

# Ovarian Cancer

## What Is Cancer?

Cancer is a group of many related diseases. All forms of cancer involve out-of-control growth and spread of abnormal cells.

Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide more rapidly until the person becomes an adult. After that, normal cells of most tissues divide only to replace worn-out or dying cells and to repair injuries.

Cancer cells, however, continue to grow and divide, and can spread to other parts of the body. These cells accumulate and form *tumors* (lumps) that may compress, invade, and destroy normal tissue. If cells break away from such a tumor, they can travel through the bloodstream, or the lymph system to other areas of the body. There, they may settle and form "colony" tumors. In their new location, the cancer cells continue growing. The spread of a tumor to a new site is called *metastasis*. When cancer spreads, though, it is still named after the part of the body where it started. For example, if prostate cancer spreads to the bones, it is still prostate cancer, and if breast cancer spreads to the lungs it is still called breast cancer.

Leukemia, a form of cancer, does not usually form a tumor. Instead, these cancer cells involve the blood and blood-forming organs (bone marrow, lymphatic system, and spleen), and circulate through other tissues where they can accumulate.

It is important to realize that not all tumors are cancerous. Benign (noncancerous) tumors do not metastasize and, with very rare exceptions, are not life-threatening.

Cancer is classified by the part of the body in which it began, and by its appearance under a microscope. Different types of cancer vary in their rates of growth, patterns of spread, and responses to different types of treatment. That's why people with cancer need treatment that is aimed at their specific form of the disease.

In America, half of all men and one-third of all women will develop cancer during their lifetimes. Today, millions of people are living with cancer or have been cured of the disease. The risk of developing most types of cancer can be reduced by changes in a person's lifestyle, for example, by quitting smoking or eating a better diet. The sooner a cancer is found, and the sooner treatment begins, the better a patient's chances are of a cure.

## What Is Ovarian Cancer?

Ovarian cancer is cancer that begins in the ovaries. In women, the ovaries produce eggs (*ova*). The ovaries are also the main source of the female hormones, estrogen and progesterone. One ovary is located on each side of the uterus in the pelvis.

## Types of Ovarian Tumors

There are many types of tumors that can start growing in the ovaries. Some are *benign* (noncancerous) and never spread beyond the ovary. These patients can be treated successfully by surgically removing one ovary or the part of an ovary containing the tumor. Other types of ovarian tumors are *malignant* (cancerous) and may spread to other parts of the body. Their treatment is more complex, and is discussed later in this document.

In general, ovarian tumors are named according to the kind of cells the tumor started from and whether the tumor is benign or cancerous. There are three main types of ovarian tumors:

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

## Epithelial Ovarian Tumors

**Benign epithelial ovarian tumors:** Most epithelial ovarian tumors are benign and therefore, do not spread and usually do not lead to serious illness. There are several types of benign epithelial tumors, including *serous adenomas*, *mucinous adenomas*, and *Brenner tumors*.

**Tumors of low malignant potential:** When viewed under the microscope, some ovarian epithelial tumors do not clearly appear to be cancerous -- these are called *tumors of low malignant potential (LMP tumors)*. They are also known as *borderline tumors*.

**Epithelial ovarian cancers:** Cancerous epithelial tumors are called *carcinomas*. About 85 percent of ovarian cancers are *epithelial ovarian carcinomas*. Epithelial ovarian carcinoma cells have several features that can be recognized under the microscope. These features are used to classify epithelial ovarian carcinomas into *serous*, *mucinous*, *endometrioid*, and *clear cell* types. *Undifferentiated* epithelial ovarian carcinomas don't look like any of these four subtypes and they also tend to grow and spread more quickly. In addition to their classification by cell type, epithelial ovarian carcinomas are also given a grade and a stage. The grade is on a scale of 1, 2, or 3. Grade 1 epithelial ovarian carcinomas more closely resemble normal tissue and tend to have a better *prognosis* (outlook). Grade 3 epithelial ovarian carcinomas less closely resemble normal tissue and usually have a worse outlook. The tumor stage describes how far the tumor has spread from where it started in the ovary. Staging is explained in detail in a later section.

## Primary Peritoneal Carcinoma

Primary peritoneal carcinoma, also called *extraovarian primary peritoneal carcinoma (EOPPC)* and *serous surface papillary carcinoma*, is a cancer closely related to epithelial ovarian cancer. It develops from cells that line the pelvis or abdomen, which are very similar to epithelial cells on

the surface of the ovaries. Because EOPPC tends to spread along the surfaces of the pelvis and abdomen, it is often difficult to tell exactly where the cancer first started. Under a microscope, EOPPC looks just like epithelial ovarian cancer. Women who have had their ovaries removed can still develop this type of cancer.

Symptoms of EOPPC 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, EOPPC may cause an elevation in the tumor marker CA 125.

Treatment for people with EOPPC usually includes surgery to remove as much of the cancer as possible, followed by chemotherapy like that given for ovarian cancer. Information on prognosis is limited since it is a newly recognized type of cancer, but early studies suggest that prognosis is similar to ovarian cancer.

## **Germ Cell Tumors**

Germ cells are the cells that usually form the *ova* or eggs. There are several subtypes of germ cell tumors. Most germ cell tumors are benign, although some are cancerous and may be life threatening. The most common germ cell tumors are teratoma, dysgerminoma, endodermal sinus tumor, and choriocarcinoma. Malignant germ cell tumors account for about 15 percent of ovarian cancers.

**Teratoma:** 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, usually affecting women of reproductive age (teens through forties). It is often called a *dermoid cyst* because its lining resembles skin. These tumors or cysts also contain a variety of other benign tissues that may resemble adult respiratory passages, bone, nervous tissue, teeth, and other tissues. Surgical removal of the cyst is curative.

Immature teratomas occur in girls and young women, usually younger than 18. These are rare cancers that resemble embryonic or fetal tissues such as connective tissue, respiratory passages, and brain. Tumors that are not very immature (*grade 1 immature teratoma*) and have not spread beyond the ovary are cured 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 surgical removal of the ovary.

