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## Menopausal Hormone Therapy and Cancer Risk

For decades, women have used hormone therapy to ease symptoms of menopause, such as hot flashes and sweating. This is called **menopausal hormone therapy**, and you may see it abbreviated as HT or MHT. You may also hear it described as hormone

can become less frequent during this time, it can be hard to know when they have actually stopped (and you have gone through menopause) until you look back at a later time.

Women who have their ovaries removed by surgery (*oophorectomy*) or whose ovaries stop working for other reasons go through menopause, too, but much more suddenly (without the menopausal transition).

Women who have had their uterus removed (hysterectomy) but still have their ovaries stop having periods, but they don't really go through menopause until their ovaries stop working. This is often determined based on symptoms, but your doctor can tell for certain by testing your blood for levels of certain hormones. Hormones made by the pituitary gland called luteinizing hormone (LH) and follicle stimulating hormone (FSH) help regulate the ovaries before menopause. When levels of estrogen get lower during menopause, the levels of FSH and LH go up. High levels of FSH and LH, along with low levels of estrogen, can be used to diagnose menopause. Blood tests for these may be helpful in a woman who has had her uterus removed.

Some drugs can turn off the ovaries and cause menstrual periods to stop for a time. Although this is not the same as menopause, it can lead to many of the same symptoms.

Most of the symptoms of menopause are linked to lower estrogen levels. Some symptoms – hot flashes and night sweats, for instance – tend to fade away at some point, whether or not they are treated. Other problems that start after menopause, like dryness and thinning of vaginal tissues and bone thinning, tend to get worse over time.

Because many of the symptoms and problems of menopause are linked to low levels of estrogen, this hormone has often been used in the past to treat menopause.

## **What hormones are used to treat the symptoms of menopause?**

The hormones most commonly used to treat symptoms of menopause are estrogen and progesterone. (Progesterone and drugs that act like it are called *progestins*). Often, these 2 hormones are used together, but some women are given estrogen alone. It's important to know which hormones you are talking about when looking at the risks.

Common estrogen preparations used to treat menopausal symptoms include

There are also many progestins available, but medroxyprogesterone acetate (MPA or Provera<sup>®</sup>), is often used with an estrogen to treat menopausal symptoms. Some preparations contain both an estrogen and a progestin.

Androgens (male hormones like testosterone) are also sometimes used to treat menopausal symptoms. This is not common, though, and because only a few studies have looked at this practice, it isn't clear how safe it is in the long run.

Tibolone is a synthetic hormone drug that can act like estrogen, progesterone, and testosterone in different tissues of the body. Because this drug isn't available in the US, it's not discussed here.

### **Taking estrogen with a progestin vs. estrogen alone**

Treating menopausal symptoms with estrogen and progestin together is known as **estrogen-progestin therapy (EPT)** or **combined hormone therapy**. Although estrogen alone improves the symptoms of menopause, it increases the risk of cancer of the uterus (endometrial cancer). Adding a progestin to the estrogen lowers the risk of endometrial cancer back to normal. Because of this, EPT is given to women who still have a uterus (those who have not had a hysterectomy). EPT can be given 2 ways:

- **Continuous EPT** means the same dose of estrogen and progestin is taken each day. Women often prefer continuous EPT because it rarely leads to menstrual-like bleeding.
- **Sequential (cyclical) EPT** means different amounts of each hormone are taken on specific days. There are different ways to do this. For example, estrogen can be taken by itself for 14 days, then estrogen plus progestin for 11 days, then neither hormone for 3 to 5 days. Other schedules involve taking progestin only every few months. This lowers the amount of progestin that you are exposed to. Monthly regimens are also thought to result in hormone levels that are more like the natural menstrual cycle. Cyclical EPT can produce bleeding like a menstrual period, but it can occur less often than monthly.

### **Bio-identical hormones**

The word "bio-identical" is sometimes used by sellers to describe hormone preparations that contain estrogens and progesterone with the same chemical structure as those found naturally in people. Sometimes, how much of the hormones the woman takes are adjusted based on blood tests of hormone levels. Marketers often describe bio-identical



osteoporosis (severe bone thinning).

## Topical hormones

Hormones, most often estrogen, can also be placed in or near the place that needs treatment. This is called **topical** hormone therapy. If small doses are used, little of the hormone is absorbed into the bloodstream, so it has little if any effect on the rest of the body.

