Endometrial (Uterine) Cancer

What is cancer?

The body is made up of trillions of living cells. Normal body cells grow, divide to make new cells, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues are what makes a cell a cancer cell.

Cells become cancer cells because of damage to DNA. DNA is in every cell and directs all its actions. In a normal cell, when DNA gets damaged the cell either repairs the damage or the cell dies. In cancer cells, the damaged DNA is not repaired, but the cell doesn’t die like it should. Instead, this cell goes on making new cells that the body does not need. These new cells will all have the same damaged DNA as the first cell does.

People can inherit damaged DNA, but most DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in our environment. Sometimes the cause of the DNA damage is something obvious, like cigarette smoking. But often no clear cause is found.

In most cases the cancer cells form a tumor. Some cancers, like leukemia, rarely form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Cancer cells often travel to other parts of the body, where they begin to grow and form new tumors that replace normal tissue. This process is called *metastasis*. It happens when the cancer cells get into the bloodstream or lymph vessels of our body.

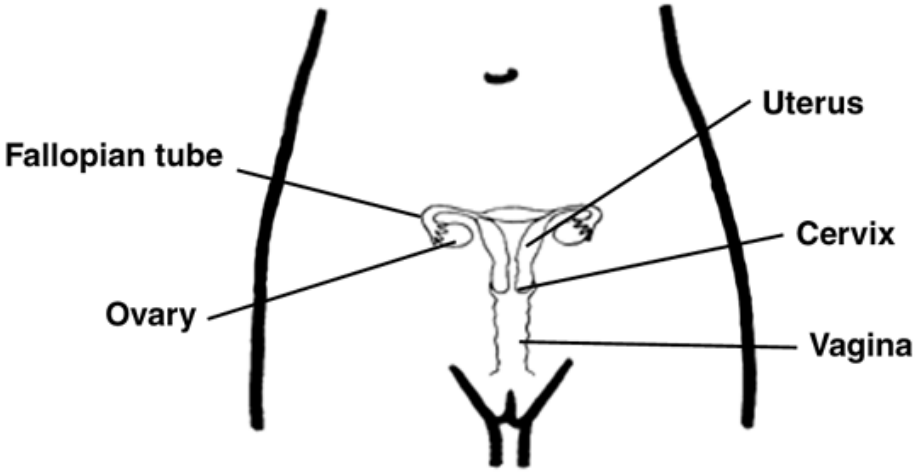
No matter where a cancer may spread, it is always named for the place where it started. For example, breast cancer that has spread to the liver is still called breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is metastatic prostate cancer, not bone cancer.

Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

Not all tumors are cancerous. Tumors that aren't cancer are called *benign*. Benign tumors can cause problems -- they can grow very large and press on healthy organs and tissues. But they cannot grow into (invade) other tissues. Because they can’t invade, they also can't spread to other parts of the body (metastasize). These tumors are almost never life threatening.

What is endometrial cancer?

Endometrial cancer starts in the endometrium, the inner lining of the *uterus* (womb). The picture below shows where the uterus is located.

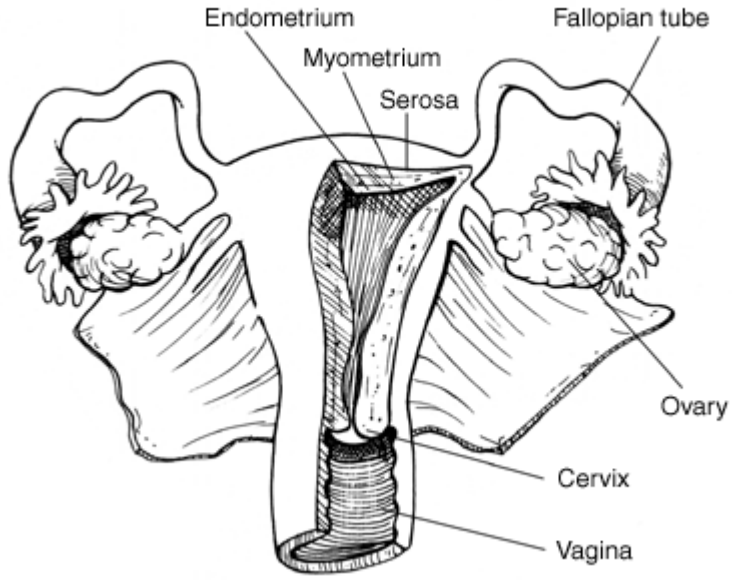


About the uterus and endometrium

The uterus is a hollow organ, which is normally about the size and shape of a medium-sized pear. The uterus is where a fetus grows and develops when a woman is pregnant. The uterus has 2 main parts (see image below):

- The *cervix* is the lower end of the uterus that extends into the vagina.
- The upper part of the uterus is called the *body* or the *corpus*. (*Corpus* is the Latin word for body.)

Although the cervix is technically part of the uterus, when people talk about cancer of the uterus, they usually mean the body, not the cervix.



The body of the uterus has 2 main layers. The inner layer or lining is called the *endometrium*. The outer layer of muscle is known as the *myometrium*. This thick layer of muscle is needed to push the baby out during birth. The tissue coating the outside of the uterus is the *serosa*.

During a woman's menstrual cycle, hormones cause the endometrium to change. During the early part of the cycle, before the ovaries release an egg (ovulation), the ovaries produce hormones called *estrogens*. Estrogen causes the endometrium to thicken so that it could nourish an embryo if pregnancy occurs. If there is no pregnancy, estrogen is produced in lower amounts and more of the hormone called *progesterone* is made after ovulation. This prepares the innermost layer of the lining to shed. By the end of the cycle, the endometrial lining is shed from the uterus and becomes the menstrual flow (period). This cycle repeats until the woman’s goes through menopause (change of life).

Cancers of the uterus and endometrium

The 2 main types of cancer of the uterus are:

- **Uterine sarcomas**, which start in the muscle layer (myometrium) or supporting connective tissue of the uterus. These include uterine leiomyosarcomas and endometrial stromal sarcomas. These cancers are not covered here, but are discussed in detail in *Uterine Sarcomas*.
- **Endometrial carcinomas**, which start in the cells of the inner lining of the uterus (the endometrium). Nearly all cancers of the uterus are this type. These cancers are the focus of the remainder of this information.

Endometrial carcinomas can be divided into different types based on how the cells look under the microscope (histologic types). These include:

- Adenocarcinoma, (most endometrial cancers are adenocarcinomas)
- Carcinosarcoma (discussed more below)
- Squamous cell carcinoma
- Undifferentiated carcinoma
- Small cell carcinoma
- Transitional carcinoma

The most common type of adenocarcinoma is known as *endometrioid cancer.* Endometrioid cancers are made up of cells in glands that look much like the normal uterine lining (endometrium). Some of these cancers contain squamous cells (squamous cells are flat, thin cells that can be found on the outer surface of the cervix), as well as glandular cells. A cancer with both types of cells is called an *adenocarcinoma with squamous differentiation.* If, under the microscope, the glandular cells look cancerous but the squamous cells don't, the tumor may be called an *adenoacanthoma*. If both the squamous cells and the glandular cells look malignant (cancerous), these tumors can be called *adenosquamous* (or *mixed cell*) carcinomas. There are other variants (or sub-types) of endometrioid cancers, such as *secretory* carcinoma, *ciliated* carcinoma, and villoglandular adenocarcinoma.

Clear-cell carcinoma, *mucinous adenocarcinoma*, and *papillary serous adenocarcinoma*. are less common types of endometrial adenocarcinomas. These types tend to be more aggressive than most endometrial cancers. They tend to grow quickly and often have spread outside the uterus at the time of diagnosis.

Classifying endometrial carcinomas

Doctors sometimes classify endometrial carcinomas based on their outlook and underlying causes.

The **grade** of an endometrial cancer is based on how much the cancer forms glands that look similar to those found in normal, healthy endometrium. In lower-grade cancers, more of the

cancerous tissue forms glands. In higher-grade cancers, more of the cancer cells are arranged in a haphazard or disorganized way and do not form glands.

- **Grade 1** tumors have 95% or more of the cancerous tissue forming glands.
- **Grade 2** tumors have between 50% and 94% of the cancerous tissue forming glands.
- **Grade 3** tumors have less than half of the cancerous tissue forming glands. Grade 3 cancers are called "high-grade." They tend to be aggressive and have a poorer outlook than lower grade cancers (grades 1 and 2).

Type 1 endometrial cancers are thought to be caused by excess estrogen. They sometimes develop from atypical hyperplasia, an abnormal overgrowth of cells in the endometrium (see the risk factors section). Type 1 cancers are usually not very aggressive and are slow to spread to other tissues. Grades 1 and 2 endometrioid cancers are “type 1” endometrial cancers.

Type 2 endometrial cancer make up a small number of endometrial cancers. Experts aren’t sure what causes type 2 cancers, but they don’t seem to be caused by too much estrogen. Type 2 cancers include all endometrial carcinomas that aren’t type 1, such as papillary serous carcinoma, clear-cell carcinoma, undifferentiated carcinoma, and grade 3 endometrioid carcinoma. These cancers don’t look at all like normal endometrium and so are called “poorly differentiated” or “high-grade.” Because type 2 cancers are more likely to grow and spread outside the uterus, they have a poorer outlook (than type 1 cancers). Doctors tend to treat these cancers more aggressively.

Uterine carcinosarcoma (CS) starts in the endometrium and has features of both endometrial carcinoma and sarcoma. In the past, CS was considered a type of uterine sarcoma, but doctors now believe that CS is a carcinoma that is abnormal and so no longer looks much like the cells it came from (poorly differentiated).

Uterine CS is considered a type 2 endometrial carcinoma. CS tumors are also known as *malignant mixed mesodermal tumors or malignant mixed mullerian tumors* (MMMTs). They make up about 4% of uterine cancers.

Cervical cancers

Cancers that start in the cervix and then spread to the body of the uterus are different from cancers that start in the body of the uterus; they are described in *Cervical Cancer*.

What are the key statistics about endometrial cancer?

In the United States, cancer of the endometrium is the most common cancer of the female reproductive organs. The American Cancer Society estimates for cancer of the uterus in the United States for 2015 are:

- About 54,870 new cases of cancer of the body of the uterus (uterine body or corpus) will be diagnosed.
- About 10,170 women will die from cancers of the uterine body.

These estimates include both endometrial cancers and uterine sarcomas. Up to 8% of uterine body cancers are sarcomas, so the actual numbers for endometrial cancer cases and deaths are slightly lower than these estimates.

Endometrial cancer is rare in women under the age of 45. Most (about 3 out of 4) cases are found in women aged 55 and over The average chance of a woman being diagnosed with this cancer during her lifetime is about 1 in 37. There are over 600,000 women who are survivors of this cancer. This cancer is slightly more common in white women, but black women are more likely to die from it.

What are the risk factors for endometrial cancer?

A risk factor is anything that changes (raises or lowers) your chance of getting a disease such as cancer. Different cancers have different risk factors. For example, unprotected exposure to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for many cancers.

There are different kinds of risk factors. Some, such as your age or race, can't be changed. Others are related to personal choices such as smoking, exercising, body weight, drinking, or diet. Some factors influence risk more than others. Although certain factors increase a woman's risk for developing endometrial cancer, they do not always cause the disease. Many women with one or more risk factors never develop endometrial cancer. Some women with endometrial cancer do not have any known risk factors. Even if a woman with endometrial cancer has one or more risk factors, there is no way to know which, if any, of these factors was responsible for her cancer.

Factors that influence the risk of endometrial cancer include:

- Things that affect hormone levels, like taking estrogen after menopause, birth control pills, or tamoxifen; the number of menstrual cycles (over a lifetime), pregnancy, obesity, , certain ovarian tumors, and polycystic ovarian syndrome

- Use of an intrauterine device
- Age
- Diet and exercise
- Diabetes
- Family history (having close relatives with endometrial or colorectal cancer)
- Having been diagnosed with breast or ovarian cancer in the past
- Having been diagnosed with endometrial hyperplasia in the past
- Treatment with radiation therapy to the pelvis to treat another cancer

Some of these, like pregnancy, birth control pills, and the use of an intrauterine device are linked to a lower risk of endometrial cancer, while many are linked to a higher risk. These factors and how they affect endometrial cancer risk are discussed in more detail below.

Hormone factors

A woman's hormone balance plays a part in the development of most endometrial cancers. Many of the risk factors for endometrial cancer affect estrogen levels. Before menopause, the ovaries are the major source of the 2 main types of female hormones -- estrogen and progesterone. The balance between these hormones changes during a woman's menstrual cycle each month. This produces a woman's monthly periods and keeps the endometrium healthy. A shift in the balance of these hormones toward more estrogen increases a woman's risk for developing endometrial cancer. After menopause, the ovaries stop making these hormones, but a small amount of estrogen is still made naturally in fat tissue. Estrogen from fat tissue has a bigger impact after menopause than it does before menopause. Female hormones can be taken as birth control pills to prevent pregnancy and as hormone therapy to treat symptoms of menopause.

Estrogen therapy

Treating the symptoms of menopause with hormones is known as *menopausal hormone therapy* (or sometimes *hormone replacement therapy*). Estrogen is the major part of this treatment. Estrogen treatment can reduce hot flashes, improve vaginal dryness, and help prevent the weakening of the bones (osteoporosis) that can occur with menopause. Doctors have found, however, that using estrogen alone (without progesterone) can lead to type I endometrial cancer in women who still have a uterus. To lower that risk back to normal, a progestin (progesterone or a drug like it) must be given along with estrogen. This approach is called *combination hormone therapy*.

Women who take progesterone along with estrogen to treat menopausal symptoms do not have an increased risk of endometrial cancer. Still, taking this combination increases a woman's chance of developing breast cancer and also increases the risk of serious blood clots.

