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Estrogen and Progesterone

HOW TO TAKE IT, WHICH ONE TO CHOOSE

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Deciding whether or not to use Hormone Therapy (HT) is a big decision and should be made with input from your healthcare provider. After the decision has been made to take HT, many women don't realize there are still two more important decisions left to make: 1) which HT regimen and 2) which specific estrogen and/or progesterone formulation to use.

Choosing a Hormone Regimen

Today there are four options for combining estrogen and progesterone. One causes monthly bleeding and two are intended to eliminate bleeding all together. The fourth regimen is a new and may reduce the risk of breast cancer, which I'll explain below. These four regimens differ by the type of estrogen and progesterone used, and by the dosing pattern of the progesterone choice. They are called **sequential, continuous combined, intermittent** and **occasional**.

Table 1

The Four Ways of Taking Estrogen and Progesterone[1]

ESTROGEN = Days of estrogen PROGESTERONE = Days of progesterone

Sequential	PROGESTERONE*PROGEST ESTROGEN*ESTROGEN*ESTROGEN*ESTROGEN*E
Continuous Combined	PROGESTERONE*PROGESTERONE*PROGESTERON ESTROGEN*ESTROGEN*ESTROGEN*ESTROGEN*E
Daily ESTROGEN/ Intermittent PROG (3 days on, 3 days off)	PROG PROG PROG PROG ESTROGEN*ESTROGEN*ESTROGEN*ESTROGEN*E
Daily ESTROGEN/ Occasional PROG (12 days per 3 – 6 months)	PROG PROG ESTROGEN*ESTROGEN_ _ _ESTROGEN*ESTROGEN

Days of the Month

The sequential regimen has been used for the longest amount of time and is designed to mimic what happens during a natural menstrual cycle. Estrogen is given every day and progesterone is added for the last 10 to 14 days of each month of treatment. This hormone pattern is similar to a natural menstrual cycle and its affect on the uterine lining is why women have menstrual cycles. This regimen will cause predictable bleeding within days after the last progesterone dose that resembles a normal period, although it may be lighter. This method is similar to many birth control pills and prevents pregnancy as well as provides HT. You are *not* ovulating even though you are having monthly bleeding.

The continuous-combined regimen uses a daily regimen of both estrogen and progesterone throughout the month. If your goal is to eventually eliminate bleeding all together, this is a good method to try. It keeps the uterine lining thin so that after a few months to one year of treatment, bleeding is greatly reduced or eliminated. It is much more likely to stop bleeding if you are a few years into perimenopause rather than just starting it.

The newest regimens are intermittent. These methods use a lower total amount of progesterone. As its name implies, the first intermittent regimen alternates 3 days of estrogen alone with 3 days of estrogen and progesterone. It is based on a theory that during the estrogen only days, the uterine lining becomes more sensitized to progesterone. So adding progesterone for only a short time at a low dose can cause the uterine lining to become thin.[2] Time will tell if this method is comparable or superior to the combined-continuous regimen or if patients will like it better.

The latest intermittent dose regimen really came into use after an April 2011 article that found women who take only estrogen and not progesterone have a 23% lower risk of breast cancer.[3] Women who don't have a uterus do not have to take progesterone.

The catch-22 is that if a woman has a uterus and takes estrogen, she must also take progesterone to lower her risk of getting uterine cancer. So to make sure that women who have a uterus and who take estrogen have the lowest risk of breast cancer and also a lower risk of uterine cancer, this new regimen gives progesterone for only about 12 days every 3 to 6 months instead of every month. That makes a lot of sense and hopefully will make it safer for more women to take estrogen. To hear my video discussion on this article, go to www.DoctorSeibel.com/menopause.

HT Formulations in the United States

After deciding which HT regimen to take, there is still one more decision – which HT formulation. There are five oral preparations that combine estrogen and progesterone into one pill, and two combination HT skin patches available in the United States.

Table 2

Oral Estrogen and Progestin Combinations in the US

Trade Name	Regimen	Estrogen Dose	Progestin Dose
COMBINED PILLS			
Activella™	Combined continuous	1 mg 17β-estradiol ($17\beta E_2$)	0.5mg norethindrone acetate (NETA)
FemHRT®	Combined continuous	5 μg ethinyl estradiol (EE)	1.0mg NETA
ORTHO-PREFEST®	Intermittent	1 mg 17β-estradiol ($17\beta E_2$)	90 μg norgestimate (NGM) 3 days off, 3 days on
PREMPRO™	Combined continuous	0.625 mg conjugated estrogens (CEE)	2.5 or 5mg medroxyprogesterone acetate (MPA)
PREMPHASE™	Sequential	0.625 mg CEE daily	5mg MPA days 15-28
COMBINED PATCHES			
Climara-Pro once per week	Combined continuous	4.4 mg estradiol; 0.045 mg/day	1.39 mg Levonorgestrel; 0.015 mg/day
Combipatch (in 2 sizes; 2 / week	Combined continuous	0.62 mg Estradiol; 0.05 mg/day	2.7 or 4.8 mg Norethindrone acetate; 0.14 or 0.25 mg/day

All of these medications contain both estrogen and progestins. Progestins are hormones that *act like* progesterone in the body but are not technically progesterone. That is why they are called progestins. These hormones are not bio-identical (see below) either. It is also possible to use Premarin or other estrogens in combination with bio-identical progesterone and create an individualized estrogen/progesterone regimen.

