Ovarian 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 way. 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. In most cases the cancer cells form a tumor. 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 isn’t 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 abnormal cell does.

People can inherit damaged DNA, but most often the 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.

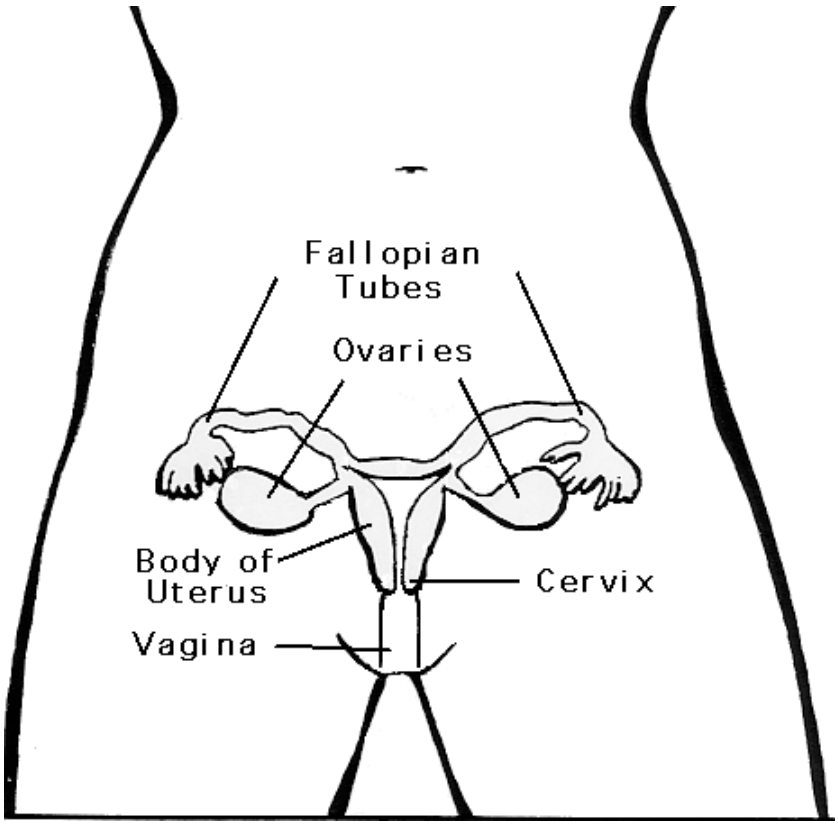
No matter where a cancer may spread, it is named (and treated) based on the place where it started. For example, breast cancer that has spread to the liver is still breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is still prostate cancer, not bone cancer.

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 ovarian cancer?

Ovarian cancer begins in the ovaries. Ovaries are reproductive glands found only in females (women). The ovaries produce eggs (ova) for reproduction. The eggs travel through the fallopian tubes into the uterus where the fertilized egg implants and develops into a fetus. The ovaries are also the main source of the female hormones estrogen and progesterone. One ovary is on each side of the uterus in the pelvis.



The ovaries are made up of 3 main kinds of cells. Each type of cell can develop into a different type of tumor:

- Epithelial tumors start from the cells that cover the outer surface of the ovary. Most ovarian tumors are epithelial cell tumors.
- Germ cell tumors start from the cells that produce the eggs (ova).
- Stromal tumors start from structural tissue cells that hold the ovary together and produce the female hormones estrogen and progesterone.

Most of these tumors are benign (non-cancerous) and never spread beyond the ovary. Benign tumors can be treated by removing either the ovary or the part of the ovary that contains the tumor.

Malignant (cancerous) or low malignant potential ovarian tumors can spread (metastasize) to other parts of the body and can be fatal. Their treatment is discussed later in this document.

Epithelial ovarian tumors

Benign epithelial ovarian tumors

Most epithelial ovarian tumors are benign, don't spread, and usually don't lead to serious illness. There are several types of benign epithelial tumors including serous cystadenomas, mucinous cystadenomas, and Brenner tumors.

Tumors of low malignant potential

When looked at under the microscope, some ovarian epithelial tumors don't clearly appear to be cancerous. These are called tumors of *low malignant potential* (LMP tumors). They are also known as *borderline epithelial ovarian cancer*. These are different from typical ovarian cancers because they don't grow into the supporting tissue of the ovary (called the ovarian *stroma*). Likewise, if they spread outside the ovary, for example, into the abdominal cavity (belly), they might grow on the lining of the abdomen but often don't grow into it.

LMP tumors tend to affect younger women than the typical ovarian cancers. These tumors grow slowly and are less life-threatening than most ovarian cancers. LMP tumors can be fatal, but this isn't common.

Malignant epithelial ovarian tumors

Cancerous epithelial tumors are called *carcinomas*. About 85% to 90% of ovarian cancers are epithelial ovarian carcinomas. When someone says that they had ovarian cancer, they usually mean that they had this type of cancer. These tumor cells have

several features (when viewed under a microscope) that can be used to classify epithelial ovarian carcinomas into different types. The *serous* type is by far the most common, but there are other types like *mucinous*, *endometrioid*, and *clear cell*.

If the cells don't look like any of these 4 subtypes, the tumor is called *undifferentiated*. Undifferentiated epithelial ovarian carcinomas tend to grow and spread more quickly than the other types. Epithelial ovarian carcinomas are classified by these subtypes, but they are also given a *grade* and a *stage*.

The grade classifies the tumor based on how much it looks like normal tissue on a scale of 1, 2, or 3. Grade 1 epithelial ovarian carcinomas look more like normal tissue and tend to have a better prognosis (outlook). Grade 3 epithelial ovarian carcinomas look less like normal tissue and usually have a worse outlook. Grade 2 tumors look and act in between grades 1 and 3.

The tumor stage describes how far the tumor has spread from where it started in the ovary. Epithelial ovarian cancers tend to spread to the lining and organs of the pelvis and abdomen (belly) first. This may lead to the build-up of fluid in the abdominal cavity (called *ascites*). As it becomes more advanced, it may spread to the lung and liver, or, rarely, to the brain, bones, or skin. Staging is explained in detail in a later section.

Other cancers that are similar to epithelial ovarian cancer

Primary peritoneal carcinoma

Primary peritoneal carcinoma (PPC) is a rare cancer closely related to epithelial ovarian cancer. At surgery, it looks the same as an epithelial ovarian cancer that has spread through the abdomen. Under a microscope, PPC also looks just like epithelial ovarian cancer. Other names for this cancer include *extra-ovarian* (meaning outside the ovary) *primary peritoneal carcinoma* (EOPPC) and *serous surface papillary carcinoma*.

PPC seems to develop from cells in the lining of the pelvis and abdomen. This lining is called the *peritoneum*. These cells are very similar to the cells on the surface of the ovaries. Some experts believe that PPC may start in the cells lining the fallopian tubes.

Like ovarian cancer, PPC tends to spread along the surfaces of the pelvis and abdomen, so it is often difficult to tell exactly where the cancer first started. This type of cancer can occur in women who still have their ovaries, but it is of more concern for women who have had their ovaries removed to prevent ovarian cancer. This cancer does rarely occur in men.

Symptoms of PPC are similar to those of ovarian cancer, including abdominal pain or bloating, nausea, vomiting, indigestion, and a change in bowel habits. Also, like ovarian cancer, PPC may elevate the blood level of a tumor marker called CA-125.

Women with PPC usually get the same treatment as those with widespread ovarian cancer. This could include surgery to remove as much of the cancer as possible (a process called debulking that is discussed in the section about surgery), followed by

chemotherapy like that given for ovarian cancer. Its outlook is likely to be similar to widespread ovarian cancer.

Fallopian tube cancer

This is another rare cancer that is similar to epithelial ovarian cancer. It begins in the tube that carries an egg from the ovary to the uterus (the fallopian tube). Like PPC, fallopian tube cancer and ovarian cancer have similar symptoms. The treatment for fallopian tube cancer is much like that for ovarian cancer, but the outlook (prognosis) is slightly better.

Ovarian germ cell tumors

Germ cells usually form the ova or eggs in females and the sperm in males. Most ovarian germ cell tumors are benign, but some are cancerous and may be life threatening. Less than 2% of ovarian cancers are germ cell tumors. Overall, they have a good outlook, with more than 9 out of 10 patients surviving at least 5 years after diagnosis. There are several subtypes of germ cell tumors. The most common germ cell tumors are *teratomas*, *dysgerminomas*, *endodermal sinus tumors*, and *choriocarcinomas*. Germ cell tumors can also be a mix of more than a single subtype.

Teratoma

Teratomas are germ cell tumors with areas that, when seen under the microscope, look like each of the 3 layers of a developing embryo: the *endoderm* (innermost layer), *mesoderm* (middle layer), and *ectoderm* (outer layer). This germ cell tumor has a benign form called *mature* teratoma and a cancerous form called *immature* teratoma.

The mature teratoma is by far the most common ovarian germ cell tumor. It is a benign tumor that usually affects women of reproductive age (teens through forties). It is often called a *dermoid cyst* because its lining is made up of tissue similar to skin (dermis). These tumors or cysts can contain different kinds of benign tissues including, bone, hair, and teeth. The patient is cured by surgical removal of the cyst, but sometimes a new cyst develops later in the other ovary.

Immature teratomas are a type of cancer. They occur in girls and young women, usually younger than 18. These are rare cancers that contain cells that look like those from embryonic or fetal tissues such as connective tissue, respiratory passages, and brain. Tumors that are relatively more mature (called *grade 1 immature teratoma*) and haven’t spread beyond the ovary are treated by surgical removal of the ovary. When they have spread beyond the ovary and/or much of the tumor has a very immature appearance (grade 2 or 3 immature teratomas), chemotherapy is recommended in addition to surgery.

Dysgerminoma

This type of cancer is rare, but it is the most common ovarian germ cell cancer**.** It usually affects women in their teens and twenties. Dysgerminomas are considered malignant (cancerous), but most don’t grow or spread very rapidly. When they are limited to the

ovary, more than 75% of patients are cured by surgically removing the ovary, without any further treatment. Even when the tumor has spread further (or if it comes back later), surgery, radiation therapy, and/or chemotherapy are effective in controlling or curing the disease in about 90% of patients.

Endodermal sinus tumor (yolk sac tumor) and choriocarcinoma

These very rare tumors typically affect girls and young women. They tend to grow and spread rapidly but are usually very sensitive to chemotherapy. Choriocarcinoma that starts in the placenta (during pregnancy) is more common than the kind that starts in the ovary. Placental choriocarcinomas usually respond better to chemotherapy than ovarian choriocarcinomas do.

Ovarian stromal tumors

About 1% of ovarian cancers are ovarian stromal cell tumors. More than half of stromal tumors are found in women older than 50, but about 5% of stromal tumors occur in young girls.

The most common symptom of these tumors is abnormal vaginal bleeding. This happens because many of these tumors produce female hormones (estrogen). These hormones can cause vaginal bleeding (like a period) to start again after menopause. In young girls, these tumors can also cause menstrual periods and breast development to occur before puberty.

Less often, stromal tumors make male hormones (like testosterone). If male hormones are produced, the tumors can cause normal menstrual periods to stop. They can also make facial and body hair grow. If the stromal tumor starts to bleed, it can cause sudden, severe abdominal pain.

Types of malignant (cancerous) stromal tumors include *granulosa cell* tumors (the most common type), *granulosa-theca* tumors, and *Sertoli-Leydig cell* tumors, which are usually considered low-grade cancers. *Thecomas* and *fibromas* are benign stromal tumors. Cancerous stromal tumors are often found at an early stage and have a good outlook, with more than 75% of patients surviving long-term.

Ovarian cysts

An ovarian cyst is a collection of fluid inside an ovary. Most ovarian cysts occur as a normal part of the process of ovulation (egg release) -- these are called *functional cysts*. These cysts usually go away within a few months without any treatment. If you develop a cyst, your doctor may want to check it again after your next cycle (period) to see if it has gotten smaller.

An ovarian cyst in a female who isn't ovulating (like a woman after menopause or a girl who hasn't started her periods), and the doctor may want to do more tests. The doctor may also order other tests if the cyst is large or if it does not go away in a few months. Even though most of these cysts are benign (not cancer), a small number of them could

be cancer. Sometimes the only way to know for sure if the cyst is cancer is to take it out with surgery. Cysts that appear to be benign (based on how they look on imaging tests) can be observed (with repeated physical exams and imaging tests), or removed with surgery.

What are the key statistics about ovarian cancer?

The American Cancer Society estimates for ovarian cancer in the United States for 2015 are:

- About 21,290 women will receive a new diagnosis of ovarian cancer.
- About 14,180 women will die from ovarian cancer.

Ovarian cancer ranks fifth in cancer deaths among women, accounting for more deaths than any other cancer of the female reproductive system. A woman's risk of getting ovarian cancer during her lifetime is about 1 in 75. Her lifetime chance of dying from ovarian cancer is about 1 in 100. (These statistics don’t count low malignant potential ovarian tumors.)

This cancer mainly develops in older women. About half of the women who are diagnosed with ovarian cancer are 63 years or older. It is more common in white women than African-American women.

The rate at which women are diagnosed with ovarian cancer has been slowly falling over the past 20 years.

What are the risk factors for ovarian cancer?

A risk factor is anything that changes your chance of getting a disease like 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 a number of cancers.

But risk factors don't tell us everything. Having a risk factor, or even several risk factors, does not mean that you will get the disease. And many people who get the disease may not have had any known risk factors. Even if a woman with ovarian cancer has a risk factor, it is very hard to know how much that risk factor may have contributed to the cancer. Researchers have discovered several specific factors that change a woman's likelihood of developing *epithelial* ovarian cancer. These risk factors don’t apply to other less common types of ovarian cancer like germ cell tumors and stromal tumors.