**Dysgerminoma:** Although this is the most common ovarian cancer of germ cells, it represents only 2% of all ovarian cancers. It usually affects women in their teens and twenties. Although dysgerminomas are considered malignant (cancerous), most do not grow or spread very rapidly. When they are limited to the ovary, over 95% are cured by surgical removal of the ovary, without any further treatment. Even when the tumor has spread further, the combination of surgery and chemotherapy is effective 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. Choriocarcinomas more commonly start in the placenta (during

pregnancy) rather than in the ovary. Placental choriocarcinomas are usually even more responsive to chemotherapy than ovarian choriocarcinomas.

### **Stromal Tumors**

These tumors account for about 5 percent of ovarian cancers. More than half are found in women over age 50, but some occur in young girls. Some, but not all, of these tumors produce female hormones or, less often, male hormones. They can cause vaginal bleeding to resume after menopause, or can cause menstrual periods and breast development in young girls. If male hormones are produced, the tumors can disrupt normal periods and cause facial and body hair to grow. Types of malignant (cancerous) stromal tumors include *granulosa cell tumors*, *granulosa-theca tumors*, and *Sertoli-Leydig cell tumors*, which are usually considered low-grade cancers. Thecomas and fibromas are benign stromal tumors.

### **Ovarian Cysts**

An ovarian cyst is a collection of fluid inside an ovary. Many cysts are completely normal. These are called functional cysts and occur as a normal part of ovulation. The fluid will usually be absorbed and the cyst will disappear without any treatment over a few months. If a woman develops a cyst, the doctor may want to check it again in a few months to see if the size has gotten smaller. If however, the mass is large, or occurs in childhood or after menopause, or does not go away, further testing is usually advised since a small number of these may be cancer. Treatment of benign cysts may consist of observation (follow-up with physical exams and imaging tests), medications, or surgical removal.

## **What Are The Key Statistics About Ovarian Cancer?**

Ovarian cancer is the sixth most common cancer among women, excluding non-melanoma skin cancers. The American Cancer Society estimates that about 23,400 new cases of ovarian cancer will be diagnosed in the United States during 2001. Ovarian cancer accounts for 4% of all cancers in women.

The good news is that the ovarian cancer *incidence rate* has been slowly decreasing since 1991. The incidence rate is a precise way for scientists to describe how common or rare a disease is. The ovarian cancer incidence rate is defined as the number of new cases diagnosed each year per 100,000 women.

Ovarian cancer ranks fifth in cancer deaths among women, accounting for more deaths than any other cancer of the female reproductive system. It is estimated that there will be about 13,900 deaths from ovarian cancer in the United States during 2001.

The five -- year survival rate is used to provide a standard way of discussing prognosis. It refers to the percentage of patients who live at least 5 years after their cancer is diagnosed, although many of these patients live much longer than 5 years after diagnosis. Five-year *relative* survival rates exclude from the calculations patients dying of other diseases, and are considered

to be a more accurate way to describe the prognosis for patients with a particular type and stage of cancer. Of course, 5-year survival rates are based on patients diagnosed and initially treated more than 5 years ago. Improvements in treatment often result in a more favorable outlook for recently diagnosed patients.

About 78% of ovarian cancer patients survive one year after diagnosis and over 50% survive longer than five years after diagnosis. If diagnosed and treated while the cancer has not spread outside the ovary, the five-year survival rate is 95%. However, only 25% of all ovarian cancers are found at this early stage. Older women with ovarian cancer tend to have a poorer prognosis than younger ones. For example, the five-year survival rate is 64% in women under 65 years of age and 30% in women over 65.

## What Are The Risk Factors For Ovarian Cancer?

A *risk factor* is anything that increases a person's chance of getting a disease. 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 cancers of the lung, mouth, larynx, bladder, kidney, and several other organs.

Researchers have discovered several specific factors that increase a woman's likelihood of developing epithelial ovarian cancer. These risk factors do not apply to other less common types of ovarian cancer such as germ cell tumors and stromal tumors.

Most women with ovarian cancer do not have any known risk factors. It is important to remember that risk factors increase the odds of getting a disease but do not guarantee it will occur. Only a small number of women who have risk factors will develop ovarian cancer.

**Age:** Most ovarian cancers develop after menopause. A woman is considered to be menopausal when she has gone a year without a menstrual period. Half of all ovarian cancers are found in women over the age of 65.

**Reproductive history:** Women who started menstruating at an early age (before age 12), had no children or had their first child after age 30, and/or experienced menopause after age 50, may have an increased risk of ovarian cancer. There seems to be a relationship between the number of menstrual cycles in a woman's lifetime and her risk of developing ovarian cancer.

**Fertility drugs:** In some studies, researchers have found that prolonged use of the fertility drug *clomiphene citrate*, especially without achieving pregnancy, may increase a woman's risk for developing ovarian tumors, particularly a type known as tumors of *low malignant potential* (LMP tumors). A woman taking this drug should discuss its potential risks with her doctor. However, infertility also increases the risk of ovarian cancer, even without use of fertility drugs. More research to clarify these relationships is now underway.

**Family history of ovarian cancer:** Ovarian cancer risk is increased among women whose mother, sister, or daughter have, or have had, ovarian cancer, especially if they developed

ovarian cancer at a young age. A woman can inherit an increased risk for ovarian cancer from relatives on her mother's side or father's side of the family. About 10% of ovarian cancers result from an inherited tendency to develop the disease. Many cases of familial epithelial ovarian cancer are due to inherited gene mutations that can be identified by genetic testing. Women with ovarian cancers due to these inherited gene mutations tend to have a better prognosis than patients who do not have any family history of ovarian cancer. Refer to the section on causes of ovarian cancer for information on these gene mutations. Genetic counseling, genetic testing, and strategies for preventing familial ovarian cancer are discussed in the prevention section of this document.

**Breast cancer:** Women who have had breast cancer also have an increased risk of developing ovarian cancer. There are several reasons for this observation. Some of the reproductive risk factors for ovarian cancer may also increase breast cancer risk. Also, inherited mutations of the BRCA1 and BRCA2 genes greatly increase a woman's risk for both cancers.

**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. Most, but not all studies suggest a 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 may explain the association with ovarian cancer in some studies. Body and face powder products have been required by law for over 20 years to be asbestos-free. However, proof of the safety of these newer products will require follow-up studies of women who have used them over a period of many years. There is no evidence at present linking cornstarch powders with any female cancers.