If you are taking (or plan to take) hormones after menopause, it is important to discuss the potential risks (including cancer, blood clots, heart attacks, and stroke) with your doctor. Like any other medicine, hormones should be used only at the lowest dose that is needed and for the shortest possible time to control symptoms. As with any other medicine you take for a long time, you'll need to see your doctor regularly. Experts recommend yearly follow-up pelvic exams. If you have any abnormal bleeding or discharge from the vagina you should see your doctor or other health care provider right away (and not wait for a check-up).

For more information about the cancer risks from taking hormones after menopause, see *Menopausal Hormone Therapy and Cancer Risk*.

Birth control pills

Using birth control pills (oral contraceptives) lowers the risk of endometrial cancer. The risk is lowest in women who take the pill for a long time, and this protection continues for at least 10 years after a woman stops taking this form of birth control. However, it is important to look at all of the risks and benefits when choosing a contraceptive method; endometrial cancer risk is only one factor to be considered. It's a good idea to discuss the pros and cons of different types of birth control with your doctor.

Total number of menstrual cycles

Having more menstrual cycles during a woman's lifetime raises her risk of endometrial cancer. Starting menstrual periods (menarche) before age 12 and/or going through menopause later in life raises the risk. Starting periods early is less a risk factor for women with early menopause. Likewise, late menopause may not lead to a higher risk in women whose periods began later in their teens.

Pregnancy

The hormonal balance shifts toward more progesterone during pregnancy. So having many pregnancies protects against endometrial cancer. Women who have never been pregnant have a higher risk, especially if they were also infertile (unable to become pregnant).

Obesity

Most of a woman's estrogen is produced by her ovaries, but fat tissue can change some other hormones (called *androgens*) into estrogens. Having more fat tissue can increase a woman's estrogen levels, which increases her endometrial cancer risk. In comparison with women who

maintain a healthy weight, endometrial cancer is twice as common in overweight women, and more than three times as common in obese women.

Tamoxifen

Tamoxifen is a drug that is used to prevent and treat breast cancer. Tamoxifen acts as an anti-estrogen in breast tissue, but it acts like an estrogen in the uterus. In women who have gone through menopause, it can cause the uterine lining to grow, which increases the risk of endometrial cancer.

The risk of developing endometrial cancer from tamoxifen is low (less than 1% per year). Women taking tamoxifen must balance this risk against the benefits of this drug in treating and preventing breast cancer. This is an issue women should discuss with their doctors. If you are taking tamoxifen, you should have yearly gynecologic exams and should be sure to report any abnormal bleeding, as this could be a sign of endometrial cancer.

Ovarian tumors

A certain type of ovarian tumor, the *granulosa cell tumor*, often makes estrogen. Estrogen release by one of these tumors is not controlled the way hormone release from the ovaries is, and can sometimes lead to high estrogen levels. The resulting hormone imbalance can stimulate the endometrium and even lead to endometrial cancer. In fact, sometimes vaginal bleeding from endometrial cancer is the first symptom of one of these tumors.

Polycystic ovarian syndrome

Women with a condition called *polycystic ovarian syndrome* (PCOS) have abnormal hormone levels, such as higher androgen (male hormones) and estrogen levels and lower levels of progesterone. The increase in estrogen relative to progesterone can increase a woman's chance of getting endometrial cancer.

Use of an intrauterine device

Women who used an intrauterine device (IUD) for birth control seem to have a lower risk of getting endometrial cancer. Information about this protective effect is limited to IUDs that do not contain hormones. Researchers have not yet studied whether newer types of IUDs that release progesterone have any effect on endometrial cancer risk. However, these IUDs are sometimes used to treat pre-cancers and early endometrial cancers in women who wish to preserve child-bearing ability.

Age

The risk of endometrial cancer increases as a woman gets older.

Diet and exercise

A high-fat diet can increase the risk of several cancers, including endometrial cancer. Because fatty foods are also high-calorie foods, a high-fat diet can lead to obesity, which is a well-known endometrial cancer risk factor. Many scientists think this is the main way in which a high-fat diet raises endometrial cancer risk. Some scientists think that fatty foods may also have a direct effect on estrogen metabolism, which increases endometrial cancer risk.

Physical activity lowers the risk of endometrial cancer. Several studies found that women who exercised more had a lower risk of endometrial cancer, while in one study women who spent more time sitting had a higher risk. To learn more, you can read the *American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention*.

Diabetes

Endometrial cancer may be as much as 4 times more common in women with diabetes. Diabetes is more common in people who are overweight, but even people with diabetes who are not overweight have a higher risk of endometrial cancer.

Family history

Endometrial cancer tends to run in some families. Some of these families also have an inherited tendency to develop colon cancer. This disorder is called *hereditary nonpolyposis colon cancer* (HNPCC). Another name for HNPCC is Lynch syndrome. In most cases, this disorder is caused by a defect in either the gene *MLH1* or the gene *MSH2*. But at least 5 other genes can cause HNPCC: *MLH3*, *MSH6*, *TGBR2*, *PMS1*, and *PMS2*. An abnormal copy of any one of these genes reduces the body's ability to repair damage to its DNA or regulate cell growth. This results in a very high risk of colon cancer, as well as a high risk of endometrial cancer. Women with this syndrome have a 40% to 60% risk of developing endometrial cancer at some point. The risk of ovarian cancer is also increased. General information about inherited cancer syndromes can be found in *Family Cancer Syndromes.*

Some families have a high rate of only endometrial cancer. These families may have a different genetic disorder that hasn't been discovered yet.

Breast or ovarian cancer

Women who have had breast cancer or ovarian cancer may have an increased risk of developing endometrial cancer, too. Some of the dietary, hormonal, and reproductive risk factors for breast and ovarian cancer also increase endometrial cancer risk.

Endometrial hyperplasia

Endometrial hyperplasia is an increased growth of the endometrium. Mild or simple hyperplasia, the most common type, has a very small risk of becoming cancerous. It may go away on its own or after treatment with hormone therapy. If the hyperplasia is called “atypical,” it has a higher chance of becoming a cancer. Simple atypical hyperplasia turns into cancer in about 8% of cases if it’s not treated. If it’s not treated, complex atypical hyperplasia (CAH) has a risk of becoming cancerous in up to 29% of cases, and the risk of having an undetected endometrial cancer is even higher. For this reason, CAH is usually treated. (Treatment is discussed in the section "Can endometrial cancer be prevented?")

Prior pelvic radiation therapy

Radiation used to treat some other cancers can damage the DNA of cells, sometimes increasing the risk of a second type of cancer such as endometrial cancer.

Do we know what causes endometrial cancer?

We do not yet know exactly what causes most cases of endometrial cancer, but we do know that there are certain risk factors, particularly hormone imbalance, for this type of cancer. A great deal of research is going on to learn more about the disease. We know that most endometrial cancer cells contain estrogen and/or progesterone receptors on their surfaces. Somehow, interaction of these receptors with their hormones leads to increased growth of the endometrium. This can mark the beginning of cancer. The increased growth can become more and more abnormal until it develops into a cancer.

As noted in the risk factors section, many of the known endometrial cancer risk factors affect the balance between estrogen and progesterone in the body.

Scientists are learning more about changes in the DNA of certain genes that occur when normal endometrial cells become cancerous. Some of these are discussed in "What's new in endometrial cancer research and treatment?"

Can endometrial cancer be prevented?

Most cases of endometrial cancer cannot be prevented, but there are some things that may lower your risk of developing this disease.

One way to lower endometrial cancer risk is to do what you can to change your risk factors whenever possible. For example, women who are overweight or obese have up to 3½ times the risk of getting endometrial cancer compared with women at a healthy weight. Getting to and maintaining a healthy weight is one way to lower the risk of this cancer.

Studies have also linked higher levels of physical activity to lower risks of endometrial cancer, so engaging in regular physical activity (exercise) may also be a way to help lower endometrial cancer risk. An active lifestyle can help you stay at a healthy weight, as well as lower the risk of high blood pressure and diabetes (other risk factors for endometrial cancer.

Estrogen to treat the symptoms of menopause is available in many different forms like pills, skin patches, shots, creams, and vaginal rings. If you are thinking about using estrogen for menopausal symptoms, ask your doctor about how it will affect your risk of endometrial cancer. Progestins (progesterone-like drugs) can reduce the risk of endometrial cancer in women taking estrogen therapy, but this combination increases the risk of breast cancer. If you still have your uterus and are taking estrogen therapy, discuss this issue with your doctor.

Getting proper treatment of pre-cancerous disorders of the endometrium is another way to lower the risk of endometrial cancer. Most endometrial cancers develop over a period of years. Many are known to follow and possibly start from less serious abnormalities of the endometrium called *endometrial hyperplasia* (see “What are the risk factors for endometrial cancer?”). Some cases of hyperplasia will go away without treatment, but it sometimes needs to be treated with hormones or even surgery. Treatment with progestins (see “Hormone therapy for endometrial cancer”) and a dilation and curettage (D&C) or hysterectomy can prevent hyperplasia from becoming cancerous. (D&C is described in “How is endometrial cancer diagnosed?”*)* Abnormal vaginal bleeding is the most common symptom of endometrial pre-cancers and cancers, and it needs to be reported and evaluated right away.

Women with hereditary nonpolyposis colon cancer (HNPCC, Lynch syndrome) have a very high risk of endometrial cancer. A woman with HNPCC may choose to have her uterus removed (a hysterectomy) after she has finished having children to prevent endometrial cancer. One study found that none of 61 women with HNPCC who had prophylactic (preventative) hysterectomies was later found to have endometrial cancer, while 1/3 of the women who didn't have the surgery were diagnosed with endometrial cancer over the next 7 years.

Can endometrial cancer be found early?

In most cases, noticing any signs and symptoms of endometrial cancer, such as abnormal vaginal bleeding or discharge (that is increasing in amount, occurring between periods, or occurring after menopause), and reporting them right away to your doctor allows the disease to be diagnosed at an early stage. Early detection improves the chances that your cancer will be treated successfully. But some endometrial cancers may reach an advanced stage before signs and symptoms can be noticed. More information can be found in “Signs and symptoms of endometrial cancer”

Early detection tests

Early detection (also called screening) refers to the use of tests to find a disease such as cancer in people who do not have symptoms of that disease.

Women at average endometrial cancer risk

At this time, there are no screening tests or exams to find endometrial cancer early in women who are at average endometrial cancer risk and have no symptoms.

The American Cancer Society recommends that, at menopause, all women should be told about the risks and symptoms of endometrial cancer and strongly encouraged to report any vaginal bleeding, discharge, or spotting to their doctor.

Women should talk to their doctors about getting regular pelvic exams. A pelvic exam can find some cancers, including some advanced uterine cancers, but it is not very effective in finding early endometrial cancers.

The Pap test (or Pap smear), which screens women for cervical cancer, can occasionally find some early endometrial cancers, but it's not a good test for this type of cancer. The Pap test is very effective in finding early cancers of the cervix (the lower part of the uterus). For information on screening tests for cervical cancer, see *Cervical Cancer: Prevention and Early Detection*.

Women at increased endometrial cancer risk

The American Cancer Society recommends that most women at increased risk should be informed of their risk and be advised to see their doctor whenever they have any abnormal vaginal bleeding. This includes women whose risk of endometrial cancer is increased due to increasing age, late menopause, never giving birth, infertility, obesity, diabetes, high blood pressure, estrogen treatment, or tamoxifen therapy.

Women who have (or may have) hereditary non-polyposis colon cancer (HNPCC, sometimes called Lynch syndrome) have a very high risk of endometrial cancer. If colon or endometrial cancer has occurred in several family members, you might want to think about having genetic counseling to learn about your family's risk of having HNPCC. If you (or a close relative) have genetic testing and are found to have a mutation in one of the genes for HNPCC, you have a high risk of getting endometrial cancer. See *Genetic Testing: What You Need to Know* for more on genetic testing.

The American Cancer Society recommends that women who have (or may have) HNPCC be offered yearly testing for endometrial cancer with endometrial biopsy beginning at age 35. Their doctors should discuss this test with them, including its risks, benefits, and limitations. This applies to women known to carry HNPCC-linked gene mutations, women who are likely to carry such a mutation (those with a mutation known to be present in the family), and

women from families with a tendency to get colon cancer where genetic testing has not been done.

Another option for a woman who has (or may have) HNPCC would be to have a hysterectomy once she is finished having children. This was discussed in “Can endometrial cancer be prevented?”

Signs and symptoms of endometrial cancer

There are a few symptoms that may point to endometrial cancer, but some are more common as this cancer becomes advanced.

Unusual vaginal bleeding, spotting, or other discharge

About 90% of women diagnosed with endometrial cancer have abnormal vaginal bleeding, such as a change in their periods or bleeding between periods or after menopause. This symptom can also occur with some non-cancerous conditions, but it is important to have a doctor look into any irregular bleeding right away. If you have gone through menopause already, it’s especially important to report any vaginal bleeding, spotting, or abnormal discharge to your doctor.

Non-bloody vaginal discharge may also be a sign of endometrial cancer. Even if you cannot see blood in the discharge, it does not mean there is no cancer. In about 10% of cases, the discharge associated with endometrial cancer is not bloody. Any abnormal discharge should be checked out by your doctor.

Pelvic pain and/or mass and weight loss

Pain in the pelvis, feeling a mass (tumor), and losing weight without trying can also be symptoms of endometrial cancer. These symptoms are more common in later stages of the disease. Still, any delay in seeking medical help may allow the disease to progress even further. This lowers the odds for successful treatment.

Although any of these symptoms can be caused by things other than cancer, it’s important to have them checked out by a doctor.

How is endometrial cancer diagnosed?

