

TREATMENT UPDATE:

Endometrial Cancer

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Treatment Update: Endometrial Cancer

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Cancer of the endometrium is the most common cancer of the female reproductive organs. In the United States, over 65,000 cases are diagnosed each year and the incidence is rising. Although endometrial cancer can occur at any age, it is typically diagnosed in post-menopausal women.

Diagnosis

The endometrium is the inner layer of the uterus. Symptoms of endometrial cancer—which is also called uterine cancer—include unusual vaginal bleeding, pain in the pelvis, uncommonly difficult or painful urination and pain during sexual intercourse. A diagnosis is usually made by the removal of endometrial tissue, which is then examined under a microscope for the presence of cancer cells.

The removal of tissue can be done in a number of minimally invasive ways:

- **Endometrial biopsy.** A small amount of tissue is removed by a thin, flexible tube that is inserted into the uterus through the cervix.

- **Dilatation and curettage (D& C).** After the cervix is dilated (widened), a spoon-shaped instrument called a curette is inserted into the uterus to remove tissue.
- **Hysteroscopy.** A hysteroscope is a thin, tube-like instrument containing a light and a lens that allows for the viewing of the inside of the uterus. It may also have a tool for the removal of tissue samples.

Another diagnostic tool, which is used to identify the presence of tumors, is called a transvaginal ultrasound exam. In this procedure, an ultrasound probe connected to a computer is inserted into the vagina. The probe bounces sound waves off internal organs and tissues, producing echoes that form a sonogram (computer picture). In endometrial cancer, the sonogram will show a thickened lining of the uterus.

Stages of Endometrial Cancer

The stages of endometrial cancer are commonly defined as follows:

- **Stage I:** Cancer that is confined to the uterus
- **Stage II:** Cancer that has spread to the cervix
- **Stage III:** Cancer that has spread to the vagina, ovaries and/or lymph nodes
- **Stage IV:** Cancer that has spread to the bladder, rectum or to organs located far from the uterus (such as the lungs or bones)

Tests used to help determine the stage of the cancer include blood tests, X-rays, computerized tomography (CT) scans and positron emission tomography (PET) scans. However, the final determination of the stage may not be able to be made until after surgery.

Treatment Options

The recommended treatment approach is personalized to the individual's specific circumstances. It is often based on discussions by a multi-disciplinary team consisting of gynecologic oncologists, radiation oncologists, medical oncologists and pathologists (doctors who examine laboratory samples of body tissue for diagnostic purposes).

Surgery

The majority of individuals with endometrial cancer undergo removal of the uterus (hysterectomy). Typically, the fallopian tube and ovaries are also removed in a procedure called a salpingo-oophorectomy.

During surgery, the areas around the uterus will be examined to look for any signs that the cancer has spread. Lymph nodes (small glands that help fight infection) may also be removed and tested, which will help determine the stage of the cancer.

As the surgery makes pregnancy impossible, other treatment options may be considered for younger women who wish to preserve their fertility. Other options are also considered if surgery is not possible for any reason, including the individual's overall health.



Radiation

External beam radiation uses a machine, called a linear accelerator, that directs multiple beams of radiation to specific parts of the body. The use of CT and PET scans allows radiation oncologists to accurately target the cancer, helping to spare healthy tissue. Internal radiation (brachytherapy) may also be used in the treatment of endometrial cancer. This approach involves placing a device filled with radiation inside the vagina for a short period of time.

Chemotherapy

Chemotherapy is the use of drugs to destroy cancer cells by stopping the ability of the cells to grow and divide. It is sometimes recommended after surgery for endometrial cancer, especially if there's an increased risk that the cancer will recur. Chemotherapy can also be given before surgery to shrink the cancer, making it more likely to be completely removed. It is often recommended for treating recurrent endometrial cancer, or cancer that has spread beyond the uterus.

Typically, a combination of chemotherapy drugs is given for the treatment of endometrial cancer. Most commonly, paclitaxel (Taxol, Abraxane) is combined with doxorubicin (Adriamycin) and either carboplatin (Paraplatin) or cisplatin (Platinol, Platinol AQ). Cisplatin, paclitaxel and ifosfamide (Ifex) may also be combined.