**Hormone replacement therapy (HRT):** Some studies suggest the use of estrogens by women after menopause may slightly increase their risk of developing ovarian cancer, while other studies have not found any effect on ovarian cancer risk. A recent review that recalculated results of other studies that have been previously published suggested that use of hormone replacement for over ten years increases ovarian cancer risk by about 30 percent, and that use for shorter periods of time increase ovarian cancer risk by about 15 percent. On the other hand, HRT reduces the risk of heart attacks and bone fractures. The decision to use hormone replacement therapy after menopause should be made by a woman and her doctor after weighing the possible risks and benefits. Factors to consider include her other risk factors for heart disease, ovarian cancer, breast cancer, osteoporosis (thinning and weakening of bones), and the severity of menopausal symptoms.

## **Do We Know What Causes Ovarian Cancer?**

We do not yet know exactly what causes most ovarian cancers, but we do know some factors that make a woman more likely to develop the most common type of ovarian cancer, epithelial ovarian cancer. Much less is known about risk factors for germ cell and stromal tumors of the ovaries. Refer to the risk factor section of this document for more information.

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 resemble our parents because they are the source of our DNA. However, DNA affects more than our outward appearance. Some *genes* (parts of our DNA) contain instructions for controlling when our cells grow and divide. Certain genes that promote cell division are called *oncogenes*. Others that slow down cell division, cause cells to die at the appropriate time, or help repair DNA damage are called *tumor suppressor genes*. It is known that cancers can be caused by DNA *mutations* (defects) that turn on oncogenes or turn off tumor suppressor genes.

### **Inherited Genetic Factors**

During the past few years, scientists have learned much about how certain genes inherited from a woman's parents can greatly increase her ovarian cancer risk. These include the BRCA1 and BRCA2 genes, and several genes related to hereditary nonpolyposis colon cancer (HNPCC).

**BRCA1 and BRCA2 genes:** Although these inherited gene mutations were originally found in women with breast cancer, they are also responsible for about 9% of ovarian cancers. Normally, these genes help to prevent cancer by making proteins that keep cells from growing abnormally. However, if a person has inherited a mutated gene from either parent, this cancer-preventing protein is less effective, and chances of developing breast and/or ovarian cancer increase. Between 56 and 87 percent of women with inherited BRCA1 or BRCA2 mutations will develop breast cancer by the age of 70. The lifetime ovarian cancer risk for women with BRCA1 or BRCA2 mutations has been estimated to be between 17 percent and 44 percent. These estimates vary considerably because they are based on studies of women of various racial and ethnic groups living in different countries. The impact of BRCA mutations on ovarian cancer risk is modified by the other risk factors discussed earlier in this document, as well as by other genes that have not yet been discovered. Differences in these other factors among the groups of women participating in each of these studies account for much of the variation in estimates of cancer risk. In comparison, the ovarian cancer lifetime risk for the general population of women is about two percent.

**Hereditary nonpolyposis colon cancer (HNPCC):** This syndrome is also caused by inherited gene mutations that reduce the body's ability to repair damage to its DNA. This results in very high risks for colorectal cancer and *endometrial* (lining of the uterus) cancer, and a somewhat increased risk for developing ovarian cancer. The risk for ovarian cancer with HNPCC syndrome is much less than with BRCA1 or BRCA2 defects. This gene mutation causes about 1% of all ovarian epithelial cancers.

### **Acquired Genetic Changes**

Most DNA mutations related to ovarian cancer occur during a woman's life rather than having been inherited. *Acquired mutations* of oncogenes and/or tumor suppressor genes may result from radiation or cancer-causing chemicals. So far, studies have not been able to identify any single chemical in the environment, or in our diets, that is specifically linked to cause 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, such as the p53 tumor suppressor gene or the HER2 oncogene, in ovarian cancers may help in predicting a woman's prognosis. The role of these tests is still not certain, and some cancer specialists feel that more research is needed. Recently, a monoclonal antibody therapy called trastuzumab (Herceptin) has been developed that specifically interrupts the growth-promoting action of the HER2 oncogene. This new treatment has been approved as a treatment for breast cancer, and is currently being tested in clinical trials to determine whether it is useful in treating ovarian cancer.

## Can Ovarian Cancer Be Prevented?

Most women have one or more risk factors for ovarian cancer. However, most of the common factors only slightly increase a woman's risk, so they only partly explain the frequency of the disease. So far, knowledge about risk factors has not been translated into practical ways to prevent most cases of ovarian cancer.

Researchers have found several ways a woman can reduce her 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 providers. They can help you consider these ideas in the context of your own situation.

**Oral contraceptives:** The use of oral contraceptives (birth control pills) decreases the risk of developing ovarian cancer, especially among women who used them for several years. Compared to women who never used oral contraceptives, those who used oral contraceptives for more than five years have about a 60 percent lower risk of developing ovarian cancer.

**Tubal ligation or hysterectomy:** Tubal ligation is a surgical procedure to "tie" the fallopian tubes to prevent pregnancy. When performed after childbearing, tubal ligation may reduce the chance of developing ovarian cancer. A hysterectomy may also reduce your risk.

One theory to explain why tubal ligation and hysterectomy reduce ovarian cancer risk 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 may explain the effect of removing the uterus or blocking the fallopian tubes on ovarian cancer risk. However, the impact of these operations on ovarian cancer risk is relatively small and they cannot prevent all or even most cases. We emphasize that these operations should be done only when there are valid medical reasons, and not exclusively for their effect on ovarian cancer risk.

If you are having a *hysterectomy* (removal of the uterus) for a valid medical reason and you have a strong family history of ovarian or breast cancer, you may wish to consider having a *bilateral*

*oophorectomy* (removal of both ovaries) as part of that procedure. If you are *postmenopausal* (after menopause) or *perimenopausal* (near menopause), the ovaries should be removed at the same time as the hysterectomy even if you do not have an increased risk of ovarian cancer. If you are having a hysterectomy and are older than 40, you should discuss the issue of ovarian removal with your doctor.

**Pregnancy and breast-feeding:** Having one or more children, particularly if your first is born before you are age 30, plus prolonged (one year or more) breast-feeding, also may decrease your risk. Although these measures slightly reduce risk, they do not guarantee protection against ovarian cancer. Doctors do not recommend making choices about when to have a child specifically for the purpose of reducing ovarian cancer risk, especially since using oral contraceptives will have a greater impact on this risk.