Most women are not screened for endometrial cancer, so it’s most often diagnosed after a woman goes to her doctor because she has symptoms.

Medical history and physical exam

If you have any of the symptoms of endometrial cancer (see “Signs and symptoms of endometrial cancer”), you should visit your doctor. The doctor will ask about your symptoms, risk factors, and medical history. The doctor will also perform a general physical exam and a pelvic exam.

Seeing a specialist

If there’s a possibility you could have endometrial cancer, you should be examined by a gynecologist, a doctor qualified to diagnose and treat diseases of the female reproductive system. Gynecologists can diagnose endometrial cancer, as well as treat some early cases. Specialists in treating cancers of the endometrium and other female reproductive organs are called gynecologic oncologists. These doctors treat both early and advanced cases of endometrial cancer.

Ultrasound

Ultrasound is often one of the first tests used to look at the uterus, ovaries, and fallopian tubes in women with a possible gynecologic problem. Ultrasound tests use sound waves to take pictures of parts of the body. A small instrument called a transducer or probe gives off sound waves and picks up the echoes as they bounce off the organs. A computer translates the echoes into pictures.

For a *pelvic ultrasound*, the transducer is placed on the skin of the lower part of the abdomen. Often, to get good pictures of the uterus, ovaries, and fallopian tubes, the bladder needs be full. That is why women getting a pelvic ultrasound are told to drink lots of water before the exam.

A *transvaginal ultrasound* (TVUS) is often preferred for looking at the uterus. For this test, the TVUS probe (that works the same way as the ultrasound transducer) is put into the vagina. Images from the TVUS can be used to see if the uterus contains a mass (tumor), or if the endometrium is thicker than usual, which can be a sign of endometrial cancer. It may also help see if a cancer is growing into the muscle layer of the uterus (myometrium).

Salt water (saline) may be put through a small tube into the uterus before the ultrasound so the doctor can see the uterine lining more clearly. This procedure is called a *saline infusion sonogram* or *hysterosonogram*. (sonogram is another term for ultrasound.) Sonography may help doctors pinpoint the area they want to biopsy if other procedures didn't detect a tumor.

Sampling endometrial tissue

To find out whether endometrial hyperplasia or endometrial cancer is present, the doctor must remove some tissue so that it can be looked at under a microscope. Endometrial tissue

can be obtained by endometrial biopsy or by dilation and curettage (D&C) with or without a hysteroscopy. A specialist such as a gynecologist usually does these procedures, which are described below.

Endometrial biopsy

An endometrial biopsy is the most commonly performed test for endometrial cancer and is very accurate in postmenopausal women. It can be done in the doctor's office. In this procedure a very thin flexible tube is inserted into the uterus through the cervix. Then, using suction, a small amount of endometrium is removed through the tube. The suctioning takes about a minute or less. The discomfort is similar to menstrual cramps and can be helped by taking a nonsteroidal anti-inflammatory drug such as ibuprofen before the procedure. Sometimes numbing medicine (local anesthetic) is injected into the cervix just before the procedure to help reduce the pain.

Hysteroscopy

For this technique doctors insert a tiny telescope (about $^{1}/_{6}$ inch in diameter) into the uterus through the cervix. To get a better view of the inside of the uterus, the uterus is filled with salt water (saline). This lets the doctor see and biopsy anything abnormal, such as a cancer or a polyp. This is usually done using a local anesthesia (numbing medicine) with the patient awake.

Dilation and curettage (D&C)

If the endometrial biopsy sample doesn't provide enough tissue, or if the biopsy suggests cancer but the results are uncertain, a D&C must be done. In this outpatient procedure, the opening of the cervix is enlarged (dilated) and a special instrument is used to scrape tissue from inside the uterus. This may be done with or without a hysteroscopy.

This procedure takes about an hour and may require general anesthesia (where you are asleep) or conscious sedation (given medicine into a vein to make you drowsy) either with local anesthesia injected into the cervix or a spinal (or epidural). A D&C is usually done in an outpatient surgery area of a clinic or hospital. Most women have little discomfort after this procedure.

Testing endometrial tissue

Endometrial tissue samples removed by biopsy or D&C are looked at under the microscope to see whether cancer is present. If cancer is found, the lab report will state what type of endometrial cancer it is (like endometrioid or clear cell) and what grade it is.

Endometrial cancer is graded on a scale of 1 to 3 based on how much it looks like normal endometrium. (This was detailed in “What is endometrial cancer?”) Women with lower grade cancers are less likely to have advanced disease or recurrences.

If the doctor suspects hereditary non-polyposis colon cancer (HNPCC) as an underlying cause of the endometrial cancer, the tumor tissue can be tested for protein changes (such as having fewer mismatch repair proteins) or DNA changes (called microsatellite instability, or MSI) that can happen when one of the genes that causes HNPCC is faulty. If these protein or DNA changes are present, the doctor may recommend that you see a genetic counselor to consider genetic testing for the genes that cause HNPCC. Testing for low mismatch repair protein levels or for MSI is most often ordered in women diagnosed with endometrial cancer at a younger than usual age or who have a family history of endometrial or colon cancer.

Tests to look for cancer spread

If the doctor suspects that your cancer is advanced, you will probably have to have other tests to look for cancer spread.Computed tomography (CT)

The CT scan is an x-ray procedure that creates detailed, cross-sectional images of your body. For a CT scan, you lie on a table while an X-ray takes pictures. Instead of taking one picture, like a standard x-ray, a CT scanner takes many pictures as the camera rotates around you. A computer then combines these pictures into an image of a slice of your body. The machine will take pictures of many slices of the part of your body that is being studied.

Before any pictures are taken, you may be asked to drink 1 to 2 pints of a liquid called oral contrast. This helps outline the intestine so that certain areas are not mistaken for tumors. You may also receive an IV (intravenous) line through which a different kind of contrast dye (IV contrast) is injected. This helps better outline structures in your body.

The injection can cause some flushing (redness and warm feeling that may last hours to days). A few people are allergic to the dye and get hives. Rarely, more serious reactions like trouble breathing and low blood pressure can occur. Medicine can be given to prevent and treat allergic reactions. Be sure to tell the doctor if you have ever had a reaction to any contrast material used for x-rays.

CT scans are not used to diagnose endometrial cancer. However, they may be helpful to see whether the cancer has spread to other organs and to see if the cancer has come back after treatment.

CT scans can also be used to precisely guide a biopsy needle into a suspected area of cancer spread. For this procedure, called a CT-guided needle biopsy, you remain on the CT scanning table while a doctor moves a biopsy needle toward the mass. CT scans are repeated until the doctor is sure that the needle is inside the mass. A fine needle biopsy sample (tiny fragment of tissue) or a core needle biopsy sample (a thin cylinder of tissue about ½ inch long and less than $^{1}/_{8}$ inch in diameter) is removed and looked at under a microscope.

CT scans take longer than regular x-rays. You might feel a bit confined by the ring you lie within when the pictures are being taken.

Magnetic resonance imaging (MRI)

MRI scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed and then released in a pattern formed by the type of tissue and by certain diseases. A computer translates the pattern of radio waves given off by the tissues into a very detailed image of parts of the body. This creates cross sectional slices of the body like a CT scanner and it also produces slices that are parallel with the length of your body.

MRI scans are particularly helpful in looking at the brain and spinal cord. Some doctors also think MRI is a good way to tell whether, and how far, the endometrial cancer has grown into the body of the uterus. MRI scans may also help find enlarged lymph nodes with a special technique that uses very tiny particles of iron oxide. These are given into a vein and settle into lymph nodes where they can be spotted by MRI.

Sometimes a contrast material is injected into a vein, just as with CT scans. The contrast used for MRI is different than the one used for CT, so being allergic to one doesn't mean you are allergic to the other. MRI scans are a little more uncomfortable than CT scans. First, they take longer, often up to an hour. Also, you have to be placed inside a tube, which is confining and can upset people with fear of enclosed places. Special, "open" MRI machines can help with this if needed, however the drawback is that the images may not be as good. The machine also makes a thumping or buzzing noise that you may find disturbing. Many places will provide headphones with music to help block out this noise.

Positron emission tomography (PET)

In this test radioactive glucose (sugar) is given to look for cancer cells. Because cancers use glucose (sugar) at a higher rate than normal tissues, the radioactivity will tend to concentrate in the cancer. A scanner can spot the radioactive deposits. This test can be helpful for spotting small collections of cancer cells. Special scanners combine a PET scan with a CT to more precisely locate areas of cancer spread. PET scans are not a routine part of the work-up of early endometrial cancer, but may be used for more advanced cases.

Cystoscopy and proctoscopy

If a woman has problems that suggest the cancer has spread to the bladder or rectum, the inside of these organs will probably be looked at through a lighted tube. In *cystoscopy* the tube is placed into the bladder through the urethra. In *proctoscopy* the tube is placed in the rectum. These exams allow the doctor to look for possible cancers. Small tissue samples can also be removed during these procedures for pathologic (microscopic) testing. They can be done using a local anesthetic but some patients may require general anesthesia. Your doctor

will let you know what to expect before and after the procedure. These procedures were used more often in the past, but now are rarely part of the work up for endometrial cancer.

Blood tests

Complete blood count

The complete blood count (CBC) is a test that measures the different cells in the blood, such as the red blood cells, the white blood cells, and the platelets. Endometrial cancer can cause bleeding, which can lead to low red blood cell counts (anemia).

CA 125 blood test

CA 125 is a substance released into the bloodstream by many, but not all, endometrial and ovarian cancers. If a woman has endometrial cancer, a very high blood CA 125 level suggests that the cancer has probably spread beyond the uterus. Some doctors check CA 125 levels before surgery or other treatment. If they are elevated, they can be checked again to find out how well the treatment is working (for example, levels will drop after surgery if all the cancer is removed).

CA 125 levels are not needed to diagnose endometrial cancer, and so this test isn't ordered on all patients.

How is endometrial cancer staged?

Staging is the process of looking at all of the information the doctors have learned about your tumor to tell how much the cancer may have spread. The stage of an endometrial cancer is the most important factor in choosing a treatment plan. Ask your doctor to explain the stage of your cancer so that you can make fully informed choices about your treatment.

A staging system is a standard way to describe how far a patient's cancer has spread. The 2 systems used for staging endometrial cancer, the *FIGO* (International Federation of Gynecology and Obstetrics) system and the American Joint Committee on Cancer TNM staging system are basically the same. They both classify this cancer on the basis of 3 factors: the extent of the tumor (T), whether the cancer has spread to lymph nodes (N) and whether it has spread to distant sites (M). The system described below is the most recent AJCC system. It went into effect January 2010. The difference between the AJCC system and the FIGO system is that the FIGO system doesn't include stage 0.

Endometrial cancer is staged based on examination of tissue removed during an operation. This is known as *surgical staging*, and means that doctors often can't tell for sure what stage the cancer is until after surgery is done.

A doctor may order tests before surgery, such as ultrasound, MRI, or CT scan, to look for signs that a cancer has spread. Although it is not as good as the surgical stage, this information can be helpful in planning surgery and other treatments. If these tests show that the cancer may have spread outside the uterus, you may be referred to a gynecologic oncologist (if you are not already seeing one).

The staging system looks at how far the cancer has spread:

- It can spread *locally* to the cervix and other parts of the uterus.
- It can also spread *regionally* to nearby lymph nodes (bean-sized organs that are part of the immune system). The regional lymph nodes are found in the pelvis and farther away along the aorta (the main artery that runs from the heart down along the back of the abdomen and pelvis). The lymph nodes along the aorta are called para-aortic nodes.
- Finally, the cancer can spread (*metastasize*) to distant lymph nodes, the upper abdomen, the omentum (a large fatty sheet of tissue in the abdomen that drapes like an apron over the stomach, intestines, and other organs), or other organs such as lung, liver, bone, and brain.

Tumor extent (T)

T0: No signs of a tumor in the uterus

Tis: Pre-invasive cancer (also called *carcinoma in-situ*). Cancer cells are only found in the surface layer of cells of the endometrium, without growing into the layers of cells below.

T1: The cancer is only growing in the body of the uterus. It may also be growing into the glands of the cervix, but is not growing into the supporting connective tissue of the cervix.

- **T1a:** The cancer is in the endometrium (inner lining of the uterus) and may have grown from the endometrium less than halfway through the underlying muscle layer of the uterus (the myometrium).
- **T1b:** The cancer has grown from the endometrium into the myometrium, growing more than halfway through the myometrium. The cancer has not spread beyond the body of the uterus.

T2: The cancer has spread from the body of the uterus and is growing into the supporting connective tissue of the cervix (called the *cervical stroma*). The cancer has not spread outside of the uterus.

T3: The cancer has spread outside of the uterus, but has not spread to the inner lining of the rectum or urinary bladder.

- **T3a:** The cancer has spread to the outer surface of the uterus (called the *serosa*) and/or to the fallopian tubes or ovaries (the *adnexa*)

- **T3b:** The cancer has spread to the vagina or to the tissues around the uterus (the parametrium).

T4: The cancer has spread to the inner lining of the rectum or urinary bladder (called the *mucosa*)

Lymph node spread (N)

NX: Spread to nearby lymph nodes cannot be assessed

N0: The cancer has not spread to nearby lymph nodes

N1: The cancer has spread to lymph nodes in the pelvis

N2: The cancer has spread to lymph nodes along the aorta (peri-aortic lymph nodes)

Distant spread (M)

M0: The cancer has not spread to distant lymph nodes, organs, or tissues

M1: The cancer has spread to distant lymph nodes, the upper abdomen, the omentum, or other organs (such as the lungs or liver)

AJCC stage grouping and FIGO stages

Information about the tumor, lymph nodes, and any cancer spread is then combined to assign the stage of disease. This process is called *stage grouping*. The stages are described using the number 0 and Roman numerals from I to IV. Some stages are divided into sub-stages indicated by letters and numbers.

