



Get the Facts



Benefits and Risks of Hormone
Therapy for Menopausal Women



THE HORMONE
FOUNDATION



What is menopause?

Menopause is the time of life when a woman's menstrual periods stop as levels of certain hormones in her body decrease. Hormones are substances formed in a body organ called a gland and carried in the bloodstream to another organ or tissue where they have a specific effect. Estrogen and progesterone are the primary female hormones that drop to low levels during menopause, causing monthly periods eventually to stop.

Many women experience symptoms such as hot flashes and vaginal dryness during this time of life. Hormone therapy (HT) is a good way for women to relieve many of these symptoms but, as with all medical treatments, HT is not without risks. Some women, for example, may be unable to take HT because of their health history.

This brochure is designed to help you learn about HT options and their associated benefits and risks, as well as alternative therapies that may help you manage symptoms during menopause. You will want to discuss the many options you read about in this brochure with your doctor.

Managing menopausal symptoms can be challenging because each individual is different, with a unique medical background and family history to consider. Throughout this brochure we share the personal stories of seven women, each with a distinct set of circumstances, who are approaching this period of their lives in somewhat different ways. Perhaps the choices of one of these women and her doctor will be helpful to you as you navigate your own very individual menopausal journey.

Menopausal management is an evolving field with new data emerging almost every day. Just a few years ago, for example, HT was prescribed to menopausal women in part to help prevent heart and bone disease. The results of a major study called the Women Health Initiative (WHI), however, triggered a shift in the way doctors think about menopause management. Now, HT is mainly prescribed to relieve symptoms.

The Women's Health Initiative

One of the biggest health stories in the past decade broke when a major clinical trial — The Women's Health Initiative — ended prematurely because of unexpected findings. (A clinical trial is a medical study that evaluates new drugs or treatments.) The WHI was a long-term national study that focused on strategies for preventing heart disease, hip fracture, and breast and colon cancer in postmenopausal women. The project included more than 27,000 healthy postmenopausal women 50 to 79 years of age. This is the largest U.S. study involving the use of hormone therapy for menopausal women to date.

The trial comprised two separate components — an estrogen-plus-progestin arm and an estrogen-alone arm.

In the first arm of the study, doctors wanted to see whether estrogen plus progestin (a synthetic progesterone) would protect a woman's heart and bone health and help prevent certain forms of cancer. Progestin was added to estrogen to prevent overgrowth of the uterine lining in women with a uterus.

In the second arm, doctors looked at estrogen alone to see if it would protect a woman's heart and bone and help to prevent certain forms of cancer. Estrogen-alone therapy was given to women who had hysterectomies, because women without a uterus do not need progestin.

Each trial had a control group — women who received a placebo, which is an inactive sugar pill. The women taking hormones then were compared with women taking placebo pills. Neither group could choose or knew which treatment they received.

Both of these trials were halted early, in 2002 and 2004, respectively, because the risks exceeded the benefits. There was a higher risk of strokes and blood clots in both studies — as well as an increased risk of breast cancer in the combined (estrogen plus progestin) hormone therapy study. The benefits of hormone therapy were not enough to justify hormone use for the average woman, unless she had significant menopausal symptoms.

Currently, women's health care providers agree with the recommendations of the U.S. Food and Drug Administration (FDA) that symptomatic women should take the lowest dose of HT that relieves their symptoms, for the shortest period of time possible.

This brochure presents information and examples that explain the issues and complexities of deciding which therapy may be best for you. You do not need to make a lifelong commitment to any one therapy. Instead, talk with your doctor about the kind of therapy you want to try. If one approach does not seem to help, or you experience side effects, ask questions and consider something else.

What happens to hormones during menopause?

Hormones are powerful chemical messengers that travel throughout the body to direct specific life-sustaining processes. One of the key hormones for women is estrogen. Estrogen controls growth of the uterine lining during the first part of the menstrual cycle, causes changes in the breasts during adolescence and pregnancy, and regulates various other metabolic processes, including bone growth and cholesterol levels.

At different times in your life, you may have any of three forms of estrogen circulating in your blood. Estradiol is naturally present in premenopausal women and increases during pregnancy. Estrone is the main estrogen in women's bodies after menopause. Estriol is a weaker form of estrogen produced as estrone and estradiol are metabolized in the body.

Progesterone is the hormone that prepares the lining of the uterus to receive and sustain a fertilized egg and, therefore, permits pregnancy.

The changes of menopause begin when your ovaries stop producing eggs, along with estrogen and progesterone. Low levels of these sex hormones will trigger an end to your monthly menstrual period and cause other changes as well. In the United States, menopause typically occurs at about age 51. The transition into menopause, however, may take anywhere from one to 10 years, beginning for some women even in their 30s.

How do I know if I'm starting to go through menopause?

Early in your menopausal transition, your estrogen levels can rise sharply and then plummet. Because of these widely fluctuating levels of hormones, you may skip periods or have a heavier flow than usual some months. Your doctor needs to rule out the possibility of benign growths called fibroids or the rare possibility of uterine cancer if you are bleeding heavily.

At the same time, more frequent bleeding is not unusual during this transition. Your periods may become increasingly irregular and then, eventually, stop altogether. A woman can still become pregnant during this transitional period. Menopause usually occurs gradually over time but may occur prematurely because of the removal of both ovaries, radiation or chemotherapy, other gland disorders, or poor health.

