream: This can be produced in a compounding pharmacy in any dose needed. The bioidentical estradiol cream is supplied in a specialized dispenser, called a topiclick. The dispenser has a dial on the bottom and a hole in the top, through which a measured dose is delivered when the bottom is twisted. The cream is low volume, non-greasy or smelly, and easy to rub into the arms or legs for daily use.

Estrogen Troches: A *troche* (pronounced “tro-kee”) is a type of oral lozenge, meant to be absorbed directly through the soft tissues of the mouth. Rather than swallowing the dissolving troche, one is intended to lodge it between the cheek and gum and allow it to dissolve slowly into the oral mucosa. This causes the hormone to bypass the liver’s metabolism so it is not like taking a pill (see below under “not optimal” ways to receive estrogen). Using a troche is safe, and it sometimes absorbs more reliably than topical estrogen, but it does not give the steady levels of a topical methods, so often twice daily dosing is required for optimal symptom relief. It is a good solution for those 5% or so of individuals, who do not absorb estrogen through the skin very well.

Vaginal Estrogen: *Vagifem* is a very low dose bioidentical estradiol tablet that is supplied in a pre-filled applicator for intra-vaginal use. It should be used twice weekly. *Estrace* cream is a brand name bioidentical estradiol cream for vaginal use.

**The following three examples of estrogen are not optimal for most of our patients, but may be prescribed in special cases:**

Oral Estrogen (pills): Oral estradiol can sometimes be less costly than brand-name products, but it is not ideal for a number of reasons. Use of oral estrogen slightly increases the risk of blood clots, because metabolism of estrogen stimulates liver production of clotting factors. Liver metabolism of oral estrogens also can cause elevated triglycerides (fat in the blood), elevation of a protein called sex-hormone binding globulin (which can bind to testosterone, thereby contributing to decreased libido), and elevation of C-Reactive Protein (a marker for inflammation in the body). Oral estrogen can also increase the risk of gallbladder disease. None of these risks are incurred when estradiol is absorbed through the skin. However, the risk of these things is small enough to be acceptable for some, if it is the only way possible to get relief of symptoms.

Intramuscular Estrogen (injection): The problem with this method, besides inconvenience of receiving injections every two weeks, is that hormone levels reach very high levels just after the biweekly injection, then drop quite low before the next injection is due. This results in side effects of too much and/or too little hormone at different times in the two-week time frame between injections. Serum hormone tests show peak levels that can be frighteningly elevated - up to 10 or 15 times normal for a **pre-menopause** woman. These high peak levels are sometimes necessary in order for the trough level (just before injection is due) to remain high enough to control symptoms. Overall, this method results in much more than physiologic doses of estrogen being administered. For typical patients, this is not the best choice.

Estrogen Pellets: Estrogen can be administered via small pellets injected beneath the skin at intervals of 3 to 6 months. The concerns are the same as the above description on intramuscular injection. With these methods, hormone levels can be extreme and inconsistent.

## **PROGESTERONE**

History has shown that estrogen therapy (when used alone) can increase risk of uterine cancer by promoting growth and thickening of the uterine lining, so progesterone is needed to oppose these estrogenic effects. Progesterone may also be used for other reasons, independent of uterine protection, thus you may be prescribed progesterone even if you've had a hysterectomy. Oral progesterone is particularly useful for helping you sleep at night. Claims have been made that progesterone protects against breast cancer, however, this is yet to be scientifically proven. Some ongoing studies may shed light on this in the future. There is no study that shows a harmful effect of oral bioidentical progesterone on the breast. That is not necessarily the case for oral *synthetic* progesterone products, known as *progestins*.

There are basically two ways to use progesterone in HT. One is to use a daily dose continuously, and avoid having any cyclic bleeding. This is preferred by most, since periods are a nuisance. However, some women have irregular, or breakthrough bleeding with this regimen. If this is persistent, it may be preferable to use the progesterone in a cyclic fashion, 12 to 14 days per month so a predictable bleed occurs once per month

When progesterone is prescribed for a woman who is using estrogen replacement, it is important to use at least the minimum dose required to protect the uterus. While progesterone skin creams can be useful for treatment of certain symptoms, absorption through the skin is limited, so blood levels do not reach concentrations adequate for uterine protection, thus we cannot recommend these creams as the only source of progesterone if a woman using estrogen still has her uterus. Similarly, bioidentical progesterone is not available as a patch because it is poorly absorbed through the skin. The following examples are choices of progesterone considered adequate for uterine protection.

Oral Progesterone: *Prometrium* is the brand name of a bioidentical progesterone that is supplied in a small oil-filled capsule to be taken by mouth. *Prometrium* contains progesterone in peanut oil. *If*

you are allergic to peanuts you should not use this product. In such cases a compounding pharmacy can prepare a progesterone pill that contains no peanut oil. *Prometrium* is best taken at night, since it can cause sleepiness, a side effect that can be quite beneficial for some.

Vaginal Progesterone: Progesterone gel or cream can be supplied as vaginal suppositories or in convenient single-use, pre-filled syringe applicators to be applied vaginally. This dosing route allows the progesterone to be absorbed directly into the bloodstream, bypassing liver, so side effects such as sedation or depression may be eliminated.

Intrauterine Progestin: Another choice for obtaining the progesterone without systemic side effects is the *Mirena Intrauterine System*. This is an intrauterine device (IUD) that contains a progestin called levonorgestrel. The progestin is continuously released into the uterus and acts locally on the uterine lining to oppose estrogen's effects of thickening the uterine lining. Only very small amounts of progestin may enter the circulation, so it is not considered a systemic progestin treatment, and therefore it is not likely to cause any progestin-related side effects or risk. This product simplifies life for those who cannot tolerate oral progesterone and find it inconvenient to use a vaginal gel. The Mirena IUD can remain in place for several years of use.

### **Monitoring and Follow-up**

After initiation of HT, typically a 2-3 month follow-up visit is recommended to assess symptom relief and side effects. Many women require two or more follow-up visits to adjust hormone dosage before satisfaction is achieved. After that, yearly visits are usually sufficient. Blood tests are sometimes indicated, but not always. If testosterone or thyroid medication is given, blood levels are important. Some sources claim that saliva testing is a good way to monitor hormone levels, but there is no scientific data to support this practice in monitoring ovarian hormone levels. The best indicator that you are using the correct dose of estrogen and progesterone is that your symptoms are controlled and you have no side effects.

### **If you are using topical hormones, please note:**

1. If you are using any cream, gel, or spray hormone product on your arms and then blood levels are tested, the blood specimen can become contaminated with some of the product from your skin. Therefore, please have blood drawn from the opposite arm, or use hormone product on your legs the day of the blood test.
2. Topical hormones can transfer to other people (rubbing the arm) or pets (licking the arm). This is particularly important to remember if you care for a small child, infant, or pet because they can actually absorb enough from your arms to affect their small bodies. If this is a possibility, you may choose to wear long sleeves, or use the topical hormone product on your legs – inner thighs and behind knees are acceptable locations.

Updated March 2016, Laura Grant, MD, FACOG, NCMP

***For a more in-depth discussion of peri-menopause, risks and benefits associated with the use of hormone therapy, the controversy surrounding it, and to determine whether hormone therapy may be right for you, please refer to Peri-menopause and Hormone Health, available on our website at***

***[www.womenswellnessnow.com](http://www.womenswellnessnow.com).***