Age

The risk of developing ovarian cancer gets higher with age. Ovarian cancer is rare in women younger than 40. Most ovarian cancers develop after menopause. Half of all ovarian cancers are found in women 63 years of age or older.

Obesity

Various studies have looked at the relationship of obesity and ovarian cancer. Overall, it seems that obese women (those with a body mass index of at least 30) have a higher risk of developing ovarian cancer.

Reproductive history

Women who have been pregnant and carried it to term before age 26 have a lower risk of ovarian cancer than women who have not. The risk goes down with each full-term pregnancy. Women who have their first full-term pregnancy after age 35 or who never carried a pregnancy to term have a higher risk of ovarian cancer.

Breastfeeding may lower the risk even further.

Birth control

Women who have used oral contraceptives (also known as *birth control pills* or *the pill*) have a lower risk of ovarian cancer. The lower risk is seen after only 3 to 6 months of using the pill, and the risk is lower the longer the pills are used. This lower risk continues for many years after the pill is stopped.

A recent study found that the women who used depot medroxyprogesterone acetate (DMPA or Depo-Provera CI®), an injectable hormonal contraceptive had a lower risk of ovarian cancer. The risk was even lower if the women had used it for 3 or more years.

Gynecologic surgery

Tubal ligation (having your tubes tied) may reduce the chance of developing ovarian cancer by up to two-thirds. A hysterectomy (removing the uterus without removing the ovaries) also seems to reduce the risk of getting ovarian cancer by about one-third.

Fertility drugs

In some studies, researchers have found that using the fertility drug clomiphene citrate (Clomid®) for longer than one year may increase the risk for developing ovarian tumors. The risk seemed to be highest in women who did not get pregnant while on this drug. Fertility drugs seem to increase the risk of the type of ovarian tumors known as "low malignant potential" (described in the section, "What is ovarian cancer?"). If you are taking fertility drugs, you should discuss the potential risks with your doctor. However,

women who are infertile may be at higher risk (compared to fertile women) even if they don’t use fertility drugs. This might be in part because they haven't carried a pregnancy to term or used birth control pills (which are protective).

Androgens

Androgens are male hormones. Danazol, a drug that increases androgen levels, was linked to an increased risk of ovarian cancer in a small study. In a larger study, this link was not confirmed, but women who took androgens were found to have a higher risk of ovarian cancer. Further studies of the role of androgens in ovarian cancer are needed.

Estrogen therapy and hormone therapy

Some recent studies suggest women using estrogens after menopause have an increased risk of developing ovarian cancer. The risk seems to be higher in women taking estrogen alone (without progesterone) for many years (at least 5 or 10). The increased risk is less certain for women taking both estrogen and progesterone.

Family history of ovarian cancer, breast cancer, or colorectal cancer

Ovarian cancer can run in families. Your ovarian cancer risk is increased if your mother, sister, or daughter has (or has had) ovarian cancer. The risk also gets higher the more relatives you have with ovarian cancer. Increased risk for ovarian cancer can also come from your father's side.

A family history of some other types of cancer such as colorectal and breast cancer is linked to an increased risk of ovarian cancer. This is because these cancers can be caused by an inherited mutation (change) in certain genes that cause a family cancer syndrome that increases the risk of ovarian cancer.

Family cancer syndromes

About 5 to 10% of ovarian cancers are a part of family cancer syndromes resulting from inherited changes (*mutations*) in certain genes.

Hereditary breast and ovarian cancer syndrome

This syndrome is caused by inherited mutations in the genes *BRCA1* and *BRCA2*, as well as possibly some other genes that have not yet been identified. This syndrome is linked to a high risk of breast cancer as well as ovarian, fallopian tube, and primary peritoneal cancers. The risk of some other cancers, such as pancreatic cancer and prostate cancer, are also increased.

Mutations in *BRCA1* and *BRCA2* are also responsible for most inherited ovarian cancers. When these genes are normal they help prevent cancer by making proteins that keep cells

from growing abnormally (they act as *tumor suppressors*). But if you have inherited a mutation (defect) in one of these genes from either parent, this cancer-preventing protein is less effective, and your chances of developing breast and/or ovarian cancer increase. Mutations in *BRCA1* and *BRCA2* are about 10 times more common in those who are Ashkenazi Jewish than those in the general U.S. population.

The lifetime ovarian cancer risk for women with a *BRCA1* mutation is estimated to be between 35% and 70%. This means that if 100 women had a *BRCA1* mutation, between 35 and 70 of them would get ovarian cancer. For women with *BRCA2* mutations the risk has been estimated to be between 10% and 30% by age 70. These mutations also increase the risks for primary peritoneal carcinoma and fallopian tube carcinoma.

In comparison, the ovarian cancer lifetime risk for the women in the general population is less than 2%.

PTEN tumor hamartoma syndrome

In this syndrome, also known as Cowden disease, people are primarily affected with thyroid problems, thyroid cancer, and breast cancer. Women also have an increased risk of ovarian cancer. It is caused by inherited mutations in the *PTEN* gene.

Hereditary nonpolyposis colon cancer

Women with this syndrome have a very high risk of colon cancer and also have an increased risk of developing cancer of the uterus (endometrial cancer) and ovarian cancer. Many different genes can cause this syndrome. They include *MLH1*, *MLH3*, *MSH2*, *MSH6*, *TGFBR2*, *PMS1*, and *PMS2*. An abnormal copy of any one of these genes reduces the body's ability to repair damage to its DNA. The lifetime risk of ovarian cancer in women with hereditary nonpolyposis colon cancer (HNPCC) is about 10%. Up to 1% of all ovarian epithelial cancers occur in women with this syndrome. An older name for HNPCC is Lynch syndrome.

Peutz-Jeghers syndrome

People with this rare genetic syndrome develop polyps in the stomach and intestine while they are teenagers. They also have a high risk of cancer, particularly cancers of the digestive tract (esophagus, stomach, small intestine, colon). Women with this syndrome have an increased risk of ovarian cancer, including both epithelial ovarian cancer and a type of stromal tumor called *sex cord tumor with annular tubules* (SCTAT). This syndrome is caused by mutations in the gene *STK11*.

MUTYH-associated polyposis

People with this syndrome develop polyps in the colon and small intestine and have a high risk of colon cancer. They are also more likely to develop other cancers, including cancers of the ovary and bladder. This syndrome is caused by mutations in the gene *MUTYH*.

Personal history of breast cancer

If you have had breast cancer, you might also have an increased risk of developing ovarian cancer. There are several reasons for this. Some of the reproductive risk factors for ovarian cancer may also affect breast cancer risk. The risk of ovarian cancer after breast cancer is highest in those women with a family history of breast cancer. A strong family history of breast cancer may be caused by an inherited mutation in the *BRCA1* or *BRCA2* genes and hereditary breast and ovarian cancer syndrome, which is linked to an increased risk of ovarian cancer.

Talcum powder

It has been suggested that talcum powder applied directly to the genital area or on sanitary napkins may be carcinogenic (cancer-causing) to the ovaries. Some, studies suggest a very slight increase in risk of ovarian cancer in women who used talc on the genital area. In the past, talcum powder was sometimes contaminated with asbestos, a known cancer-causing mineral. This might explain the association with ovarian cancer in some studies. Since the 1970s, however, body and face powder products have been required by law to be asbestos-free. Proving the safety of these newer products will require follow-up studies of women who have used them for many years. There is no evidence at present linking cornstarch powders with any female cancers.

Diet

A study of women who followed a low-fat diet for at least 4 years showed a lower risk of ovarian cancer. Some studies have shown a reduced rate of ovarian cancer in women who ate a diet high in vegetables, but other studies disagree. The American Cancer Society recommends eating a variety of healthful foods, with an emphasis on plant sources. Eat at least 2 ½ cups of fruits and vegetables every day, as well as several servings of whole grain foods from plant sources such as breads, cereals, grain products, rice, pasta, or beans. Limit the amount of red meat and processed meats you eat. Even though the effect of these dietary recommendations on ovarian cancer risk remains uncertain, following them can help prevent several other diseases, including some other types of cancer.

Analgesics

In some studies, both aspirin and acetaminophen have been shown to reduce the risk of ovarian cancer. However, the information isn’t consistent. Women who don’t already take these medicines regularly for other health conditions should not start doing so to try to prevent ovarian cancer. More research is needed on this issue.

Smoking and alcohol use

Smoking doesn’t increase the risk of ovarian cancer overall, but it is linked to an increased risk for the mucinous type.

Drinking alcohol is not linked to ovarian cancer risk.

Do we know what causes ovarian cancer?

We don't yet know exactly what causes most ovarian cancers. As discussed in the previous section, we do know some factors that make a woman more likely to develop epithelial ovarian cancer. Much less is known about risk factors for germ cell and stromal tumors of the ovaries.

There are many theories about the causes of ovarian cancer. Some of them came from looking at the things that change the risk of ovarian cancer. For example, pregnancy and taking birth control pills both lower the risk of ovarian cancer. Since both of these things reduce the number of times the ovary releases an egg (ovulation), some researchers think that there may be some relationship between ovulation and the risk of developing ovarian cancer.

Also, we know that tubal ligation and hysterectomy lower the risk of ovarian cancer. One theory to explain this is that some cancer-causing substances may enter the body through the vagina and pass through the uterus and fallopian tubes to reach the ovaries. This would explain how removing the uterus or blocking the fallopian tubes affects ovarian cancer risk. Another theory is that male hormones (androgens) can cause ovarian cancer.

Researchers have made great progress in understanding how certain mutations (changes) in DNA can cause normal cells to become cancerous. DNA is the chemical that carries the instructions for nearly everything our cells do. We usually look like our parents because they are the source of our DNA. However, DNA affects more than the way we look. Some genes (parts of our DNA) contain instructions for controlling when our cells grow and divide. DNA mutations (defects) in these genes can lead to the development of cancer.

Inherited genetic mutations

A small portion of ovarian cancers occur in women with inherited gene mutations linked to an increased risk of ovarian cancer. These include mutations in the *BRCA1* and *BRCA2* genes, as well as the genes related to other family cancer syndromes linked to an increased risk of ovarian cancer, such as *PTEN* (PTEN tumor hamartoma syndrome), *STK11* (Peutz-Jeghers syndrome), *MUTYH* (MUTYH-asociated polyposis, and the many genes that can cause hereditary nonpolyposis colon cancer (*MLH1*, *MLH3*, *MSH2*, *MSH6*, *TGFBR2*, *PMS1*, and *PMS2).* (These syndromes were discussed in the previous section).

Genetic tests can detect gene mutations associated with these inherited syndromes. If you have a family history of cancers linked to these syndromes, such as breast and ovarian cancers, thyroid and ovarian cancer, and/or colorectal and endometrial (uterine) cancer, you might want to ask your doctor about genetic counseling and testing. The American Cancer Society recommends discussing genetic testing with a qualified cancer genetics

professional before any genetic testing is done. For more on this, see our document *Genetic Testing: What You Need to Know*.

Acquired genetic changes

Most DNA mutations related to ovarian cancer are not inherited but instead occur during a woman's life. In some cancers, acquired mutations of certain genes leading to the development of cancer may result from radiation or cancer-causing chemicals, but there is no evidence for this in ovarian cancer. So far, studies haven't been able to specifically link any single chemical in the environment or in our diets to mutations that cause ovarian cancer. The cause of most acquired mutations remains unknown.

Most ovarian cancers have several acquired gene mutations. Research has suggested that tests to identify acquired changes of certain genes in ovarian cancers, like the *TP53* tumor suppressor gene or the *HER2* oncogene, can help predict a woman's prognosis. The role of these tests is still not certain, and more research is needed.

For more information about genetic changes that can lead to cancer, see our document *Genes and Cancer*.

Can ovarian cancer be prevented?

Most women have one or more risk factors for ovarian cancer. But most of the common factors only slightly increase your risk, so they only partly explain the frequency of the disease. So far, what is known about risk factors has not translated into practical ways to prevent most cases of ovarian cancer.

There are several ways you can reduce your risk of developing epithelial ovarian cancer. Much less is known about ways to lower the risk of developing germ cell and stromal tumors of the ovaries. The remainder of this section refers to epithelial ovarian cancer only. It is important to realize that some of these strategies reduce the risk only slightly, while others decrease it much more. Some strategies are easily followed, and others require surgery. If you are concerned about your risk of ovarian cancer, you may want to discuss this information with your health care professionals. They can help you consider these ideas as they apply to your own situation.

Oral contraceptives

Using oral contraceptives (birth control pills) decreases the risk of developing ovarian cancer, especially among women who use them for several years. Women who used oral contraceptives for 5 or more years have about a 50% lower risk of developing ovarian cancer compared with women who never used oral contraceptives. Still, birth control pills do have some serious risks and side effects. Women considering taking these drugs for any reason should first discuss the possible risks and benefits with their doctor.

Gynecologic surgery

Both tubal ligation and hysterectomy may reduce the chance of developing ovarian cancer, but experts agree that these operations should only be done for valid medical reasons -- not for their effect on ovarian cancer risk.

If you are going to have a hysterectomy for a valid medical reason and you have a strong family history of ovarian or breast cancer, you may want to consider having both ovaries and fallopian tubes removed (called a *bilateral salpingo-oophorectomy*) as part of that procedure.

Even if you don't have an increased risk of ovarian cancer, some doctors recommend that the ovaries be removed with the uterus if a woman has already gone through menopause or is close to menopause. If you are older than 40 and you are going to have a hysterectomy, you should discuss the potential risks and benefits of having your ovaries removed with your doctor.

Prevention strategies for women with a family history of ovarian cancer or BRCA mutation

If your family history suggests that you (or a close relative) might have a syndrome linked with a high risk of ovarian cancer, you might want to consider genetic counseling and testing. During genetic counseling (by a genetic counselor or other health care professional with training in genetic risk evaluation), your personal medical and family history is reviewed. This can help predict whether you are likely to have one of the gene mutations associated with an increased ovarian cancer risk.