For women in menopause, very small doses of estrogen can be placed inside the vagina as topical therapy to help treat dry or thinned vaginal tissues. This type of estrogen comes in the form of vaginal creams, rings, and tablets. Even though tiny amounts of hormone may enter the blood, most of it stays in the vaginal tissues. Because so little of the hormone gets into the blood, topical treatment doesn't help with problems like hot flashes, night sweats, or osteoporosis. Generally, topical estrogen is not needed in women taking systemic hormones.

(As noted earlier, there's a type of vaginal ring that delivers high doses of hormones to the whole body, which would be considered systemic treatment. If you're unsure about the type of ring you have, check with your doctor.)

## Types of studies of hormone therapy and cancer risk

Different types of studies can be used to look at cancer risk from menopausal hormone therapy (MHT).

**Randomized controlled trials:** In this kind of study, a group of patients get the drug being studied (like MHT), and another (control) group gets a placebo (like a sugar pill). Results from this kind of study are powerful because which group a patient is in is based on chance. This helps assure that the groups are similar in all ways, such as risk for cancer, except for the drug that's being studied. This is the best way to see the effects of a drug. These types of studies can also be **double-blinded**, which means neither the people in the study nor their doctors know which group they are in. This lowers the chance that thoughts or opinions about treatment could affect the study results. Unfortunately, these kinds of studies are costly, which limits the number of people in the study, how long the study can continue, and the number of studies done.

**Observational studies:** These kinds of studies collect information about a large group of people but don't give them a certain treatment, such as a drug. In observational studies of MHT, the women and their doctors decide what hormone drugs, if any, the women take and for how long. These kinds of studies can also gather information about

other factors that can influence cancer risk. Some observational studies gather data about what happened over previous years. Others follow (observe) people for years to look at how different factors (like MHT) affect cancer risk. Observational studies can be less costly than randomized clinical trials, so they're more common and often enroll many more patients.

A major drawback of observational studies is that the people getting the treatment being studied may have different cancer risk factors than the people who aren't. Plus, the treatment (like which drugs are used for MHT and how long they're taken) can differ between the people being studied. This makes it less clear that the differences seen are only due to the drug being studied (like MHT) and not other factors.

When observational studies and randomized controlled trials have different results, most experts give more weight to the results of the randomized controlled trial.

### **Womens Health Initiative studies of hormone therapy and cancer risk**

Several large studies have looked at possible links between systemic hormone therapy in menopausal women and different types of cancer.

Million Women Study. It enrolled over a million women aged 50 to 64 in the UK, collected information about hormone use and other health and personal details, and

randomized controlled trials and observational studies. This analysis found that women who took estrogen and progestin (progesterone) after menopause did have an increased risk of getting ovarian cancer. The risk was highest for women taking hormones, and decreased over time after the hormones were stopped.

To put the risk into numbers, if 1,000 women who were 50 years old took hormones for menopause for 5 years, one extra ovarian cancer would be expected to develop.

### ***Colorectal cancer***

In the WHI study of EPT, the results were mixed. Women who took EPT had a lower risk of getting [colorectal cancer](#)<sup>4</sup> at all, but the cancers they got were more advanced (more likely to have spread to lymph nodes or distant sites) than the cancers in the women not taking hormones.

Some observational studies have found a lower risk of colorectal cancer in women taking EPT, but some did not. So far, though, observational studies have not linked EPT with a higher risk of colorectal cancer.

### ***Lung cancer***

EPT is not linked to a higher risk of getting [lung cancer](#)<sup>5</sup>, but it is linked to a higher risk of dying from lung cancer.

### ***Skin cancer***

EPT is not linked to a higher risk of any type of [skin cancer](#)<sup>6</sup> (including both [melanoma](#)<sup>7</sup> and other types of skin cancer).

## **Estrogen therapy (ET) and cancer risk**

### ***Endometrial cancer***

In women who still have a uterus, using systemic ET has been shown to increase the risk of endometrial cancer (cancer of the lining of the uterus). The risk remains higher than average even after ET is no longer used. Although most studies that showed an increased risk were of women taking estrogen as a pill, women using a patch or high-dose vaginal ring can also expect to have an increased risk of endometrial cancer.

Because of this increased cancer risk, women who have gone through menopause and who still have a uterus are given a progestin along with estrogen. Studies have shown



that EPT does not increase the risk for endometrial cancer.