**Diet:** results of some studies suggest that a high fat diet may increase ovarian cancer risk. Other studies disagree, however. The American Cancer Society recommends choosing most foods from plant sources (fruits, vegetables, whole grain products) and limiting intake of high fat foods, especially those from animal sources. Even though the impact of these dietary recommendations on ovarian cancer risk remains uncertain, following these recommendations can help prevent several other diseases, including some types of cancer.

**Prevention strategies for women with a family history of ovarian cancer:** Genetic counseling can predict whether a woman is likely to have one of the gene mutations associated with an increased ovarian cancer risk. If a woman's family history suggests that she might have one of these gene mutations, genetic testing can be done. Before undergoing genetic testing, a woman should discuss its benefits and potential drawbacks. Genetic testing can determine if you or members of your family carry certain gene mutations that cause a high risk of ovarian cancer. For some women with a strong family history of ovarian cancer, knowing that 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 very stressful, but many women find this information very helpful in making important decisions about certain prevention strategies for them and their children.

Use of oral contraceptives is one way to decrease ovarian cancer in women at high risk for this disease. However, some studies have indicated that oral contraceptives might increase breast cancer risk in women with a strong family history of breast cancer. Other studies, on the other hand, have not found any increase in breast cancer risk among women with BRCA mutations who take oral contraceptives. Additional research is needed to learn more about the risks and benefits of oral contraceptives to women at high ovarian and breast cancer risk.

Surgery to remove one or both ovaries is called an *oophorectomy*. A *prophylactic oophorectomy* is surgery to remove both of the ovaries before an ovarian cancer occurs. This is a controversial operation because it causes premature menopause in premenopausal women, and may be unnecessary. It generally is recommended only for certain very high-risk patients over age 40. This operation lowers ovarian cancer risk a great deal but does not entirely eliminate it. In some women with a very high risk of ovarian cancer (due to a strong family history) who have had both ovaries removed, cancers can still form from the lining cells of the pelvic cavity where the

ovaries were previously located. This type of cancer, known as *primary peritoneal carcinoma* occurs more often in women with BRCA gene mutations. Recent studies suggest that having both ovaries removed can also lower the risk of developing breast cancer among women with BRCA gene mutations.

As noted in the section on finding ovarian cancer early, women with high risk gene mutations, and women with a strong family history who have not undergone genetic testing may benefit from screening tests.

## Can Ovarian Cancer Be Found Early?

About 25% of ovarian cancers are found at an early stage. Early detection improves the chances that ovarian cancer can be treated successfully. When ovarian cancer is found early at a localized stage, about 90% of patients live longer than 5 years after diagnosis.

**Routine pelvic examination:** Annual pelvic examinations and Pap smears to check the pelvic area both internally and externally should begin at age 18 or when a woman becomes sexually active, whichever is earlier. During this exam, the health care professional feels the ovaries and uterus for size, shape, and consistency. Although the Pap test is effective in early detection of cervical cancer, it cannot detect most ovarian cancers. Most of the ovarian cancers that are detected through Pap smears are already advanced. Although a pelvic examination is routinely recommended because it can find some reproductive system cancers at an early stage, most early ovarian tumors are difficult or impossible for even the most skilled examiner to feel.

**Seek medical attention if symptoms appear:** The ovaries are deep inside the pelvis and cannot be seen directly without surgery. Small ovarian tumors are difficult for even the most skilled examiner to feel. Early cancers of the ovaries tend to cause symptoms that are relatively nonspecific. These symptoms include swelling of the abdomen (due to a mass or accumulation of fluid), unusual vaginal bleeding, pelvic pressure, back pain, leg pain, and digestive problems such as gas, bloating, indigestion, or long-term stomach pain. Most of these symptoms can also be caused by other less serious conditions. By the time ovarian cancer is considered as a possible cause of these symptoms, it may have already spread beyond the ovaries. Also, some types of ovarian cancer can rapidly spread to the surface of nearby organs. Nonetheless, prompt attention to symptoms can improve the odds of early diagnosis and successful treatment. If you have symptoms of ovarian cancer, report them to your health care provider right away.

**Screening tests for ovarian cancer:** *Screening* refers to tests and examinations used to detect a disease, such as cancer, in people who do not have any symptoms. Women with a high risk of developing epithelial ovarian cancer, such as those with a very strong family history of this disease, may be screened with *transvaginal sonography* (an ultrasound test performed with a small instrument placed in the vagina) and blood tests. Transvaginal sonography is helpful in finding a mass in the ovary, but it does not accurately predict which masses are cancers and which are due to benign diseases of the ovary. Blood tests for ovarian cancer may include measuring the amount of CA 125 (also known as OC 125). The amount of this protein is increased in the blood of many women with ovarian cancer. However, some noncancerous

diseases of the ovaries can also increase the blood levels of CA 125 and some ovarian cancers may not produce enough CA 125 to cause a positive test. When these tests are positive, it may be necessary to do more x-ray studies or to take samples of fluid from the abdomen or tissue from the ovaries to find out if a cancer is really present.

In preliminary studies of women at average risk of ovarian cancer, these tests did not make any difference in the number of deaths caused by ovarian cancer. For this reason, transvaginal sonography and the CA 125 blood test are not recommended for ovarian cancer screening of women without known strong risk factors. However, some recent studies found that cancers detected by these tests tend to be somewhat less advanced than cancers of women who did not have any screening tests. Additional research is in progress to improve ovarian cancer screening tests. It is hoped that further improvements will make these tests effective enough to lower the ovarian cancer death rate.

There are no tests recommended for screening women for germ cell tumors or stromal tumors. Some germ cell cancers release certain markers (proteins) 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 as a sign that the cancer may be coming back.

## **How Is Ovarian Cancer Diagnosed?**

### **Signs and Symptoms of Ovarian Cancer**

There are several signs and symptoms that may be caused by ovarian cancer. However, most of these may also be caused by benign (noncancerous) diseases and by cancers of other organs.