The counselor will also discuss the benefits and potential drawbacks of genetic testing with you. Genetic testing can help determine if you or members of your family carry certain gene mutations that cause a high risk of ovarian cancer. Still, the results are not always clear cut, and a genetic counselor can help you sort out what the results mean to you.

For some women with a strong family history of ovarian cancer, knowing they do not have a mutation that increases their ovarian cancer risk can be a great relief for them and their children. Knowing that you do have such a mutation can be stressful, but many women find this information very helpful in making important decisions about certain prevention strategies for them and their children. More information about genetic testing can be found in our document, *Genetic Testing: What You Need to Know*.

Using oral contraceptives is one way that many women can reduce their risk of developing ovarian cancer. Oral contraceptives also seem to reduce this risk for women with *BRCA1* and *BRCA2* mutations. But birth control pills can increase breast cancer risk in women without these mutations. This increased risk continues for some time after these pills are stopped. Studies that have looked at this issue in women with *BRCA* mutations haven't agreed about what effect birth control pills have on breast cancer risk. Some studies have shown an increased risk of breast cancer, while some have not.

Research is continuing to find out more about the risks and benefits of oral contraceptives for women at high ovarian and breast cancer risk.

It isn't clear if tubal ligation effectively reduces the risk of ovarian cancer in women who have *BRCA1* or *BRCA2* mutations. Studies that have looked at this issue haven't agreed about this. Researchers do agree that removing both ovaries and fallopian tubes (salpingo-oophorectomy) helps protect women with *BRCA1* or *BRCA2* mutations against ovarian (and fallopian tube) cancer.

Sometimes a woman has this surgery to reduce her risk of ovarian cancer before cancer is even suspected. If the ovaries are removed to prevent ovarian cancer, the surgery is called *risk-reducing* or *prophylactic*. Generally, salpingo-oophorectomy is recommended only for very high-risk women after they have finished having children. This operation lowers ovarian cancer risk a great deal but does not entirely eliminate it. That's because some women who have a high risk of ovarian cancer already have a cancer at the time of surgery. These cancers can be so small that they are only found when the ovaries and fallopian tubes are looked at under the microscope (after they are removed). Also, women with *BRCA1* or *BRCA2* gene mutations have an increased risk of primary peritoneal carcinoma. Although the risk is low, this cancer can still develop after the ovaries and fallopian tubes are removed.

The risk of fallopian tube cancer is also increased in women with mutations in *BRCA1* or *BRCA2*. Sometimes early fallopian tube cancers are found unexpectedly when the fallopian tubes are removed as a part of a risk-reducing surgery. In fact, some cancers that were thought to be ovarian or primary peritoneal cancers may have actually started in the fallopian tubes. That is why experts recommend that women at high risk of ovarian cancer who are having their ovaries removed should have their fallopian tubes completely removed as well (salpingo-oophorectomy).

Research has shown that premenopausal women who have *BRCA* gene mutations and have had their ovaries removed reduce their risk of breast cancer as well as their risk of ovarian cancer. The risk of ovarian cancer is reduced by 85% to 95%, and the risk of breast cancer cut by 50% or more.

Another option for women who do not wish to have their ovaries removed because they don't want to lose ovarian function (and go through menopause early) is to have just the fallopian tubes removed (a salpingectomy). They may choose to have their ovaries removed later. This has not been studied as well as removing both the ovaries and fallopian tubes at the same time, so it isn't clear how much this affects the risk of cancer. It is clear that to have the greatest effect on breast cancer risk, the ovaries need to be removed by the time the woman is 35.

Some women who have a high risk of ovarian cancer due to *BRCA* gene mutations feel that having their ovaries and fallopian tubes removed is not right for them. Often doctors recommend that those women have screening tests to try to find ovarian cancer early. These tests are discussed in the next section.

Can ovarian cancer be found early?

About 20% of ovarian cancers are found at an early stage. When ovarian cancer is found early at a localized stage, about 94% of patients live longer than 5 years after diagnosis. Several large studies are in progress to learn the best ways to find ovarian cancer in its earliest stage.

Ways to find ovarian cancer early

Regular women's health exams

During a pelvic exam, the health care professional feels the ovaries and uterus for size, shape, and consistency. A pelvic exam can be useful because it can find some reproductive system cancers at an early stage, but most early ovarian tumors are difficult or impossible for even the most skilled examiner to feel. Pelvic exams may, however, help identify other cancers or gynecologic conditions. Women should discuss the need for these exams with their doctor.

The Pap test is effective in early detection of cervical cancer, but it isn’t a test for ovarian cancer. Rarely, ovarian cancers are found through Pap tests, but usually they are at an advanced stage.

See a doctor if you have symptoms

Early cancers of the ovaries often cause no symptoms. When ovarian cancer causes symptoms, they tend to be symptoms that are more commonly caused by other things. These symptoms include abdominal swelling or bloating (due to a mass or a buildup of fluid), pelvic pressure or abdominal pain, difficulty eating or feeling full quickly, and/or urinary symptoms (having to go urgently or often). Most of these symptoms can also be caused by other less serious conditions. These symptoms can be more severe when they are caused by ovarian cancer, but that isn’t always true. What is most important is that they are a change from how a woman usually feels.

By the time ovarian cancer is considered as a possible cause of these symptoms, it usually has already spread beyond the ovaries. Also, some types of ovarian cancer can rapidly spread to the surface of nearby organs. Still, prompt attention to symptoms may improve the odds of early diagnosis and successful treatment. If you have symptoms similar to those of ovarian cancer almost daily for more than a few weeks, and they can't be explained by other more common conditions, report them to your health care professional -- preferably a gynecologist -- right away.

Screening tests for ovarian cancer

Screening tests and exams are used to detect a disease, like cancer, in people who don’t have any symptoms. Perhaps the best example of this is the mammogram, which can often detect breast cancer in its earliest stage, even before a doctor can feel the cancer.

There has been a lot of research to develop a screening test for ovarian cancer, but there hasn't been much success so far. The 2 tests used most often to screen for ovarian cancer are *transvaginal ultrasound* (TVUS) and the *CA-125* blood test.

TVUS is a test that uses sound waves to look at the uterus, fallopian tubes, and ovaries by putting an ultrasound wand into the vagina. It can help find a mass (tumor) in the ovary, but it can't actually tell if a mass is cancer or benign. When it is used for screening, most of the masses found are not cancer.

CA-125 is a protein in the blood. In many women with ovarian cancer, levels of CA-125 are high. This test can be useful as a tumor marker to help guide treatment in women known to have ovarian cancer, because a high level often goes down if treatment is working.

But checking CA-125 levels has not been found to be as useful as a screening test for ovarian cancer. The problem with using this test for screening is that common conditions other than cancer can also cause high levels of CA-125. In women who have not been diagnosed with cancer, a high CA-125 level is more often caused by one of these other conditions and not ovarian cancer. Also, not everyone who has ovarian cancer has a high CA-125 level. When someone who is not known to have ovarian cancer has an abnormal CA-125 level, the doctor might repeat the test (to make sure the result is correct). The doctor could also consider ordering a transvaginal ultrasound test.

In studies of women at average risk of ovarian cancer, using TVUS and CA-125 for screening led to more testing and sometimes more surgeries, but did not lower the number of deaths caused by ovarian cancer. For that reason, no major medical or professional organization recommends the routine use of TVUS or the CA-125 blood test to screen for ovarian cancer.

Some organizations state that these tests may be offered to screen women who have a high risk of ovarian cancer due to an inherited genetic syndrome (discussed in the section, "Do we know what causes ovarian cancer?"). Still, even in these women, it's not clear that using these tests for screening lowers their chances of dying from ovarian cancer.

Better ways to screen for ovarian cancer are being researched. Hopefully, improvements in screening tests will eventually lead to a lower ovarian cancer death rate.

There are no recommended screening tests for germ cell tumors or stromal tumors. Some germ cell cancers release certain protein markers such as human chorionic gonadotropin (HCG) and alpha-fetoprotein (AFP) into the blood. After these tumors have been treated by surgery and chemotherapy, blood tests for these markers can be used to see if treatment is working and to determine if the cancer is coming back.

Researchers continue to look for new tests to help diagnose ovarian cancer early but currently there are no reliable screening tests.

Signs and symptoms of ovarian cancer

Ovarian cancer may cause several signs and symptoms. Women are more likely to have symptoms if the disease has spread beyond the ovaries, but even early- stage ovarian cancer can cause them. The most common symptoms include:

- Bloating
- Pelvic or abdominal pain
- Trouble eating or feeling full quickly
- Urinary symptoms such as urgency (always feeling like you have to go) or frequency (having to go often)

These symptoms are also commonly caused by benign (non-cancerous) diseases and by cancers of other organs. When they are caused by ovarian cancer, they tend to be *persistent* and represent a *change from normal* − for example, they occur more often or are more severe. If a woman has these symptoms more than 12 times a month, she should see her doctor, preferably a gynecologist.

Others symptoms of ovarian cancer can include:

- Fatigue
- Upset stomach
- Back pain
- Pain during sex
- Constipation
- Menstrual changes
- Abdominal swelling with weight loss

However, these symptoms are more likely to be caused by other conditions, and most of them occur just about as often in women who don’t have ovarian cancer.

How is ovarian cancer diagnosed?

If you have symptoms of ovarian cancer you should see your doctor, who will examine you and may order some tests.

Physical exam

Your doctor will first take your history and do a physical exam to look for signs of ovarian cancer. These include an enlarged ovary (on a pelvic exam) and signs of fluid in the abdomen (which is called *ascites*).

If there is reason to suspect you have ovarian cancer based on your symptoms and/or physical exam, your doctor will order some tests to check further.

Consultation with a specialist

If the results of your pelvic exam or other tests suggest that you have ovarian cancer, you will need a doctor or surgeon who specializes in treating women with this type of cancer. A *gynecologic oncologist* is an obstetrician/gynecologist who is specially trained in treating cancers of the female reproductive system. Treatment by a gynecologic oncologist helps ensure that you get the best kind of surgery for your cancer. It has also has been shown to help patients with ovarian cancer live longer. Anyone suspected of having ovarian cancer should see this type of specialist before having surgery.

Imaging tests

Imaging tests like computed tomography (CT) scans, magnetic resonance imaging (MRI) scans, and ultrasound studies can confirm whether a pelvic mass is present. These studies cannot confirm that the mass is a cancer, but they may be useful if your doctor is looking to see if ovarian cancer has spread (metastasized) to other tissues and organs.

Ultrasound

Ultrasound (ultrasonography) is the use of sound waves to create an image on a video screen. Sound waves are released from a small probe placed in the woman's vagina or on the surface of her abdomen. The sound waves create echoes as they enter the ovaries and other organs. The same probe detects the echoes that bounce back, and a computer translates the pattern of echoes into a picture.

Ultrasound is often the first test done if a problem with the ovaries is suspected. It can be useful finding an ovarian tumor and seeing if it is a solid mass (tumor) or a fluid-filled cyst. It can also be used to get a better look at the ovary to see how big it is and how it looks inside (the internal appearance or complexity). These factors help the doctor decide which masses or cysts are more worrisome.

Computed tomography (CT) scans

The CT scan is an x-ray procedure that produces detailed cross-sectional images of your body. Instead of taking one picture, like a conventional x-ray, a CT scanner takes many pictures as it rotates around you. A computer then combines these pictures into an image

of a slice of your body. The machine will take pictures of multiple slices of the part of your body that is being studied.

A CT scanner has been described as a large donut, with a narrow table in the middle opening. You will need to lie still on the table while the scan is being done. CT scans take longer than regular x-rays, and you might feel a bit confined by the ring while the pictures are being taken.

CT scans do not show small ovarian tumors well, but they can see larger tumors, and may be able to see if the tumor is growing into nearby structures. A CT scan may also find enlarged lymph nodes, signs of cancer spread to liver or other organs, or signs that an ovarian tumor is affecting your kidneys or bladder.

You may be asked to drink 1 to 2 pints of a liquid before the CT scan called *oral contrast*. You might also receive an IV (intravenous) line through which a different kind of contrast dye is injected. Contrast dyes help 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 imaging tests.

CT scans are not usually used to biopsy (see biopsy in the section "Other tests") an ovarian tumor, but they can be used to biopsy a suspected metastasis. For this procedure, called a *CT-guided needle biopsy*, the patient stays on the CT scanning table, while a radiologist moves a biopsy needle toward the location of the mass. CT scans are repeated until the doctors are confident that the needle is within 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 examined under a microscope.

Barium enema x-ray

This is a test to see if the cancer has invaded the colon (large intestine) or rectum (it is also used to look for colorectal cancer). After taking laxatives the day before, barium sulfate, a chalky substance, is put into the rectum and colon and x-rays are taken. Because x-rays don’t penetrate (go through) barium, the colon and rectum are outlined on the x-rays. This test is rarely used now in women with ovarian cancer. Colonoscopy may be done instead.

Magnetic resonance imaging (MRI) scans

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. Not only does this produce cross-sectional slices of the body like a CT scanner, it can also produce slices that are parallel with the

length of the body. A contrast material might be injected into a vein (same as with a CT scan). MRI scans are not used often to look for ovarian cancer.

MRI scans are particularly helpful to examine the brain and spinal cord. MRI scans take longer than CT scans, -- often up to 30 minutes or more. Also, you have to be placed inside a tube, which is confining and can upset people with claustrophobia (fear of enclosed spaces). The machine also makes a thumping noise that you may find disturbing. Some places will provide headphones with music to block the sound.

Chest x-ray

This procedure may be done to determine whether ovarian cancer has spread (metastasized) to the lungs. This spread may cause one or more tumors in the lungs and more often causes fluid to collect around the lungs. This fluid, called a *pleural effusion*, can be seen with chest x-rays as well as other types of scans.