What symptoms might I encounter during menopause?

As estrogen drops to very low levels, your body may respond in several ways:

- You may have hot flashes, which can make your face red and cause a sudden sensation of body warmth.
- Your sleep may be interrupted by night sweats or you may not sleep as soundly as you used to.
- Your vaginal tissues may become thinner, which can cause vaginal dryness, itching, and pain during sexual intercourse.

- Your bones may become thinner and lose calcium, which can lead to spine fractures later in life, or even a curved spine, sometimes called a “dowager’s hump.” Thinning bones can also cause hip fractures, a major cause of hospitalization and even death in older women.
- You may experience mood swings, some memory loss, irritability, depression, or a general lack of well-being.
- The cholesterol level in your bloodstream may increase.

You may experience other symptoms too. If you are not feeling well, ask your doctor if your complaints could be related to menopause. There are many approaches to treating symptoms. A careful assessment of your options and treatment goals can lead the way to prompt relief and put you back in control.

Anita: Two years ago, I had a hysterectomy because I had large fibroid tumors and heavy bleeding. I wanted to keep my ovaries so I wouldn't go into menopause, since I was only 37. Over the last few months I've been pretty moody, which isn't like me. I also sometimes feel warm around my face and neck, but I don't think they're hot flashes — I'm too young for menopause. I wonder if I'm depressed.



Comment: Development and growth of uterine fibroids is common in the years leading up to menopause as estrogen levels can, at times, be higher than before the menopause transition started. While the hysterectomy relieved the problem of heavy bleeding, Anita is probably still having some hormonal fluxes that may be contributing to mood changes and episodes that sound like hot flashes. While she is indeed young, we know that symptoms of the menopause transition can occur in women as early as their 30s.

Anita might benefit from a measurement of the pituitary hormone, follicle stimulating hormone (FSH), to check on her ovarian function. (FSH levels rise as the ovaries stop working.) Her symptoms may improve with estrogen therapy. She does not need a progestin since she has no uterus. Anita's doctor should keep an eye on her mood to evaluate her for depression, if necessary. Depression is more common during the menopause transition than afterwards, and estrogen alone is not a sufficient treatment for depression, although it might help antidepressant medications work more efficiently.

How will I know when my menopause transition is over and I'm postmenopausal?

There is no simple test to tell you that your menopausal transition is over and you have reached menopause. Only after your periods have stopped completely for a year are you considered to be postmenopausal. At this stage, you are very unlikely to get pregnant naturally. Menopausal symptoms usually do not stop after a woman reaches this point but, for many women, they will slowly subside as estrogen stays at a consistent, although low level. For other women, symptoms may continue for months or even years after menstrual periods stop.

What is the role of hormones in symptom relief?

By far, estrogen is the most studied and most effective of the hormone therapies for relieving troubling menopausal symptoms. Progesterone or progestins may be used with estrogen to protect the uterus, or alone to treat specific symptoms. Other hormones that may be helpful in some circumstances, but that are not yet FDA approved for menopause treatment, include testosterone and dehydroepiandrosterone (DHEA).

FDA-approved hormones for women

- **ESTROGEN** has been used by millions of women for more than 60 years to effectively relieve many of the symptoms of menopause. One form of “bioidentical” estrogen (so called because it is identical to the hormone produced naturally by your ovaries) is estradiol. Other preparations include conjugated equine estrogens (a formula containing several types of estrogen), estrone, and synthetic estrogens.
- **PROGESTINS** include bioidentical progesterone and synthetic progestins. Progestins are prescribed along with estrogen as a combination therapy to prevent uterine cancer only in women who have a uterus. While estrogen is highly effective in relieving menopausal symptoms, it can increase the risk of uterine cancer if taken alone. A progestin may also be used to control heavy or irregular bleeding, which is a common temporary problem during a woman’s menopausal transition.

Other hormones under consideration by the FDA

- **TESTOSTERONE** is present in all females in small amounts, and is produced in larger amounts in males. Studies comparing combination oral testosterone–estrogen with estrogen alone found improvements in sexual arousal in menopausal women. Bioidentical testosterone patches have also been tested and found to be effective but are not yet FDA approved or available for prescription. The long-term risks of taking testosterone are currently being studied in large clinical trials.
Side effects may include acne, weight gain, unhealthy changes in cholesterol levels, enlargement of the clitoris, and an increase in hair growth, sometimes leading to male-pattern hair growth in a woman. Mood or personality changes such as aggressiveness or hostility may also occur. Some of these side effects may be irreversible, but appear to be rare in doses appropriate for women.
- **DHEA** is made from cholesterol by the adrenal glands (two small glands in the abdomen) and is converted by the body into testosterone and estrogen. Research data are inconsistent and the effectiveness and safety of DHEA for healthy women remain unclear. Currently, it is only available for people with adrenal gland insufficiency.

What do I need to know about bioidentical hormones?

Bioidentical hormones are natural or synthetic hormones that have the same chemical structure as hormones produced by the human body. There are two general classes of bioidentical hormones. The first class consists of pharmaceutical products approved by the FDA and available by prescription only. FDA-approved bioidentical hormones are monitored for dosage and purity, and come with package inserts providing important FDA-mandated safety information.

