

Hormone Therapy

*Important information from Women's Health America
for you and your health care provider*

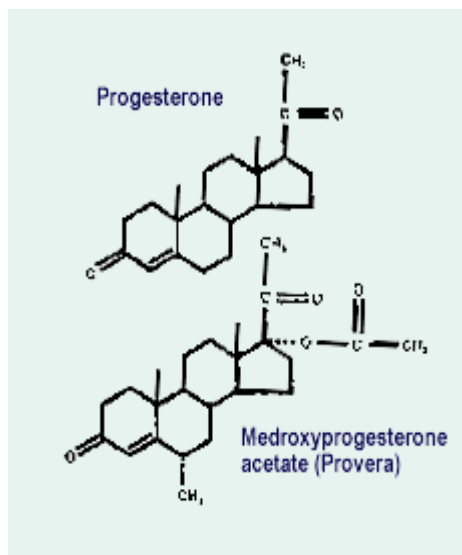
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What is the Difference Between Natural and Synthetic Hormones?

The term "*natural*" can be confusing when used in connection with hormones.



You can see that the synthetic hormone medroxyprogesterone acetate, commonly known as Provera® (bottom), has a different chemical structure than natural progesterone (top).

When we say a hormone is "natural," we are referring to the molecules that make up the structure of the hormone. A natural hormone has a chemical structure that is identical to the hormone naturally produced by the body, which is why natural hormones are also called "bioidentical" hormones.

A "natural" hormone does not mean that it is an organic product purchased in a health food store. In fact, many "natural" hormones are synthesized in laboratories using pharmaceutical-grade products. The important thing to remember is that, for a hormone to be considered "natural," its structure must replicate exactly the structure of hormones your body produces.

A "synthetic" hormone, on the other hand, may have a structure similar to, but not exactly the same as, a hormone produced by your body. These chemical differences, however, can mean that the synthetic hormone acts differently in your body and produces substantially different effects. "Natural" and "synthetic" hormones should not be considered the same or used interchangeably.

Because of these differences, it should not be assumed that the results of studies using synthetic hormones, like the Women's Health Initiative, also apply to natural (bioidentical) hormones.



HT -- The Right Regimen for You

You've discussed your symptoms and risk factors with your doctor, you've done some research, and you've decided you would like to try hormone therapy (HT).¹ Before you take any pills, apply patches, or rub in creams, you need the answers to some questions: What should you take, how much should you take, and when should you take it?

What to take

While there is no set combination or dosage of hormones that works for every woman, an HT regimen may commonly include a combination of:

- a form of estrogen
- a form of progesterone
- and, if needed, an androgen such as testosterone

The estrogens: Not all alike

While we tend to think of estrogen's relationship to our reproductive function first, this hormone actually nourishes and protects our bodies in hundreds of ways, from our hearts, to our bones, to our skin and hair. In the uterus, estrogen causes the lining (endometrium) to thicken and build up each month until it is sloughed as a menstrual period.

"Estrogen" is often used as a general term, but it is actually a category of hormones. Of the many types of estrogen our bodies make, these are the three produced in major amounts:

- Estradiol is the most potent form of estrogen, and the one produced in the largest amounts by a woman's ovaries before menopause. Estradiol levels fall after menopause. The brand names Estrace®, Estraderm®, Vivelle®, Alora®, FemPatch®, Estring®, and Climara® contain natural estradiol.
- Estrone is the predominant estrogen in a woman's body after menopause. When ovarian function declines, the fat cells in a woman's body take over the role of synthesizing estrone. Premarin® and Ogen® contain estrone (Premarin® also contains other estrogens derived from the urine of pregnant horses).
- Estriol is known as the "weak" or "forgotten" estrogen. Produced in large amounts by the placenta during pregnancy, estriol is also converted in small amounts by the liver. Estriol is not commercially available in the U.S., but must be compounded by a pharmacist.

You have a variety of estrogen preparations to choose from. Commonly prescribed natural estrogens include:

- Estraderm® (transdermal skin patch)
- Estring® (vaginal ring)
- Climara® (transdermal skin patch)

- Vivelle® (transdermal skin patch)
- FemPatch® (transdermal skin patch)
- Estrace® (oral tablet, vaginal cream)
- Ogen® (oral tablet, vaginal cream)
- Premarin® (oral tablet)
- And specially compounded estrogens like BiEst or Tri-Est that combine the natural estrogens: estradiol, estrone, and estriol.