Positron emission tomography (PET) scan

In this test, radioactive glucose (sugar) is given to look for the cancer. Because cancers use glucose 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 in spotting small collections of cancer cells. In some instances this test has proved useful in finding ovarian cancer that has spread. It is even more valuable when combined with a CT scan (PET/CT scan). PET scans can help find cancer when it has spread, but they are expensive and are not always covered by insurance when they are used to look for ovarian cancer.

Other tests

Laparoscopy

This procedure uses a thin, lighted tube through which a doctor can look at the ovaries and other pelvic organs and tissues in the area. The tube is inserted through a small incision (cut) in the lower abdomen and sends the images of the pelvis or abdomen to a video monitor. Laparoscopy provides a view of organs that can help plan surgery or other treatments and can help doctors confirm the stage (how far the tumor has spread) of the cancer. Also, doctors can manipulate small instruments through the laparoscopic incision(s) to perform biopsies.

Colonoscopy

A colonoscopy is a way to examine the inside of the large intestine (colon). Before this test can be done, the colon and rectum must be cleaned out to remove any stool. This often means drinking a large amount (2 to 4 quarts) of a liquid laxative the night before and the morning of the procedure, and spending hours in the bathroom. Just before the procedure, the patient is given intravenous (IV) medicine to make him or her relaxed or

even asleep (sedation). Then a colonoscope (a long, flexible, tube with a light and video camera on the end) is inserted through the rectum and into the colon. The images are sent to a video monitor. Any abnormal areas seen can be biopsied. Because sedation is used for this procedure, patients need someone they know to take them home afterwards (not just a cab). This procedure is more commonly used to look for colorectal cancer.

Biopsy

The only way to determine for certain if a growth is cancer is to remove a sample of the growth from the suspicious area and examine it under a microscope. This procedure is called a *biopsy*. For ovarian cancer, the biopsy is most commonly done by removing the tumor.

In rare cases, a suspected ovarian cancer may be biopsied during a laparoscopy procedure or with a needle placed directly into the tumor through the skin of the abdomen. Usually the needle will be guided by either ultrasound or CT scan. This is only used in patients who cannot have surgery because of advanced cancer or some other serious medical condition, because there is concern that a biopsy could spread the cancer.

In patients with ascites (fluid buildup inside the abdomen), samples of the fluid can also be used to diagnose the cancer. In this procedure, called *paracentesis*, the skin of the abdomen is numbed and a needle attached to a syringe is passed through the abdominal wall into the fluid in the abdominal cavity. Ultrasound may be used to guide the needle. The fluid is sucked up into the syringe and then sent for analysis to see if it contains cancer cells.

In all these procedures, the tissue or fluid obtained is sent to the laboratory. There it is examined under the microscope by a *pathologist*, a doctor who specialize in diagnosing and classifying diseases by examining cells under a microscope and using other lab tests.

Blood tests

Your doctor will order blood count tests to make sure you have enough red blood cells, white blood cells and platelets (cells that help stop bleeding). There will also be tests to measure your kidney and liver function as well as your general health status. Finally the doctor will order a CA-125 test. Women who have a high CA-125 level are often referred to a gynecologic oncologist, but any woman with suspected ovarian cancer should see a gynecologic oncologist, as well.

Some germ cell cancers can cause elevated blood levels of the tumor markers human chorionic gonadotropin (HCG), alpha-fetoprotein (AFP), and/or lactate dehydrogenase (LDH). These may be checked if your doctor suspects that your ovarian tumor could be a germ cell tumor.

Some ovarian stromal tumors cause the blood levels of a substance called *inhibin* and hormones such as estrogen and testosterone to go up. These levels may be checked if your doctor suspects that you have this type of tumor.

How is ovarian cancer staged?

Staging is the process of finding out how widespread a cancer is. Most ovarian cancers that are not obviously widespread are staged at surgery. One of the goals of surgery for ovarian cancer is to take tissue samples for diagnosis and staging. To stage the cancer, samples of tissues are taken from different parts of the pelvis and abdomen and examined under the microscope.

Staging is very important because ovarian cancers have different prognoses at different stages and are treated differently. The accuracy of the staging may determine whether or not a patient will be cured. If the cancer isn't accurately staged, then cancer that has spread outside the ovary might be missed and not treated. Once the cancer has been given a stage it does not change, even when it comes back (recurs) or spreads (metastasizes) to new locations.

Ask your cancer care team to explain the staging procedure. After surgery, ask what your cancer's stage is. In this way, you will be able to make informed decisions about your treatment. One of the reasons it is important to be operated on by a gynecologic oncologist is that you are more likely to be staged accurately.

Ovarian and fallopian tube cancer is most often staged using the *FIGO system*. This system relies on the results of surgery to determine the extent of the primary tumor (often described by the letter T), the absence or presence of metastasis to nearby lymph nodes (described by the letter N), and the absence or presence of distant metastasis (described by the letter M). This information is combined to determine the final stage. Primary peritoneal cancer (PPC) is staged in a similar way, but there is no stage I.

The American Joint Committee on Cancer has another way to stage ovarian, fallopian tube, and primary peritoneal cancers. This also uses T, N, and M categories, however this staging is slightly different from the most recent FIGO staging.

Stages of ovarian and fallopian tube cancer

Once a patient's T, N, and M categories have been determined, this information is combined in a process called *stage grouping* to determine the stage, expressed in Roman numerals from stage I (the least advanced stage) to stage IV (the most advanced stage). Many stages are divided into substages designated by adding letters and sometimes additional numbers to the Roman numerals.

Stage I

The cancer is only within the ovary (or ovaries) or fallopian tube(s). It has not spread to organs and tissues in the abdomen or pelvis, lymph nodes, or to distant sites.

Stage IA (T1a, N0, M0): Cancer has developed in one ovary, and the tumor is confined to the inside of the ovary; or the cancer has developed in one fallopian tube, and is only inside the fallopian tube. There is no cancer on the outer surface of the ovary or fallopian

tube. Laboratory examination of washings from the abdomen and pelvis did not find any cancer cells.

Stage IB (T1b, N0, M0): Cancer has developed in both ovaries or fallopian tubes but not on their outer surfaces. Laboratory examination of washings from the abdomen and pelvis did not find any cancer cells.

Stage IC (T1c, N0, M0): The cancer is present in one or both ovaries or fallopian tubes and any of the following are present:

- The tissue (capsule) surrounding the tumor broke during surgery, which could allow cancer cells to leak into the abdomen and pelvis (called *surgical spill*). This is stage IC1.
- Cancer is on the outer surface of at least one of the ovaries or fallopian tubes or the capsule (tissue surrounding the tumor) has ruptured (burst) before surgery (which could allow cancer cells to spill into the abdomen and pelvis). This is stage IC2
- Laboratory examination found cancer cells in fluid or washings from the abdomen. This is stage IC3.

Stage II

The cancer is in one or both ovaries or fallopian tubes and has spread to other organs (such as the uterus, fallopian tubes, bladder, the sigmoid colon, or the rectum) within the pelvis. It has not spread to lymph nodes or distant sites.

Stage IIA (T2a, N0, M0): Either

- Cancer that started in the ovaries has spread to or has invaded (grown into) the uterus or the fallopian tubes, or both,

  OR

- Cancer that started in the fallopian tubes has spread to the ovaries, the uterus or both.

Stage IIB (T2b, N0, M0): The cancer has grown into other nearby pelvic organs such as the bladder, the sigmoid colon, or the rectum.

Stage III

The cancer is in one or both ovaries or fallopian tubes, and one or both of the following are present:

- Cancer has spread beyond the pelvis to the lining of the abdomen
- Cancer has spread to lymph nodes in the back of the abdomen (retroperitoneal lymph nodes)

Stage IIIA1 (T1 or T2, N1, M0): Cancer is in one or both ovaries or fallopian tubes, and it may have spread or grown into nearby organs in the pelvis. Areas of cancer spread are found in retroperitoneal lymph nodes, but there are no other areas of cancer spread.

- Stage IIIA1(i): the areas of cancer spread in the lymph nodes is 10 mm (millimeters) across or smaller
- Stage IIIA1(ii): the areas of cancer spread in the lymph nodes is greater than 10 mm across

Stage IIIA2 (T3a2, N0 or N1, M0): Cancer is in one or both ovaries or fallopian tubes, and it may have spread or grown into nearby organs in the pelvis. During surgery, no cancer is visible to the naked eye in the abdomen (outside of the pelvis). However, when biopsies are checked under a microscope, tiny deposits of cancer are found in the lining of the upper abdomen. The cancer may also have spread to retroperitoneal lymph nodes, but it has not spread to distant sites.

Stage IIIB (T3b, N0 or N1, M0): There is cancer in one or both ovaries or fallopian tubes, and it may have spread or grown into nearby organs in the pelvis. Deposits of cancer large enough for the surgeon to see, but 2 cm (about 3/4 inch) or smaller across, are in the abdomen. These deposits may be on the outside (the capsule) of the liver or spleen. Cancer may have also spread to the lymph nodes, but it has not spread to the inside of the liver or spleen or to distant sites.

Stage IIIC (T3c, N0 or N1, M0): The cancer is in one or both ovaries or fallopian tubes, and it may have spread or grown into nearby organs in the pelvis. Deposits of cancer larger than 2 cm (about 3/4 inch) across are seen in the abdomen and these may be on the outside (the *capsule*) of the liver or spleen. Cancer may have also spread to the lymph nodes, but it has not spread to the inside of the liver or spleen or to distant sites.

Stage IV (any T, any N, M1)

This is the most advanced stage of ovarian cancer. In this stage the cancer has spread to the inside of the spleen, liver, lungs, or other organs located outside the peritoneal cavity. (The peritoneal cavity is the area enclosed by the peritoneum, a membrane that lines the inner abdomen and some of the pelvis and covers most of its organs.)

Stage IVA: Cancer cells are found in the fluid around the lungs (this is called a *malignant pleural effusion*) with no other areas of cancer spread outside the pelvis or peritoneal cavity.

Stage IVB: Cancer has spread to the inside of the spleen or liver, to lymph nodes besides the retroperitoneal lymph nodes, and/or to other organs or tissues outside the peritoneal cavity. This includes the lungs, the brain, and the skin.

Stages of primary peritoneal cancer

Stage II

Cancer is not inside the ovaries or fallopian tubes (if it was, then it would be ovarian or fallopian tube cancer). Cancer is only in the tissue lining the pelvis (the peritoneum) and has not spread elsewhere, including the upper part of the abdomen or outside the abdomen or pelvis.

Stage III

Cancer is not inside the ovaries or fallopian tubes (if it was, then it would be ovarian or fallopian tube cancer). The cancer is in the tissue lining the pelvis and abdomen (the peritoneum). It may be on the surface (the capsule) of the liver or spleen, but not inside these organs. It has not spread outside the abdomen or pelvis.

Stage IV

Cancer is not inside the ovaries or fallopian tubes (if it was, then it would be ovarian or fallopian tube cancer). Cancer is in the tissue lining the pelvis and abdomen (the peritoneum) and has spread further, such as to the inside of the liver or spleen, the lungs, brain, skin, or bones.

Survival rates for ovarian cancer, by stage

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 and skip to the next section.

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 even are cured).

Five-year relative survival rates assume that some people will die of other causes and compare the observed survival with that expected for people without the cancer. This is a more accurate way to see the impact of the cancer on survival.

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 ovarian cancer.

Survival rates are often based on previous outcomes of large numbers of people who had the disease, but they cannot predict what will happen in any individual's case. Many other factors can affect a person's outlook, such as their general health, the grade of the cancer, the treatment received, and how well the cancer responds to treatment. Your doctor can

tell you how the numbers below apply to you, as he or she is familiar with the aspects of your situation.

For all types of ovarian cancer, the 5-year relative survival is 45%. Women diagnosed when they are younger than 65 do better than older women. If ovarian cancer is found (and treated) before the cancer has spread outside the ovary (stages IA and IB), the 5-year relative survival rate is 92%. However, only 15% of all ovarian cancers are found at this early stage.

The survival rates given below are for the different types of ovarian cancer. They come from the National Cancer Institute, SEER Data Base and are based on patients diagnosed from 2004 to 2010. The most recent FIGO staging system came out in January of 2014, and so statistics for survival based on that staging are not yet available. These numbers are based on a previous version of the staging system, which had different and fewer substages.

Invasive epithelial ovarian cancer

Stage	**Relative 5-Year Survival Rate**
I	90%
IA	94%
IB	92%
IC	85%
II	70%
IIA	78%
IIB	73%
III	39%
IIIA	59%
IIIB	52%
IIIC	39%
IV	17%

Ovarian stromal tumors

Stage	Relative 5-yr Survival Rate
I	95%
II	78%
III	65%
IV	35%

Germ cell tumors of the ovary

Stage	Relative 5-yr Survival Rate
I	98%
II	94%
III	87%
IV	69%

Fallopian tube carcinoma

Stage	Relative 5-yr Survival Rate
I	87%
II	86%
III	52%
IV	40%

How is ovarian 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 the diagnostic tests are done, your cancer care team will recommend 1 or more treatment options. The main treatments for ovarian cancer are:

- Surgery
- Chemotherapy
- Hormone therapy
- Targeted therapy
- Radiation therapy

Often, 2 or more different types of treatments are used.

Consider the options without feeling rushed. If there is anything you don’t understand, ask to have it explained. The choice of treatment depends largely on the type of cancer and the stage of the disease., The exact stage may not be known in patients who did not have surgery as their first treatment. Treatment then is based on other available information.

Other factors that could play a part in choosing the best treatment plan might include your general state of health, whether you plan to have children, and other personal considerations. Age alone isn’t a determining factor since several studies have shown that older women tolerate ovarian cancer treatments well. Be sure you understand all the risks and side effects of the various therapies before making a decision about treatment.