A second class is custom-mixed (compounded) formulas, prepared for an individual by a compounding pharmacy. Although the individual ingredients may be FDA approved, these custom-mixed formulas are not. Compounded hormones are supposedly tailored to a woman’s individual hormonal needs based on a saliva test. However, saliva testing has not been proven to be a reliable measure of blood hormone levels.

When many people think of bioidentical hormones, they think of these compounded products. Custom-mixed doses of hormones are not tested for purity, potency, effectiveness, or safety. They do not require the same safety information package inserts for patients that FDA preparations must provide. The exact composition of the preparation cannot be verified for custom-mixed hormones. Although compounded hormones have been touted as being more “natural,” there is no evidence that they are safer or more effective than FDA-approved hormone products. In fact, they may pose a risk to women.

Tri-estrogen cream is of particular concern to many physicians (and the FDA) because it includes estriol, a form of estrogen that has not been FDA approved for any use. Another concern is inconsistency in the content of compounded formulas from batch to batch. In each batch, there could be too much or too little hormone. Too much estrogen can cause vision and thinking disturbances, excessive bleeding, breast pain, and more serious conditions in the long term. Large-scale scientific studies on these combinations of hormones have not yet been done. So the medical community is appropriately concerned.

The Endocrine Society – the world’s largest and most influential professional society of physicians and researchers who specialize in hormone science – issued a Position Statement recommending against the use of compounded bioidentical hormones. They call for FDA regulation of this treatment, because hormones should be considered medications and not supplements. In October 2006, the Society wrote: “Claims about these hormones being superior to laboratory-manufactured hormones are not supported by scientific data. Further, post-market surveys of compounded hormone preparations have uncovered inconsistencies in dose and quality.”

This position statement has been adopted by the American Medical Association and endorsed by the North American Menopause Society.

Jackie: Over the last six months, I've been getting more and more irritable and have slept poorly, waking up sweating at night. I recently skipped two periods and I'm the right age for menopause — 47. I want relief of my symptoms but I'm worried about using hormone therapy, since my mother and maternal aunt both had breast cancer at a young age. I've had a couple of breast biopsies, which were negative, but I'm still concerned that hormone therapy might increase the odds that I'll develop breast cancer in the future.



Comment: Jackie's situation illustrates the dilemma that clinicians face when their patients have clear-cut symptoms related to their menopause transition, but who also have some compelling reasons to be wary of estrogen therapy. It's possible that Jackie has a genetic mutation linked to breast cancer, which would put her at high risk for this disease. Because of her strong family history and her concerns, she may want to seek genetic counseling and testing.

Jackie may also be a candidate for tamoxifen or raloxifene, medications used to prevent breast cancer. These treatments, however, are likely to make her hot flashes worse.

The best first step in Jackie's treatment is a careful and accurate assessment, with her doctor, of the potential risks and benefits of HT. A very short-term course of hormones may be appropriate for immediate control of her symptoms. As a long-term option, however, non-hormonal methods are probably safest for Jackie. If lifestyle changes do not provide enough relief, she may want to try gabapentin or a selective serotonin reuptake inhibitor (SSRI) or serotonin norepinephrine reuptake inhibitor (SNRI) antidepressant to improve her sleep.

What does the Women's Health Initiative tell us about the risks and benefits of hormone therapy?

Each woman is a unique individual, so each woman has her own risk and benefit profile. However, doctors have a clearer picture of the overall risks involved in HT as a result of the WHI study (see table on page 7).

When this study began in the 1990s, the combination of estrogen and progestin was the most commonly prescribed menopausal therapy for women with a uterus. The typical daily dose was 0.625 mg conjugated equine estrogen, along with 2.5 mg medroxyprogesterone acetate (a progestin). This combination therapy effectively helped women manage troublesome symptoms of menopause while protecting the uterus.

Many in the medical community believed that HT also offered protection from certain health problems of aging, such as heart attacks, hip fractures, and colon cancer. Before the WHI study, the benefits of HT appeared to outweigh the risks. As the results of the study became known, women and doctors across the country reevaluated their choice of HT.

Estrogen-plus-progestin risks and benefits

The estrogen-plus-progestin trial was stopped in 2002 after 5.6 years of follow-up when investigators found that the risk of breast cancer, coronary heart disease (heart attacks caused by narrowing of the small blood vessels that supply blood and oxygen to the heart),

strokes, and blood clots outweighed the benefits of hormones in preventing fractures and reducing colon cancer.

An individual woman's risk of developing breast cancer was relatively small, about 8 cases per 10,000 women who took hormones for one year. In further analysis, the risk of breast cancer did not appear to increase until after three years of combined therapy. However, because of the huge numbers of women who could potentially use HT, the total number of women who might develop breast cancer was significant. For this reason, the investigators discontinued the trial and published their findings early. The WHI concluded that estrogen plus progestin should no longer be prescribed to women after menopause for preventing chronic diseases of aging.

Estrogen-alone risks and benefits

The estrogen-alone study was stopped in 2004 after an average of 7.1 years of follow-up because there appeared to be an increased risk of strokes and no benefit to heart health. These findings were also published early. Unlike the combined therapy study, however, the estrogen-alone study found no increase in risk of breast cancer or heart attacks. Further analysis confirmed that women with prior hysterectomy do not have an increased risk of breast cancer for at least seven years after starting estrogen-alone therapy.