In addition to these pharmaceutical preparations, there has been a lot of attention given to bio-identical hormones. Bio-identical means that their chemical structure is identical to what is biologically made in the body. They are not "natural;" they are made in pharmaceutical plants rather than squeezed out of botanical plants. Some are compounded to include ratios of the body's three principle estrogens (estrone or E1, estradiol or E2, and estriol or E3) in ratios that are typically found in women. The commonest brand is *Tri-Estrogen* or *Tri-Est* for short because it contains E1, E2 and E3. Tri-Est was developed in the early 1980s by Jonathan Wright, MD and contains 80% estriol, 10% estradiol and 10% estrone. A similar product called Bi-Est contains E2 and E3. Bi-Est contains 80% E3 and 20% E. These estrogens are usually available only in compounding drug stores and not the traditional chain drug stores.[4] They are available as capsules, topical creams and gels, sublingual drops, vaginal creams, suppositories, and lozenges. They do not come as a patch.

Pharmaceutical companies also make bio-identical estrogen and progesterone (see below). It is the type of estrogen that usually comes in the patches sold in traditional drugstore chains. Because estradiol cannot be patented, the actual patch is what makes each product unique. Patches differ in how they stick to the surface of your skin and how the estrogen inside them is absorbed into your body. Although the medicine is exactly the same, some work better than others for different individuals because of each patch's technology and differences in people's skin. The most common examples of estradiol only patches are Vivelle Dot and Climara. Estradiol is also produced by pharmaceutical companies in other forms listed in Table 3:

Table 3

Pharmaceutical Preparations of Bio-identical Estradiol

Estrogen Type	How Taken	How Prepared	Examples
Estradiol	Transdermal	Patch	Vivelle Dot, Climara, etc…
Estradiol	Transdermal	Gel	Estrogel
Estradiol	Transdermal	Lotion	Estrasorb
Estradiol	Transdermal	Spray	Evamist
Estradiol	Oral	Tablet	Estrace, Gynodiol, etc…
Estradiol	Vaginal	Ring	Femring

Intravaginal Estrogen

Many women think that vaginal estrogen stays only in the vagina. In fact, many vaginal estrogens are well absorbed into the bloodstream, though some less than others. Women who are having a particular problem with upset stomach taking estrogen find vaginal creams a big improvement. In addition to Tri-Est mentioned above, several other intravaginal estrogens are also available (see Table 4 below). Estrace, Premarin or Dienestrol vaginal creams and Estring can all be substituted for oral estrogen. Because they are absorbed through the vagina and not through the intestinal tract, the liver does not metabolize them. So the actual amount available to your body is even greater than if you took the same dosage orally. That's why the dosages and preparations are often different. To know how much you are absorbing, it is necessary to

measure estradiol levels in your blood to be certain that the amount you are given is in the therapeutic range. In addition to the vaginal creams, there is also a vaginal gel tablet (Vagifem) and an estrogen ring (Estring Vaginal Ring):

Table 4: Types of Vaginal Estrogen

Brand	**Estrogen**	**Content**
Ogen	Estropipate (purified estrone)	1.5 mg/gm
Premarin	Conjugated equine estrogens	0.3 mg (green), 0.45 mg (blue), 0.625 mg (maroon), 0.9 mg (white), 1.25 mg (yellow)
Estrace	Estradiol	0.1 mg/gm
Ortho Dienestrol	Dienestrol	0.01 mg/gm
Vagifem vaginal gel tab	Estradiol hemihydrate	10 & 25 mcg = 10 & 25 micrograms of estradiol; daily x 14 days then twice weekly
Estring vaginal ring	Estradiol	2 mg per ring releases 7.5 micrograms/24 hrs for 90 days

Progesterone and Progestins

Progesterone is the hormone of ovulation. It gets its name from "pro gestation" because after ovulation it prepares the lining of the uterus to receive a fertilized egg and to help sustain the pregnancy. In addition to its role in reproduction, progesterone also keeps the menstrual cycle regular and normal, and balances estrogen's potential negative effects on the body. Progesterone also plays a role in protecting the uterus from developing cancer, increases HDL or "good" cholesterol, improves the breakdown of fat into energy and cuts the body's craving for carbohydrates and sweets. In fact, progesterone deficiency is commonly a cause of PMS symptoms and painful, lumpy breasts.[5]

Bio-identical progesterone is available in compounding drugstores with a doctor's directions on a prescription. The same progesterone is available in chain drug stores as a gel cap (Prometrium 100 mg or 200 mg) or a vaginal gel (Crinone 4% or 8%).

Sometimes bio-identical progesterone is confused with the synthetic class of hormones called progestins or progestogens. These are patented, chemically modified molecules that act similar to progesterone in the body. They are also responsible for many of the side effects attributed to progesterone. There are two main types of progestins: 1) Provera (medroxyprogesterone acetate) and similar generic products are chemical alterations of the progesterone molecule and are called 17 – OH or hydroxyprogesterones; and 2) a chemical alteration of testosterone called 19 – nortestosterones.

As you can see, there are many things to consider when deciding on a HT treatment plan. The information in this eBook provides basic information to help you make an informed decision. You can find more detailed information on menopause and its treatments in my eBook *Doctor Seibel's Menopause Handbook*.

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