Stage 0

Tis, N0, M0: This stage is also known as *carcinoma in-situ*. Cancer cells are only found in the surface layer of cells of the endometrium, without growing into the layers of cells below. The cancer has not spread to nearby lymph nodes or distant sites. This is a pre-cancerous lesion. This stage is not included in the FIGO staging system.

Stage I

T1, N0, M0: The cancer is only growing in the body of the uterus. It may also be growing into the glands of the cervix, but is not growing into the supporting connective tissue of the cervix**.** The cancer has not spread to lymph nodes or distant sites.

- **Stage IA (T1a, N0, M0):** In this earliest form of stage I, the cancer is in the endometrium (inner lining of the uterus) and may have grown from the endometrium less than halfway

through the underlying muscle layer of the uterus (the myometrium). It has not spread to lymph nodes or distant sites.

- **Stage IB (T1b, N0, M0):** The cancer has grown from the endometrium into the myometrium, growing more than halfway through the myometrium. The cancer has not spread beyond the body of the uterus.

Stage II

T2, N0, M0: The cancer has spread from the body of the uterus and is growing into the supporting connective tissue of the cervix (called the *cervical stroma*). The cancer has not spread outside of the uterus. The cancer has not spread to lymph nodes or distant sites.

Stage III

T3, N0, M0: Either the cancer has spread outside of the uterus or into nearby tissues in the pelvic area.

- **Stage IIIA (T3a, N0, M0):** The cancer has spread to the outer surface of the uterus (called the serosa) and/or to the fallopian tubes or ovaries (the adnexa). The cancer has not spread to lymph nodes or distant sites.

- **Stage IIIB (T3b, N0, M0):** The cancer has spread to the vagina or to the tissues around the uterus (the *parametrium*). The cancer has not spread to lymph nodes or distant sites.

- **Stage IIIC1 (T1 to T3, N1, M0):** The cancer is growing in the body of the uterus. It may have spread to some nearby tissues, but is not growing into the inside of the bladder or rectum. The cancer has spread to pelvic lymph nodes but not to lymph nodes around the aorta or distant sites.

- **Stage IIIC2 (T1 to T3, N2, M0):** The cancer is growing in the body of the uterus. It may have spread to some nearby tissues, but is not growing into the inside of the bladder or rectum. The cancer has spread to lymph nodes around the aorta (peri-aortic lymph nodes) but not to distant sites.

Stage IV

The cancer has spread to the inner surface of the urinary bladder or the rectum (lower part of the large intestine), to lymph nodes in the groin, and/or to distant organs, such as the bones, omentum or lungs.

- **Stage IVA (T4, any N, M0):** The cancer has spread to the inner lining of the rectum or urinary bladder (called the mucosa). It may or may not have spread to nearby lymph nodes but has not spread to distant sites.

- **Stage IVB (any T, any N, M1):** The cancer has spread to distant lymph nodes, the upper abdomen, the omentum, or to organs away from the uterus, such as the bones, omentum, or lungs. The cancer can be any size and it may or may not have spread to lymph nodes.

Survival by stage of endometrial cancer

Survival rates are often used by doctors as a standard way of discussing a person's prognosis (outlook). Some patients with cancer may want to know the survival statistics for people in similar situations, while others may not find the numbers helpful, or may even not want to know them. If you decide that you don’t want to know them, stop reading here.

The 5-year survival rate refers to the percentage of patients who live at least 5 years after their cancer is diagnosed. Of course, many people live much longer than 5 years (and many are cured). Also, although some people die of their cancer, others die from something else. These are *observed* survival rates, and include deaths from all causes, not just from cancer.

In order to get 5-year survival rates, doctors have to look at people who were treated at least 5 years ago. Improvements in treatment since then may result in a more favorable outlook for people now being diagnosed with endometrial cancer.

The survival rates below are based on the stage of the cancer at the time it was diagnosed. These rates do not apply to cancers that have come back after treatment or have spread after treatment starts.

Survival rates are based on previous outcomes of large numbers of people who had the disease, but they cannot predict what will happen in any particular person's case. Many other factors may affect a person's outlook, such as their general health and how well the cancer responds to treatment. Your doctor can tell you how the numbers below may apply to you, as he or she is familiar with the aspects of your particular situation.

The numbers below come from the National Cancer Data Base as published in the AJCC Staging Manual in 2010, and are based on people diagnosed between 2000 and 2002.

Endometrial adenocarcinoma

Stage	**5-year survival**
Stage 0	90%
Stage IA	88%
Stage IB	75%
Stage II	69%
Stage IIIA	58%

Stage IIIB	50%
Stage IIIC	47%
Stage IVA	17%
Stage IVB	15%

The statistics for **uterine carcinosarcoma** are different from those given for endometrial adenocarcinoma in some important ways.

- The numbers given are for 5-year *relative* survival. These rates assume that some people will die of other causes and compare the observed survival with that expected for people without the cancer. This can better show the impact of a particular type and stage of cancer on survival. Relative survival is generally higher than observed survival.
- These numbers come from a different source -- the SEER program from the National Cancer Institute.
- The stages listed are based on an older version of staging. In the most recent staging system, some of the cancers that were stage III might actually be considered stage I or II.

These differences in staging may make it more difficult to apply these numbers to your own situation.

Uterine carcinosarcoma

Stage	**5-year relative survival**
Stage I	70%
Stage II	45%
Stage III	30%
Stage IV	15%

How is endometrial cancer treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

General treatment information

After all of the test results have been reviewed, your doctor will recommend one or more treatment options. The four basic types of treatment for women with endometrial cancer are:

- Surgery
- Radiation therapy
- Hormonal therapy
- Chemotherapy

Surgery is the main treatment for most women with this cancer. But in certain situations, a combination of these treatments may be used. The choice of treatment depends largely on the type of cancer and stage of the disease when it is found. Other factors could play a part in choosing the best treatment plan. These might include your age, your overall state of health, whether you plan to have children, and other personal considerations.

It is important to discuss all of your treatment options with your doctors to help make the decision that best fits your needs. (See the section “What should you ask your doctor about endometrial cancer?”) Be sure you understand all the risks and side effects of the different treatment options before making a decision. If there is anything you do not understand, ask to have it explained again.

When considering your treatment options it is often a good idea to seek a second opinion, if possible. This can provide more information and help you feel confident about the treatment plan you choose. Some insurance companies require a second opinion before they will pay for certain treatments, but a second opinion is usually not required for routine cancer treatments..

Surgery for endometrial cancer

Surgery is often the main treatment for endometrial cancer and consists of a **hysterectomy**, often along with a **salpingo-oophorectomy**, and **removal of lymph nodes**. In some cases, pelvic washings are obtained, the omentum is removed, and/or peritoneal biopsies are obtained. If the cancer has spread throughout the pelvis and abdomen, a debulking procedure (removal of as much cancer as possible) may be done.

These are discussed in detail below.

Hysterectomy

The main treatment for endometrial cancer is an operation to remove the uterus and cervix (called a hysterectomy). When the uterus is removed through an incision in the abdomen, it is called a *simple* or *total abdominal hysterectomy*. If the uterus is removed through the vagina, it is known as a vaginal hysterectomy. Removing the ovaries and fallopian tubes, a *bilateral salpingo-oophorectomy* (BSO), is not actually part of a hysterectomy; it is a separate procedure that is often done during the same operation (see below).

For endometrial cancer, removing the uterus but not the ovaries or fallopian tubes is seldom recommended, but it may be considered in women who are premenopausal. To decide what stage the cancer is in, lymph nodes in the pelvis and around the aorta will also need to be removed (see below). This can be done through the same incision as the abdominal hysterectomy. If the hysterectomy is done vaginally, lymph nodes can be removed by laparoscopy.

When endometrial cancer has spread to the cervix or the area around the cervix (called the *parametrium*), a *radical hysterectomy* is done. In this operation, the entire uterus, the tissues next to the uterus (parametrium and uterosacral ligaments), and the upper part of the vagina (next to the cervix) are all removed. Both fallopian tubes and ovaries are removed at the same time. This operation is most often done through an incision in the abdomen, but it can also be done through the vagina.

When a vaginal approach is used, *laparoscopy* is used to help safely remove the necessary organs and tissues. Laparoscopy is a technique that lets the surgeon look at the inside of the abdomen and pelvis through tubes inserted into very small incisions. Small surgical instruments can be controlled through the tubes, allowing the surgeon to operate without a large incision in the abdomen. This can shorten the time needed for recovery from surgery. Both a hysterectomy and a radical hysterectomy can also be done through the abdomen using laparoscopy.

Surgery for endometrial cancer using laparoscopy seems to be just as good as more traditional open procedures if done by a surgeon who has a lot of experience in laparoscopic cancer surgeries. The DaVinci® robot is increasingly used to perform laparoscopic procedures.

For any of these procedures, either general anesthesia or regional anesthesia will be used so the patient is asleep or sedated during these operations.

Bilateral salpingo-oophorectomy

This operation removes both fallopian tubes and both ovaries. This procedure is usually done at the same time the uterus is removed (either by simple hysterectomy or radical hysterectomy) to treat endometrial cancers. Removing both ovaries means that you will go into menopause if you have not done so already.

If you are younger than 45 when you get stage I endometrial cancer, you may discuss keeping your ovaries with your surgeon, because although women whose ovaries were removed had a lower chance of the cancer coming back, removing the ovaries didn't seem to help them live longer.

Lymph node surgery

Pelvic and para-aortic lymph node dissection: This operation removes lymph nodes from the pelvis and the area next to the aorta to see if they contain cancer cells that have spread from the endometrial tumor. It is called a *lymph node dissection* when most or all of the lymph nodes in a certain area are removed. This procedure is usually done at the same time as the operation to remove the uterus. If you are having an abdominal hysterectomy, the lymph nodes can be removed through the same incision. In women who have had a vaginal hysterectomy, these lymph nodes may be removed by laparoscopic surgery.

Laparoscopy is a technique that lets the surgeon look at the inside the abdomen and pelvis through tubes inserted into very small incisions. Small surgical instruments can be controlled through the tubes, allowing the surgeon to remove lymph nodes. This approach avoids the need for a large incision in the abdomen so the recovery time is often shorter.

Lymph node sampling: When only a few of the lymph nodes in an area are removed, it's called *lymph node sampling*.

Depending on the grade, the amount of cancer in the uterus and how deeply the cancer invades the muscle of the uterus, lymph nodes may not need to be removed.

Pelvic washings

In this procedure, the surgeon "washes" the abdominal and pelvic cavities with salt water (saline) and sends the fluid to the lab to see if it contains cancer cells. This is also called *peritoneal lavage*.

Other procedures that may be used to look for cancer spread

- **Omentectomy:** The omentum is a layer of fatty tissue that covers the abdominal contents like an apron. Cancer sometimes spreads to this tissue. When this tissue is removed, it is called an *omentectomy*. This may be done during a hysterectomy if cancer has spread there or to check for cancer spread.
- **Peritoneal biopsies:** The tissue lining the pelvis and abdomen is called the *peritoneum*. Peritoneal biopsies remove small pieces of this lining to check for cancer cells.

Tumor debulking

If cancer has spread throughout the abdomen, the surgeon may attempt to remove as much of the tumor as possible. This is called *debulking*. Debulking a cancer can help other treatments, like radiation or chemotherapy, work better. Tumor debulking is helpful for other types of cancer, and it may also be helpful in treating some types of endometrial cancer.

Recovery after surgery

The hospital stay for an **abdominal hysterectomy** is usually from 3 to 7 days. The average hospital stay after a **radical hysterectomy** is about 5 to 7 days. Complete recovery can take about 4 to 6 weeks. A laparoscopic procedure and **vaginal hysterectomy** usually require a hospital stay of 1 to 2 days and 2 to 3 weeks for recovery. Complications are unusual but could include excessive bleeding, wound infection, and damage to the urinary or intestinal systems.

A radical hysterectomy affects the nerves that control the bladder, so a catheter is used to drain urine and is kept in place for at least a few days after surgery. If the bladder hasn't recovered completely when it is removed, it may be replaced for a time or you may be shown how to insert a catheter yourself several times a day to empty your bladder until bladder function returns.

For more information on surgery for cancer, see *A Guide to Cancer Surgery*.

Side effects

Any hysterectomy causes infertility (not being able to start or maintain a pregnancy). For women who were premenopausal before surgery, removing the ovaries will cause menopause. This can lead to symptoms such as hot flashes, night sweats, and vaginal dryness. Removing lymph nodes in the pelvis can lead to a build-up of fluid in the legs, a condition called *lymphedema*. This happens more often if radiation is given after surgery. To learn more, see *Understanding Lymphedema: For Cancers Other than Breast Cancer*.

Surgery and menopausal symptoms can also affect your sex life. For more, you can read our booklet *Sexuality for the Woman With Cancer*.

Radiation therapy for endometrial cancer

Radiation therapy uses high-energy radiation (such as x-rays) to kill cancer cells. It can be given in 2 ways to treat endometrial cancer:

- By placing radioactive materials inside the body near the tumor. This is called internal radiation therapy or **brachytherapy**.

- By using a machine that focuses a beam of radiation at the tumor, much like having an x-ray. This is called **external beam radiation therapy**.

In some cases, both brachytherapy and external beam radiation therapy are given. When that is done, usually the external beam radiation is given first, followed by the brachytherapy. The stage and grade of the cancer help determine what areas need to be exposed to radiation therapy and which methods are used.

If your treatment plan includes radiation after surgery, you will be given time to heal from the operation before starting radiation. Often, at least 4 to 6 weeks are needed.