Because of the overall findings that health risks exceeded benefits in both of these clinical trials, the use of HT is now generally recommended only for short-term relief of symptoms.

The WHI balanced the risks and benefits for disease prevention only — it was not designed to look at symptom relief. For women with symptoms, however, HT has added benefit that might change the balance in favor of hormones.

Facts from the Women's Health Initiative

If 10,000 postmenopausal women age 50 to 54 years took hormone therapy for one year, these would be the numbers of cases of different outcomes:

Risks	ESTROGEN and PROGESTERONE	ESTROGEN alone
Cardiovascular disease	2.6 more cases	No change
Stroke	2.0 more cases	2.0 more cases
Pulmonary embolus (blood clot in the lungs)	4.5 more cases	No change
Breast cancer	9.3 more cases	No change
Colon cancer	1.8 fewer cases	No change
Hip fractures	1.0 fewer case	1.2 fewer cases
Total events per 10,000 women for one year	15.6 more cases	0.8 more cases

SOURCE: Grady D. Clinical practice. Management of menopausal symptoms. *New England Journal of Medicine*, 2006;355(22):2338-47.

What are the limitations of the Women's Health Initiative study?

The WHI study was limited to measuring risks for heart disease, stroke, blood clots, hip fracture, and breast and colon cancer. It did not address whether hormone replacement would help relieve hot flashes or vaginal dryness, which can be intense and troubling to women. The WHI study was not designed to evaluate the risks and benefits of HT in women under age 50.

Keisha: I've been having severe hot flashes, along with spotty periods, even though I'm only 39. I'd like to take hormones to relieve those intense hot flashes, but I know blood clots are a possible side effect of hormone therapy. That concerns me because I was recently treated for a blood clot in my lower leg. You see, my job takes me on long flights around the world and I don't find much time to exercise, which makes it more likely I'll get another clot.



Comments: At age 39, Keisha is more than 10 years younger than the youngest woman in the WHI study, so its results may not apply to her. She is also just shy of age 40, before which the onset of menopause is considered premature, so her symptoms might be related to other medical conditions.

We know that the risk of blood clots increases with age. At her age, Keisha may not be at a very high risk of blood clots. However, since she has already had one blood clot, she's much more likely to have another than someone who has never had a blood clot.

It is also possible that Keisha carries a family gene that puts her at increased risk for blood clots. While she can be screened for some inherited syndromes, others have not been identified. If other family members have had an unprovoked blood clot or clots, Keisha may not be a candidate for HT at all, especially because of the increased risk of blood clots on long airplane flights. Given her severe symptoms, it is unlikely that she will get relief through lifestyle changes alone. Keisha may want to consider a non-hormonal alternative, such as gabapentin or an SSRI or SNRI medication, to provide short-term relief.

How do the risks differ for menopausal women in their 50s vs. women over 60?

The women in the WHI study were 50 to 79 years old, with an average age of 63, so the findings more directly relate to older postmenopausal women. In general, the older a woman is, the greater the overall risk. The evidence is becoming clearer that women over age 60 should probably not start HT because their risk of stroke starts to climb at this age. In women over 70, the risk of heart attack also increases.

Young women who start HT within five years of menopause may have more benefits with less risk. Among the 3,310 women in the estrogen-only arm of the WHI study who

were age 50 to 59 when the trial began, those taking estrogen were no more likely to have a heart attack or die of heart disease than those taking a placebo, or sugar pill. Researchers even suggested that the risk for heart disease in this group might have been slightly reduced. (There was a very small risk in women taking estrogen plus progestin.)

The other risks of HT, such as blood clots, stroke, and breast cancer, do not seem to be reduced by starting hormones early, however. In fact, a woman who starts HT close to the time of menopause might have a higher risk of breast cancer if she takes hormones for many years. These complexities make it important for a woman to consult her physician and arrive at a careful, individualized assessment of risks and benefits.

Do the results of the WHI apply to women who have premature menopause in their 30s and 40s?

Strictly speaking, the results of the WHI do not apply to women in their 30s and 40s. Symptoms are often worse in women who have menopause in this age group. The risks of developing osteoporosis and fractures also are greater with many years of life ahead after the onset of early menopause. The benefits of HT in women with premature menopause seem to outweigh the risks, and these women can probably safely take hormones until the average age of menopause (around 51), when they can reassess their treatment.

If my body naturally produces estrogen throughout my many childbearing years, why is it that replacing estrogen when levels drop during menopause may be a health risk? I find it puzzling that a hormone that is safe as a young adult becomes worrisome when I am menopausal. Can you explain the biology?

It's mostly about aging. As we age, our blood vessels get more and more plaque — so-called hardening of the arteries. When we are younger and we have less plaque, estrogen keeps the blood vessels limber, and this helps prevent heart attacks. However, with further aging, the plaque in our arteries becomes more complex and prone to clotting. This seems to be when estrogen, our former friend, becomes an enemy and can increase the clotting, leading to an increased risk of strokes and heart attacks.