When taken alone as a medication, estrogen can cause the cells in the uterine lining to become crowded or malformed. Progesterone, on the other hand, controls that effect, protecting you from endometrial abnormalities. You can choose between synthetic forms of progesterone, called progestins, and natural progesterone (progesterone USP), which must be compounded by a pharmacist.²

Arriving at the right HT formulation for you can take some time and adjustment. For many women, 1 mg Estrace® is a good starting dosage of estrogen. Dosages of progesterone will vary depending on the type of progesterone you are taking, and whether you are on a continuous or cyclical regimen (see below).

If the initial HT dose gives you uncomfortable side effects or doesn't alleviate your symptoms, your doctor can adjust the dose, try a different form of estrogen, or use natural progesterone instead of synthetic progestin, depending on your individual situation.

Patch, pill, or cream?

In choosing the form of hormone therapy that is best for you, there are several factors you will want to consider, including which symptoms are most important for you to manage.

Because the level of heart and bone protection differs with various forms of HT, your individual profile and family history of these conditions may come into play. Some women value convenience very highly, and choose a form of HT that is easiest for them to remember how and when to take. Finally, some women weigh the costs of various forms, and factor that into their decision.

Points you may want to keep in mind in deciding between oral (taken by mouth), transdermal (skin) patch, transdermal (skin) cream, or vaginal cream estrogen:

- The skin patch may be a good choice for you if your triglyceride levels are abnormally high. Transdermal estrogen enters the body through the skin and does not raise triglyceride levels. Oral estrogen appears to increase triglyceride levels somewhat because it passes through the liver.
- The adhesive on the estrogen skin patch sometimes causes skin irritation and the patch is more expensive than oral estrogen.
- Estrogen in cream form is very effective in treating urinary and vaginal problems. (Premarin®, Estrace®, and Ogen® are commercially available as vaginal creams; the "weak" estrogen, estriol, while not commercially available, can be compounded as a cream or suppository by a pharmacist.)
- Vaginal estrogen creams may not protect against heart disease or bone loss.

Natural hormone options

When we say "natural" hormone, we mean chemically identical to the hormones produced in your body. That's the key difference between the synthetic progestins and natural progesterone, for example. The synthetic progestins (Provera® is a commonly-prescribed synthetic progestin) are similar to the progesterone your body produces, but the subtle chemical differences can significantly influence the hormone's action and side effects in the body. Synthetic progestins can cause side effects of irritability, nausea, depression, and water retention in some women. Natural progesterone is identical to the hormone made in the body, and many women find it easier to tolerate.

Many women call Women's Health America and the consulting pharmacists at Madison Pharmacy Associates to ask if there is a "natural estrogen" they can take with their natural progesterone. They are often surprised to learn that commercially manufactured and frequently prescribed forms of estrogen (Estrace® and Estraderm® for example) are "natural" estrogens. Choosing among estradiol, estrone (both potent forms of estrogen), and estriol (the weaker estrogen) is a decision best made based on the specific symptoms that need to be managed.

For instance, estriol, the "weak" estrogen, has been used to manage vaginal dryness, urinary infections, hot flashes, and stress incontinence. The fact that estriol is "weak" has pluses and minuses. Estriol does not provide as much heart and bone protection as other more potent estrogens like estradiol and estrone. But it has little or no effect for most women on breast or uterine tissue when used in low doses, so estriol avoids the risk of breast or uterine cell abnormalities associated with estradiol and estrone.

Unlike estradiol or estrone, estriol can be taken alone, without progesterone, because it has no effect on the uterine lining. A woman, who has no family history of heart disease or osteoporosis, has cholesterol levels and bone density levels within normal ranges but who suffers from vaginal dryness and/or incontinence and hot flashes, may be a good candidate for estriol.

Women who are taking the hormone testosterone to alleviate lack of sex drive also have the option of taking the natural form of this hormone. Natural testosterone is not commercially available and must be compounded by a pharmacist. The section on "Checking Testosterone" tells more about how to decide if testosterone may be helpful for you.

When to take it

If you're taking HT, you can choose between two types of regimens: cyclical and continuous combined.