Chemotherapy given along with radiation (chemoradiation) can increase the effectiveness of the radiation, but can lead to increased side effects.

Hormone therapy

Cancer cells that rely on hormones to grow might be stopped or slowed by medications that lower hormone levels in the body. Hormone therapy is a possible option for endometrial cancer that has spread beyond the uterus or has recurred after a different type of treatment.

The use of progestins is the primary hormone therapy used to treat endometrial cancer. The two most common types of progestins are medroxyprogesterone acetate (Provera) and megestrol acetate (Megace). Progestins can slow the growth of endometrial cancer by mimicking the activity of the female hormone progesterone.

Other hormone treatments involve estrogen, a female steroid hormone produced by the ovaries that can stimulate the growth of cancer cells:

- **Tamoxifen (Soltamox, Nolvadex)** blocks estrogen.
- **Aromatase inhibitors (AIs)** block the action of the enzyme aromatase, which cuts off the supply of estrogen. AIs include letrozole (Femara), anastrozole (Arimidex) and exemestane (Aromasin).
- **Luteinizing hormone-releasing hormone agonists (LHRH agonists)** prevent the ovaries from making estrogen. LHRH antagonists, which are given as an injection, include goserelin (Zoladex) and leuprolide (Lupron).

Early-stage endometrial cancer is sometimes treated with an intrauterine device (IUD) that contains a progestin called levonorgestrel (Plan B, Mirena, Kyleena) which can be combined with medroxyprogesterone acetate or an LHRH antagonist.

Hormone therapy is often used in combination with chemotherapy.

Targeted Therapy

Targeted therapy focuses on specific molecules and cell mechanisms thought to be important for cancer cell survival and growth, taking advantage of what researchers have learned in recent years about how cancer cells grow. Targeted therapies are meant to spare healthy tissues and provide treatment against cancer cells that is more focused than chemotherapy. Molecular characterization of endometrial cancer is becoming critical in directing treatment for advanced and recurrent disease.

The use of targeted therapy in the treatment of endometrial cancer is still fairly new, and is the subject of ongoing research. The following therapies can be used for the treatment of endometrial cancer that is at an advanced stage, or has recurred after prior treatment.

- **Bevacizumab (Avastin)** is an angiogenesis inhibitor, preventing the formation of new blood vessels that cancer cells need to grow and spread. Bevacizumab is used in combination with chemotherapy after second- or third-line treatment of endometrial cancer.
- **Lenvatinib (Lenvima)** targets proteins called kinases that help cancer cells grow. It can be used in combination with the immunotherapy pembrolizumab.
- **Everolimus (Afinitor) and temsirolimus (Torisel)** block a cell protein called mTOR that normally helps cells grow and divide. mTOR inhibitors can be given alone or in combination with chemotherapy or hormone therapy.

The targeted therapy trastuzumab (Herceptin) is being studied in clinical trials for the treatment of uterine serous carcinoma (USC), an aggressive type of endometrial cancer that accounts for less than 10 percent of all cases. In the trial participants, the USC had spread beyond the uterus or recurred after previous treatment and had high levels of HER2, a protein that can fuel the growth of cancer cells. Trastuzumab is a standard treatment for HER2-positive breast cancer.



Immunotherapy

Our immune system works constantly to keep us healthy. It recognizes and fights against danger, such as infections, viruses and growing cancer cells. In general terms, immunotherapy uses our own immune system as a treatment against cancer.

Immunotherapy is typically considered as an option for endometrial cancer that is at an advanced stage, or after another treatment approach has failed.

- **Pembrolizumab (Keytruda)**, a PD-1 inhibitor, was approved by the FDA for second-line treatment of advanced endometrial cancer that has progressed after prior therapy, and which has a high- microsatellite instability-high (MSI-H) or mismatch repair deficiency (dMMR). Pembrolizumab, in combination with the targeted therapy lenvatinib, is FDA-approved for the treatment of high-grade tumors that do not have a genetic mutation called microsatellite instability-high (MSI-H). High grade tumors have cancer cells that tend to spread more quickly.
- **Dostarlimab (Jemperli)**. In April 2021, the FDA approved dostarlimab, a PD-1 inhibitor, for the treatment of advanced or recurrent endometrial cancer that was previously treated with platinum-containing therapy and which exhibits the genetic abnormality dMMR (mismatch repair deficient), which can prevent DNA within cells from repairing itself.