When it comes to breast cancer risk, the answer is slightly different. Prior to menopause, all women are bathed in estrogen and progesterone from the time they go through puberty. The cycles of estrogen alternating with progesterone take their toll on women, who have a greater overall risk of breast cancer than men because they are exposed to cyclical hormones for many years. After menopause, women no longer have much estrogen and progesterone circulating in their bloodstreams. When the estrogen/progesterone state of a woman's reproductive years is artificially continued into her menopausal years, this increases her breast cancer risk when compared to women who became menopausal but who did not take any hormones.

Carol: I went to my doctor recently because I was having mood swings, crying a lot, and having what I thought were panic attacks. This started happening after I had six rounds of chemotherapy. It was my second cancer — I had a mastectomy for breast cancer seven years ago. My periods stopped after this latest chemo, but it didn't occur to me that it might be menopause since I'm just 37. I knew I wasn't pregnant since I had a tubal ligation after my second daughter was born. My doctor did a blood test that showed I was in menopause, and after asking me more about my panic attacks, told me they were actually hot flashes.



Comment: Carol's case clearly illustrates the very challenging situation of chemotherapy-induced ovarian failure. Though women are more susceptible to the effects of chemotherapy at older ages, depending upon the type, dose, and duration of chemotherapy, the ovaries can fail at any age. Because she had so many other concerns with her breast cancer, Carol did not notice the absence of menstrual cycles, and menopause was the farthest thing from her mind.

What is the best approach? Considering her history of breast cancer, Carol should not use HT because of concerns that estrogen and progesterone will contribute to the growth of breast cancer cells. SSRI antidepressant medications have been shown to provide symptom relief in women with breast cancer. They are not quite as effective at reducing hot flashes as estrogen, but still provide a significant improvement. Research suggests that some SSRIs may interfere with the actions of tamoxifen, so Carol should check with her oncologist.

What are the risks of hormone therapy for women over 80?

Women over 80 years of age also are not covered by the WHI study. Some interesting studies suggest that their risks may be somewhat different. Specifically, very low dose estrogen (about 1/2 the dose used in the WHI), when reintroduced to women in their 80s, has a protective effect on bone. In the small studies completed to date, very low doses of transdermal (absorbed through the skin) estrogen do not seem to have the same risks of blood clots and stroke as does oral HT given to younger menopausal women. But these studies included far fewer women than the WHI did and we can't say for certain that these low doses are safer.

Who should not take hormone therapy?

Certain women probably should not take estrogen, either alone or in combination with progesterin. These women include those who are or think they might be pregnant, have unexplained bleeding from the uterus, or have a history of breast or other hormone-sensitive cancer such as ovarian or endometrial cancer. Women with liver disease, history of blood clots, heart disease, stroke, or blood vessel disease should also — generally speaking — avoid hormones to relieve their menopause symptoms. If you have migraine headaches and experience symptoms such as slurred speech, visual field cuts, or trouble moving an arm or leg, you should carefully discuss the risks and benefits of HT with your doctors.

How many ways are there to take hormones?

Women have a choice of ways to take hormones to relieve menopausal symptoms. Discussing your personal medical history and all of the choices with your doctor will help you get the best therapy.

Systemic treatments

Systemic treatments affect the whole body system.

- **PILLS** taken orally can help relieve symptoms such as hot flashes and protect against vaginal thinning and bone loss. Pills are easy to remember to take in simple daily doses. Estrogen and combination estrogen-progestin pills are now available in lower doses than the pills used in the WHI. Many women have opted to take lower dose pills to minimize their risk.
- **TRANSDERMAL ESTROGEN** skin patches are easy to use and provide relief of symptoms, too. New research shows that an estrogen patch that delivers 14 micrograms per day (compared to 50 or more in most full-dose estrogen patches) also provides bone benefit in older women. A combination patch provides both estrogen and progesterin. Estrogen is also available as a gel applied to and absorbed through the skin.
- **A VAGINAL ESTROGEN RING** releases enough estrogen to reduce symptoms such as hot flashes and to prevent loss of bone. If you have your uterus, you will need to take some sort of progesterin to counter the effects of the estrogen on your uterus.

Local treatments

Another way to take hormones is by way of local vaginal treatment, which gets the hormone more directly to where it is needed. Local treatments include vaginal tablets, creams, a low-dose estrogen ring, and a progesterone-secreting intrauterine device.

Lynn: I can't sleep well at night and I wake up sweating all the time. Sometimes I feel like I can't think as quickly and clearly as usual. I'm thinking about hormone therapy but at 5 feet and 180 pounds, I'm afraid my extra weight could cause heart or other problems if I take hormones. I've been eating right, walking, and exercising at the gym so I've lost 20 pounds, but I still have about 80 pounds to lose. I plan to keep working toward a healthy weight but I don't know if hormone therapy is safe for me right now.



Comment: Lynn is clearly on the right track as increased body weight is known to increase menopausal symptoms, particularly hot flashes. Her night sweats may continue to improve with weight loss alone, but if this is not enough, some lifestyle changes may help to improve her sleep. If she still needs medication for relief, hormones are an option, unless they are inadvisable for some other health problem. Given that excess weight increases the risk of blood clots, a transdermal patch or gel might be a better choice than pills, although this has not been proven conclusively.