Surgery for ovarian cancer

Surgery is the main treatment for most ovarian cancers. How much surgery you have depends on how far your cancer has spread and on your general health. For women of childbearing age who have certain kinds of tumors and whose cancer is in the earliest stage, it may be possible to treat the disease without removing both ovaries and the uterus.

For epithelial ovarian cancer, surgery has 2 main goals: staging and debulking (this is discussed in detail further on). It’s important that this surgery is done by someone who’s experienced in ovarian cancer surgery.

Experts recommend that patients see a gynecologic oncologist for surgery. Gynecologic oncologists are specialists who have training and experience in treating, staging, and debulking ovarian cancer. If your cancer isn’t properly staged and debulked, you may need to have more surgery later. It has been shown that gynecologic oncologists are more likely than general surgeons and gynecologists to stage and debulk ovarian cancer optimally (see below).

For other types of ovarian cancer (germ cell tumors and stromal tumors), the main goal of surgery is to remove the cancer.

Staging epithelial ovarian cancer

Surgery for ovarian cancer has 2 main goals. The first goal is to *stage* the cancer − to see how far the cancer has spread from the ovary. Usually this means removing the uterus (this operation is called a *hysterectomy*), along with both ovaries and fallopian tubes (this is called a *bilateral salpingo-oophorectomy* or BSO). In addition, the omentum is also removed (an *omentectomy*). The omentum is a layer of fatty tissue that covers the abdominal contents like an apron, and ovarian cancer sometimes spreads to this tissue. Some lymph nodes in the pelvis and abdomen are biopsied (taken out to see if the cancer has spread from the ovary).

If there is fluid in the pelvis or abdominal cavity, it will also be removed for analysis. The surgeon may "wash" the abdominal cavity with salt water (saline) and send that fluid for analysis. He or she may also remove tissue samples from different areas inside the abdomen and pelvis. All the tissue and fluid samples taken during the operation are sent to a lab to be examined for cancer cells. Staging is very important because ovarian cancers at different stages are treated differently. If the staging isn't done correctly, the doctor may not be able to decide on the best treatment.

Debulking epithelial ovarian cancer

The other important goal of surgery is to remove as much of the tumor as possible − this is called *debulking.* Debulking is very important in any patient with ovarian cancer that has already spread widely throughout the abdomen at the time of surgery. The aim of debulking surgery is to leave behind no tumors larger than 1 cm. This is called *optimally debulked*. Patients whose tumors have been optimally debulked, have a better outlook than those left with larger tumors after surgery (called *sub-optimally debulked*).

Sometimes the surgeon will need to remove a piece of colon to debulk the cancer properly. In some cases, a piece of colon is removed and then the 2 ends that remain are sewn back together. In other cases, though, the ends can’t be sewn back together right away. Instead, the top end of the colon is attached to an opening (stoma) in the skin of the abdomen to allow body wastes to get out. This is known as a *colostomy.* Most often, this

is only temporary, and the ends of the colon can be reattached later in another operation. For more information, see our document, *Colostomy: A Guide*.

Debulking surgery might also mean removing a piece of the bladder. If this occurs, a catheter (to empty the bladder) will be placed during surgery. This will be left in place until the bladder recoveis enough to be able to empty on its own. Then, the catheter can be removed.

Debulking may also require removing the spleen and/or the gallbladder, as well as part of the stomach, liver, and/or pancreas.

If both ovaries and/or the uterus are removed, you will not be able to become pregnant. It also means that you will go into menopause if you haven't done so already. Most women will stay in the hospital for 3 to 7 days after the operation and can resume their usual activities within 4 to 6 weeks.

Surgery for ovarian germ cell tumors and ovarian stromal tumors

Most ovarian germ cell tumors are treated with a hysterectomy and bilateral salpingo-oophorectomy. If the cancer is in only one ovary and the patient still wants to be able to have children, only the ovary containing the cancer and the fallopian tube on the same side are removed (leaving behind the other ovary and fallopian tube and the uterus).

Ovarian stromal tumors are often confined to just one ovary, so surgery may just remove that ovary. If the cancer has spread, more tissue may need to be removed. This could mean a hysterectomy and bilateral salpingo-oophorectomy and even debulking surgery.

Chemotherapy for ovarian cancer

Chemotherapy (chemo) is the use of drugs to treat cancer. Most often, chemo is a systemic treatment − the drugs are given in a way that lets them enter the bloodstream and reach all areas of the body. Systemic chemo can be useful for cancers that have metastasized (spread). Most of the time, systemic chemo uses drugs that are injected into a vein (IV) or given by mouth. For some cases of ovarian cancer, chemotherapy may also be injected through a catheter (thin tube) directly into the abdominal cavity. This is called *intraperitoneal (IP) chemotherapy*. Drugs given this way are also absorbed into the bloodstream, so IP chemotherapy is also a type of systemic chemo. This is discussed in more detail later in this section.

If you'd like more information on a drug used in your treatment or a specific drug mentioned in this section, see our Guide to Cancer Drugs , or call us with the names of the medicines you're taking.

Chemotherapy for epithelial ovarian cancer

Chemo for ovarian cancer is most often a combination of 2 or more drugs, given IV every 3- to 4-weeks. Giving combinations of drugs rather than just one drug alone seems to be more effective in the initial treatment of ovarian cancer.

The standard approach is the combination of a platinum compound, such as cisplatin or carboplatin, and a taxane, such as paclitaxel (Taxol®) or docetaxel (Taxotere®). For IV chemotherapy, most doctors favor carboplatin over cisplatin because it has fewer side effects and is just as effective.

The typical course of chemo for epithelial ovarian cancer involves 3 to 6 cycles. A cycle is a schedule of regular doses of a drug, followed by a rest period. Different drugs have varying cycles; your doctor will let you know what schedule planned for your chemo.

Epithelial ovarian cancer often shrinks or even seems to go away with chemo, but the cancer cells may eventually begin to grow again. If the first chemo seemed to work well and the cancer stayed away for a long time (at least 6 to 12 months), it can be treated with additional cycles of the same chemotherapy used the first time. In some cases, different drugs may be used. Some of the other chemo drugs that are helpful in treating ovarian cancer include (in alphabetical order):

- Albumin bound paclitaxel (nab-paclitaxel, Abraxane®)
- Altretamine (Hexalen®)
- Capecitabine (Xeloda®)
- Cyclophosphamide (Cytoxan®)
- Etoposide (VP-16)
- Gemcitabine (Gemzar®)
- Ifosfamide (Ifex®)
- Irinotecan (CPT-11, Camptosar®)
- Liposomal doxorubicin (Doxil®)
- Melphalan
- Pemetrexed (Alimta®)
- Topotecan
- Vinorelbine (Navelbine®)

The different drug combinations used to treat germ cell tumors are described later on in the section “Treatment for germ cell tumors.”

Chemotherapy drugs kill cancer cells but also damage some normal cells. Therefore, your doctor will be careful to avoid or minimize side effects, which depend on the type of drugs, the amount taken, and the length of treatment.

Common temporary side effects include:

- Nausea and vomiting

- Loss of appetite
- Loss of hair
- Hand and foot rashes
- Mouth sores

Chemotherapy can damage the blood-producing cells of the bone marrow, so patients may have low blood cell counts. This can result in:

- Increased chance of infection (caused by a shortage of white blood cells)
- Bleeding or bruising after minor cuts or injuries (caused by a shortage of blood platelets)
- Fatigue (caused by low red blood cell counts)

Most side effects disappear once treatment is stopped. Hair will grow back after treatment ends, although it may look different. There are remedies for many of the temporary side effects of chemotherapy. For example, drugs can be given to prevent and treat nausea and vomiting. For more information about chemotherapy and its side effects, please see our document, *A Guide to Chemotherapy*. A list of some other documents that you may find helpful can be found in the section called "Additional resources for ovarian cancer."

Some chemo drugs may have long-term or even permanent side effects. For example, cisplatin can cause kidney damage. To help prevent this, doctors give lots of IV fluid before and after this drug is given. Both cisplatin and the taxanes can cause nerve damage (called *neuropathy*). This can lead to problems with numbness, tingling, or even pain in the hands and feet. Cisplatin can also damage the nerves to the ear, which can lead to hearing loss (called *ototoxicity*). Other drugs can have other side effects, so ask your doctor what side effects to expect from the drugs that you will receive. Most side effects improve once treatment is stopped, but some can last a long time and may never go away completely.

Chemo can also cause early menopause and infertility (inability to become pregnant), which may be permanent. This is rarely an issue in the treatment of epithelial ovarian cancer, since most women have both ovaries removed as a part of treatment.

Rarely, some chemo drugs can permanently damage bone marrow. This can later cause a bone marrow cancer such as myelodysplastic syndrome or even acute myeloid leukemia. This is called a *secondary malignancy*. Your health care team knows which drugs can cause this problem and will discuss this possibility with you. Their positive effects against ovarian cancer offset the small chance that any of these drugs will cause another cancer.

Intraperitoneal chemotherapy

In intraperitoneal (IP) chemotherapy for ovarian cancer, in addition to giving the chemo drug paclitaxel IV, the drugs cisplatin and paclitaxel are injected into the abdominal cavity through a catheter (thin tube). The tube can be placed during the staging/debulking

surgery, but sometimes it is placed later. If it is done later, it can be placed by a surgeon using laparoscopy, or by an interventional radiologist under x-ray guidance. The catheter is usually connected to a *port*, a half dollar-sized disk topped with a pliable diaphragm. The port is placed under the skin against a bony structure of the abdominal wall, such as a rib or pelvic bone. A needle can be placed through the skin and into the port to give chemo and other drugs. Over time, problems may rarely occur with the catheter. − it may become plugged or infected or even damage the bowel.

Giving chemo this way gives the most concentrated dose of the drugs to the cancer cells in the abdominal cavity. This chemo also gets absorbed into the bloodstream and so can reach cancer cells outside the abdominal cavity. IP chemotherapy works well, but the side effects are often more severe than with regular chemo. In a study of women with advanced ovarian cancer, women getting the IP chemotherapy had more abdominal pain, nausea, vomiting, and other side effects than the women getting chemo through the vein. These side effects actually made some women stop their treatment early. Still, the women getting IP chemotherapy lived longer than the women getting regular chemo.

IP chemotherapy currently is only given to some of the women with ovarian cancer that has spread to the inside of the abdomen. It was only studied in women whose cancer had not spread outside the abdomen (stage III) and who had no tumors larger than 1 cm after surgery (optimally debulked). Also, because it can be so toxic, women must have normal kidney function and be in good overall shape for their doctor to be willing to try IP chemo. They also cannot have a lot of adhesions or scar tissue inside their abdomen because this can prevent the chemo from spreading well.

Germ cell tumors

Patients with germ cell cancer often need to be treated with combination chemo. The combination used most often is called PEB (or BEP), and includes the chemotherapy drugs cisplatin (Platinol), etoposide, and bleomycin. Dysgerminomas are usually very sensitive to chemotherapy, and can sometimes be treated with the less toxic combination of carboplatin and etoposide. Other drug combinations may be used if the cancer isn’t responding to treatment or to treat cancer that has recurred (come back). These include:

- TIP: paclitaxel (Taxol), ifosfamide, and cisplatin
- VeIP: vinblastine, ifosfamide, and cisplatin
- VIP: etoposide (VP-16), ifosfamide, and cisplatin

Chemo for germ cell tumors has some of the same risks and side effects as the chemo for epithelial ovarian cancer. These include:

- Nausea and vomiting
- Loss of appetite
- Loss of hair

- Increased chance of infection (caused by a shortage of white blood cells)
- Bleeding or bruising after minor cuts or injuries (caused by a shortage of blood platelets)
- Fatigue (caused by low red blood cell counts)

Other possible side effects include kidney damage from cisplatin. To help prevent this, doctors give lots of IV fluid before and after this drug is given. Both cisplatin and the taxanes can cause nerve damage (called *neuropathy*). This can lead to problems with numbness, tingling, or even pain in the hands and feet. Cisplatin can also damage the nerves to the ear, which can lead to hearing loss (called *ototoxicity*). will cause another cancer. Rarely, bleomycin can lead to lung damage, so doctors may test lung function before using this drug. Ifosfamide can cause hemorrhagic cystitis (irritation and bleeding of the bladder lining). This can usually be prevented by giving the drug mesna with the ifosfamide.

Other other side effects can occur depending on what drugs are used, so ask your doctor what side effects to expect from the drugs that you will receive.

Most side effects improve once treatment is stopped, but some can last a long time and may never go away completely.

Chemo can also cause early menopause and infertility (inability to become pregnant), which may be permanent. This can be a particular concern for young women treated for germ cell tumors.

Rarely, some chemo drugs can permanently damage bone marrow. This can later cause a bone marrow cancer such as myelodysplastic syndrome or even acute myeloid leukemia. This is called a *secondary malignancy*. Your health care team knows which drugs can cause this problem and will discuss this possibility with you. Their positive effects against ovarian cancer offset the small chance that any of these drugs

Stromal tumors

Ovarian stromal tumors are not often treated with chemotherapy, but when they are, the combination of carboplatin plus paclitaxel or PEB (cisplatin/Platinol, etoposide, and bleomycin) is most often used.

Chemo for stromal tumors has some of the same risks and side effects as the chemo for epithelial ovarian cancer. These include

- Nausea and vomiting
- Loss of appetite
- Loss of hair
- Increased chance of infection (caused by a shortage of white blood cells)

- Bleeding or bruising after minor cuts or injuries (caused by a shortage of blood platelets)
- Fatigue (caused by low red blood cell counts)

Other possible side effects include kidney damage from cisplatin. To help prevent this, doctors give lots of IV fluid before and after this drug is given. Both cisplatin and the taxanes can cause nerve damage (called *neuropathy*). This can lead to problems with numbness, tingling, or even pain in the hands and feet. Cisplatin can also damage the nerves to the ear, which can lead to hearing loss (called *ototoxicity*). will cause another cancer. Rarely, bleomycin can lead to lung damage, so doctors may test lung function before using this drug. Ifosfamide can cause hemorrhagic cystitis (irritation and bleeding of the bladder lining). This can usually be prevented by giving the drug mesna with the ifosfamide.