Taking HT cyclically, which is recommended for women still cycling, mimics a menstrual pattern: you take progesterone for days 14-28 of a 28-day cycle; estrogen (if needed) days 1-21; and testosterone (if needed) daily. When you finish taking progesterone each month, you experience bleeding as your body "withdraws" from the hormone progesterone, and the endometrial lining sloughs away.

Continuous combined therapy, in which women take estrogen and progesterone every day, is recommended for women who are no longer having menstrual cycles. It eliminates the breakthrough bleeding after some initial spotting in the first one to three months. Women also experience fewer side effects with this regimen.

Evaluating your choices

Whatever HT regimen you choose, be aware of two very important points, says Dr. Wulf H. Utian:

- 1) The therapy must be evaluated at least annually by both you and your doctor, sooner if you experience side effects or problems. No hormone therapy should ever be considered permanent, although you may be taking the hormones indefinitely.
- 2) No single hormone "recipe" exists that will fit every woman. The first regimen you try may not work for you, but don't give up. Your doctor should fine-tune your hormone regimen to your individual needs, your risk factors, your symptoms before and during therapy, and your lifestyle.

The consulting pharmacists at Madison Pharmacy Associates routinely work with women and their health care providers to individualize HT regimens, and are available to advise you. Health care providers may call 800.558.7046 for a comprehensive consultation with a pharmacist.

¹ Some women should not take estrogen: women who have had breast or uterine cancer; women with chronic blood-clotting problems, unexplained vaginal bleeding, or serious gall bladder or liver disease; or women who are or might be pregnant.

² Women's Health America, Madison Pharmacy Associates, Inc. specializes in compounding natural hormones.

³ "More reasons than ever for HT," T.L. Bush, R.D. Gambrell, Jr., and V. Miller, Patient Care, Nov. 15, 1993, pp. 103-132.



HT Objective Measures: Your Evaluation Checklist

This checklist can help you and your doctor evaluate your hormone therapy (HT).

- 1) Before starting HT, get a "baseline" hormone profile – a blood or saliva test to measure your:
 - **FSH** (Follicle stimulating hormone – tells whether you have reached menopause; also helps show whether HT is absorbed by the body. Blood test only.)
 - **Estradiol** (The most active estrogen – replacement levels should be greater than 60 pg/ml to protect against bone loss; for optimal benefit and well-being, levels should be 100-200 ng/dl when measured in blood; 0.5-10.0 pg/ml when measured in saliva.)
 - **Progesterone** (5-15 ng/dl in blood; 0.1-0.5 pg/ml in saliva. Progesterone is measured during the second half of the menstrual cycle.)
 - **Testosterone** (Normal levels for women are between 30-50 ng/dl in blood; 10-50 pg/ml in saliva.)
- 2) After starting HT, write down how you feel, side effects, etc.
- 3) Four to eight weeks after starting HT, retest your hormone levels, as above. Thereafter, a yearly evaluation will let you and your doctor know if your hormone levels are within normal ranges.



The FDA and North American Menopause Society agree — hormone therapy should be “individualized” and “low-dose”

Since the Women’s Health Initiative Study was halted prematurely in July 2002, women, health care providers, and health organizations have scrambled to understand what the study results mean for the future of hormone therapy.

Individualized, Low-Dose Therapy

Recent statements by The North American Menopause Society (NAMS), American College of Obstetricians and Gynecologists, and Food and Drug Administration (FDA) caution against overreacting to results of this single study and indicate hormone replacement is still a viable option to consider, however, they advise clinicians to evaluate the risks and benefits for each individual patient and prescribe customized HT, using the lowest effective dose.

“Use the lowest effective dose’ has always been a simple, yet important principle of clinical medicine,” says Professor Leon Speroff, M.D., Ph.D., a recognized expert in women’s health care. “In the wake of the announcements from the Women’s Health Initiative, this axiom has never been more attractive.”

Dr. Mark McClellan, M.D., Ph.D., Commissioner of the FDA agrees. “Our recommendation is that if you choose to use hormone therapy...take the lowest dose for the least duration required to provide relief.” The NAMS 2003 position statement regarding hormone replacement in peri- and postmenopausal women echoes the same concepts, adding that a complete health evaluation and “individual risk profile is essential for every woman contemplating any regimen of EPT or ET.”

Is Low-Dose As Effective?