- **ESTROGEN CREAMS** are applied into the vagina with an applicator. While the creams can be very effective in improving vaginal dryness, estrogen absorption into the rest of the body might be more likely with creams than with other vaginal estrogens.
- **VAGINAL ESTROGEN TABLETS** are usually used daily for the first several weeks of therapy. After that, most women find their symptoms are still improved with use just a couple of times per week.
- **A LOWER-DOSE VAGINAL ESTROGEN RING** can be inserted in the vagina to target tissues directly and fight vaginal dryness and thinness. Some women experience tender breasts the first week of the ring and may have vaginal discharge that looks like a yeast infection. The amount of estrogen absorbed into the body is low and actually decreases with each new ring (usually replaced every three months) as the vaginal tissues become healthier. It is okay to have intercourse with the ring in place.
- **AN INTRAUTERINE PROGESTIN SYSTEM (IUS)** may help a woman who has heavy bleeding. The system releases progestin automatically from the device directly into the uterus. This device is very much like an intrauterine device inserted to prevent pregnancy. Only very rarely do women experience side effects from the hormone. The biggest drawback of the IUS is that it causes persistent spotting in about 15 percent of women who use it.
- **A VAGINAL PROGESTERONE GEL** concentrates effects on the uterus rather than the entire body.

prescription medications, botanicals, mind/body techniques, and diet and exercise.

A major scientific review of non-hormonal therapies found that they are generally less effective than estrogen. Non-hormonal treatments may also have some unwanted side effects. There are large differences between individuals in how they respond to medications, however. One woman may find relief from a non-prescription remedy that does not improve symptoms in another. Always let your doctor know if you are taking an over-the-counter remedy.

June: I had my last period three years ago at age 51. Because I'm small (5'1" and 95 pounds) and postmenopausal, I was concerned about bone loss, so I recently had a DEXA bone scan. Unfortunately, it showed that I'm already losing calcium from my bones, and the doctor told me I'm at high risk for osteoporosis. I'm wondering if I should take estrogen to treat my bone loss and also relieve another problem I'm having – vaginal dryness. That's really bothering me because I'm in a new relationship and vaginal lubricants just aren't working for me.



Comment: Findings from the WHI show that women like June did not get enough bone protecting benefit from hormones to outweigh the potential risk for strokes, blood clots, or breast cancer. Since June is experiencing vaginal menopausal symptoms, she would be a good candidate for vaginal estrogen, given as a ring, vaginal insert, or cream. The dose can be reduced to as low a dose as provides relief, and is often considerably less than what systemic HT supplies.

For improved bone health, June should first evaluate her lifestyle for any changes she could make, such as getting enough calcium in her diet, exercising more, and stopping smoking. Her doctor might want to evaluate her for any other condition that might contribute to her low bone mineral density. This would include checking her thyroid function, blood calcium and phosphate levels, total blood count, kidney function, and vitamin D level. If everything is in order, June might want to consider taking a bone-sparing drug like a bisphosphonate or raloxifene.

Other prescription medications

While non-hormonal prescription drugs have been used to treat hot flashes, they are not FDA approved for this use. Some of these drugs may be approved for hot flashes in the near future, however. Their use is supported by scientific studies.

- **SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIs) AND SEROTONIN NOREPINEPHRINE REUPTAKE INHIBITORS (SNRIs)** are antidepressants that typically are used to help mood disorders. Women taking these drugs also have fewer hot flashes. SSRIs and SNRIs can reduce sexual desire and prevent orgasm, both of which are reversible upon discontinuing the drug. Some of these medications may reduce the effectiveness of tamoxifen, a drug used to treat breast cancer or to prevent breast cancer in women at high risk. If you have had breast cancer and are taking tamoxifen, be sure your oncologist helps you select the best SSRI or SNRI for you.

Is transdermal estrogen safer than estrogen taken by mouth?

Many physicians believe transdermal estrogen may be safer for women than pills. This is because the transdermal estrogen bypasses the liver, so it may not induce the same level of clotting factors that oral hormones induce. Few clinical trials have provided enough evidence about safety, but preliminary findings from small clinical trials are promising. About 10 percent of women experience rashes or other side effects, however, so these patches are not for everyone.

What are the alternatives if I can't or don't want to take hormone therapy?

The unexpected results of the WHI study in 2002 led to increased fear about hormone use among menopausal women and their physicians. Many women stopped taking HT, only to find that their symptoms came back. As a result, women and their doctors began looking for alternate ways to treat menopausal symptoms. Alternative therapies include other

- **GABAPENTIN** is a medication approved for treating seizures and some types of nerve-related pain. One new study found that gabapentin is as effective as estrogen in reducing hot flashes when given in large doses. Side effects can include sleepiness, dizziness, nausea, leg swelling, and balance problems.
- **CLONIDINE**, a blood pressure medication, may reduce the frequency of hot flashes. This medication may cause dizziness, tiredness, dry mouth, and constipation. For many women, the side effects are not worth the improvement in hot flashes. The transdermal clonidine patch may have fewer side effects than the pill.

Botanicals

Many women use non-drug therapies such as treatments derived from plants. Scientific studies to date have found no clear and consistent evidence that they are effective, and new studies are underway. In general, the study of botanicals is difficult because the amount of active substances in plants is inconsistent and unreliable, making scientific measurement difficult.