Long-term use of vaginal creams, rings, or tablets containing topical estrogen doses may also increase the levels of estrogen in the body. It's not clear if this leads to health risks, but the amounts of hormone are much smaller than systemic therapies.

### ***Breast cancer***

ET is not linked to a higher risk of breast cancer. In fact, certain groups of women taking ET, such as women who had no family history of breast cancer and those who had no history of benign breast disease, had a slightly lower risk of breast cancer.

### ***Ovarian cancer***

The WHI study of ET did not report any results about ovarian cancer.

However, a recent analysis combined the results of more than 50 studies, including randomized controlled trials and observational studies. This analysis found that women who took estrogen after menopause did have an increased risk of getting ovarian cancer. The risk was highest for women currently taking estrogen, and decreased over time after estrogen was stopped.

To put the risk into numbers, if 1,000 women who were 50 years old took estrogen for menopause for 5 years, one extra ovarian cancer would be expected to develop.

Observational studies have shown that women who take ET have a higher risk for ovarian cancer compared with women who take no hormones after menopause. The overall risk remains low, but it does increase the longer a woman uses ET. The risk of ovarian cancer goes down after a woman stops taking the hormone.

### ***Colorectal cancer***

In the WHI study, ET did not seem to have any effect on the risk of colorectal cancer.

Observational studies have found a lower risk of colorectal cancer in women who have used ET for many years.

### ***Lung cancer***

ET does not seem to have any effect on the risk of lung cancer.

## ***Skin cancer***

ET is not linked to a higher risk of any type of skin cancer (including both melanoma and other types of skin cancer).

## **Deciding to use menopausal hormone therapy (MHT)**

The decision to use estrogen, alone (ET) or with a progestin therapy (EPT), after menopause should be made by each woman and her doctor after weighing the possible risks and benefits. Things to think about include:

- The woman's baseline risk of breast, endometrial, ovarian, and other types of cancer, and how much this might be affected by hormone therapy
- The risks of other serious conditions affected by hormone therapy that aren't covered here, like heart disease, stroke, serious blood clots, and effects on the brain
- What other medicines might be used to treat menopausal symptoms or osteoporosis instead

Other factors to consider include how bad the woman's menopausal symptoms are and the type and dose of the hormones the doctor recommends.

The American Cancer Society has no position or guidelines regarding menopausal hormone therapy.

## **Reducing the cancer risks of hormone therapy**

If you and your doctor decide that MHT is the best way to treat symptoms or problems caused by menopause, keep in mind that it is medicine and like any other medicine it's best to use it at the lowest dose needed for as short a time as possible. And just as you would if you were taking another type of medicine, you need to see your doctor regularly. Your doctor can see how well the treatment is working, monitor you for side effects, and let you know what other treatments are available for your symptoms.

All women should report any vaginal bleeding that happens after menopause to their doctors right away – it may be a symptom of endometrial cancer. A woman who takes EPT does not have a higher risk of endometrial cancer, but she can still get it.

Women using vaginal cream, rings, or tablets containing only estrogen should talk to their doctors about follow-up and the possible need for progestin treatment.



## Hyperlinks

1. [www.cancer.org/cancer/endometrial-cancer.html](http://www.cancer.org/cancer/endometrial-cancer.html)
2. [www.cancer.org/cancer/breast-cancer.html](http://www.cancer.org/cancer/breast-cancer.html)
3. [www.cancer.org/cancer/ovarian-cancer.html](http://www.cancer.org/cancer/ovarian-cancer.html)
4. [www.cancer.org/cancer/colon-rectal-cancer.html](http://www.cancer.org/cancer/colon-rectal-cancer.html)
5. [www.cancer.org/cancer/lung-cancer.html](http://www.cancer.org/cancer/lung-cancer.html)
6. [www.cancer.org/cancer/skin-cancer.html](http://www.cancer.org/cancer/skin-cancer.html)
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8. [www.cancer.org/cancer/breast-cancer/screening-tests-and-early-detection.html](http://www.cancer.org/cancer/breast-cancer/screening-tests-and-early-detection.html)
9. [www.cancer.org/treatment/treatments-and-side-effects/complementary-and-alternative-medicine/dietary-supplements.html](http://www.cancer.org/treatment/treatments-and-side-effects/complementary-and-alternative-medicine/dietary-supplements.html)

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