- Prolonged swelling of the abdomen (due to a mass or accumulation of fluid)
- Digestive problems including gas, loss of appetite, bloating, long-term abdominal pain, or indigestion
- Unusual vaginal bleeding is a rare sign of ovarian cancer. It is a strong warning of some type of abnormality, although not necessarily ovarian cancer. Bleeding that occurs between periods, is heavier, or lasts longer than usual, is considered abnormal. Any postmenopausal bleeding, staining, or persistent vaginal discharge is abnormal. A woman of any age who has unusual vaginal bleeding should alert her doctor immediately.
- Pelvic pressure (feeling as though you have to urinate or defecate all the time)
- Pelvic pain is a nonspecific symptom. It may be caused by ovarian cancer, other cancers, or by several benign conditions.
- Leg pain
- Back pain

If there is reason to suspect you may have ovarian cancer, your doctor will use one or more methods to be absolutely certain that the disease is present and to determine the stage of the cancer.

## Consultation with a Specialist

If your pelvic examination or other tests suggest that you may 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.

## Imaging Studies

Imaging methods such as computed tomography (CT) scans, magnetic resonance imaging (MRI) scans, and ultrasound studies can confirm whether a pelvic mass is present. Although these studies cannot confirm if the mass is a cancer, they are useful in looking for spread of ovarian cancer to other tissues and organs.

**Ultrasound:** *Ultrasound* or *ultrasonography* uses 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. Because ovarian tumors and normal ovarian tissue often reflect sound waves differently, this test may be useful in detecting tumors and in determining whether a mass is solid or a fluid-filled cyst.

**Color-flow Doppler:** This procedure uses a special type of ultrasound instrument to assess blood flow to the ovaries. In ovarian cancer there is usually an increase in blood flow. However, several benign conditions can also increase blood flow to the ovaries.

**Computed tomography:** Commonly referred to as a CT or CAT scan, this test uses a rotating x-ray beam to create a series of pictures of the body from many angles. A computer combines the information from these pictures, producing a detailed cross-sectional image. *Contrast material* is usually injected into a vein before CT scanning to help produce clearer pictures.

**Chest x-ray:** This test may be done to determine whether ovarian cancer has spread to the lungs. This spread may cause one or more tumors in the lungs and often causes fluid to collect around the lungs. This fluid, called a *pleural effusion*, can be seen with chest x-rays.

**Magnetic resonance imaging (MRI):** Like computed tomography, MRI displays a cross-section of the body. However, MRI uses powerful magnetic fields instead of radiation. The procedure can present cross-sectional views from several angles.

## Tissue Sampling

The only way to determine for certain if a growth in the pelvic region is cancer is to *biopsy* (removing a sample of tissue) the suspicious area and examine the tissue sample under a microscope. In patients with *ascites* (collection of fluid inside the abdomen), samples of fluid can also be used to diagnose the cancer. A biopsy is usually done at the time of surgery. Depending on the extent of disease, the surgical procedure may be a *laparotomy* (surgery through an

abdominal incision) or *laparoscopy* (surgery done through a lighted tube inserted into a very small incision in the pelvis ). The goal of surgery for ovarian cancer is to obtain tissue samples for diagnosis and staging, and to remove all deposits of cancer larger than 1 cm (about one-half inch). Another diagnostic method is to obtain small samples of the cancer using CT scanning or ultrasound to guide a thin biopsy needle. This method might be used if the patient cannot have surgery because of advanced cancer or some other serious medical condition.

## 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 the time of surgery. This is done by sampling tissues from different parts of the pelvis and abdomen to be examined under the microscope. Staging is very important because ovarian cancers of different stages have a different prognosis and are treated differently. The accuracy of the staging may determine whether or not a patient will be cured. If the cancer is not properly staged, then cancer that has spread outside the ovary may be missed and not treated. Once a stage has been assigned, it does not change, even when the cancer recurs or spreads to new locations in the body.

Ask your cancer care team to explain the staging procedure. Also ask them if they will perform a thorough staging procedure. After surgery, ask what your cancer's stage is. In this way, you will be able to take part in making informed decisions about your treatment.

### What the Stages of Ovarian Cancer Mean

Staging of ovarian cancer is described using the *FIGO system*. FIGO stands for International Federation of Gynecologists and Obstetricians.

**Stage I:** The cancer is still contained within the ovary (or ovaries).

**Stage IA:** Cancer has developed in one ovary and the tumor is confined to the inside of the ovary. There is no cancer on the outer surface of the ovary. Laboratory examination of washings from the abdomen and pelvis did not find any cancer cells.

**Stage IB:** Cancer has developed within both ovaries without any tumor on their outer surfaces. Laboratory examination of washings from the abdomen and pelvis did not find any cancer cells.

**Stage IC:** The tumor is present in one or both ovaries and one or more of the following are present: (1) cancer on the outer surface of at least one of the ovaries, (2) in the case of cystic tumors (fluid-filled tumors), the capsule (outer wall of the tumor) has ruptured (burst), (3) laboratory examination found cancer cells in fluid or washings from the abdomen.

**Stage II:** The cancer involves one or both ovaries and has involved other organs (such as the uterus, fallopian tubes, bladder, the sigmoid colon, or the rectum) within the pelvis.

**Stage IIA:** The cancer has extended to, or has actually invaded the uterus or the fallopian tubes, or both. Laboratory examination of washings from the abdomen did not find any cancer cells.

**Stage IIB:** The cancer has extended to other nearby pelvic organs such as the bladder, the sigmoid colon, or the rectum. Laboratory examination of fluid from the abdomen did not find any cancer cells.

**Stage IIC:** The cancer involves pelvic organs as in stages IIA or IIB and one or more of the following are present: (1) cancer on the outer surface of at least one of the ovaries, (2) in the case of cystic tumors (fluid-filled tumors), the capsule (outer wall of the tumor) has ruptured (burst), (3) laboratory examination found cancer cells in fluid or washings from the abdomen.

**Stage III:** The cancer involves one or both ovaries, and one or both of the following are present: (1) cancer has spread beyond the pelvis to the lining of the abdomen, (2) cancer has spread to lymph nodes (glands that fight infection and produce some types of blood cells.)

**Stage IIIA:** During the staging operation, the surgeon can see cancer involving the ovary or ovaries, but no cancer is grossly visible (can be seen without using a microscope) in the abdomen and the cancer has not spread to lymph nodes. However, when biopsies are checked under a microscope, tiny deposits of cancer are found in the lining of the upper abdomen.