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Chemo can also cause early menopause and infertility (inability to become pregnant), which may be permanent.

Rarely, some chemo drugs can permanently damage bone marrow. This can later cause a bone marrow cancer such as myelodysplastic syndrome or even acute myeloid leukemia. This is called a *secondary malignancy*. Your health care team knows which drugs can cause this problem and will discuss this possibility with you. Their positive effects against ovarian cancer offset the small chance that any of these drugs

For more information about chemotherapy and its side effects, please see our document, *A Guide to Chemotherapy*. A list of some other documents that you may find helpful can be found in the section called “Additional resources for ovarian cancer.”

Targeted therapy for ovarian cancer

Targeted therapy is a newer type of cancer treatment that uses drugs or other substances to identify and attack cancer cells while doing little damage to normal cells. These therapies attack the cancer cells' inner workings − the programming that makes them different from normal, healthy cells. Each type of targeted therapy works differently, but all alter the way a cancer cell grows, divides, repairs itself, or interacts with other cells.

Bevacizumab

Bevacizumab (Avastin®) belongs to a class of drugs known as *angiogenesis inhibitors*. In order for cancers to grow and spread, they need new blood vessels to form to nourish the tumors (called angiogenesis). This drug binds to a substance called VEGF that signals new blood vessels to form. This can slow or stop the growth of cancers.

In studies, bevacizumab has been shown to shrink or slow the growth of advanced epithelial ovarian cancers. Trials to see if bevacizumab works even better when given along with chemotherapy have shown good results in terms of shrinking (or stopping the growth of) tumors. But it doesn't seem to help women live longer.

This drug is given as an infusion into the vein (IV) every 2 to 3 weeks.

Common side effects include high blood pressure, tiredness, bleeding, low white blood cell counts, headaches, mouth sores, loss of appetite, and diarrhea. Rare but possibly serious side effects include blood clots, severe bleeding, slow wound healing, holes forming in the colon (called perforations), and the formation of abnormal connections between the bowel and the skin or bladder (fistulas). If a perforation or fistula occurs it can lead to severe infection and may require surgery to correct.

Olaparib

Olaparib (Lynparza™) is a type of drug known as a *PARP (poly(ADP)-ribose polymerase) inhibitor*. PARP enzymes are normally involved in one pathway to help repair damaged DNA inside cells. The *BRCA* genes (*BRCA1* and *BRCA2*) are also normally involved in a different pathway of DNA repair, and mutations in those genes can block that pathway. By blocking the PARP pathway, olaparib makes it very hard for tumor cells with a *BRCA* gene that doesn't work to repair damaged DNA, which often leads to the death of these cells.

This drug is used to treat advanced epithelial ovarian cancer. Because it relies on a blocked *BRCA* pathway to work, at this time it is only used in patients who have mutations in the *BRCA* genes. Only a small portion of women with ovarian cancer have mutated *BRCA* genes. If you are not known to have a *BRCA* mutation, your doctor will test your blood to be sure you have one before starting treatment with this drug.

In studies, this drug helped some advanced ovarian cancers in women who had *BRCA* mutations stop growing or shrink for a time. So far though, it hasn't been shown to help the women live longer.

This drug is taken by mouth, twice a day.

Side effects tend to be mild and include nausea, vomiting, diarrhea, fatigue, loss of appetite, and muscle and joint pain. Rarely, some patients treated with olaparib have developed a blood cancer, such as myelodysplastic syndrome and acute myeloid leukemia.

Other targeted therapy drugs are being studied.

Our document *Targeted Therapy* has more information about these kinds of drugs. If you'd like more information on a drug used in your treatment or a specific drug mentioned in this section, see our Guide to Cancer Drugs , or call us with the names of the medicines you're taking.

Hormone therapy for ovarian cancer

Hormone therapy is the use of hormones or hormone-blocking drugs to fight cancer. This type of systemic therapy is rarely used to treat epithelial ovarian cancer, but is more often used to treat ovarian stromal tumors.

Luteinizing-hormone-releasing hormone (LHRH) agonists

LHRH agonists (sometimes called *GnRH agonists*) switch off estrogen production by the ovaries. These drugs are used to lower estrogen levels in women who are premenopausal. Examples of LHRH 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. If they are taken for a long time (years), these drugs can weaken bones (sometimes leading to osteoporosis).

Tamoxifen

Tamoxifen is a drug that is often used to treat breast cancer. It can also be used to treat ovarian stromal tumors and is rarely used to treat advanced epithelial ovarian cancer. Tamoxifen acts as an anti-estrogen in many tissues in the body, but as a weak estrogen in others. The goal of tamoxifen therapy is to keep any estrogens circulating in the woman's body from stimulating cancer cell growth. The anti-estrogen activity of this drug can lead to hot flashes and vaginal dryness. Because tamoxifen acts like a weak estrogen in some areas of the body, it does not cause bone loss but can increase the risk of serious blood clots in the legs.

Aromatase inhibitors

Aromatase inhibitors are drugs that block an enzyme (called *aromatase*) that turns other hormones into estrogen in post-menopausal women. They don't stop the ovaries from making estrogen, so they are only helpful in lowering estrogen levels in women after menopause. These drugs are mainly used to treat breast cancer, but can also be used to treat some ovarian stromal tumors that have come back after treatment. They include letrozole (Femara®), anastrozole (Arimidex®), and exemestane (Aromasin®). These drugs are taken as pills once a day.

Common side effects of aromatase inhibitors include hot flashes, joint and muscle pain, and bone thinning. The bone thinning can lead to osteoporosis and bone that break easily.

If you'd like more information on a drug used in your treatment or a specific drug mentioned in this section, see our Guide to Cancer Drugs , or call us with the names of the medicines you're taking.

Radiation therapy for ovarian cancer

Radiation therapy uses high energy x-rays or particles to kill cancer cells. These x-rays may be given in a procedure that is much like having a regular (diagnostic) x-ray. In the

past radiation was used more often for ovarian cancer, at this time radiation therapy is only rarely used in this country as the main treatment for this cancer. It can be useful in treating areas of cancer spread.

External beam radiation therapy

In this procedure, radiation from a machine outside the body is focused on the cancer. This is the main type of radiation therapy used to treat ovarian cancer. Treatments are given 5 days a week for several weeks. Each treatment lasts only a few minutes and is similar to having a regular x-ray. As with a regular x-ray, the radiation passes through the skin and other tissues before it reaches the tumor. The actual time you are exposed to the radiation is very short, and most of the visit is spent getting precisely positioned so that the radiation is aimed accurately at the cancer.

Some common side effects include:

- Skin changes – the skin in the treated area may look and feel sunburned or even blister and peel
- Fatigue (tiredness)
- Nausea and vomiting
- Diarrhea
- Vaginal irritation, sometimes with a discharge (if the pelvis is being treated)

These side effects improve after treatment is stopped. Skin changes gradually fade, and the skin returns to normal in 6 to 12 months.

If you are having side effects from radiation, discuss them with your cancer care team. There may be things you can do to obtain relief.

Brachytherapy

Radiation therapy also may be given as an implant of radioactive materials, called *brachytherapy*, placed near the cancer. This is rarely done for ovarian cancer.

Radioactive phosphorus

Radioactive phosphorus was used in the past, but is no longer part of the standard treatment for ovarian cancer. For this treatment, a solution of radioactive phosphorus is instilled into the abdomen. The solution gets into cancer cells lining the surface of the abdomen and kills them. It has few immediate side effects but can cause scarring of the intestine and lead to digestive problems, including bowel blockage.

More information on radiation therapy can be found in the radiation section of our website, or in our document *Understanding Radiation Therapy: A Guide for Patients and Families.*

Ovarian cancer clinical trials

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.

You must meet requirements to take part in any clinical trial. But if you do qualify for a clinical trial, you still get to decide whether or not to enter (enroll in) it.

Clinical trials are one way to get state-of-the art cancer treatment. In some cases, 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 on clinical trials in our document called *Clinical Trials: What You Need to Know*. You can read it on our website or call our toll-free number (1-800-227-2345) and have it sent to you.

Ovarian cancer complementary and alternative therapies

When you have ovarian 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 might 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 haven't been tested. Some have been proven not to be helpful, and a few have even been found harmful.

Alternative treatments: Alternative treatments may be offered as cancer cures. These treatments haven't 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. Delaying or interrupting 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 haven't 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 Medicine and Cancer* in general or read about specific methods, in the *Complementary and Alternative Medicine* section of our website.

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 of invasive epithelial ovarian cancers, by stage

The first step in treating most stages of ovarian cancer is surgery to remove and stage the cancer. Debulking is also done as needed (see the section about surgery for details).

Stage I

The initial treatment for stage I ovarian cancer is surgery to remove the tumor. Most often the uterus, both fallopian tubes, and both ovaries are removed (a hysterectomy with bilateral salpingo-oophorectomy) (this is discussed in the surgery section).

In **stages IA and IB** (T1a or T1b, N0, M0), cancer was found inside one or both ovaries, without spread to lymph nodes or other organs. The treatment after surgery depends on the way the cancer cells look under the microscope (called the *tumor grade*).

The tumor is grade 1 when the cancer cells look a lot like normal ovarian cells. The outlook is good for grade 1 tumors, and most patients require no treatment after surgery. If someone with a grade 1, Stage IA ovarian cancer wants to be able to have children after treatment, the initial surgery may be changed. Instead of removing the uterus, both ovaries, and both fallopian tubes, the surgeon may offer the option of removing only the ovary containing the cancer along with the fallopian tube on the same side.

For a grade 2 cancer (meaning the cancer looks something like normal ovarian cells), patients are either watched closely after surgery without further treatment, or they are treated with chemotherapy (chemo). The chemo used most commonly is carboplatin and paclitaxel (Taxol) for 3-6 cycles, but cisplatin can be used instead of carboplatin, and docetaxel (Taxotere) can be used instead of paclitaxel.

Grade 3 cancers don't look very much like normal ovarian tissue under the microscope. The treatment of these tumors usually includes chemotherapy (like the chemo that is given for grade 2).

Stage IC (**T1c, N0, M0)**: For stage IC ovarian cancer (including stage IC1, IC2, and IC3), standard surgery to remove the cancer is still the first treatment. After surgery, chemo is recommended, usually 3 to 6 cycles of treatment with carboplatin and paclitaxel.

Stage I fallopian tube cancer is treated the same way as stage I ovarian cancer.

Stage II (including IIA and IIB)

For all stage II cancers, treatment starts with surgery for staging and debulking. This includes a hysterectomy and bilateral salpingo-oophorectomy (see the section about surgery for details). The surgeon will try to remove as much of the tumor as is possible.

After surgery, chemo is recommended for at least 6 cycles. The combination of carboplatin and paclitaxel is most often used. Some women with stage II ovarian cancer are treated with intraperitoneal (IP) chemotherapy instead of intravenous (IV) chemotherapy. This was discussed in more detail in the section about chemotherapy.

Stage II fallopian tube cancers are also treated with surgery for staging and debulking, followed by chemo.

Stage III ovarian, fallopian tube, and primary peritoneal cancers

Stage III cancers (includes IIIA1, IIIA2, IIIB, and IIIC) are given similar treatments as stage II cancers. First, the cancer is surgically staged and the tumor is debulked (like stage II). The uterus, both fallopian tubes, both ovaries, and omentum (fatty tissue from the upper abdomen near the stomach and intestines) are removed. The surgeon will also try to remove as much of the tumor as possible. The goal is to leave behind no tumor larger than 1 cm. When this goal is reached, the cancer is said to have been *optimally debulked*.

Sometimes tumor is growing on the intestines, and in order to remove the cancer, part of the intestine will have to be removed. Sometimes pieces of other organs (like the bladder or liver) may have to be removed to remove the cancer (this was discussed in the section about surgery). The smaller the remaining tumor, the better the outlook will be.

After recovery from surgery, combination chemo is given. The combination used most often is carboplatin (or cisplatin) and a taxane, such as paclitaxel (Taxol), given IV (into a vein) for 6 cycles.

Another option is to give intra-abdominal (intraperitoneal or IP) chemo after surgery. This was discussed in more detail in the section about chemotherapy. Since IP chemo means giving the drug paclitaxel IV along with the drugs cisplatin and paclitaxel into the abdomen (IP), women who get IP chemo are actually getting both IV and IP chemo. IP chemo is usually only considered if the cancer was optimally debulked − it may not work as well if a lot of tumor is left in the abdomen. IP chemo seems to work better than IV chemo, but it also causes worse side effects. These side effects can make it hard for someone to continue their treatment. For that reason, IP chemo may not be for everyone. Still, it is an option for women with advanced ovarian cancer to consider.

After surgery, and during and after chemo, blood tests will be done to determine if you have normal levels of a tumor marker called *CA-125*. A CT scan, PET-CT scan, or MRI could also be done to evaluate your response to treatment.

Patients who are too weak or ill to have full staging and debulking surgery sometimes get chemo as the first treatment. If the chemo works and the patient becomes stronger, surgery to debulk the cancer may be done, often followed by more chemo. Most often, 3 cycles of chemo are given before surgery, with at least 3 more after surgery (for a total of at least 6 cycles). Giving chemo before surgery is also sometimes an option for some women with advanced cancers that aren't likely to be able to be optimally debulked if the surgery is done first.

Second look surgery: In the past, many experts recommended another operation (laparoscopy/laparotomy) to see if the cancer was gone after chemo. This is known as a *second look surgery*. These operations haven't been shown to have any real benefit, and so are no longer a standard part of ovarian cancer care. Still, they may be done as part of a clinical trial. In a clinical trial of new treatments, the second-look operation may be worthwhile to help determine how effective the new treatment is.