The Women’s Health, Osteoporosis, Progestin, Estrogen (Women’s HOPE) Study conducted in 2,673 postmenopausal women with an intact uterus, average age 53.3, indicates that low-dose HT is as effective at the standard doses usually prescribed. The study compared the standard daily dose of estrogens (0.625 mg of CEE) with a ¾ dose and ½ dose with and without a progestin. Two of the combined regimens used a lower-than-standard progestin dose (1.5 mg MPA).

Women’s HOPE Study results showed lower-than-standard HT doses:

- Are effective in relieving vasomotor symptoms.
- Are associated with reduced incidence of endometrial bleeding, a side effect that commonly leads to patient dissatisfaction and discontinuation.
- Are effective in maintaining bone density.
- Show the same positive lipid changes associated with standard doses, though the overall impact of HT on clinical cardiovascular outcomes has yet to be resolved.



Getting Started with Individualized HT

Individualized, low-dose HT is the wave of the future, but it is new for many health care providers. Fortunately Women's Health America, Inc. (WHA) has successfully used this approach for more than twenty years. WHA's well-established RestoreSM program takes the guesswork out of prescribing and provides all the tools and expertise for patient case management.

The RestoreSM Program



The Women's Health America **RestoreSM program** integrates the very latest in leading laboratory technology and pharmaceutical science with traditional values in health care: listening to patients and responding to their individual needs. It's medicine for this millennium – where patients are treated as individuals and practitioners can use this new technology to return to the art of patient care. In the wake of the controversy over hormone therapy, this approach is more important than ever.

"The Restore program from Women's Health America provides customized dosing for individual patients, merging the patient clinical needs with supporting laboratory data. It's the future of hormone therapy." - **Claude Hughes, M.D., Ph.D., Consulting Professor, Department of Obstetrics & Gynecology, Duke University Medical Center**

RestoreSM Consists of Three Components

- 1) **Analytical measurement** of saliva to determine hormone levels, and of urine to measure rate of bone loss.
- 2) **Customized prescriptions** specific to each patient's results and medical history, always taking into account that each person produces, metabolizes, absorbs, and responds to hormones differently. Our pharmacists use pure, pharmaceutical-grade products to hand-prepare each prescription. These natural hormones (*derived from soy*) are biologically identical to what the body produces.
- 3) **Ongoing case management** provided to the health care provider and patients (when prescriptions are ordered through Women's Health America, Madison Pharmacy Associates, Inc.). Pharmacists and nursing staff will assist the health care provider in evaluating and adjusting the plan of care to attain optimal therapeutic outcomes.

The RestoreSM Process

- 1) The health care provider completes and signs the Restore enrollment form and returns it to Women's Health America.
- 2) A Women's Health America Restore program consultant contacts the patient to:
 - Explain the program and how to test correctly.
 - Verify payment and shipping information.
- 3) The patient receives the test kit with instructions for testing and mailing.

- 4) The patient collects samples according to enclosed instructions, completes the health history form included with test kit, and returns the kit to the lab.
- 5) The Women's Health America laboratory processes the samples and produces results for the nursing staff.
- 6) A Women's Health America nurse receives and evaluates results. The results and a letter with considerations for the patient's individualized therapy are faxed to the health care provider.
- 7) The patient is notified that results have been faxed and it is time to follow up with her or his health care provider.
- 8) The health care provider discusses the test results and suggestions with the patient.
- 9) The health care provider calls/faxes prescription(s) to Women's Health America, Madison Pharmacy Associates, Inc.
- 10) The patient is contacted for prescription insurance information and shipping.
- 11) A Restore case manager provides ongoing consultation and monitoring through follow-up testing at 30-60 days after beginning HT, six months, and annually.



RestoreSM Testing to Measure Hormone Levels and Bone Loss

Restore testing uses saliva and urine testing to evaluate hormone levels and rate of bone breakdown.

"Saliva testing to determine hormone levels means we can get good baseline information," says Marla Ahlgrimm, R.Ph. "The baseline sheds light on which hormones a woman needs, and how much. Through Restore testing, women of perimenopausal age can also learn if they need to take steps to prevent bone loss, or osteoporosis."

How does saliva testing differ from blood testing of hormones?

When we test hormone levels in the body, we want to know how much of the hormone is available to work for us. This is the available, or "free," form of the hormone. Saliva contains only the free form of our hormones, so it is an excellent way to look at levels. Blood tests, on the other hand, measure both the free and inactive, or "bound," form of hormones. The bound form of hormones cannot get into cells to do its work. Blood tests don't always distinguish between free and bound forms of hormones, so the results of a blood test are less precise than saliva testing.