**Stage IIIB:** There is cancer in one or both ovaries, and deposits of cancer are present in the abdomen which are large enough for the surgeon to see but smaller than 2 cm (about 3/4 inch) across. Cancer has not spread to the lymph nodes.

**Stage IIIC:** The tumor is in one or both ovaries, and one or both of the following is present: (1) cancer has spread to lymph nodes, (2) deposits of cancer larger than 2 cm (about 3/4 inch) across are seen in the abdomen.

**Stage IV:** This is the most advanced stage of ovarian cancer. The tumor is in one or both ovaries. Distant *metastasis* (spread of the cancer to the inside of the liver, the lungs, or to other organs located outside of the peritoneal cavity) has occurred. Finding ovarian cancer cells in *pleural fluid* (from the cavity that surrounds the lungs) is also evidence of stage IV disease.

**Recurrent ovarian cancer:** This means that the disease has *recurred* (come back) after completion of treatment.

## How Is Ovarian Cancer Treated?

After the diagnostic tests are done, your cancer care team will recommend one or more treatment options. Consider the options without feeling rushed. If there is anything you do not understand, ask to have it explained. The choice of treatment depends largely on the type of cancer and the stage of the disease. In patients who do not have surgery as their initial treatment, the exact stage may not be known. Treatment then is based on other available information. Other factors could play a part in choosing the best treatment plan. This might include your general state of health,

whether you plan to have children, and other personal considerations. Age alone is not 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.

The main treatments for ovarian cancer are surgery, chemotherapy, and radiation therapy. In some cases two or even all of these treatments will be recommended.

## **Surgery**

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 early stage, an effort will be made to treat the disease without removing both ovaries and the uterus.

There are several surgical techniques used to treat ovarian cancer. The medical vocabulary for these operations is based on the Greek or Latin medical names of the organs they remove. The medical name of an operation that removes something usually ends with "-ectomy." So, removing the uterus is a hysterectomy, removing the omentum is an *omentectomy*, removing lymph nodes is a *lymphadenectomy* (also called lymph node biopsy or dissection). Because there are two ovaries and two fallopian tubes, we must distinguish between removing one or both. Removing one ovary is a *unilateral* (one side) *oophorectomy* and removing both is a *bilateral* (two sides) *oophorectomy*. Likewise, removing one or two fallopian tubes is a *unilateral salpingectomy* or *bilateral salpingectomy*. Often, an operation removes several organs. For example removing both ovaries and fallopian tubes is a *bilateral salpingo-oophorectomy*.

The other important surgical procedure is *cytoreduction or debulking*. In this procedure, the surgeon removes as much tumor as possible, even though all of it can't be removed. Most doctors feel this greatly improves a patient's prognosis (outlook for survival). This partial list of names of operations should help you in understanding information you may read about ovarian cancer and in discussing your cancer with your health care providers. Don't be afraid to ask your cancer care team to explain your condition and recommend treatments in simple, nonmedical terms.

It is important that a surgeon experienced in ovarian cancer surgery do the surgery. Many general gynecologists are not prepared to do the appropriate cancer operation, which requires careful staging and perhaps, debulking. Ask your doctor if he or she is experienced in treating ovarian cancer, will stage your cancer properly, and can perform a debulking procedure if that is needed. Otherwise you may need a second operation if debulking is required.

Removal of both ovaries and/or the uterus means that you will not be able to become pregnant. It also means that you will go into menopause if you have not done so already. There is also the recovery period from surgery. Most women will remain in the hospital for three to seven days after the operation and can resume their usual activities within four to six weeks.

## Chemotherapy

*Systemic chemotherapy* uses anticancer drugs that are injected into a vein or given by mouth. These drugs enter the bloodstream and reach all areas of the body, making this treatment potentially useful for cancers that have *metastasized* (spread) beyond the organ they started in. *Intraperitoneal chemotherapy* is injected directly into the abdomen. This approach concentrates the dose of chemotherapy reaching the cancer cells on the abdominal lining and limits the amount reaching the rest of the body, thereby reducing some side effects.

Chemotherapy drugs kill cancer cells but also damage some normal cells. Therefore, careful attention must be given to avoiding or minimizing side effects, which depend on the type of drugs, the amount taken, and the length of treatment. Temporary side effects might include nausea and vomiting, loss of appetite, loss of hair, hand and foot rashes, and mouth sores. Because chemotherapy can damage the blood-producing cells of the bone marrow, patients may have low blood cell counts. This can result in an increased chance of infection (due to a shortage of white blood cells), bleeding or bruising after minor cuts or injuries (due to a shortage of blood platelets), and fatigue (due to low red blood cell counts).

Most side effects disappear once treatment is stopped. Hair will grow back after treatment ends, though it may look different. There are remedies for many of the temporary side effects of chemotherapy. For example, *antiemetic* drugs to prevent or reduce nausea and vomiting can be given.

Potentially permanent side effects include premature menopause and infertility (inability to become pregnant).

Some anticancer drugs may rarely cause *acute myeloid leukemia* a life-threatening cancer of white blood cells. This is called a *secondary malignancy*. Your health care team knows which drugs can cause this problem and will discuss this possibility with you. The small chance that any of these drugs will cause leukemia is offset by their positive effects against ovarian cancer.

The typical course of chemotherapy for epithelial ovarian cancer involves six *cycles*. A *cycle* is a schedule that allows regular doses of a drug, followed by a rest period. Different drugs have varying cycles; the particular cycle or schedule for your chemotherapy will be prescribed by your oncologist (cancer doctor).

These drugs are usually administered intravenously in a three to four week cycle. This chemotherapy may also be given via *intraperitoneal* injection directly into the abdominal cavity. If chemotherapy treatment is chosen, you will probably receive a combination of drugs. Most oncologists in the United States believe that combination chemotherapy is more effective in treating ovarian cancer than one drug alone.

Combination therapy using a platinum compound, such as cisplatin or carboplatin, and a taxane, such as paclitaxel, is the standard approach. There are several reasons why two or more drugs work better than one. Because each drug has certain side effects a combination of drugs allows higher dosages of chemotherapy without risking the extreme reaction that an equivalent amount

of one drug would cause. Also, cancer cells do have the ability to develop a resistance to drugs; by combining drugs, the chances of resistance may be decreased.

