



## Hormones and Menopause

### *Tips from the National Institute on Aging*

*Waking up flushed and sweaty several times a night left Cathy feeling tired all day. But when she began to feel hot on and off during the day as well, she went to see Dr. Kent. He told Cathy she was having hot flashes—a sign that she was starting the menopause transition. Dr. Kent talked about several ways to control her hot flashes. One was to use the hormone estrogen for a short time. He talked about the benefits and risks of this choice. Cathy said she remembered hearing something on a TV talk show about using hormones around menopause. Were they helpful? Were they safe? She didn't know.*

A hormone is a chemical substance made by an organ like the thyroid gland or ovary. Hormones control different body functions. Examples of hormones are estrogen, progesterone, testosterone, and thyroid hormone. In a woman's body during the menopause transition, the months or years right before menopause (her final menstrual period), levels of several hormones, including estrogen and progesterone, go up and down irregularly. This happens as the ovaries begin working less and less well.

Menopause is a normal part of aging. It is not a disease or disorder. Women who have

symptoms like hot flashes and night sweats may decide to use hormones like estrogen because of the benefits, but there are also side effects and risks to consider.

*Dr. Kent told Cathy to call back for a prescription if she decided to try using hormones to relieve her symptoms. She read pamphlets from the doctor's office and talked to her friends. Lily, who had surgery to remove her uterus and ovaries, has been taking the hormone estrogen since the operation. Sandy said she's had a few hot flashes, but isn't really uncomfortable enough to take hormones. Melissa is bothered by hot flashes and can't sleep, but her doctor thinks she should not use estrogen because her younger sister has breast cancer. Each friend had a different story. Cathy wanted more information.*

### **What about hormones?**

Symptoms such as hot flashes might result from the changing hormone levels during the menopause transition. After a woman's last menstrual period, when her ovaries make much less estrogen and progesterone, some symptoms of menopause might disappear, but others may continue or get worse.

To help relieve these symptoms, some women use hormones. This is called menopausal hormone therapy (MHT). This approach used to be called hormone replacement therapy or HRT. MHT is a more current, umbrella term that describes several different hormone combinations available in a variety of forms and doses.

## How would I use menopausal hormone therapy?

Estrogen is a hormone used to relieve the symptoms of menopause. A woman whose uterus has been removed can use estrogen only (E). But a woman who still has a uterus must add progesterone or a progestin (synthetic progesterone) along with the estrogen (E+P). This combination lowers the chance of an unwanted thickening of the lining of the uterus and reduces the risk of cancer of the uterus, an uncommon, but possible result of using estrogen alone.

*Cathy's friend Stephanie takes a pill containing estrogen and progestin, but Cathy has trouble swallowing pills. If MHT is only available as a pill, that is something she'd consider when making her decision.*

Estrogen comes in many forms. Cathy could use a skin patch, vaginal tablet, or cream; take a pill; or get an implant, shot, or vaginal ring insert. She could even apply a gel or spray. There are also different types of estrogen (such as estradiol and conjugated estrogens). Estradiol is the most important type of estrogen in a woman's body before menopause. Other hormones, progesterone or progestin, can be taken as a pill, sometimes in the same pill as the estrogen, as well as a patch (combined with estrogen), shot, IUD (intrauterine device), gel, or vaginal suppository.

The form of MHT your doctor suggests may depend on your symptoms. For example, an estrogen patch (also called transdermal estrogen) or pill (oral estrogen) can relieve hot flashes, night sweats (hot flashes that bother you at night), and vaginal dryness. Other forms—vaginal creams, tablets, or rings—are used mostly for vaginal dryness alone. The vaginal ring insert might also help some urinary tract symptoms.

The dose can also vary, as can the timing of those doses. Some doctors suggest that estrogen be used every day, but that the progesterone or progestin be used cyclically—for 10 to 14 straight days every 4 weeks. A cyclic schedule is thought to mimic how the body makes estrogen and progesterone before menopause. This approach can cause some spotting or bleeding, like a light period, which might get lighter or go away in time. Alternatively, some women take estrogen and progesterone or progestin continuously—every day of the month.

## Is there a downside to taking hormones?

*A lot of the information Cathy read said that taking estrogen is the most effective way to relieve hot flashes, night sweats, and vaginal dryness. Estrogen also helps keep bones strong. Cathy thought that those seemed like good reasons to use MHT. But she wondered, is there a downside?*

Research has found that, for some women, there are serious risks, including an increased chance of heart disease, stroke, blood clots, and breast cancer, when using MHT. The Women's Health Initiative (see page 3) also found an increased risk of possible dementia in women who started MHT after age 65. These concerns are why every woman

needs to think a lot before deciding to use menopausal hormone therapy.