For laparoscopy, a small opening is made below the navel and a slender tube with a light is placed so the doctor can inspect the abdominal cavity to see how successful treatment has been.

Laparotomy requires an incision (cut) or surgical opening long enough for the surgeon to look inside the pelvis and abdomen and take biopsy samples. Your cancer care team can decide if you need more chemo based on the results of the second-look surgery.

Consolidation therapy: For some patients, the doctor will recommend additional chemo after the cancer appears to be gone after the initial treatment. This is called *maintenance* or *consolidation therapy.* It is aimed at killing any cancer cells that were left behind after treatment but are too small to be seen with medical tests. The goal of consolidation therapy is to keep the cancer from coming back after treatment. One study showed that giving paclitaxel (every 4 weeks) for a year lengthened the time before the cancers came back, but didn't help the women live longer. Another study found no benefit, but the drug was given on a different schedule. This is still being studied in clinical trials.

Stage IV ovarian, fallopian tube, and primary peritoneal cancers

In stage IV, the cancer has spread to distant sites, like the inside the liver, the lungs, or bones. This stage isn’t able to be cured with current treatment, but it can still be treated. The goals of treatment are to help patients feel better and live longer. Stage IV can be treated like stage III − with surgery to remove the tumor and debulk the cancer, followed by chemo. Another option is to treat with chemo first. Then, if the tumors shrink from the chemo, surgery may be done, which is followed by more chemo. Most often, 3 cycles of chemo are given before surgery, with at least 3 more after surgery. Another option is to limit treatment to those aimed at improving comfort (but not at fighting the cancer). This type of treatment is called *palliative,* and is discussed later in more detail.

Recurrent or persistent ovarian 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 like the lungs or bone). Persistent tumors are those that never went away completely after treatment. Advanced epithelial ovarian cancer often comes back months or years after the initial treatment.

Sometimes, more surgery is recommended. Most patients with recurrent or persistent ovarian cancer are treated with some form of chemo. Which chemo drugs are used depends on what was used the first time and how well it worked (how long the cancer stayed away). The longer it takes for the cancer to come back after treatment, the better the chance that additional chemo will work. If it has been at least 6 months since any chemo, the patient may be treated with carboplatin and paclitaxel (even if these drugs were given before). Giving carboplatin with another drug is also an option.

If the cancer comes back in less than 6 months (or if it never went away at all), different chemo drugs usually will be tried. The targeted drug bevacizumab (Avastin) may be given with chemo. For women with mutations in the *BRCA1* or *BRCA2* genes, olaparib (Lynparza) may be an option at some point. Some women may receive several different

chemo regimens over several years. Many chemo drugs can be used to treat ovarian cancer (see the section about chemotherapy). In addition, some patients benefit from hormonal treatment with drugs like anastrozole, letrozole, or tamoxifen. Someone who didn't initially receive chemo can be treated with the same drugs that are used for newly diagnosed cancer − usually carboplatin and paclitaxel.

A clinical trial for new treatments might provide important advantages for women with recurrent or persistent ovarian cancer. Ask your cancer care team for information about suitable clinical trials for your type of cancer.

High-dose chemotherapy with stem cell rescue (sometimes known as *stem cell transplant*) has been used for women with recurrent or persistent ovarian cancer. This treatment has very serious side effects, however, and has not been proven to help patients live longer. It is best done as part of a clinical trial that is studying improvements to this procedure. More information about stem cell transplants is available on our website, or you can call 1-800-227-2345 for our document *Stem Cell Transplant (Peripheral Blood, Bone Marrow, and Cord Blood Transplants*.

Palliative treatments: Women with ovarian cancer can have a buildup of fluid in the abdomen. This is called *ascites*. It can be very uncomfortable but can be treated with a procedure called *paracentesis*. After the skin is numbed, a needle is used to withdraw the fluid, often several quarts, into a bottle. Often, ultrasound is used to guide the needle. Often the fluid builds up again, and this procedure needs to be repeated. Sometimes a catheter (a thin flexible tube) is placed into the abdomen and left there so that fluid can be removed as often as is needed without using a needle. Another option is to inject chemo directly into the abdomen to slow the buildup of fluid. Treatment with bevacizumab (Avastin) may also help slow fluid buildup. These treatments can relieve symptoms for some patients and, rarely, might extend life. Often, however, their effects are temporary, and the cancer returns or persists.

Ovarian cancer can also block the intestinal tract. This is called *obstruction*, and can cause abdominal pain, nausea, and vomiting. Dealing with an intestinal blockage can be difficult. Often, the cancer has grown so much in the abdomen that surgery to unblock the intestine doesn't work. To help make the patient comfortable, doctors may place a tube through the skin and into the stomach to allow the stomach juices to drain, so that the digestive tract isn’t completely blocked. This can help with pain, nausea, and vomiting.

Sometimes a stent (a stiff tube) can be put into the large intestine to relieve a blockage. Since this option has a high risk of complications, you should discuss the risks and benefits with your doctor first.

In some patients, surgery can be done to relieve intestinal obstruction. This is often only offered to patients who are well enough to get additional treatments (like chemo) after surgery.

Treatment for epithelial tumors of low malignant potential

These tumors are also called *LMP tumors*, *atypical proliferating tumors*, or *borderline tumors*. When seen on ultrasound and CT scan, these tumors look the same as invasive epithelial ovarian cancers. To know for certain that the tumor isn't an invasive epithelial ovarian cancer, a biopsy must be done. A biopsy sample is usually taken during surgery. Surgery for LMP tumors is similar to the surgery for invasive ovarian cancer, with the goals of removing the tumor along with full staging and debulking (see the section about surgery for details).

For women who have finished having children, the uterus, both fallopian tubes, and both ovaries are removed. Surgical staging is done to see if the tumor has spread outside the ovary or pelvis. This means removing the omentum and some lymph nodes, and doing washings of the abdomen and pelvis. If the patient wants to be able to become pregnant in the future, only the ovary with the tumor and the fallopian tube on that side is removed. Rarely, just the part of the ovary containing the ovarian cyst with the tumor is removed (ovarian cystectomy). These patients still should have surgical staging to see if the tumor has spread. If the tumor is only in one ovary, the patient is usually observed without further treatment. Experts recommend follow-up visits at least every 6 months for the first 5 years after diagnosis. Chemotherapy (chemo) and radiation therapy are not generally the first treatments used for tumors that haven't spread outside the ovary.

If the tumor has spread outside the ovary when it is first diagnosed, the surgeon will remove as much of it as possible (debulk it). Treatment after surgery depends on something called *invasion* (when one kind of cell grows into organs or tissues where it doesn't belong). Part of what makes a cancer cell dangerous is its ability to invade other tissues. When LMP tumors spread, they can form tumor implants (deposits) on the lining of the abdomen (the peritoneum) and on the surface of organs in the abdomen and pelvis. Most often, these implants are *non-invasive*, meaning they haven't grown into the abdominal lining or organs. When they are growing into the peritoneum or the organs, they are said to be *invasive.*

Patients with non-invasive spread from an LMP tumor are usually observed without further treatment after debulking surgery. If the tumor implants are invasive, chemo may be offered. The chemo given is usually the same as that used for invasive ovarian cancer. Observation is often recommended for LMP tumors because they grow very slowly and even when they spread they are rarely fatal.

If the tumor comes back after initial surgery, further debulking surgery may be considered. Chemo and, rarely, radiation therapy are also options for recurrent LMP tumors.

Treatment for germ cell tumors of the ovary

Benign germ cell tumors

Women with benign (non-cancerous) germ cell tumors such as mature teratomas (dermoid cysts) are cured by removing the part of the ovary that has the tumor (ovarian cystectomy) or by removing the entire ovary.

Malignant germ cell tumors

As with epithelial ovarian cancers, it is a good idea to consult with a gynecologic oncologist for treating malignant germ cell tumors, especially because these are so uncommon. Less than 2% of all ovarian cancers are germ cell tumors.

Most types and stages of germ cell cancers of the ovary are treated the same way, with surgery and chemotherapy (chemo). The exceptions are stage I, grade 1, immature teratoma and stage IA dysgerminoma. Their treatment is discussed in detail later in this section.

Surgery: In general, all patients with malignant germ cell tumors will have the same staging surgery that is done for epithelial ovarian cancer. If the patient is still interested in having children, the cancerous ovary and the fallopian tube on the same side are removed, but the uterus, the ovary, and the fallopian tube on the opposite side can be left behind. This isn’t an option when the cancer is in both ovaries. If the patient has finished having children, complete staging including removing both ovaries, both fallopian tubes, and the uterus is generally recommended.

Sometimes, the doctor might consider removing only a part of one ovary to allow a woman to keep her ovarian function. Even when both ovaries need to be removed, a patient may wish to keep her uterus to allow future pregnancy through the use of in-vitro fertilization. Consulting a gynecologic oncologist is advised in these cases.

If cancer has spread beyond the ovaries (stage IC and higher), debulking may be done as a part of the initial surgery. This removes as much cancer as possible without damaging or removing essential organs.

For stage IA dysgerminoma and stage I, grade 1, immature teratoma, surgery is usually the only treatment needed. Patients with these germ cell cancers are watched closely after surgery. If the cancer comes back later, the patient is usually given chemo.

Chemotherapy: Most patients with germ cell cancer will need to be treated with combination chemo for at least 3 cycles. The combination used most often is PEB (or BEP), and includes the chemo drugs cisplatin, etoposide, and bleomycin. Dysgerminomas are usually very sensitive to chemo, and can sometimes be treated with the less toxic combination of carboplatin and etoposide. Other drug combinations may be used to treat cancer that has recurred (come back) or hasn't responded to treatment.

Germ cell cancers can elevate blood levels of the tumor markers human chorionic gonadotropin (HCG), alpha-fetoprotein (AFP), and/or lactate dehydrogenase (LDH). If the blood levels of these are elevated before treatment starts, they are rechecked during chemo (usually before each cycle). If the chemo is working, the levels will go down to normal. If the levels stay up, it can be a sign that a different treatment is needed.

Stage IA dysgerminoma

If dysgerminoma is limited to one ovary, the patient may be treated by removing only that ovary and the fallopian tube on the same side, without chemo after surgery. This approach requires close follow-up so that if the cancer comes back it can be found early and treated. Most patients in this stage are cured with surgery and never need chemo.

Grade 1 immature teratoma

A grade 1 immature teratoma is made up mostly of non-cancerous tissue, and only a few cancerous areas seen under the microscope look immature (look like fetal organs). These tumors rarely come back after being removed. If careful staging has determined that a grade 1 immature teratoma is limited to one or both ovaries, the patient may be treated by removing the ovary or ovaries containing the cancer and the fallopian tube or tubes. If implants (tumor deposits) are found outside the ovary but they appear mature under a microscope (look like adult tissues), no chemo is needed after surgery.

Recurrent or persistent germ cell tumors

Recurrent tumors are those that come back after initial treatment. Persistent tumors are those that never disappeared even after treatment. Sometimes increased blood levels of the tumor markers HCG and AFP will be the only sign that a germ cell cancer is still there (or has come back).

Treatment for recurrent or persistent germ cell tumors may include chemo or, rarely, radiation therapy. For chemo, a combination of drugs is used most often. PEB (cisplatin, etoposide, and bleomycin) may be used if the patient did not receive this combination of drugs before. For patients who had already been treated with PEB, other combinations are used (see the section about chemotherapy).

For recurrent or persistent germ cell cancer, a clinical trial for new treatments may provide important advantages. Ask your cancer care team for information about clinical trials for your type of cancer.

Treatment for stromal tumors of the ovary, by stage

Stage I

All stage I tumors are treated with surgery to remove the ovary with the tumor. Most patients with stage I tumors are watched closely after the operation and don't require further treatment. Some stage I tumors are more likely to come back after surgery. These cancers are said to be at *high-risk* for recurrence. Features that make a stage I tumor high-risk include very large tumors, tumors where the cyst broke open (ruptured), and poorly-

differentiated tumors (also called high grade − the cancer cells don’t look very much like normal tissue when examined under the microscope). Patients with high-risk stage I stromal cancers have 3 options after surgery: observation (being watched closely), chemotherapy (chemo), or (rarely) radiation therapy

Stages II, III, and IV

These cancers are treated with surgery to remove the ovary with the tumor. Surgery is also used to stage and debulk the cancer, as needed (this is discussed in the section about surgery). This may be followed by chemo or hormone therapy. Often, the chemo used is what’s used in the treatment of germ cell tumors (PEB: cisplatin, etoposide, and bleomycin). The combination of carboplatin and paclitaxel (Taxol) may also be used. Hormone treatment is most often used to treat advanced stromal tumors in women who cannot tolerate chemo, but who want to try treatment. This can mean treatment with a drug such as leuprolide (Lupron) and goserelin (Zoladex), the drug tamoxifen, or an aromatase inhibitor. Rarely, radiation therapy is an option as well.

Recurrence

Cancer that comes back after treatment is said to be *recurrent*. This can happen years later for stromal tumors. Even so, the prognosis (outlook) may still be good because they grow so slowly. Surgery may be repeated. Any of the chemo regimens used initially can also be used to treat a relapse. Hormone therapy is also an option to treat recurrence. There really isn't a standard treatment for recurrent stromal cancer, so treatment as part of a clinical trial is also a good option. Radiation therapy may sometimes be helpful for recurrent cancer.

For tumors that produce hormones, the hormone blood levels may be checked at regular intervals after surgery to check for increased levels that could suggest the tumor has returned. The level of inhibin can also go up with some stromal tumors and may be useful to in finding a recurrence

More ovarian cancer treatment information

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 ovarian cancer?