The Importance of Clinical Trials

Clinical trials are the standard by which we measure the worth of new treatments and the quality of life of patients as they receive those treatments. For this reason, doctors and researchers urge people with cancer to take part in clinical trials.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things that you should know:

- Often, people who take part in clinical trials gain access to and benefit from new treatments.
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial, including any possible side effects.
- Most clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- You can stop taking part in a clinical trial at any time for any reason.

Treatment Side Effects

All cancer treatments can cause side effects. It's important that you report any side effects that you experience to your health care team so they can help you manage them. Report them right away—don't wait for your next appointment. Doing so will improve your quality of life and allow you to stick with your treatment plan. It's important to remember that not all people experience all side effects, and people may experience side effects not listed here.

Side Effects of Radiation Therapy

Changes to the skin are the most common side effects of external radiation therapy; those changes can include dryness, swelling, peeling, redness and blistering. If a reaction occurs, contact your health care team so the appropriate treatment can be prescribed. It's especially important to contact your health care team if there is any open skin or painful areas, as this could indicate an infection. Infections can be treated with an oral antibiotic or topical antibiotic cream.

Side effects of internal radiation (brachytherapy) can include swelling, bruising, bleeding and pain at the spot where the radiation was delivered. It can also lead to short-term urinary symptoms, including incontinence or pain when urinating.



Side Effects of Chemotherapy

The side effects of chemotherapy depend on the type and dose of drugs given and the length of time they are used, and can include:

- Hair loss
- Anemia (decrease in red blood cells)
- Increased risk of infection (from having too few white blood cells)
- Easy bruising or bleeding (from having a low platelet count)
- Changes in memory or thinking
- Peripheral neuropathy (numbness or tingling in hands and feet)

Side Effects of Hormone Therapy

The side effects of hormone therapy can include hot flashes, night sweats, weight gain, increased blood sugar levels in people with diabetes and (rarely) serious blood clots.

Side Effects of Targeted Therapy

Targeted therapy doesn't have the same effect on the body as do chemotherapy drugs, but can still cause side effects. Side effects of targeted therapies can include diarrhea, liver problems (such as hepatitis and elevated liver enzymes), nerve damage, rash, high blood pressure and problems with blood clotting and wound healing.

Side Effects of Immunotherapy

Immunotherapy travels through the bloodstream, helping to prompt an immune response. Because it can trigger an attack on healthy cells as well as cancer cells, certain side effects may be experienced, including fatigue, decreased appetite and digestive tract symptoms (including colitis). Immunotherapy can also affect the thyroid, lungs, liver, pancreas, adrenal glands and kidneys.

General Side Effects

Some side effects may occur across treatment approaches. This section provides tips and guidance on how to manage these side effects should they occur.

Managing Digestive Tract Symptoms

Nausea and vomiting

- Avoid food with strong odors, as well as overly sweet, greasy, fried or highly seasoned food.
- Eat meals that are chilled, which often makes food more easily tolerated.
- Nibble on dry crackers or toast. These bland foods are easy on the stomach.
- Having something in your stomach when you take medication may help ease nausea.

Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade which provide electrolytes. Electrolytes are body salts that must stay in balance for cells to work properly.
- Over-the-counter medicines such as loperamide (Imodium A-D and others) and prescription drugs are available for diarrhea but should be used only if necessary. If the diarrhea is bad enough that you need medicine, discuss it with your doctor or nurse.
- Choose fiber-dense foods such as whole grains, fruits and vegetables, all of which help form stools.
- Avoid food high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol.

Loss of appetite

- Eating small meals throughout the day is an easy way to take in more protein and calories, which will help maintain your weight. Try to include protein in every meal.
- To keep from feeling full early, avoid liquids with meals or take only small sips (unless you need liquids to help swallow). Drink most of your liquids between meals.
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, ice cream, granola bars, liquid nutritional supplements, puddings, nuts, canned tuna or trail mix.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.