Also, some women develop noticeable side effects from using hormones:

- Breast tenderness
- Spotting or a return of monthly periods
- Cramping
- Bloating

By changing the type or amount of the hormones, the way they are taken, or the timing of the doses, your doctor may be able to help control these side effects. Or, over time, they may go away on their own.

### What more should I know about the benefits and risks of hormones?

*Cathy knows there have been news stories about menopausal hormone therapy research findings. But, several years ago, when she first heard about the risks of using estrogen, she didn't really pay attention. Now she wants to know more about the risks.*

Over the years, research findings have led to a variety of positive, negative, and sometimes conflicting reports about menopausal hormone therapy. Some of these findings came from randomized clinical trials, the most convincing type of research. Historically, clinical trials often used one type of estrogen called conjugated estrogens. Several other types of estrogen, as well as progesterone and progestins, have also been tested in small trials to see if they have an effect on heart disease, breast cancer, or dementia.

Let's look more closely at what we have learned from these small studies.

**Hot flashes and night sweats.** Estrogen will relieve most women's hot flashes and night sweats. If you stop using estrogen, you may again start having hot flashes. Lifestyle changes and certain prescription medicines also might help some women with hot flashes. For most women, hot flashes and night sweats go away in time.

**Vaginal dryness.** Estrogen improves vaginal dryness, probably for as long as you continue to use it. If vaginal dryness is your only symptom, your doctor might prescribe a vaginal estrogen. A water-based lubricant, but not petroleum jelly, may also relieve vaginal discomfort.

**Cholesterol levels.** Estrogen improves cholesterol levels, lowering LDLs (the "bad" kind of cholesterol) and raising HDLs (the "good" kind of cholesterol). The pill form of estrogen can cause the level of triglycerides (a type of fat in the blood) to go up. The estrogen patch does not seem to have this effect, but it also does not improve cholesterol to the same degree as the pill form. But, improving cholesterol levels is not a reason to take estrogen. Other medicines and lifestyle changes will improve cholesterol levels more effectively.

### What is the Women's Health Initiative? What have we learned from it?

Before menopause, women generally have a lower risk of heart disease than men. This led experts to wonder whether giving women estrogen after menopause might help prevent heart disease. In 1992, the National Institutes of Health (NIH), the nation's premier medical research agency, began the Women's Health Initiative (WHI) to explore ways postmenopausal

women might prevent heart disease, as well as osteoporosis and cancer. One part of the WHI, the Hormone Trial, looked at oral conjugated estrogens used alone (E therapy or ET) or with a particular progestin (EPT) to see if, in postmenopausal women, estrogen could prevent heart disease without increasing the chance of breast cancer.

In July 2002, the EPT part of the WHI Hormone Trial was stopped early because it became clear to the researchers that the overall risk of taking E+P outweighed the benefits:

#### *Benefits*

- Fewer fractures
- Less chance of cancer in the colon and/or rectum

#### *Risks*

- More strokes
- More serious blood clots
- More heart attacks
- More breast cancers

In April 2004, the rest of the Hormone Trial, the E alone or ET trial, was also halted because using estrogen alone increased the risk of stroke, and it was not likely that there would be a positive effect on heart attacks. Unlike using estrogen plus progestin, using estrogen alone did not increase the risk of heart attacks or breast cancer, but like the EPT trial, there were fewer fractures.

During the first 3 years after stopping the WHI EPT trial, women were no longer at greater risk of heart disease, stroke, or serious blood clots than women who had not used MHT. On the other hand, they also no longer had greater protection from fractures. The women still had an increased risk of breast cancer, but their risk was smaller than it was

while they were using hormones. During the first 4 years after stopping the WHI ET trial, the increased risk of stroke disappeared, there was no effect on risk of heart attack, but the slightly lower risk of breast cancer continued.

It appears from the WHI that women **should not** begin using MHT to protect their health—it does not appear to prevent heart disease or dementia when started several years after menopause. In fact, older women in the study using MHT were at increased risk of certain diseases. Women who were less than age 60 did not appear to be at increased risk of heart disease but were at increased risk of stroke. For these women, the overall risks and benefits appeared to be balanced, but there is no strong evidence to support women under age 60 using MHT to prevent chronic diseases of aging, such as heart disease and dementia.