Brachytherapy

Patients who have had their uterus (and cervix) removed may have the upper part of the vagina treated with brachytherapy. To do this, called *vaginal brachytherapy*, a source of radiation is placed into a cylinder and inserted into the vagina. The length of the cylinder (and how much of the vagina is treated) can vary, but the upper part of the vagina is always treated. With this method, the radiation mainly affects the area of the vagina in contact with the cylinder. Nearby structures such as the bladder and rectum get less radiation exposure. The most common side effect is changes to the lining of the vagina (discussed in more detail below).

This procedure is done in the radiation suite of the hospital or care center. The radiation oncologist inserts a special applicator into the woman's vagina, and pellets of radioactive material are inserted into the applicator. There are 2 types of brachytherapy used for endometrial cancer, low-dose rate (LDR) and high-dose rate (HDR).

- In **LDR brachytherapy**, the radiation devices are usually left in place for about 1 to 4 days. The patient needs to stay immobile to keep the radiation sources from moving during treatment, and so she is usually kept in the hospital overnight. Several treatments may be necessary. Because the patient has to stay immobile, this form of brachytherapy carries a risk of serious blood clots in the legs (called *deep venous thrombosis* or *DVT*). LDR is less commonly used now in this country.

- In **HDR brachytherapy**, the radiation is more intense. Each dose takes a very short time (usually less than an hour), and the patient can go home the same day. For endometrial cancer, HDR brachytherapy is often given weekly or even daily for at least 3 doses.

External beam radiation therapy

In this type of treatment the radiation is delivered from a source outside of the body.

External beam radiation therapy is often given 5-days-a-week for 4 to 6 weeks. The skin covering the treatment area is carefully marked with permanent ink or injected dye similar to a tattoo. A special mold of the pelvis and lower back is custom made to ensure that the

woman is placed in the exact same position for each treatment. Each treatment takes less than a half-hour, but the daily visits to the radiation center may be tiring and inconvenient.

Sometimes chemotherapy is given along with the radiation to help it work better. This is called *chemoradiation*.

Side effects of radiation therapy

Short-term side effects: Common side effects of radiation therapy include tiredness, upset stomach, or loose bowels. Serious fatigue, which may not occur until about 2 weeks after treatment begins, is a common side effect. Diarrhea is common, but usually can be controlled with over-the-counter medicines. Nausea and vomiting may also occur, but can be treated with medication. These side effects are more common with pelvic radiation than with vaginal brachytherapy. Side effects tend to be worse when chemotherapy is given with radiation.

Skin changes are also common, which can range from mild redness to peeling and blistering. The skin may release fluid, which can lead to infection, so care must be taken to clean and protect the area exposed to radiation. Sometimes, as it heals, the skin in the treated area becomes darker or less flexible (harder).

Radiation can irritate the bladder, and problems with urination may occur. Irritation to the bladder, called *radiation cystitis*, can result in discomfort, blood in the urine, and an urge to urinate often.

Radiation can also cause similar changes in the intestine. When there is rectal irritation or bleeding, it is called *radiation proctitis*. This is sometimes treated with enemas that contain a steroid (like hydrocortisone) or suppositories that contain an anti-inflammatory.

Radiation can irritate the vagina, leading to discomfort and drainage (a discharge). This is called *radiation vaginitis* and if it occurs, your radiation doctor may recommend douching with a dilute solution of hydrogen peroxide. When the irritation is severe, open sores can develop in the vagina, which may need to be treated with an estrogen cream.

Radiation can also lead to low blood counts, causing anemia (low red blood cells) and leukopenia (low white blood cells). The blood counts usually return to normal within a few weeks after radiation is stopped.

Long-term side effects: Radiation therapy may cause changes to the lining of the vagina leading to vaginal dryness. This is more common after vaginal brachytherapy than after pelvic radiation therapy. In some cases scar tissue can form in the vagina. The scar tissue can make the vagina shorter or more narrow (called *vaginal stenosis*), which can make sex (vaginal intercourse) painful. A woman can help prevent this problem by stretching the walls of her vagina several times a week. This can be done by having sexual intercourse 3 to 4 times a week or by using a vaginal dilator (a plastic or rubber tube used to stretch out the vagina). Still, vaginal dryness and pain with intercourse can be a long-term side effect of radiation. Some centers have physical therapists who specialize in pelvic floor therapy which

can help to treat these vaginal symptoms and sometimes improve sexual function. You should ask your physician about this if you are bothered by these problems. You can also find some helpful information in our booklet *Sexuality for the Woman With Cancer*.

Pelvic radiation can damage the ovaries, resulting in premature menopause. However, this is not an issue for most women who are being treated for endometrial cancer because they have already gone through menopause, either naturally or as a result of surgery to treat the cancer (hysterectomy and removal of the ovaries).

Pelvic radiation therapy can also lead to a blockage of the fluid draining from the leg. This can lead to severe swelling, known as *lymphedema*. Lymphedema is a long-term side effect; it doesn't go away after radiation is stopped. In fact it may not appear for several months after treatment ends. This side effect is more common if pelvic lymph nodes were removed during surgery to remove the cancer. There are specialized physical therapists who can help treat this. It is important to begin treatment early if you develop it. For more on lymphedema, you can read *Understanding Lymphedema: For Cancers Other than Breast Cancer*.

Radiation to the pelvis can also weaken the bones, leading to fractures of the hips or pelvic bones. It is important that women who have had endometrial cancer contact their doctor right away if they have pelvic pain. Such pain might be caused by a fracture, recurrent cancer, or other serious conditions.

Pelvic radiation can also lead to long-term problems with the bladder (*radiation cystitis*) or bowel (*radiation proctitis*). Rarely, radiation damage to the bowel can cause a blockage (called *obstruction*) or for an abnormal connection to form between the bowel and the vagina or outside skin (called a *fistula*). These conditions may need to be treated with surgery.

If you are having side effects from radiation, discuss them with your doctor. There are things you can do to get relief from these symptoms or to prevent them from happening.

For more information, please see the “Radiation Therapy” section of our website.

Chemotherapy for endometrial cancer

Chemotherapy (often called “chemo”) is the use of cancer-fighting drugs given into a vein or by mouth. These drugs enter the bloodstream and reach throughout the body, making this treatment potentially useful for cancer that has spread beyond the endometrium. If this treatment is chosen, you may receive a combination of drugs. Combination chemotherapy sometimes works better in treating cancer than one drug alone.

Chemo is often given in cycles: a period of treatment, followed by a rest period. The chemo drugs may be given on one or more days in each cycle.

Drugs used in treating endometrial cancer may include:

- Paclitaxel (Taxol®)

- Carboplatin
- Doxorubicin (Adriamycin®) or liposomal doxorubicin (Doxil®)
- Cisplatin

Most often, 2 or more drugs are combined for treatment. The most common combinations include carboplatin with paclitaxel and cisplatin with doxorubicin. Less often, paclitaxel and doxorubicin and cisplatin/paclitaxel/doxorubicin may be used.

For carcinosarcoma, the chemo drug ifosfamide (Ifex®), either alone or in combination with either carboplatin, cisplatin or paclitaxel, is often used. However, the combination of carboplatin and paclitaxel is also often being used for carcinosarcoma.

Sometimes chemo is given for a few cycles, followed by radiation. Then chemo is given again. This is called *sandwich therapy* and is sometimes used for endometrial papillary serous cancer and uterine carcinosarcoma.

Another treatment option is to give chemo with radiation (called *chemoradiation*). The chemo can help the radiation work better, but it can be harder on the patient because it causes more side effects.

Side effects of chemotherapy

These drugs kill cancer cells but can also damage some normal cells, which in turn can cause side effects. Side effects of chemotherapy depend on the specific drugs, the amount taken, and the length of time you are treated. Common side effects include:

- Nausea and vomiting
- Loss of appetite
- Mouth and vaginal sores
- Hair loss

Also, most chemotherapy drugs can damage the blood-producing cells of the bone marrow. This can result in low blood cell counts, such as:

- Low white blood cells which increases the risk of infection
- Low platelet counts which can cause bleeding or bruising after minor cuts or injuries
- Low red blood cells (anemia) which can cause problems like fatigue and shortness of breath

Most of the side effects of chemotherapy stop when the treatment is over, but some can last a long time. Different drugs can cause different side effects. For example, the drug doxorubicin

can damage the heart muscle over time. The chance of heart damage goes up as the total dose of the drug goes up, so doctors place a limit on how much doxorubicin is given. Cisplatin can cause kidney damage, so you will be given large amounts of IV fluids before and after chemotherapy to help protect the kidneys. Both cisplatin and paclitaxel can cause nerve damage (called *neuropathy*). This can lead to numbness, tingling, or even pain in the hands and feet. Ifosfamide can injure the lining of the bladder, causing it to bleed (called *hemorrhagic cystitis*). To prevent this, you might be given large amounts of IV fluids and a drug called mesna along with the chemo. Before starting chemotherapy, be sure to discuss the drugs and their possible side effects with your health care team.

If you have side effects while on chemotherapy, remember that there are ways to prevent or treat many of them. For example, modern anti-nausea drugs can prevent or reduce nausea and vomiting. Be sure to talk with your doctor or nurse about any side effects you are having.

For more information, please see the "Chemotherapy" section of our website, or our document *A Guide to Chemotherapy*.

Hormone therapy for endometrial cancer

This type of treatment uses hormones or hormone-blocking drugs to fight cancer. It's not the same as the hormone therapy given to treat the symptoms of menopause (menopausal hormone therapy).

Hormone treatment for endometrial cancer can include:

- Progestins – which are the main hormone treatment used
- Tamoxifen
- Lutenizing hormone releasing hormone agonists
- Aromatase inhibitors

Progestins

The main hormone treatment for endometrial cancer uses progesterone or similar drugs (called *progestins*). The 2 most commonly used progestins are medroxyprogesterone acetate (Provera®, which can be given as an injection or as a pill) and megestrol acetate (Megace®, which is given as a pill). These drugs work by slowing the growth of endometrial cancer cells. Side effects can include hot flashes, night sweats, weight gain (from fluid retention and an increased appetite), and worsening of depression. For women with diabetes, progestins can cause increased blood sugar levels. Rarely, serious blood clots can happen.

Sometimes endometrial hyperplasia and early endometrial cancers can be treated with an intrauterine device that contains levonorgestrel, a progestin. This may be combined with

another hormone drug, such as medroxyprogesterone acetate or a luteinizing hormone-releasing hormone agonist (see below).

Tamoxifen

Tamoxifen, an anti-estrogen drug often used to treat breast cancer, may also be used to treat advanced or recurrent endometrial cancer. The goal of tamoxifen therapy is to prevent any estrogens circulating in the woman's body from stimulating growth of the cancer cells. Even though tamoxifen may prevent estrogen from nourishing the cancer cells, it acts like a weak estrogen in other areas of the body. It does not cause bone loss, but it can cause hot flashes and vaginal dryness. People taking tamoxifen also have an increased risk of serious blood clots in the leg.

Luteinizing hormone-releasing hormone agonists

Most women with endometrial cancer have had their ovaries removed as a part of treatment. In others, radiation treatments have made their ovaries inactive. This reduces the production of estrogen and may also slow the growth of the cancer. Luteinizing hormone-releasing hormone agonists (LHRH agonists) are a way to lower estrogen levels in women who still have functioning ovaries. These drugs switch off estrogen production by the ovaries in women who are premenopausal. Examples of GNRH agonists include goserelin (Zoladex®) and leuprolide (Lupron®). These drugs are injected every 1 to 3 months. Side effects can include any of the symptoms of menopause, such as hot flashes and vaginal dryness. They can also cause muscle and joint aches. If they are taken for a long time (years), these drugs can weaken bones (sometimes leading to osteoporosis). These drugs are also called *gonadotropin-releasing hormone (GNRH) agonists*.

Aromatase inhibitors

Even after the ovaries are removed (or are not functioning), estrogen is still made in fat tissue. This becomes the body's main source of estrogen. Drugs called aromatase inhibitors can stop this estrogen from being formed and lower estrogen levels even further. Examples of aromatase inhibitors include letrozole (Femara®), anastrozole (Arimidex®), and exemestane (Aromasin®). These drugs are most often used to treat breast cancer, but may be helpful in treating endometrial cancer, too. Side effects can include joint and muscle pain as well as hot flashes. If they are taken for a long time (years), these drugs can weaken bones (sometimes leading to osteoporosis). These drugs are still being studied for use in treating endometrial cancer.

Clinical trials for endometrial cancer

You may have had to make a lot of decisions since you've been told you have cancer. One of the most important decisions you will make is choosing which treatment is best for you. You

may have heard about clinical trials being done for your type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you.

Clinical trials are carefully controlled research studies that are done with patients who volunteer for them. They are done to get a closer look at promising new treatments or procedures.

If you would like to take part in a clinical trial, you should start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service for a list of clinical trials that meet your medical needs. You can reach this service at 1-800-303-5691 or on our website at www.cancer.org/clinicaltrials. You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials website at www.cancer.gov/clinicaltrials.

There are requirements you must meet to take part in any clinical trial. If you do qualify for a clinical trial, it is up to you whether or not to enter (enroll in) it.

Clinical trials are one way to get state-of-the art cancer treatment. They are the only way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

You can get a lot more information in *Clinical Trials: What You Need to Know*.

Complementary and alternative therapies for endometrial cancer

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to social media groups and websites offer ideas for what might help you. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

What exactly are complementary and alternative therapies?

Not everyone uses these terms the same way, and they are used to refer to many different methods, so it can be confusing. We use *complementary* to refer to treatments that are used *along with* your regular medical care. *Alternative* treatments are used *instead of* a doctor's medical treatment.