It is important for you to have honest, open discussions with your cancer care team. They want to answer all of your questions, no matter how trivial you might think they are. Here are some questions to consider:

- What type of ovarian cancer do I have?
- Has my cancer spread beyond the ovaries?
- What are the cell type, microscopic grade, and stage of my cancer? What does that mean?
- What treatments do you recommend for me? Why?
- What risks or side effects should I expect?
- What are the chances my cancer will recur (come back) with the treatments we have discussed?
- What should I do to be ready for treatment?
- Should I follow a special diet?
- Will I be able to have children after my treatment?
- What is my expected prognosis?
- Will I lose my hair?
- What do I tell my children, husband, parents, and other family members?

In addition to these sample questions, be sure to write down some of your own. For instance, you might want specific information about anticipated recovery times so that you can plan your work schedule. You may also want to ask about second opinions or about experimental programs or clinical trials for which you may qualify.

What will happen after treatment for ovarian cancer?

For some people with ovarian cancer, treatment may remove or destroy the cancer. Completing treatment can be both stressful and exciting. You will be relieved to finish treatment, yet it is hard not to worry about cancer coming back. (When cancer returns, it is called *recurrence*.) This is a very common concern for those 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 live with this uncertainty and are leading full lives. Our

document, *Living With Uncertainty: The Fear of Cancer Recurrence*, gives more detailed information on this.

For other people, the cancer never goes away completely. These women may be treated with chemotherapy on and off for years. 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*, gives more information 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.

Follow-up for ovarian cancer usually includes a careful general physical exam and blood tests for tumor markers that help recognize recurrence. For epithelial ovarian cancer, it is not clear if checking for CA-125 levels and treating you before you have symptoms will help you live longer. Treatment based only on CA-125 levels and not symptoms can increase side effects, so it is important to discuss the pros and cons of CA-125 monitoring and quality of life with your doctor.

The choice of which tumor marker blood tests to check depends on the type of cancer a woman has. CA-125 is the tumor marker used most often to follow-up women with epithelial ovarian cancers. Others, such as CA 19-9, CEA, and HE-4, are used most often in patients whose CA-125 levels never went up.

For women with germ cell tumors, blood is tested for alpha-fetoprotein (AFP) and/or human chorionic gonadotropin (HCG). Checking levels of hormones like estrogen, testosterone, and inhibin is sometimes helpful for women with stromal cancers.

After your cancer treatment is finished, you will probably need to still see your cancer doctor for many years. So, ask what kind of follow-up schedule you can expect.

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, our document, *When Your Cancer Comes Back: Cancer Recurrence* can give 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. Gathering these details soon after treatment may be easier than trying to get them at some point in the future. Make sure you have this information handy:

- A copy of your pathology report(s) from any biopsy or surgery
- If you had surgery, a copy of your operative report(s)
- If you were hospitalized, a copy of the discharge summary that every doctor must prepare when patients are sent home from the hospital
- If you had radiation therapy, a copy of the treatment summary
- If you had drug therapy (such as chemotherapy, hormone therapy, or targeted therapy), a list of your drugs, drug doses, and when you took them
- Copies of x-rays and imaging tests (these can be put on a DVD)

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

Lifestyle changes after having ovarian 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 the 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. The tobacco cessation and coaching service can help increase your chances of quitting for good.

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 might 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 to 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.

See the section called “Additional resources for ovarian cancer” to get more of our nutrition information.

Rest, fatigue, 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. A person who has not been physically active will not be able to take on the same amount of exercise as someone who plays tennis twice a week. 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 activity plans. Then, try to find a buddy so you're not doing it alone. Having family or friends involved when starting a new activity 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 dealing with fatigue, please see *Fatigue in People With Cancer* and *Anemia in People With Cancer*. A list of some other documents that you may find helpful can be found in the “Additional resources for ovarian cancer” section

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 helps you feel better about yourself.

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

How does having ovarian cancer affect your emotional health?

When treatment ends, you may find yourself overcome with many different emotions. This happens to a lot of people. You may have been going through so much during treatment that you could only focus on getting through each day. Now it may feel like a lot of other issues are catching up with you.

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 isn’t 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 don’t 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.

If ovarian cancer treatment 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 isn't 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 isn't 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 isn't the same as treatment to try to cure the cancer.

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 documents *Hospice Care* and *Nearing the End of Life.* They can be read online, or call us to have free copies mailed to you.

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 ovarian cancer research and treatment?

Risk factors and causes

Scientists continue to study the genes responsible for familial ovarian cancer. This research is beginning to yield clues about how these genes normally work and how disrupting their action can lead to cancer. This information eventually is expected to lead to new drugs for preventing and treating familial ovarian cancer.

Research in this area has already led to better ways to detect high-risk genes and assess a woman's ovarian cancer risk. A better understanding of how genetic and hormonal factors (such as oral contraceptive use) interact may also lead to better ways to prevent ovarian cancer.

Prevention

New information about how much *BRCA1* and *BRCA2* gene mutations increase ovarian cancer risk is helping women make practical decisions about prevention. For example, mathematical models have been developed that help estimate how many years of life an average woman with a *BRCA* mutation might gain by having both ovaries and fallopian tubes removed to prevent a cancer from developing. Studies have shown that fallopian tube cancers develop in women with *BRCA* gene mutations more often than doctors had previously suspected. However, it is important to remember that although doctors can predict the average outcome of a group of many women, it is still impossible to accurately predict the outcome for any individual woman.

Recent studies suggest that many primary peritoneal cancers and some ovarian cancers (such as high-grade serous carcinomas) actually start in the fallopian tubes. According to this theory, the early changes of these cancers can start in the fallopian tubes. Cells from these very early fallopian tube cancers can become detached and then stick to the surface of the peritoneum or the ovaries. For reasons that are still not understood, these cancer cells may grow more rapidly in their new locations.

This theory has important implications for preventing ovarian cancer because having the ovaries removed early can cause problems from lack of estrogen, such as bone loss, cardiovascular disease, and menopause symptoms. Some experts have suggested recently that some women who are concerned about their ovarian cancer risk (especially those

with a strong family history and/or *BRCA* gene mutations) consider having just their fallopian tubes removed first. They then can have their ovaries removed when they are older. This approach lets women keep their ovaries functioning for longer, but because of that, it might not help breast cancer risk as much. This is an active area of research.

Other studies are testing new drugs for ovarian cancer risk reduction.

Researchers are constantly looking for clues such as lifestyle, diet, and medicines that may alter the risk of ovarian cancer.

Early detection

Accurate ways to detect ovarian cancer early could have a great impact on the cure rate. Researchers are testing new ways to screen women for ovarian cancer, and a national repository for blood and tissue samples from ovarian cancer patients is being established to aid in these studies. One method being tested is looking at the pattern of proteins in the blood (called *proteomics*) to find ovarian cancer early.

From time to time, lab companies have marketed unproven tests to look for early ovarian cancer. Because these tests had not yet been shown to help find early cancer, the US Food and Drug Administration (FDA) told the companies to stop selling them. So far, this occurred with 2 different tests looking at protein patterns: OvaSure and OvaCheck. Both were taken off the market at the request of the FDA.

Two large studies of screening have been completed. One was in the United States, and the other was in the United Kingdom. Both studies looked at using the CA-125 blood test along with ovarian (transvaginal) ultrasound to find ovarian cancer. In these studies, more cancers were found in the women who were screened. Some of these were found at an early stage. But the outcomes of the women who were screened were not better than the women who weren't screened. - the screened women did not live longer and were not less likely to die from ovarian cancer.

Diagnosis

A test called OVA1 is meant to be used in women who have an ovarian tumor. It measures the levels of 4 proteins in the blood. The levels of these proteins, when looked at together, are used to put women with tumors into 2 categories − low risk and high risk. The women labeled low risk are not likely to have cancer. The women called "high risk" are more likely to have a cancer, and so should have surgery by a specialist (a gynecologic oncologist). This test is NOT a screening test − it is only meant for use in women who have an ovarian tumor.

Treatment

Treatment research includes testing the value of currently available methods as well as developing new approaches to treatment.

Chemotherapy

New chemotherapy (chemo) drugs and drug combinations are being tested. The drugs trabectedin (Yondelis®) and belotecan have shown promise in some studies.

When the drugs cisplatin and carboplatin stop working, the cancer is said to be *platinum resistant*. Studies are looking for ways (like other drugs) to make these cancers sensitive to these drugs again.

Although carboplatin is preferred over cisplatin in treating ovarian cancer if the drug is to be given IV, cisplatin is used in intraperitoneal (IP) chemotherapy. Studies are looking at giving carboplatin for IP chemo.

Another approach is to give IP chemo during surgery using heated drugs. This, known as heated intraperitoneal chemotherapy or HIPEC, can be effective, but is very toxic. It still needs to be studied and compared with standard IP chemo to see if it actually works better.

Targeted therapy

Targeted therapy is a newer type of cancer treatment that uses drugs or other substances to identify and attack cancer cells while doing little damage to normal cells. Each type of targeted therapy works differently, but they all attack the cancer cells' inner workings − the programming that makes them different from normal, healthy cells. Bevacizumab (Avastin) is the targeted therapy that has been studied best in ovarian cancer, but other drugs are also being looked at, as well.

Pazopanib (Votrient®) is a targeted therapy drug that, like bevacizumab, helps stop new blood vessels from forming. It has shown some promise in studies.

Poly(ADP-ribose) polymerases (PARPs) are enzymes that have been recently recognized as key regulators of cell survival and cell death. Drugs that inhibit PARP-1 help fight cancers caused by mutations in *BRCA1* and *BRCA2*. In one study, the PARP inhibitor olaparib was also able to shrink tumors in ovarian cancer patients who did not have *BRCA* mutations. Clinical trials of this type of drug are being done to see who will benefit most from them.

Vintafolide (EC145) is a newer drug that targets the folic acid receptor. This receptor is found on some ovarian cancers. In one study, it helped stop the growth of cancers that had the folic acid receptor.

Immunotherapy

Another approach is to develop tumor vaccines that program the immune system to better recognize cancer cells. Also, monoclonal antibodies that specifically recognize and attack ovarian cancer cells are being developed. These antibodies are man-made versions of the antibodies our bodies make to fight infection. They can be designed to home in on certain sites on the cancer cell. Farletuzumab is a monoclonal antibody that is directed against

the folic acid receptor, which is on the surface of some ovarian cancer cells. It has shown promise in treating ovarian cancer in early studies. Another monoclonal antibody being studied in ovarian cancer is called catumaxomab. It binds to a protein that is in some cancer cells and some immune system cells. When it is administered into the abdominal cavity, it can help treat fluid build up (ascites) that can occur when cancer is present.

Additional resources for ovarian cancer

More information from your American Cancer Society

Here is more information you might find helpful. You also can order free copies of our documents from our toll-free number, 1-800-227-2345, or read them on our website, www.cancer.org.

Dealing with diagnosis and treatment

Health Professionals Associated With Cancer Care

Talking With Your Doctor (also in Spanish)

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

Nutrition for the Person With Cancer During Treatment: A Guide for Patients and Families (also in Spanish)

Coping With Cancer in Everyday Life (also in Spanish)

Family and caregiver concerns

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

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

What It Takes to Be a Caregiver

Insurance and financial issues

Financial Guidance for Cancer Survivors and Their Families:In Treatment (also in Spanish)

Health Insurance and Financial Assistance for the Cancer Patient (also in Spanish)

More on cancer treatments

A Guide to Cancer Surgery (also in Spanish)

A Guide to Chemotherapy (also in Spanish)

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

Targeted Therapy

Imaging (Radiology) Tests

Clinical Trials: What You Need to Know

Cancer treatment side effects

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

Distress in People With Cancer

Anxiety, Fear, and Depression

Nausea and Vomiting

Guide to Controlling Cancer Pain (also in Spanish)

Get Relief From Cancer Pain

Pain Diary

Anemia in People With Cancer

Fatigue in People With Cancer

Sexuality for the Woman With Cancer

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 (1-800-227-2345), other sources of patient information and support include:

Foundation for Women's Cancer (formerly Gynecologic Cancer Foundation)

Has a directory of trained gynecologic oncologists practicing in the US; free information; and an online "survivor section" featuring articles on personal issues such as fertility, sexuality and quality of life aimed at creating an online community for women with cancer.

Toll-free number: 1-800-444-4441
Website: www.foundationforwomenscancer.org

Gilda Radner Familial Ovarian Cancer Registry
Offers literature on ovarian cancer, referrals to available support groups nationwide, a

hotline staffed by cancer information specialists, and an online version of the Gilda Radner Familial Ovarian Cancer Registry Newsletter

Toll-free number: 1-800-OVARIAN (1-800-682-7426)
Website: www.ovariancancer.com

National Cancer Institute
Their Cancer Information Service offers free, accurate, up-to-date information about cancer to patients, their families, and the general public; also can help people find clinical trials in their area.

Toll-free number: 1-800-422-6237 (1-800-4-CANCER)
TYY: 1-800-332-8615
Website: www.cancer.gov

National Ovarian Cancer Coalition
Services include: Information and materials on ovarian cancer (many available in Spanish); events throughout the country promoting awareness and education; the *NOCC*, a quarterly newsletter; clinical trial information and access; and a free Newly Diagnosed Patient Kit with a resource guide, book of survivor stories, personal journal, stories of Hope DVD and more

Toll-free number: 1-888-682-7426 (1-888-OVARIAN)
Website: www.ovarian.org

womenshealth.gov
Offers a lot of information on women's health issues − including cancers in women

Toll-free number: 1-800-994-9662 (1-800-994-WOMAN)
TTY: 1-888-220-5446
Website: www.womenshealth.gov

Ovarian Cancer National Alliance
This survivor-led group offers information specific to survivors, newly diagnosed patients, family, and friends; public education and awareness programs; Fact Sheets covering ovarian cancer, treatment, and other related issues; quarterly e-newsletters; treatment and clinical trials information; and their online store, Shop Teal, with items such as wristbands, awareness ribbons, etc.

Telephone number: 1-866-399-6262
Website: www.ovariancancer.org

**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.

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