Constipation

- As hydration is important to avoid constipation, make sure to drink plenty of fluids. Also, limit your intake of caffeine and alcoholic beverages, as they can cause dehydration.
- Include foods high in fiber in your daily diet, such as fruit (especially pears and prunes), vegetables and cereals. If your health care team approves, you may want to add synthetic fiber to your diet, such as Metamucil, Citrucel or FiberCon.
- Be as physically active as you can, after checking with your health care team on the level of physical activity that is right for you.
- If your doctor has prescribed a “bowel regimen,” make sure to follow it exactly.

Managing Fatigue

Fatigue (extreme tiredness not helped by sleep) is one of the most common side effects of many cancer treatments. If you are taking a medication, your doctor may lower the dose of the drug, as long as it does not make the treatment less effective. If you are experiencing fatigue, talk to your doctor about whether taking a smaller dose is right for you.

There are a number of other tips for reducing fatigue:

- Take several short naps or breaks during the day.
- Take short walks or do some light exercise, if possible.
- Try easier or shorter versions of the activities you enjoy.
- Ask your family or friends to help you with tasks you find difficult or tiring.
- Save your energy for things you find most important.

Fatigue can be a symptom of other illnesses, such as anemia, diabetes, thyroid problems, heart disease, rheumatoid arthritis and depression. So be sure to ask your doctor if they think any of these conditions may be contributing to your fatigue.

Managing Pain

To help your doctor prescribe the best medication, it's useful to give an accurate report of your pain. Keep a journal that includes information on:

- Where the pain occurs
- When the pain occurs
- How long it lasts
- How strong it is on a scale of 1 to 10, with 1 being the least amount of pain and 10 the most intense
- What makes the pain feel better and what makes it feel more intense

There are a number of options for pain relief, including prescription and over-the-counter medications. It's important to talk to a member of your health care team before taking any over-the-counter medication to determine if they are safe and will not interfere with your treatments.

Physical therapy, acupuncture and massage may also be of help in managing your pain. Consult with a member of your health care team before beginning any of these activities.



Communicating With Your Health Care Team

As you manage your endometrial cancer, it's important to remember that you are a consumer of health care. The best way to make decisions about health care is to educate yourself about your diagnosis and the members of your health care team, including doctors, nurses, nurse practitioners, physician assistants, dietitians, social workers and patient navigators. Here are some tips for improving communication with your health care team:

Start a health care journal. Having a health care journal or notebook (either on paper or in a digital format) will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor. Keep a diary of your daily experiences with cancer and treatment. You can separate your journal or notebook into different sections to help keep it organized.

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, you should ask your most important questions first, and be as specific as possible.

Bring someone with you to your appointments. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support when you go to your appointments. The person who accompanies you can serve as a second set of ears. They may also think of questions to ask your doctor or remember details about your symptoms or treatment that you may have forgotten.

Write down your doctor's answers. Taking notes will help you remember your doctor's responses, advice and instructions. If you cannot write down the answers, ask the person who accompanies you to do that for you. If you have a mobile device, like a tablet or smartphone, ask if you can use it to take notes. Writing notes will help you review the information later.

Record your visit if your doctor allows it. Recording the conversation with your doctor gives you a chance to hear specific information again or share it with family members or friends.

Incorporate other health care professionals into your team.

Your medical oncologist is an essential member of your health care team, but there are other health care professionals who can help you manage your diagnosis and treatment:

- Your primary care physician should be kept updated about your cancer treatment and any test results.
- Your local pharmacist is a great source of knowledge about the medications you are taking. Have all of your prescriptions filled at the same pharmacy to avoid the possibility of harmful drug interactions.
- Make sure your oncologist knows of any other medical conditions you have or any pain you are experiencing so that they can consult with your primary care physician or specialists as needed.
- Ask your oncologist to send a summary of your visits to your primary care physician and all doctors involved in your care.

Remember, there is no such thing as over-communication.

CancerCare's Free Support Services and Programs

It can be very difficult to receive a diagnosis of endometrial cancer, and adjusting to the necessary changes in your life can be challenging.