Although epithelial ovarian cancer tends to respond to chemotherapy, the cells may eventually begin to grow again. Tumor recurrence is sometimes treated with additional cycles of a platinum compound and/or a taxane. In other cases, recurrence is treated with *second line* agents such as topotecan, anthracyclines such as doxorubicin (Adrimycin) and liposomal doxorubicin (Doxil), gemcitabine, cyclophosphamide, vinorelbine (Navelbine), hexamethylmelamine, ifosfamide, etoposide and fluorouracil.

Different drug combinations are often used to treat germ cell tumors and are described in the section on treatment of germ cell tumors.

**Radiation therapy:** Radiation therapy uses high energy x-rays to kill cancer cells. These x-rays may be given externally in a procedure that is much like having a diagnostic x-ray.

*External beam radiation therapy* focuses radiation on the cancer from a machine outside the body called a *linear accelerator*. This is one type of radiation therapy recommended for people with ovarian cancer. Treatments are given five days a week for several weeks. Each treatment lasts only a few minutes, and is similar to having a diagnostic x-ray test. As with a diagnostic x-ray, the radiation passes through the skin and other tissues before it reaches the tumor. The actual radiation exposure is very short, and most of the time is spent precisely positioning the patient so that the radiation is aimed accurately at the cancer.

Radiation therapy also may be given as an implant of radioactive materials, called *brachytherapy*, placed near the tumor or as a radioactive fluid placed into the abdominal cavity. This is rarely done for ovarian cancer.

Although in the past it was often used, radiation therapy is now only rarely used in this country as the main treatment for ovarian cancer.

During the course of radiation therapy, skin in the treated area may look and feel sunburned. This gradually fades, returning to a normal appearance in six to 12 months. Because the abdomen and pelvis is sensitive to radiation, many women also notice tiredness, nausea, or diarrhea. 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.

## **Clinical Trials**

Studies of promising new or experimental treatments in patients are known as clinical trials. During a course of treatment for ovarian cancer, the doctor may suggest that a patient take part in a clinical trial of a new treatment. A clinical trial is only done when there is some reason to believe that the treatment being studied may be of value to the patient. Treatments used in clinical trials are often found to have real benefits.

There are three phases of clinical trials in which a treatment is studied before the treatment is eligible for approval by the FDA (Food and Drug Administration).

The purpose of a Phase I study is to find the best way to give a new treatment and how much of it can be given safely. Physicians watch patients carefully for any harmful side effects. The research treatment has been well tested in laboratory and animal studies, but the side effects in patients are not completely predictable.

Phase II trials determine the effectiveness of a research treatment after safety has been evaluated in a Phase I trial. Patients are closely observed for an anti-cancer effect by careful measurement of cancer sites present at the beginning of the trial. In addition to monitoring patients for response, any side effects are carefully recorded and assessed.

Phase III trials require entry of large numbers of patients; some trials enroll thousands of patients. One of the groups may receive standard (the most accepted) treatment, so the new treatments can be directly compared. The group that received the standard treatment is called the "control group." For example, one group of patients (the control group) may receive the standard chemotherapy for a certain type of cancer, while another patient group may receive another type of chemotherapy that may or may not contain an investigational drug to see if this improves survival. All patients in Phase III trials are monitored closely for side effects, and treatment is discontinued if the side effects are too severe.

Researchers conduct studies of new treatments to answer the following questions:

- Is the treatment likely to be helpful?
- Does this new type of treatment work?
- Does it work better than other treatments already available?
- What side effects does the treatment cause?
- Do the benefits outweigh the risks, including side effects?
- In which patients is the treatment most likely to be helpful?

However, there are some risks. No one involved in the study knows in advance whether the treatment will work or exactly what side effects will occur. That is what the study is designed to discover. While most side effects will disappear in time, some can be permanent or even life threatening. Keep in mind, though, that even standard treatments have side effects. Depending on many factors, you may decide that a clinical trial will be beneficial in your case.

Enrollment in any clinical trial is completely up to you. Your doctors and nurses will explain the study to you in detail and will give you a form to read and sign indicating your desire to take part. This process is known as giving your informed consent. Even after signing the form and after the clinical trial begins, you are free to leave the study at any time, for any reason. Taking part in the study does not prevent you from getting other medical care you may need.

To find out more about clinical trials, ask your cancer care team. Among the questions you should ask are:

- What is the purpose of the study?
- What kinds of tests and treatments does the study involve?

- What does this treatment do?
- What is likely to happen in my case with, or without, this new research treatment?
- What are my other choices and their advantages and disadvantages?
- How could the study affect my daily life?
- What side effects can I expect from the study? Can the side effects be controlled?
- Will I have to be hospitalized? If so, how often and for how long?
- Will the study cost me anything? Will any of the treatment be free?
- If I am harmed as a result of the research, what treatment would I be entitled to?
- What type of long-term follow-up care is part of the study?
- Has the treatment been used to treat other types of cancers?

You can get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll free at 1-800-4-CANCER or visiting the NCI clinical trials websites for patients ([cancertrials.nci.nih.gov](http://cancertrials.nci.nih.gov)) or healthcare professionals ([cancernet.nci.nih.gov/prot/protsrch.shtml](http://cancernet.nci.nih.gov/prot/protsrch.shtml)).

### **Treatment for Epithelial Ovarian Cancers by Stage**

**Stages IA and IB:** For both stages, surgery is the treatment of choice. If the laboratory results indicate a grade 1 or grade 2 cancer (meaning the cancer has some similarities to normal glandular tissue) surgery alone may be enough. The surgery can include a *hysterectomy* (removal of the uterus), *bilateral salpingectomy* (removal of the fallopian tubes), *bilateral oophorectomy* (removal of both ovaries) and an *omentectomy* (removal of part of the omentum, which is fatty tissue from the upper part of the abdominal cavity near the stomach and intestines). During surgery, biopsies (tissue samples) of organs, omentum, lymph nodes, and the lining surfaces of the pelvic and abdominal cavities may be collected and sent to the laboratory for microscopic examination. This is done to find out if the cancer has spread. Stage IA and IB, grade 3 cancers are treated the same as stage IC cancers - with surgery and adjuvant chemotherapy. The overall 5-year survival rate for stage I is over 90%.

**Stage IC:** For stage IC (or grade 3) cancer, surgery, as described for stages IA and IB, is the main treatment of choice. Chemotherapy will also be used as well. The 5-year survival rate is 80% to 90%.