**The U.S. Food and Drug Administration (FDA) now recommends that women with moderate to severe menopausal symptoms who want to try menopausal hormone therapy for relief use it for the shortest time needed and at the lowest effective dose.**

It is important to remember that the WHI findings are based on the specific oral form (rather than patch, gel, etc.), dose, and type of estrogen and progestin studied in the WHI. Which hormones and dose you use and the way you take them might change these benefits and risks. We don't know how the WHI findings apply to these other types, forms, and doses of estrogen and progesterone or progestin.

### **What are some other options?**

*Cathy is like a lot of women bothered by symptoms of menopause. After learning about some research results, she is concerned*

*about using menopausal hormone therapy for relief of her symptoms. But it's been several years since some study findings raised concerns, and now Cathy is wondering whether there is anything new.*

Women now have more options than when the WHI study was first planned. More types of estrogens are available, and some of them come in a variety of forms. For example, synthetic estradiol, now available in several forms (pill, patch, cream, gel, etc.), is chemically identical to the estrogen most active in women's bodies before menopause. If it is not taken by mouth, but rather applied to the skin or taken as a shot, estradiol appears to work the same way as estradiol made in the body. Lower doses of estrogen are available. Investigators are now studying a low-dose estradiol patch (transdermal estradiol) compared to a low-dose conjugated-estrogens pill to see whether one or both slow hardening of the arteries in women around the age of menopause and whether the estradiol patch is as effective and, perhaps, safer than the conjugated-estrogens pill. These alternatives are creating more choices for women seeking relief from their menopausal symptoms, as well as a variety of new opportunities for research.

Besides a pill, some estrogens come in different and sometimes new forms—skin patch, gel, emulsion, spray, and vaginal ring, cream, and tablet. These forms work in the body somewhat differently than a pill by entering your body directly through the skin or walls of the vagina. Oral estrogen (a pill) is chemically changed in the liver before reaching your tissues. Some studies suggest that if estrogen enters through the skin and bypasses the liver, the risk of serious blood clots might be lower. Others suggest a lower risk of gallbladder disease. This may also

allow a change in dosage—further testing may show that the same benefits might come from lower doses than are needed with a pill.

## What questions remain unanswered?

*Cathy was beginning to understand more about the benefits and risks of using hormones, but she wondered whether there are still questions about the WHI results and menopausal hormone therapy in general. What else needs to be looked at?*

Experts now know more about menopause and have a better understanding of what the WHI results mean. But, they have new questions also.

- The average age of women participating in the trial was 63, more than 10 years older than the average age of menopause, and the WHI was looking at reducing the risk of chronic diseases of growing older like heart disease and osteoporosis. Do the WHI results apply to younger women choosing MHT to relieve symptoms around the time of menopause or to women who have early surgical menopause (surgery to remove both ovaries or the uterus)?
- Other studies show that lower doses of estrogen than were studied in the WHI provide relief from symptoms of menopause for some women and still help women maintain bone density. What are the long-term benefits and risks of lower doses of estrogen?
- In the WHI, women using E alone did not seem to have a greater risk of heart disease than women not using hormones. Does this mean that healthy women in their 50s who start using estrogen alone are not at higher eventual

risk for heart disease than women who don't use estrogen?

- Would using progesterone or a different progestin than the one used in the WHI be less risky to a woman's heart, blood vessels, and breasts?
- The combination menopausal hormone therapy used in the WHI makes it somewhat more likely that a woman could develop breast cancer, especially with long-term use. Is using a different type of estrogen, a smaller dose of estrogen or progesterone, or a different progestin (instead of medroxyprogesterone acetate) safer?
- Does using estrogen around the time of menopause increase the risk of possible dementia in later life, as starting it after age 65 did in the WHI Memory Study (WHIMS)? Or does it decrease the risk of dementia later in life?

The National Institute on Aging and other parts of the National Institutes of Health, along with other medical research centers, continue to explore questions such as these. They hope that in the future these studies will give women additional facts needed to make informed decisions about relieving menopausal symptoms.

### What are “natural hormones”?

*Cathy's friend Susan thinks she is not at risk for serious side effects from menopausal hormone therapy because she uses “natural hormones” to treat her hot flashes and night sweats. Cathy asked Dr. Kent about them. He told her that there is very little reliable scientific information from high-quality clinical trials about the safety of “natural” or compounded hormones, how well they control the symptoms of menopause, and whether*

*they are as good or better to use than FDA-approved estrogens, progesterone, and progestins.*

The “natural hormones” Susan uses are estrogen and progesterone made from plants such as soy or yams. Some people also call them bioidentical hormones because they are supposed to be chemically the same as the hormones naturally made by a woman's body. These so-called natural hormones are put together (compounded) by a compounding pharmacist. This pharmacist follows a formula decided on by a doctor familiar with this approach. Compounded hormones are not regulated or approved by the FDA. So, we don't know much about how safe or effective they are or how the quality and quantity vary from batch to batch.