CancerCare® can help. We are a national nonprofit organization providing free, professional services to anyone affected by cancer. Our master's-prepared oncology social workers can provide support and education, help in navigating the complicated health care system and offer information on support groups and other resources.

To learn more about how CancerCare helps, call us at 800-813-HOPE (4673) or visit www.cancercare.org.

You will likely also build your own personal support network, composed of family and friends. In doing so, it's best to take some time to think about the people in your life and how they are best suited to help. Match the task to their strengths—ask a family member who loves to shop to pick up something for you at the store; ask a friend who's a good listener to come over for a chat.



Frequently Asked Questions

Q: Does endometrial cancer have a known cause?

A: While researchers don't know what causes endometrial cancer, certain risk factors have been identified, including:

- **Balance of female hormones.** The two main hormones made by the ovaries are estrogen and progesterone. A medical condition that increases the amount of estrogen in the body can increase the risk of endometrial cancer; examples include polycystic ovary syndrome, obesity and diabetes. Additionally, the risk of endometrial cancer is increased by taking tamoxifen for the treatment of breast cancer, and taking hormones post-menopause that contain estrogen but not progesterone.
- **Years of menstruation.** As menstruation exposes the endometrium to estrogen, starting menstruation early (before the age of 12) and/or beginning menopause later than the average age increases the risk of endometrial cancer. (The average age of menopause in the United States is 51.)
- **Age.** The risk of endometrial cancer increases with age. Most cases occur after menopause.
- **Obesity.** Excess body fat can alter the body's balance of estrogen and progesterone.
- **Never having been pregnant.** Having had at least one pregnancy reduces the risk of endometrial cancer.
- **Lynch syndrome.** Lynch syndrome is a hereditary disorder caused by a mutation in a mismatch repair gene. Most commonly Lynch syndrome is associated with an increased risk for colorectal cancer, but it also increases the risk of endometrial and other cancers.
- **Family history.** Increased risk is associated with having close relatives with either endometrial or colorectal cancer.

Q. Should a person diagnosed with endometrial cancer seek a second opinion?

A: At the time of diagnosis, it makes sense to seek a consultation from a major cancer center or a group of physicians who are experts in managing endometrial cancer. Another time to seek a consultation or second opinion is if the cancer is not responding to treatment and/or if a change in treatment is warranted. Discussions can include possible changes in treatment approaches, and if participation in a clinical trial should be considered.

Q. I've been recently diagnosed with endometrial cancer. Should I see a genetic counselor?

A: Genetic counseling can help people make informed decisions about genetic testing. In a genetic counseling session for endometrial cancer, the counselor will typically collect a detailed family and medical history and discuss genetic mutations, such as microsatellite instability-high (MSI-H) or mismatch repair deficiency (dMMR).



Q: What is a treatment summary and why is it important?

A: Keeping your own records up-to-date in the form of a treatment summary can be helpful, as it allows you and your family members to have instant access to the specifics of your endometrial cancer diagnosis and treatment. A treatment summary should include:

- Your name and date of birth
- Date of diagnosis
- Prescribed therapy/therapies, including dates started and stopped and dosages when appropriate
- Dates and types of baseline and post-diagnosis testing and the results of these tests
- Other medications and supplements you are taking
- Names, affiliations and contact information of all members of your health care team

Ask the members of your health care team what they suggest be included. Take your personal record with you when you visit any doctor, not just your oncologist.



Resources

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www.cancercaresupport.org

American Cancer Society

800-227-2345
www.cancer.org

Cancer.Net

Patient information from
the American Society of
Clinical Oncology
888-651-3038
www.cancer.net

National Cancer Institute

800-422-6237
www.cancer.gov

CLINICAL TRIALS WEBSITES

EmergingMed

www.emergingmed.com

National Cancer Institute

www.cancer.gov

Cancer Support Community

888-793-9355
www.cancersupportcommunity.org

National Coalition for Cancer Survivorship

877-622-7937
www.canceradvocacy.org

Foundation for Women's Cancer

www.foundationforwomenscancer.org

Medicine Assistance Tool

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