- **BLACK COHOSH** is the most studied of the plant-based therapies. It helps to relieve hot flashes according to some studies, but other studies show no overall effect. Some doctors support the temporary use of black cohosh for treating menopausal symptoms, because it appears to be safe when used for six months or less. Rarely, it causes liver toxicity, so as always, check with your doctor.
- **PHYTOESTROGENS** (also called isoflavones) are chemicals produced by plants such as soy that act like estrogens in our bodies. Several studies of soy extracts suggest they may help to relieve hot flashes, but most studies did not show a benefit. Little information is available about short- or long-term side effects of isoflavone supplements. Women with estrogen-dependent cancers (including most types of breast cancer) should not take phytoestrogens.
- **OTHER BOTANICAL PRODUCTS** for menopause have not shown clear proof of usefulness. If you want to try these products, be sure to tell your doctor, because they may interact in harmful ways with prescription drugs. Some of the botanicals women try for symptom relief include the following:
 - **Dong quai** root is used widely for many symptoms, but may not be effective for hot flashes. Women taking warfarin, a blood thinner, should avoid dong quai root because it can lead to excessive bleeding.
 - **Kava** may help reduce anxiety, but there is no evidence that it reduces hot flashes. Kava may be dangerous to the liver. The FDA has issued a warning to patients and health care providers about potential harm.
 - **Ginseng** may help improve well-being, moodiness, and sleep disorders, but it does not appear to lessen hot flashes.
 - **Valerian** may help with sleep disturbances. It can cause mild side effects such as headaches, dizziness, upset stomach, and tiredness the morning after its use.

Maureen: Five months ago, at age 47, I had an emergency hysterectomy, and my ovaries were removed too. Since then, I've been having severe hot flashes. I don't sleep well either and I often feel tired. I want to get rid of the hot flashes, but I'd rather use natural remedies.



Comment: Severe hot flashes are not uncommon after the removal of the ovaries prior to menopause. Maureen's hot flashes may continue to be severe, or may subside over time. She may find temporary relief by keeping the room about five degrees cooler than usual, layering her clothes, and avoiding caffeine and alcohol. Paced respiration exercises also may help. If these measures are unsuccessful, some studies suggest that vitamin E (400 IU/day), black cohosh, or soy isoflavones may improve hot flashes somewhat. None of these agents have been proven safe for long-term use, however. Maureen should be followed by a doctor while she is taking these sorts of therapies, because they may have unexpected side effects.

Non-botanical supplements

Studies on the use of other supplements for the treatment of menopausal symptoms are limited, and the effects of long-term use are not known. Tell your doctor if you are taking either of these supplements.

- **VITAMIN E** may have a modest effect in relieving hot flashes in some women, although study results are inconsistent.
- **MELATONIN** is a hormone produced in the brain that helps regulate sleep and wake cycles. Melatonin supplements may help in falling asleep and staying asleep.

Mind/body therapies

Many mind/body therapies are based on Asian medicine, most of which have not been studied using conventional Western clinical trials. Some women find mind/body therapies useful in relieving hot flashes or the emotional symptoms of menopause.

- **YOGA** is a form of exercise in which you are very aware of your breathing as you move through a series of positions that stimulate strength, flexibility, and relaxation.
- **FOCUSED BREATHING** alone (without the yoga body positions) may also help you relax, easing symptoms. You take a slow, deep breath, hold it several seconds, and then exhale slowly. Some women find that slow, focused breathing relieves a hot flash when they sense one is starting.
- **MINDFULNESS MEDITATION** can take many forms. Overall, it is the practice of becoming intentionally aware of your thoughts and actions in the present moment and not judging these. Sitting quietly and noticing thoughts, and then letting them go, can help manage or reduce stress.

- **ACUPUNCTURE** aims to restore and maintain health through the stimulation of specific points on the body. It is believed to help a variety of menopausal symptoms. Thin needles are inserted into the surface of the skin by an expert who targets specific points to create relaxation or relief.
- **AROMATHERAPY** is based on the belief that smells can produce effects in the body. Oils produced from different parts of aromatic plants can be used in concentrated amounts in the bath or for massage.
- **MASSAGE** itself is another form of relaxation therapy. Clinical trials have shown massage to be an effective way to manage fatigue, stress, pain, and other conditions.

Diet and exercise

The Hormone Foundation strongly recommends good nutrition, maintaining a healthy body weight, regular exercise, and no smoking. In fact, women with a higher percentage of body fat have more hot flashes. So exercise and increased muscle mass will not only make your heart and bones healthier, but just might help with hot flashes too. (Avoiding hot and spicy foods, caffeine, and alcohol may also help reduce hot flashes.) All of these are important steps to staying healthy and can make a big difference in the quality of your life during and beyond menopause.

If I decide to take hormones, how long should I take them?

Consider managing your menopausal symptoms in two phases, with an eye to short-term goals and long-term goals. Short-term therapy is designed primarily to relieve symptoms such as hot flashes, while long-term therapy helps prevent bone loss.

If you are a healthy woman and take hormones for fewer than three to five years, your overall risks of heart disease, blood clots, or cancer appear to be relatively low. Any excess risk disappears within several years of stopping the hormones. Discuss your options with your doctor before beginning HT. He or she can help you decide if this is really your best choice or whether an alternative therapy might be better.