Complementary methods: Most complementary treatment methods are not offered as cures for cancer. Mainly, they are used to help you feel better. Some methods that are used along with regular treatment are meditation to reduce stress, acupuncture to help relieve pain or peppermint tea to relieve nausea. Some complementary methods are known to help, while others have not been tested. Some have been proven not be helpful, and a few have even been found harmful.

Alternative treatments: Alternative treatments may be offered as cancer cures. These treatments have not been proven safe and effective in clinical trials. Some of these methods may pose danger, or have life-threatening side effects. But the biggest danger in most cases is that you may lose the chance to be helped by standard medical treatment. Delays or interruptions in your medical treatments may give the cancer more time to grow and make it less likely that treatment will help.

Finding out more

It is easy to see why people with cancer think about alternative methods. You want to do all you can to fight the cancer, and the idea of a treatment with few or no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or they may no longer be working. But the truth is that most of these alternative methods have not been tested and proven to work in treating cancer.

As you consider your options, here are 3 important steps you can take:

- Look for "red flags" that suggest fraud. Does the method promise to cure all or most cancers? Are you told not to have regular medical treatments? Is the treatment a "secret" that requires you to visit certain providers or travel to another country?
- Talk to your doctor or nurse about any method you are thinking about using.
- Contact us at 1-800-227-2345 to learn more about complementary and alternative methods.

The choice is yours

Decisions about how to treat or manage your cancer are always yours to make. If you want to use a non-standard treatment, learn all you can about the method and talk to your doctor about it. With good information and the support of your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

Treatment options for endometrial cancer by stage

Endometrial cancer is often diagnosed when a woman who is having symptoms has an endometrial biopsy or D&C. Diagnosis is often followed by surgery to treat and stage the cancer.

This operation includes removing the uterus, fallopian tubes, and ovaries (total hysterectomy bilateral salpingo-oophorectomy or TH/BSO). Lymph nodes from the pelvis and around the aorta may also be removed (a pelvic and para-aortic lymph node dissection [LND] or sampling) and examined for cancer spread. Pelvic washings may be done, too. The tissues removed at surgery are examined under a microscope to see how far the cancer has spread

(the stage). Depending on the stage of the cancer, other treatments, such as radiation and/or chemotherapy may be recommended.

For some women who still want to be able to get pregnant, surgery may be put off for a time and other treatments tried instead.

If the cancer has spread outside the uterus, a different surgery may be planned. If the cancer has spread to the inside of the liver, the lungs, or other organs, surgery may not be helpful, and so chemotherapy or other treatments may be used instead.

Stage I

An endometrial cancer is stage I if the cancer is limited to the body of the uterus and has not spread to lymph nodes or distant sites. Surgery and other treatment often differ for cancers that aren't endometrioid. These cancers are discussed separately in this section.

Endometrioid cancers

Standard treatment includes surgery to remove and stage the cancer (see above).

Stage I cancers that have been staged with surgery may not need any further treatment. For some patients, especially those with higher grade tumors, doctors are more likely to recommend radiation after surgery. Either vaginal brachytherapy (VB), pelvic radiation, or both can be used.

Some younger women with early endometrial cancer may have the uterus removed without removing the ovaries. Although this does increase the chance that the cancer will come back, it doesn’t make it more likely that you will die from your cancer. This may be something that you want to discuss with your doctor.

Women who cannot have surgery because of other medical problems or who are frail due to age are often treated with radiation alone.

Fertility-sparing treatment for stage IA grade 1 cancers: In young women who still want to have children, surgery may be postponed for a time while progestin therapy is used to treat the cancer. Progestin treatment, as a pill, injection, or as a progestin-containing intrauterine device, can cause the cancer to shrink or even go away for some time, giving the woman a chance to get pregnant. This approach is experimental and can be risky if the patient isn't watched closely.

Often, this does not work and the cancer doesn’t get better or keeps growing. Putting off surgery can give the cancer time to spread outside the uterus. If the cancer doesn’t go away, surgery to remove and stage the cancer is recommended (including a hysterectomy and removal of both fallopian tubes and ovaries).

Sometimes the tumor gets smaller or goes away for a while, but then comes back again. Because the cancer often comes back again, doctors often recommend surgery to remove the uterus, fallopian tubes, and ovaries after childbearing is complete.

A second opinion from a gynecologic oncologist and pathologist (to confirm the grade of the cancer) before starting progestin therapy is important. Women need to understand that this is not a standard treatment and may increase risk.

Other endometrial cancers

Cancers such as papillary serous carcinoma, clear cell carcinoma, or carcinosarcoma are more likely to have already spread outside the uterus when diagnosed. Women with these types of tumors do not do as well as those with lower grade tumors. If the biopsy done before surgery showed a high-grade cancer, the surgery may be more extensive. In addition to the total hysterectomy, removal of both fallopian tubes and ovaries, and the pelvic and para-aortic lymph node dissections, the omentum is often removed. After surgery, both chemotherapy (chemo) and radiation therapy are often given to help keep the cancer from coming back. The chemo usually includes the drugs carboplatin and paclitaxel (Taxol), but other combinations can also be used.

Stage II

When an endometrial cancer is stage II, it has spread to the connective tissue of the cervix but still has not grown outside the uterus.

One treatment option is to have surgery first, possibly followed by radiation therapy. The surgery would include a radical hysterectomy (the entire uterus, the tissues next to the uterus, and the upper part of the vagina are all removed), removal of both fallopian tubes and ovaries (BSO), and pelvic and para-aortic lymph node dissection (LND) or sampling. Radiation therapy, often including both vaginal brachytherapy and external pelvic radiation may be given after the patient has recovered from surgery. The other option is to give the radiation therapy first, followed by a simple hysterectomy, BSO, and possible LND or lymph node sampling.

The lymph nodes that have been removed are checked for cancer cells. If lymph nodes show cancer, then the cancer is not really a stage II – it’s a stage IIIC.

In some cases, a woman with early stage endometrial cancer might be too frail or ill from other diseases to safely have surgery. These women are treated with radiation therapy alone.

For women with high-grade cancers, such as papillary serous carcinoma or clear cell carcinoma, the surgery may include omentectomy and peritoneal biopsies in addition to the total hysterectomy, removal of both fallopian tubes and ovaries, pelvic and para-aortic lymph node dissections, and pelvic washings. After surgery, chemo, radiation therapy, or both may be given to help keep the cancer from coming back. The chemo usually includes the drugs carboplatin and paclitaxel or possibly cisplatin and doxorubicin.

Someone with a stage II uterine carcinosarcoma often has the same type of surgery that's used for a high-grade cancer. After surgery, radiation, chemo, or both may be used. The chemo often includes paclitaxel and carboplatin but may instead include ifosfamide, along with paclitaxel or cisplatin.

Stage III

Stage III endometrial cancers have spread outside of the uterus.

If the surgeon thinks that all visible cancer can be removed, a hysterectomy is done and both ovaries and fallopian tubes are removed. Sometimes women with stage III cancers need a radical hysterectomy. A pelvic and para-aortic lymph node dissection may also be done. Pelvic washings will be done and the omentum may be removed. Some doctors will try to remove any remaining cancer (debulking), but it isn't clear that this will help patients live longer.

If tests done before surgery reveal that the cancer has spread too far to be removed completely, radiation therapy may rarely be given before any surgery. The radiation may shrink the tumor enough to make surgery an option.

Stage IIIA: A cancer is considered stage IIIA when it has spread to the tissue covering the uterus (the serosa) or to other tissues in the pelvis like the fallopian tubes or the ovaries (the adnexa). For these cancers, treatment after surgery may include chemo, radiation, or a combination of both. Radiation is given to the pelvis or to both the abdomen and the pelvis. Sometimes vaginal brachytherapy is used as well.

Stage IIIB: In this stage, the cancer has spread to the vagina. After surgery, stage IIIB may be treated with chemo and/or radiation.

Stage IIIC: This includes cancers that have spread to the lymph nodes in the pelvis (stage IIIC1) and those that have spread to the lymph nodes around the aorta (stage IIIC2). Treatment includes surgery, followed by chemo and/or radiation.

For women with high-grade cancers, such as papillary serous carcinoma or clear cell carcinoma, the surgery may include omentectomy and peritoneal biopsies in addition to the total hysterectomy, removal of both ovaries and fallopian tubes, pelvic and para-aortic lymph node dissections, and pelvic washings. After surgery, chemo, radiation therapy, or both may be given to help keep the cancer from coming back. The chemo usually includes the drugs carboplatin and paclitaxel or cisplatin and doxorubicin.

Women with stage III uterine carcinosarcoma often have the same type of surgery that's used for a high-grade cancer. After surgery, radiation, chemo, or both may be used. The chemo often includes the drug paclitaxel and carboplatin, but ifosfamide, along with paclitaxel or cisplatin may be used.

Stage IV

Stage IVA: These endometrial cancers have grown inside the bladder or bowel.

Stage IVB: These endometrial cancers have spread to lymph nodes outside the pelvis or para-aortic area. This stage also includes cancers that have spread to the liver, lungs, omentum, or other organs.

Some endometrial cancers are stage IV because they have spread to lymph nodes in the abdomen (and not just the pelvis and para-aortic area), but the cancers have not spread to any other areas. Women with this kind of cancer spread may have the best chance if all the cancer that's seen can be removed (debulked) and biopsies of other areas in the abdomen do not show cancer cells.

However, in most cases of stage IV endometrial cancer, the cancer has spread too far for it all to be removed with surgery and a surgical cure is not possible. A hysterectomy and removal of both fallopian tubes and ovaries may still be done to prevent excessive bleeding. Radiation therapy may also be used for this reason. When the cancer has spread to other parts of the body, hormone therapy may be used. Drugs used for hormone therapy include progestins and tamoxifen. Aromatase inhibitors may also be useful and are being studied. High-grade cancers and those without detectable progesterone and estrogen receptors are not likely to respond to hormone therapy.

Combinations of chemo drugs may help some women with advanced endometrial cancer for a time. The drugs used most often are paclitaxel, doxorubicin, and either carboplatin or cisplatin. These drugs are often used together in combination. Stage IV carcinosarcoma is often treated with similar chemo. Cisplatin, ifosfamide, and paclitaxel may also be combined. Women with stage IV endometrial cancer should consider taking part in clinical trials of chemotherapy or other new treatments.

Recurrent endometrial cancer

Cancer is called recurrent when it come backs after treatment. Recurrence can be local (in or near the same place it started) or distant (spread to organs such as the lungs or bone). Treatment depends on the amount and location of the cancer.

For local recurrences, such as in the pelvis, surgery (sometimes followed with radiation therapy may provide a cure. For women who have other medical conditions that make them unable to have surgery, radiation therapy alone or combined with hormone therapy is generally used.

For a distant recurrence, surgery and/or focused radiation therapy may also be used when the cancer is only in a few small spots (like in the lungs or bones). Women with more extensive recurrences (widespread cancer) are treated like those with stage IV endometrial cancer. Either hormone therapy or chemo is recommended. Low-grade cancers containing progesterone receptors are more likely to respond well to hormone therapy. Higher-grade

cancers and those without detectable receptors are unlikely to shrink during hormone therapy but may respond to chemo. Clinical trials of new treatments are another option.

More treatment information about endometrial cancer

For more details on treatment options -- including some that may not be addressed in this document -- the National Comprehensive Cancer Network (NCCN) and the National Cancer Institute (NCI) are good sources of information.

The NCCN, made up of experts from many of the nation's leading cancer centers, develops cancer treatment guidelines for doctors to use when treating patients. Those are available on the NCCN website (www.nccn.org).

The NCI provides treatment guidelines via its telephone information center (1-800-4-CANCER) and its website (www.cancer.gov). Detailed guidelines intended for use by cancer care professionals are also available on www.cancer.gov.

What should you ask your doctor about endometrial cancer?

As you cope with cancer, you need to have honest, open talks with your doctor. You should feel free to ask any question that's on your mind, no matter how small it might seem. Nurses, social workers, and other members of the treatment team may also be able to answer many of your questions. Here are some questions you might want to ask:

- What type and grade of endometrial cancer do I have?
- Has my cancer spread outside the uterus?
- What is the stage of my cancer and what does that mean in my case?
- What treatments might be right for me? What do you recommend? Why?
- Am I eligible for a clinical trial?
- What is the goal of this treatment?
- How will you monitor my response to treatment?
- What should I do to be ready for treatment?
- What risks or side effects should I expect?
- What are the chances my cancer will come back with the treatments we have discussed?
- Should I follow a special diet?

- Will I be able to have children after my treatment?
- What is my expected prognosis, based on my cancer as you view it?
- Does this cancer prevent me from considering estrogen replacement therapy?
- How will I feel during treatment?
- When can I resume my usual activities at work and/or around the house?

Along with these sample questions, be sure to write down some of your own. For instance, you might want to ask about getting a second opinion, or you may need specific information about how long it might take you to recover so you can plan your work schedule. You can find more information about communicating with your health care team in our document *Talking With Your Doctor*.

What will happen after treatment for endometrial cancer?

For many women with endometrial cancer, treatment may remove or destroy the cancer. Completing treatment can be both stressful and exciting. You may be relieved to finish treatment, but find it hard not to worry about cancer coming back. (When cancer comes back after treatment, it is called *recurrence*.) This is a very common concern in people who have had cancer.

It may take a while before your fears lessen. But it may help to know that many cancer survivors have learned to accept this uncertainty and are living full lives. Our document *Living With Uncertainty: The Fear of Cancer Recurrence* gives more detailed information on this.

For other women, this cancer may never go away completely. They may get regular treatments with chemotherapy, radiation therapy, or other therapies to try to help keep the cancer in check. Learning to live with cancer that does not go away can be difficult and very stressful. It has its own type of uncertainty. Our document *When Cancer Doesn't Go Away* talks more about this.