Some drug companies also make estrogens and progesterone from plants like soy and yams. Some of these are also chemically identical to the hormones made by your body. These other forms of MHT are available by prescription. Importantly, these estrogens and progesterone made by drug companies are regulated and approved by the FDA.

There are also “natural” treatments for the symptoms of menopause that are available over-the-counter, without a prescription. Black cohosh is one that women use, but a couple of clinical trials have shown that it did not relieve hot flashes in postmenopausal women or those approaching menopause. Because of rare reports of serious liver disease, scientists are concerned about the possible effects of black cohosh on the liver. Other “natural” treatments are made from soy or yams. None of these are regulated or approved by the FDA.

## What's right for me?

There is no single answer for all women who are trying to decide whether to use MHT. You have to look at your own needs and weigh your own risks. Here are some questions you can ask yourself and talk to your doctor about:

- *Do menopausal symptoms such as hot flashes or vaginal dryness bother me a lot?* Like many women, your hot flashes or night sweats will likely go away over time, but vaginal dryness may not. MHT can help with troubling symptoms.
- *Am I at risk for developing osteoporosis?* Estrogen might protect bone mass while you use it. However, there are other drugs that can protect your bones without MHT's risks. Talk to your doctor about the risks and benefits of those medicines for you.
- *Do I have a history of heart disease or risk factors such as high blood cholesterol?* If so, using estrogen and progestin can increase that risk even more.
- *Do I have a family history of breast cancer?* If you have a family history of breast cancer, check with your doctor about your risk.
- *I have high levels of triglycerides and a family history of gallbladder disease. Can I use MHT?* The safety of any kind of MHT in women with high levels of triglycerides or a family history of gallbladder disease is not known. But some experts think that using a patch will not raise your triglyceride level or increase your chance of gallbladder problems. Using an oral estrogen pill might.
- *Do I have liver disease or a history of stroke or blood clots in my veins?* MHT, especially taken by mouth, might not be safe for you to use.

In all cases, talk to your doctor about how best to treat or prevent your menopause symptoms or diseases for which you are at risk.

If you are already using menopausal hormone therapy and think you would like to stop, first ask your doctor how to do that. Some doctors suggest tapering off slowly.

Whatever decision you make now about using MHT is not final. You can start or end the treatment at any time, although, as we learned from the WHI, it appears that it is best not to start MHT many years after menopause. If you stop, some of your risks will lessen over time, but so will the benefits. Discuss your decision about menopausal hormone therapy with your doctor at your annual checkup.

## MHT is not one size fits all

*Cathy realized that talking to her friends about what each is doing to relieve menopause symptoms was helpful, but that her decision needed to be just for her. And she was sure that basing her decision just on what she heard on a TV show might not be the best way to choose. She tried to find sources of information that seemed to be unbiased and didn't have a product to promote. She felt most comfortable with science-based websites like the National Institutes of Health, the U.S. Food and Drug Administration, or doctors' professional groups.*

Each woman is different, and the decision for each one about menopausal hormone therapy will probably also be different. But, almost every research study helps give women and their doctors more information to answer the question: *Is menopausal hormone therapy right for me?*

## For More Information

Other resources on menopausal hormone therapy include:

### National Institutes of Health

Menopausal Hormone Therapy Information  
[www.nih.gov/PHTindex.htm](http://www.nih.gov/PHTindex.htm)

### The National Library of Medicine MedlinePlus

[www.medlineplus.gov](http://www.medlineplus.gov)

The National Library of Medicine website has information on many health subjects, including menopause. Click on Health Topics. Choose any topic you are interested in, such as menopause, menopausal hormone therapy, or osteoporosis, by clicking on the first letter of the topics and scrolling down the list to find it.

### American College of Obstetricians and Gynecologists

409 12th Street, SW  
P.O. Box 70620  
Washington, DC 20024-9998  
1-202-638-5577  
1-800-673-8444 (toll-free)  
[www.acog.org](http://www.acog.org)

### Food and Drug Administration

10903 New Hampshire Avenue  
Silver Spring, MD 20993-0002  
1-888-463-6332 (toll-free)  
[www.fda.gov](http://www.fda.gov)

### North American Menopause Society

5900 Landerbrook Drive  
Suite 390  
Mayfield Heights, OH 44124  
1-440-442-7550  
[www.menopause.org](http://www.menopause.org)

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## For more information about health and aging, contact:

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P.O. Box 8057  
Gaithersburg, MD 20898-8057  
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