Making the most of your doctor visit

- Document and prioritize your symptoms, including how often you have them and how severe they are.
- Learn about hormone therapy in general ahead of time.
- Think through your own comfort level with the risks and benefits of hormone therapy.
- Document your family health history.
- Come to your doctor's office with a list of questions prepared.

Remember that right now, the best advice doctors can give women about taking hormones is to take the lowest dose for the shortest time. It is also wise to periodically reevaluate your hormone regimen (at least yearly at your annual visit), because new information is coming out on a regular basis in this very active field of research.

How often should I follow up with my health care provider and what should I report?

If you decide on menopausal HT, schedule a follow-up appointment about eight to 12 weeks after you start. Most women beginning HT will notice relief of symptoms in about a month, but with the new lower doses, it might take longer to see the full effect. Taking hormones for 12 weeks is almost always long enough for a woman to know if she will get relief from the therapy or will need to try something else.

A 12-week follow-up appointment is especially useful if your doctor prescribed HT for a symptom that is not clearly linked with menopause and that could be caused by another condition. Examples include aches and pains, insomnia, foggy thinking, or difficulty recalling things. If these symptoms are not improving with hormones, your doctor may suggest that you stop HT and try a different medication.

Your doctor will also want you to have an annual breast exam and mammogram. If members of your family have had breast cancer, or if you have ever had breast lumps or an abnormal mammogram, you may need to have more frequent breast exams or more intensive screening. HT can make the breast look denser on mammograms, so you may need additional views and possibly a biopsy to examine your breasts thoroughly.

Ask your doctor if you should have a bone density exam, called a dual energy x-ray absorptiometry (DEXA) scan. This scan, which takes about 30 minutes, is a painless, non-invasive test to find out if your bones are thin and prone to fracture. The best way to prevent the bone-thinning disease osteoporosis is by eating lots of calcium-rich foods or taking a supplement, if necessary. Each day, menopausal women should get about 1,200 mg of calcium and about 1,000 IU (international units) of vitamin D, which is needed for your body to absorb calcium. Exercise is also important for strong bones and maintaining balance to prevent falls.

If you already have thinning bones, your doctor may prescribe a medication to help halt bone loss or build new bone. Talk with your doctor about the best option for you.

When it is time to stop taking hormones, should I taper off or go cold turkey?

It's not clear whether you should taper off your hormone use by reducing your dose a bit at a time, or if you should stop all at once. Women with the most severe symptoms might benefit from tapering off, either by decreasing the dose or by extending the time between doses. About half of women continue to have symptoms once they stop HT. Don't be surprised if your symptoms peak two to three months after stopping hormones. You may want to try different therapies after discontinuing hormones. Your doctor can help you to decide which therapy might be best for you.

Be aware of any worrisome side effects that might mean you need to stop HT promptly. Spotting or bleeding is not uncommon initially, but a change in bleeding pattern after being on hormones for some time should be evaluated. Warning signs that you need to discontinue the medication include symptoms of:

- stroke (slurred speech, loss or blurred vision, numbness of a limb, or difficulty moving a limb)
- heart attack (chest pain or tightness, shortness of breath)
- blood clots in the legs (swelling or calf pain)
- blood clots in the lungs (sudden shortness of breath or pain with breathing)

If you develop a breast mass, it is a good idea to stop hormones until you have been evaluated. Call your doctor promptly if you notice any of these symptoms.

How might hormone therapy be used in the future?

Doctors and research scientists are working every day to learn more about how hormones affect our bodies and how HT might affect the quality of life during menopause. They are exploring possible heart and brain benefits in women who start HT very close to the start of their menopause. Doctors and researchers are evaluating the effectiveness of lower doses and designing better ways to screen women for risk. They are also investigating whether modified versions of estrogen and progesterone may prove to be effective treatments for menopausal symptoms.

Researchers also hope to better identify the needs of different populations of women. For example, does a woman who started menopause in her early 30s have different HT needs than a woman who starts at age 50? Do heavy smokers need a certain type of therapy? Different ethnic populations also have different risks, with African American women less likely to develop osteoporosis but more likely to have hot flashes than Chinese women. It stands to reason that all of these groups of women will have different needs as they journey through menopause.

How should I keep abreast of ever-changing research on menopausal management?

Remember that research on menopause management is evolving all the time. Reevaluate your choices periodically. In addition to talking with your doctor, stay in tune with stories in the news. While the Internet is an excellent source of information, be careful to get your information from legitimate sources, as suggested on page 20 of this brochure. With all of these resources, a continuous stream of research, and a trusted specialist you can communicate with, you will be empowered to make all the decisions necessary to navigate this period of change in your life.

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Resources

American Cancer Society: www.cancer.org

American College of Obstetricians and Gynecologists: www.acog.org

American Heart Association: www.americanheart.org

The Hormone Foundation: www.hormone.org

National Center for Complementary and Alternative Medicine: www.nccam.nih.gov

National Osteoporosis Foundation: www.nof.org

North American Menopause Society: www.menopause.org



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For more information on menopause and related conditions and to find a menopause specialist, visit www.hormone.org

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