Follow-up care

When treatment ends, your doctors will still want to watch you closely. It is very important to go to all of your follow-up appointments. During these visits, your doctors will ask questions about any problems you may have and may do exams and lab tests or x-rays and scans to look for signs of cancer or treatment side effects. Almost any cancer treatment can have side effects. Some may last for a few weeks to months, but others can last the rest of your life.

This is the time for you to talk to your cancer care team about any changes or problems you notice and any questions or concerns you have.

Endometrial cancer is most likely to come back within the first few years after treatment, so an important part of your treatment plan is a specific schedule of follow-up visits after treatment is finished. How often you need to be seen depends mostly on what stage your cancer was.

- Women who had stage IA low-grade endometrioid cancers (grades 1 and 2) may be seen every 6 months for the first year after treatment, and then yearly after that.
- If the cancer was stage IB or II low-grade endometrioid cancers (grades 1 and 2), follow-up visits are every 3 months for the first year, then every 6 months for the next 4 years, and then once a year.
- For women with higher stage or grade cancers (stages III or IV, or cancers that were grade III, including papillary serous, clear cell, or carcinosarcomas), experts recommend visits every 3 months for the first 2 years, every 6 months for the next 3 years, and then yearly after that.

During each follow-up visit, the doctor will do a pelvic exam (using a speculum) and check for any enlarged lymph nodes in the groin area. A Pap test may also be done to look for cancer cells in the upper part of the vagina, near the area where the uterus used to be, but it is no longer recommended as a matter of routine due to the low chance of detecting a recurrence. Sometimes a CA 125 blood test is done as a part of follow-up, but this is also not needed in all patients. The doctor will also ask about any symptoms that might point to cancer recurrence or side effects of treatment. Most endometrial cancer recurrences are found because of symptoms, so it’s very important that you tell your doctor exactly how you are feeling.

If your symptoms or the physical exam results suggest the cancer may have come back, imaging tests (such as CT scans or ultrasound studies), a CA 125 blood test, and/or biopsies may be done. Studies of many women with endometrial cancer show that if no symptoms or physical exam abnormalities are present, routine blood tests and imaging tests are not needed.

It is important to keep health insurance. Tests and doctor visits cost a lot, and even though no one wants to think of their cancer coming back, this could happen.

Should your cancer come back, *When Your Cancer Comes Back: Cancer Recurrence* gives you information on how to manage and cope with this phase of your treatment.

Seeing a new doctor

At some point after your cancer diagnosis and treatment, you may find yourself seeing a new doctor who does not know anything about your medical history. It is important that you be

able to give your new doctor the details of your diagnosis and treatment. Make sure you have this information handy:

- A copy of your pathology reports from any biopsies or surgeries
- If you had surgery, a copy of your operative report(s)
- If you were hospitalized, a copy of the discharge summary that doctors prepare when patients are sent home from the hospital
- If you were treated with radiation, a copy of your treatment summary
- If you had chemotherapy (or hormone therapy), a list of the drugs, drug doses, and when you took them

The doctor may want copies of this information for his records, but always keep copies for yourself.

Can I get another cancer after having endometrial cancer?

Cancer survivors can be affected by a number of health problems, but often their greatest concern is facing cancer again. If a cancer comes back after treatment it is called a "recurrence." But some cancer survivors may develop a new, unrelated cancer later. This is called a "second cancer." No matter what type of cancer you have had, it is still possible to get another (new) cancer, even after surviving the first.

Unfortunately, being treated for cancer doesn't mean you can't get another cancer. People who have had cancer can still get the same types of cancers that other people get. In fact, certain types of cancer and cancer treatments can be linked to a higher risk of certain second cancers.

Survivors of endometrial cancer can get any type of second cancer, but they have an increased risk of:

- Breast cancer
- Colon cancer
- Rectal cancer
- Small intestine cancer
- Bladder cancer
- Vaginal cancer
- Soft tissue cancer

- Acute leukemia

Colon and breast cancers are the second cancers most often seen.

The increased risks of acute myeloid leukemia (AML) and cancers of the rectum, bladder, and soft tissue seem to be linked to treatment with radiation.

Follow-up after treatment

After completing treatment for endometrial cancer, you should see your doctor regularly to look for signs the cancer has come back. Experts do not recommend additional testing to look for second cancers in patients without symptoms. Let your doctor know about any new symptoms or problems, because they could be caused by the cancer coming back or by a new disease or second cancer.

Survivors of endometrial cancer should follow the American Cancer Society guidelines for the early detection of cancer and stay away from tobacco products. Smoking increases the risk of many cancers, as well as other health problems.

To help maintain good health, survivors should also:

- Achieve and maintain a healthy weight
- Adopt a physically active lifestyle
- Consume a healthy diet, with an emphasis on plant foods
- Limit consumption of alcohol to no more than 1 drink per day

These steps may also lower the risk of some cancers.

See *Second Cancers in Adults* for more information about causes of second cancers.

Lifestyle changes after treatment for endometrial cancer

You can't change the fact that you have had cancer. What you can change is how you live the rest of your life -- making choices to help you stay healthy and feel as well as you can. This can be a time to look at your life in new ways. Maybe you are thinking about how to improve your health over the long term. Some people even start during cancer treatment.

Making healthier choices

For many people, a diagnosis of cancer helps them focus on their health in ways they may not have thought much about in the past. Are there things you could do that might make you healthier? Maybe you could try to eat better or get more exercise. Maybe you could cut down on alcohol, or give up tobacco. Even things like keeping your stress level under control may

help. Now is a good time to think about making changes that can have positive effects for the rest of your life. You will feel better and you will also be healthier.

You can start by working on those things that worry you most. Get help with those that are harder for you. For instance, if you are thinking about quitting smoking and need help, call the American Cancer Society at 1-800-227-2345.

Eating better

Eating right can be hard for anyone, but it can get even tougher during and after cancer treatment. Treatment may change your sense of taste. Nausea can be a problem. You may not feel like eating and lose weight when you don't want to. Or you may have gained weight that you can't seem to lose. All of these things can be very frustrating.

If treatment caused weight changes or eating or taste problems, do the best you can and keep in mind that these problems usually get better over time. You may find it helps to eat small portions every 2 to 3 hours until you feel better. You may also want to ask your cancer team about seeing a dietitian, an expert in nutrition who can give you ideas on how to deal with these treatment side effects.

One of the best things you can do after cancer treatment is start healthy eating habits. You may be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Getting to and staying at a healthy weight, eating a healthy diet, and limiting your alcohol intake may lower your risk for a number of types of cancer, as well as having many other health benefits. Get more information from *Nutrition and Physical Activity During and After Cancer Treatment: Answers to Common Questions*.

Rest, fatigue, work, and exercise

Extreme tiredness, called *fatigue*, is very common in people treated for cancer. This is not a normal tiredness, but a "bone-weary" exhaustion that doesn't get better with rest. For some people, fatigue lasts a long time after treatment, and can make it hard for them to exercise and do other things they want to do. But exercise can help reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel better physically and emotionally and can cope better, too.

If you were sick and not very active during treatment, it is normal for your fitness, endurance, and muscle strength to decline. Any plan for physical activity should fit your own situation. If you haven't exercised in a few years, you will have to start slowly -- maybe just by taking short walks.

Talk with your health care team before starting anything. Get their opinion about your exercise plans. Then, try to find an exercise buddy so you're not doing it alone. Having family or friends involved when starting a new exercise program can give you that extra boost of support to keep you going when the push just isn't there.

If you are very tired, you will need to balance activity with rest. It is OK to rest when you need to. Sometimes it's really hard for people to allow themselves to rest when they are used to working all day or taking care of a household, but this is not the time to push yourself too hard. Listen to your body and rest when you need to. (For more information on fatigue and other side effects, please see the “Physical Side Effects” section of our website or “Additional resources for endometrial cancer” to get a list of available information.)

Keep in mind exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- Along with a good diet, it will help you get to and stay at a healthy weight.
- It makes your muscles stronger.
- It reduces fatigue and helps you have more energy.
- It can help lower anxiety and depression.
- It can make you feel happier.
- It can help you feel better about yourself.

And long term, we know that exercise plays a role in helping to lower the risk of some cancers, as well as having other health benefits.

How might having endometrial cancer affect your emotional health?

During and after treatment, you may find yourself overcome with many different emotions. This happens to a lot of people.

You may find yourself thinking about death and dying. Or maybe you're more aware of the effect the cancer has on your family, friends, and career. You may take a new look at your relationship with those around you. Unexpected issues may also cause concern. For instance, as you feel better and have fewer doctor visits, you will see your health care team less often and have more time on your hands. These changes can make some people anxious.

Almost everyone who has been through cancer can benefit from getting some type of support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, church or spiritual groups, online support communities, or one-on-one counselors. What's best for you depends on your situation and personality. Some people feel safe in peer-support groups or education groups. Others would rather talk in an informal setting, such as church. Others may feel more at ease talking one-on-one with a trusted friend or counselor. Whatever your source of strength or comfort, make sure you have a place to go with your concerns.

The cancer journey can feel very lonely. It is not necessary or good for you to try to deal with everything on your own. And your friends and family may feel shut out if you do not include them. Let them in, and let in anyone else who you feel may help. If you aren't sure who can help, call your American Cancer Society at 1-800-227-2345 and we can put you in touch with a group or resource that may work for you. You can also read *Distress in People with Cancer* or see the "Emotional Side Effects" section of our website for more information.

If treatment for endometrial cancer stops working

If cancer keeps growing or comes back after one kind of treatment, it is possible that another treatment plan might still cure the cancer, or at least shrink it enough to help you live longer and feel better. But when a person has tried many different treatments and the cancer has not gotten any better, the cancer tends to become resistant to all treatment. If this happens, it's important to weigh the possible limited benefits of a new treatment against the possible downsides. Everyone has their own way of looking at this.

This is likely to be the hardest part of your battle with cancer -- when you have been through many medical treatments and nothing's working anymore. Your doctor may offer you new options, but at some point you may need to consider that treatment is not likely to improve your health or change your outcome or survival.

If you want to continue to get treatment for as long as you can, you need to think about the odds of treatment having any benefit and how this compares to the possible risks and side effects. In many cases, your doctor can estimate how likely it is the cancer will respond to treatment you are considering. For instance, the doctor may say that more chemo or radiation might have about a 1% chance of working. Some people are still tempted to try this. But it is important to think about and understand your reasons for choosing this plan.

No matter what you decide to do, you need to feel as good as you can. Make sure you are asking for and getting treatment for any symptoms you might have, such as nausea or pain. This type of treatment is called *palliative care*.

Palliative care helps relieve symptoms, but is not expected to cure the disease. It can be given along with cancer treatment, or can even be cancer treatment. The difference is its purpose - .the main purpose of palliative care is to improve the quality of your life, or help you feel as good as you can for as long as you can. Sometimes this means using drugs to help with symptoms like pain or nausea. Sometimes, though, the treatments used to control your symptoms are the same as those used to treat cancer. For instance, radiation might be used to help relieve bone pain caused by cancer that has spread to the bones. Or chemo might be used to help shrink a tumor and keep it from blocking the bowels. But this is not the same as treatment to try to cure the cancer. You can learn more about the changes that occur when curative treatment stops working, and about planning ahead for yourself and your family, in our documents *Nearing the End of Life* and *Advance Directives*.

At some point, you may benefit from hospice care. This is special care that treats the person rather than the disease; it focuses on quality rather than length of life. Most of the time, it is given at home. Your cancer may be causing problems that need to be managed, and hospice focuses on your comfort. You should know that while getting hospice care often means the end of treatments such as chemo and radiation, it doesn't mean you can't have treatment for the problems caused by your cancer or other health conditions. In hospice the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult time. You can learn more about hospice in our document *Hospice Care*.

Staying hopeful is important, too. Your hope for a cure may not be as bright, but there is still hope for good times with family and friends -- times that are filled with happiness and meaning. Pausing at this time in your cancer treatment gives you a chance to refocus on the most important things in your life. Now is the time to do some things you've always wanted to do and to stop doing the things you no longer want to do. Though the cancer may be beyond your control, there are still choices you can make.

What's new in endometrial cancer research and treatment?

Molecular pathology of endometrial cancer

Recent research has improved our understanding of how changes in certain molecules can cause normal endometrial cells to become cancerous. For several years we have known that damaged or defective DNA (called mutations) can alter important genes that regulate cell growth. If these genes are damaged, out-of-control growth may result in cancer.

Sometimes, endometrial cancer and colon cancer may seem to “run in a family.” We now know that some of these families have a higher risk for these cancers because they have an inherited defect in certain genes that normally help repair damage to DNA. If these repair enzymes are not working properly, damage to DNA is more likely to persist and cause cancer. Similar DNA repair defects have also been found in endometrial cancer cells from some patients without an inherited tendency to develop this disease. One of the normal genes responsible for suppressing tumor growth, called *PTEN*, is often abnormal in endometrial cancers.

Tests for this and other DNA changes may someday help find endometrial cancers early. Endometrial cancers without other tumor suppressor genes (or with inactive ones), such as the retinoblastoma (*Rb*) gene and the *TP53* gene, tend to be more likely to come back after initial treatment. Tests for these and other DNA changes may someday be used to help predict how aggressive the cancer might be and to select the best treatment for each woman with this disease. The long-range goal of this field of research is gene therapy that can correct the DNA abnormalities that caused the endometrial cells to become cancerous.

New treatments

Researchers are examining new drugs, combinations of drugs and “targeted therapies” in patients with advanced endometrial cancer. The use of adjuvant chemotherapy, with or without radiation is also under investigation.