"The convenience of Restore testing is another plus," says Ms. Ahlgrimm. "You simply collect saliva and urine samples using the test kit we mail to you. Mail the samples back to the lab for evaluation in the mailer provided, and your doctor receives results in a few weeks." Restore testing results can be used to determine the correct hormonal balance for your body. The consulting pharmacists at Madison Pharmacy Associates are available to work with your doctor to develop any hormonal medications you may need.

Bone markers such as the NTx bone loss analysis are essential

Though many believe osteoporosis is part of the normal aging process, this is not true. Younger generations, due to lifestyle and diet, are putting themselves at a larger risk than the generations that went before them.

The Restore (NTx) bone loss test is an affordable and economic test that can be used to help assess individuals who will receive the greatest long-term skeletal benefit from hormonal antiresorptive therapy and determine the probability for a decrease in bone mass in postmenopausal individuals if they do not initiate HT. The NTx bone loss test may also be used to monitor response to antiresorptive therapy in postmenopausal individuals as well as those diagnosed with or at risk for osteoporosis. In as soon as three months, NTx can determine the effect of an antiresorptive therapy on bone resorption, providing vital information to help health care professionals counsel individuals on the effect of antiresorptive therapy on bone resorption and encourage patient compliance and continuation of therapy. Compared to the one to two years required for BMD testing, you can understand why bone marker technology plays such an essential role in patient management. BMD testing simply is not enough.



About Women's Health America

Since the first woman suffering from hormone imbalance walked through our doors almost thirty years ago, our mission has been one thing and one thing only – to provide women with options for good health, quality of life, and healthy aging by supporting hormonal balance – one woman at a time.

Women's Health America was the first in the United States to:

- Identify PMS.
- Use natural progesterone therapy to treat PMS.
- Educate women about self-care diet, lifestyle and supplementation options for hormone management, creating a *continuum of care* that starts with self-care and includes prescriptive therapy only when needed.
- Recognize and use a case management approach for identifying and managing an individual woman's transitions in hormone levels that occur over time.
- Pair diagnostic testing with hormone therapy, introducing the concept of individualized treatment and paving the way for the current trend toward lowest effective dose.
- Develop innovative dosage forms for natural hormone medication (such as the sustained release oral tablet).
- Create a free educational resource for women including a toll-free women's health information line and monthly newsletter.

Our Products and Services

SELF-CARE FORMULATIONS: Hormonal balance starts with self-care. Our proprietary formulas, designed specifically for women, include ProCycle™ nutritional formulas, RestoreSM BioBalance personal care, and DermaFex™ therapeutic skin care. We also offer a full line of nutritional supplements and other unique products.

INDIVIDUALLY COMPOUNDED PRESCRIPTIONS: Our specialized pharmacy can fill any prescription including oral capsules, sublingual tablets, topical gels and creams, and patches. We specialize in customized, low-dose hormone therapy using only natural (bioidentical) hormones. Women's Health America is the only compounding pharmacy in America that tests each prescription using sensitive HPLC (liquid chromatography) to eliminate over- or under-dosing.

RESTORESM MANAGEMENT AND MONITORING: Our innovative Restore program brings together a team of registered nurses and our in-house nurse practitioner, health educator, and registered pharmacists to work with patients and health care providers in monitoring and successfully managing even the most challenging cases of hormone imbalance.

RESTORESM TESTING AND SCREENING: Our full-service laboratory performs testing processes in-house, from measuring baseline hormone levels to assessing rate of bone loss using the sensitive NTx test with results returned to the health care provider.

EDUCATION: Women's Health America provides the most current women's health care information through website articles, online mini-courses, and a monthly electronic newsletter. Marla Ahlgrimm, R.Ph., is available to answer your specific questions online at Ask Marla. Our online Health Library has many articles of interest and our Book Store carries recommended books, including *The HT Solution* and *Self-Help for Premenstrual Syndrome*, co-authored by our founder, Marla Ahlgrimm, R.Ph. Visit us at www.womenshealth.com.

CUSTOMER SERVICE AND RESTORESM HEALTH EDUCATION: Expert Customer Service Representatives and Restore Health Educators are available to answer questions and assist you in ordering. No question is too big or too small – we'll always help you find the answer.



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