Targeted therapy

As researchers have learned more about the gene and protein changes in cancer cells, they have been able to develop newer drugs that specifically target these changes. These targeted drugs work differently from standard chemotherapy (chemo) drugs. They often have different side effects. Some targeted therapy that are being studied to treat endometrial cancer include temsirolimus, brivanib, and gefitinib.

Hormone therapy

Although hormone therapy of endometrial cancer has often involved progestins, drugs that affect estrogen may also be helpful. A recent study looked at using fulvestrant (Faslodex®), a drug that blocks estrogen receptors.

Surgery

Another way to see if cancer has spread to the lymph nodes in the pelvis is to identify and remove the lymph nodes that most likely are draining the cancer. This is called sentinel lymph node biopsy. In this procedure, radioactive tracer and/or blue dye is injected into the area with the cancer. The lymph nodes that turn blue (from the dye) or that become radioactive (from the tracer) are removed at surgery. These lymph nodes are examined closely to see if they contain any cancer cells. This technique is commonly used for some other tumors, such as breast cancer, but it is still new in the treatment of endometrial cancer. It is not yet known if sentinel lymph node biopsy is as good as lymph node dissection for staging and treating endometrial cancer, so it is not currently part of the standard surgery for this cancer.

Additional resources for endometrial cancer

More information from your American Cancer Society

The following related information may also be helpful to you. These materials may be ordered from our toll-free number, 1-800-227-2345.

Living with Cancer

After Diagnosis: A Guide for Patients and Families (also available in Spanish)

Distress in People With Cancer

Genetic Testing: What You Need to Know

Sexuality for the Woman With Cancer (also available in Spanish)

Guide to Controlling Cancer Pain (also available in Spanish)

When Cancer Doesn't Go Away

When Your Cancer Comes Back: Cancer Recurrence

Understanding cancer treatments

A Guide to Cancer Surgery (also available in Spanish)

A Guide to Chemotherapy (also available in Spanish)

Understanding Radiation Therapy: A Guide for Patients and Families (also available in Spanish)

Cancer treatment side effects

Nausea and Vomiting

Anemia in People With Cancer

Fatigue in People With Cancer

Peripheral Neuropathy Caused by Chemotherapy

Family and caregiver concerns

Talking With Friends and Relatives About Your Cancer (also in Spanish)

What It Takes to Be a Caregiver

Caring for the Patient With Cancer at Home: A Guide for Patients and Families (also available in Spanish)

Helping Children When a Family Member Has Cancer: Dealing With Diagnosis (also available in Spanish)

Work, insurance, and finances

Health Insurance and Financial Assistance for the Cancer Patient

Returning to Work After Cancer Treatment

Working During Cancer Treatment

Your American Cancer Society also has books that you might find helpful. Call us at 1-800-227-2345 or visit our bookstore online at cancer.org/bookstore to find out about costs or to place an order.

National organizations and websites*

In addition to the American Cancer Society, other sources of patient information and support include:

Foundation for Women's Cancer
Toll-free number: 1-800-444-4441
Website: www.foundationforwomenscancer.org

> Offers referrals to gynecologic oncologists and has information about how to prevent, detect, and treat female cancer; also the booklet, “Renewing Intimacy and Sexuality After Gynecologic Cancer.” Educational materials are offered online, and educational programs for survivors are offered throughout the country.

National Cancer Institute
Telephone: 1-800-422-6237 (1-800-4-CANCER)
Website: www.cancer.gov

> Offers current information about breast cancer screening, diagnosis, and treatment as well as information on other types of cancer, as well as information for the family and children of people with cancer

**Inclusion on this list does not imply endorsement by the American Cancer Society.*

No matter who you are, we can help. Contact us anytime, day or night, for information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

References: Endometrial cancer detailed guide

Abu-Rustum NR, Khoury-Collado F, Pandit-Taskar N, et al. Sentinel lymph node mapping for grade 1 endometrial cancer: is it the answer to the surgical staging dilemma? *Gynecol Oncol.* 2009;113:163-169.

Alektiar KM, Abu-Rustum NR, Fleming GF. Cancer of the uterine body. In: DeVita VT, Hellman S, Rosenberg SA, eds. *DeVita, Hellman, and Rosenberg‘s Cancer: Principles and*

Practice of Oncology. 10th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2015: 1048-1064.

Alvarez EA, Brady WE, Walker JL, et al. Phase II trial of combination bevacizumab and temsirolimus in the treatment of recurrent or persistent endometrial carcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol*. 2013;129(1):22-27.

Amant F, Moerman P, Neven P, et al. Endometrial cancer. *Lancet*. 2005; 366:491-505.

American Cancer Society. *Cancer Facts and Figures 2015.* Atlanta, Ga: American Cancer Society; 2015.

American College of Obstetricians and Gynecologists. ACOG practice bulletin, clinical management guidelines for obstetrician-gynecologists, number 65, August 2005: management of endometrial cancer. *Obstet Gynecol*. 2005;106(2):413-425.

American Joint Committee on Cancer. Uterine Cancer. In: *AJCC Cancer Staging Manual*. 7th ed. New York, NY: Springer; 2010: 403-409.

Barlin JN, Puri I, Bristow RE. Cytoreductive surgery for advanced or recurrent endometrial cancer: a meta-analysis. *Gynecol Oncol*. 2010;118(1):14-18.

Beining RM, Dennis LK, Smith EM, Dokras A. Meta-analysis of intrauterine device use and risk of endometrial cancer. *Ann Epidemiol.* 2008;18:492-499.

Boggess JF, Kilgore JE. Uterine cancer. In: Niederhuber JE, Armitage JO, Doroshow JH,. Kastan MB, Tepper JE, eds. *Abeloff's Clinical Oncology.* 5th ed. Philadelphia, Pa: Elsevier; 2014: 1575-1591.

Cardenes HR, Look K, Michael H, Cerezo L. Endometrium. In: Halperin EC, Perez CA, Brady LW, eds. *Perez and Brady's Principles and Practice of Radiation Oncology*. 5th ed. Philadelphia, Pa: Lippincott Williams and Wilkins; 2008: 1610-1628.

Chao KSC, Perez CA, Brady LW. *Radiation Oncology Management Decisions*. 3rd edition. Philadelphia, Pa: Lippincott Williams and Wilkins; 2011.

Colombo N, McMeekin DS, Schwartz PE, et al. Ridaforolimus as a single agent in advanced endometrial cancer: results of a single-arm, phase 2 trial. *Br J Cancer*. 2013;108(5):1021-1026.

Creasman WT, Odicino F, Maisonneuve P, et al. Carcinoma of the corpus uteri. *Int J Gynecol Obs.* 2003;83:79-118.

Emons G, Günthert A, Thiel FC, et al. Phase II study of fulvestrant 250 mg/month in patients with recurrent or metastatic endometrial cancer: a study of the Arbeitsgemeinschaft Gynäkologische Onkologie. *Gynecol Oncol*. 2013;129(3):495-499.

Freedman DM, Curtis RE, Travis LB, Fraumeni Jr JF. New Malignancies Following Cancer of the Uterine Corpus and Ovary. In: Curtis RE, Freedman DM, Ron E, Ries LAG, Hacker

DG, Edwards BK, Tucker MA, Fraumeni JF Jr. (eds). New Malignancies Among Cancer Survivors: SEER Cancer Registries, 1973-2000. National Cancer Institute. NIH Publ. No. 05-5302. Bethesda, MD, 2006. Accessed on 4/18/2014 at http://seer.cancer.gov/archive/publications/mpmono/MPMonograph_complete.pdf.

Howlader N, Noone AM, Krapcho M, et al (eds). SEER Cancer Statistics Review, 1975-2011, National Cancer Institute. Bethesda, MD, http://seer.cancer.gov/csr/1975_2011/, based on November 2013 SEER data submission, posted to the SEER web site, April 2014.

Keys HM, Roberts JA, Brunetto VL, et al. A phase III trial of surgery with or without adjunctive external pelvic radiation therapy in intermediate risk endometrial adenocarcinoma: a Gynecologic Oncology Group study. *Gynecol Oncol*. 2004;92(3):744-751.

Kim MK, Yoon BS, Park H, et al. Conservative treatment with medroxyprogesterone acetate plus levonorgestrel intrauterine system for early-stage endometrial cancer in young women: pilot study. *Int J Gynecol Cancer*. 2011;21(4):673-677.

Kosary CL. Cancer of the Corpus Uteri. In: Ries LAG, Young JL, Keel GE, Eisner MP, Lin YD, Horner M-J (editors). SEER Survival Monograph: Cancer Survival Among Adults: U.S. SEER Program, 1988-2001, Patient and Tumor Characteristics. National Cancer Institute, SEER Program, NIH Pub. No. 07-6215, Bethesda, MD, 2007.

Kushi LH, Doyle C, McCullough M, et al. American Cancer Society guidelines on nutrition and physical activity for cancer prevention: Reducing the risk of cancer with healthy food choices and physical activity. *CA Cancer J Clin*. 2012;62:30-67.

Leslie KK, Sill MW, Fischer E, et al. A phase II evaluation of gefitinib in the treatment of persistent or recurrent endometrial cancer: a Gynecologic Oncology Group study. *Gynecol Oncol*. 2013;129(3):486-494.

Malzoni M, Tinelli R, Cosentino F, et al. Total laparoscopic hysterectomy versus abdominal hysterectomy with lymphadenectomy for early-stage endometrial cancer: a prospective randomized study. *Gynecol Oncol*. 2009;112:126-133.

McCullough ML, Patel AV, Patel R, et al. Body mass and endometrial cancer risk by hormone replacement therapy and cancer subtype. *Cancer Epidemiol Biomarkers Prev*. 2008;17:73-79.

Minig L, Franchi D, Boveri S, et al. Progestin intrauterine device and GnRH analogue for uterus-sparing treatment of endometrial precancers and well-differentiated early endometrial carcinoma in young women. *Ann Oncol*. 2011;22(3):643-649.

Moore SC, Gierach GL, Schatzkin A, Matthews CE. Physical activity, sedentary behaviours, and the prevention of endometrial cancer. *Br J Cancer*. 2010;103(7):933-938.

Nag S, Scruggs GR. Clinical Aspects and Applications of High-Dose Rate Brachytherapy. In: Halperin EC, Perez CA, Brady LW, eds. *Perez and Brady's Principles and Practice of*

Radiation Oncology. 5th ed. Philadelphia, Pa: Lippincott Williams and Wilkins; 2008: 560-582.

National Cancer Institute. Physician Data Query (PDQ). Endometrial cancer treatment. 4/23/2014. Accessed at www.cancer.gov/cancertopics/pdq/treatment/endometrial/healthprofessional on January 22, 2015.

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Uterine Neoplasms. V.2.2015. Accessed at www.nccn.org on January 9, 2015.

Nout RA, Smit VT, Putter H, et al. Vaginal brachytherapy versus pelvic external beam radiotherapy for patients with endometrial cancer of high-intermediate risk (PORTEC-2): an open-label, non-inferiority, randomized trial. *Lancet*. 2010;375(9717):816-823.

Online Mendelian Inheritance in Man, OMIM. Lynch syndrome. McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine (Bethesda, MD). Accessed at www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=120435 on August 24, 2009.

Pellegrino A, Signorelli M, Fruscio R, et al. Feasibility and morbidity of total laparoscopic radical hysterectomy with or without pelvic limphadenectomy [sic] in obese women with stage I endometrial cancer. *Arch Gynecol Obstet.* 2009;279:655-660.

Perrone AM, Casadio P, Formelli G, et al. Cervical and hysteroscopic injection for identification of sentinel lymph node in endometrial cancer. *Gynecol Oncol*. 2008;111:62-67.

Powell MA, Sill MW, Goodfellow PJ, et al. A phase II trial of brivanib in recurrent or persistent endometrial cancer: an NRG Oncology/Gynecologic Oncology Group Study. *Gynecol Oncol*. 2014;135(1):38-43.

Rahaman J, Cohen CJ. Endometrial cancer. In: Kufe DW, Pollock RE, Weichselbaum RR, Bast RC, Gansler TS, Holland JF, Frei E, eds. *Cancer Medicine*. 6th ed. Hamilton, Ontario: B.C. Decker; 2003: 1809-1823.

Ray-Coquard I, Favier L, Weber B, et al. Everolimus as second- or third-line treatment of advanced endometrial cancer: ENDORAD, a phase II trial of GINECO. *Br J Cancer*. 2013;108(9):1771-1777.

Richter CE, Qian B, Martel M, et al. Ovarian preservation and staging in reproductive-age endometrial cancer patients. *Gynecol Oncol*. 2009;114(1):99-104.

Rosai J. Uterus-corpus. In: Rosai J, ed. Rosai and Ackerman's *Surgical Pathology.* 9th ed. Philadelphia, PA. Elsevier, 2004. 1565-1635.

Salani R, Backes FJ, Fung MF, Holschneider CH, Parker LP, Bristow RE, Goff BA. Posttreatment surveillance and diagnosis of recurrence in women with gynecologic

malignancies: Society of Gynecologic Oncologists recommendations. *Am J Obstet Gynecol*. 2011;204(6):466-478.

Schmeler KM, Lynch HT, Chen LM, et al. Prophylactic surgery to reduce the risk of gynecologic cancers in the Lynch syndrome. *N Engl J Med.* 2006;354:261-269.

Simpson AN, Feigenberg T, Clarke BA, et al. Fertility sparing treatment of complex atypical hyperplasia and low grade endometrial cancer using oral progestin. *Gynecol Oncol*. 2014;133(2):229-233.

Wright JD, Barrena Medel NI, Sehouli J, Fujiwara K, Herzog TJ. Contemporary management of endometrial cancer. *Lancet*. 2012;379(9823):1352-1360.

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