**Stage II (including IIA, IIB, IIC):** Not many tumors are diagnosed at this stage. In such cases, the same type of surgery as described for stage I is performed. Additional treatment will consist of combination chemotherapy or, less often, radiation therapy. The 5-year survival rates for stages IIA, IIB, and IIC are about 75%, 50%, and 40%, respectively.

**Stage III and IV:** For stages IIIA, IIIB, IIIC, and IV, the options are the same. Initial surgical treatment is usually the same as for 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 tumor also will be "*debulked*." This means that its size will be reduced as much as possible. The smaller the remaining tumor, the better the outlook for the patient's future will be. Most surgeons try to leave behind no tumor larger than 2 cm. (about 3/4 inch), but less residual cancer is even better. Sometimes this kind of surgery will require removing parts of the intestinal tract.

After recovery from surgery, combination chemotherapy will be used. The most used combination is carboplatin (or cisplatin) and a taxane, such as paclitaxel, usually for four to five months.

After surgery, during chemotherapy, and after chemotherapy, blood tests will be given to determine if you have normal levels of a tumor marker called CA 125. If CA 125 levels and imaging studies (such as CT scans or sonograms) are normal, your cancer care team may want to do a "second-look" surgery (laparoscopy and/or laparotomy).

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 or surgical opening long enough to allow your surgeon to look inside the pelvis and abdomen and take biopsy samples. Based on the results of the "second-look" surgery, your cancer care team can decide whether more radiation therapy or chemotherapy treatment is needed.

"Second-look" operations have not been shown to lead to improved outcomes. Because of this, they are not a standard part of ovarian cancer care but are usually performed as part of clinical trials. In a clinical trial of new treatments, the second look operation may be worthwhile to help determine how effective the new treatment is.

The 5-year survival rate for stages III is 20 to 40 percent. The rate is about 11 percent for stage IV.

**Recurrent or persistent ovarian cancer:** *Recurrent* tumors are those that reappear after initial treatment. *Persistent* tumors are those that never disappeared even after treatment. If epithelial ovarian cancer recurs after initial treatment over a period of months or years, you may be offered additional surgery, followed by combination chemotherapy. Follow-up treatment like this is usually less successful than the initial treatment. However, if the initial disease-free period was long (a few years), there may be a good response to a second course of treatment.

The most common problems that can occur in women with recurrent ovarian cancer are fluid accumulation in the abdomen and blockage of the intestinal tract. The doctor can treat the fluid in the abdomen with a procedure called *paracentesis*. This simply means the doctor places a needle into the abdomen after numbing the skin, and withdraws the fluid, usually about 2-4 quarts, into a bottle. This will often need to be repeated from time to time. Infusion of interferon alpha into the abdominal cavity can also help slow growth of cancer and accumulation of fluid within the abdomen. All these treatments can extend life and relieve symptoms for some patients. Often, however, their effects are temporary and the cancer returns.

Dealing with the intestinal blockage can be harder. Often times the cancer has grown into the intestinal tract so much, that surgery cannot fix the problem. Doctors can place a tube into the stomach to help relieve painful accumulation of fluid inside the digestive tract. At this point, the main concern is usually to relieve pain and keep the patient comfortable.

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

High dose chemotherapy with stem cell rescue (sometimes known as bone marrow 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 should only be done as part of a clinical trial that is studying improvements to this procedure.

### **Treatment for Epithelial Tumors of Low Malignant Potential (also called LMP Tumors or Borderline Tumors)**

The ovary with the tumor and the fallopian tube on that side are usually removed. In certain cases, just the ovarian cyst containing the tumor is removed; this operation is called an *ovarian cystectomy*. If there is no cancer seen beyond the one involved ovary and if the patient may want to become pregnant in the future, no further surgery is done at that time. In cases where ovarian cystectomy or removal of only one ovary is considered, it is a good idea to consult with a *gynecologic oncologist* (specialist in female reproductive system cancers). If the patient is not interested in remaining fertile, both ovaries and fallopian tubes as well as the uterus are removed. If the tumor is in more advanced stages, it is debulked as much as possible. Chemotherapy and radiation therapy are not generally used in the initial treatment of tumors that have not spread outside the ovary. If the tumor comes back after initial surgery, chemotherapy and radiation therapy may be considered. Further surgery can also be considered. The 5-year survival rate, considering women with all stages of borderline tumors together, is around 90 percent.

### **Treatment for Germ Cell Tumors of the Ovary**

Women with *benign* (noncancerous) germ cell tumors such as mature *teratomas* (dermoid cysts) are cured by removal of a portion of the ovary (*ovarian cystectomy*) containing the tumor or rarely by removal of the entire ovary. As with epithelial ovarian cancers, it is a good idea to consult with a gynecologic oncologist for the treatment of malignant germ cell tumors especially because these are so uncommon. Less than 5% of all ovarian cancers are of germ cell origin.

**Chemotherapy:** With the exception of some patients with grade 1 immature teratoma, and some patients with stage IA dysgerminoma, all patients with germ cell cancers receive combination chemotherapy. A frequently used combination chemotherapy treatment is called BEP, combining three drugs called **bleomycin**, **etoposide**, and **cisplatin (Platinol)**. However, other drug combinations may be used, particularly as part of a clinical trial or for treatment of cancer which has *recurred* (come back) after initial treatment.

**Radiation therapy:** In the past, radiation therapy was often used for treating dysgerminomas. However, results with current combination chemotherapy are as good or better. For younger women who want to keep the option of future pregnancy and who have had only one ovary removed, chemotherapy is less damaging to the remaining ovary and less likely to cause difficulty in becoming pregnant. For these reasons, radiation therapy is rarely used as the main treatment for dysgerminoma.

In some situations, such as cancer recurrence, radiation rarely may be given in addition to chemotherapy.

**All stages of germ cell ovarian cancer (except for stage IA dysgerminoma and stage I, grade 1 immature teratoma):** Most types and stages of germ cell cancers of the ovary are treated the same, with a few important exceptions. In order to identify these special cases, precise classification of the tumor and attention to staging is needed.

If only one ovary is involved (stage IA) and you want to become pregnant later, only the involved ovary and the fallopian tube on that side are removed. The uterus, the ovary, and the fallopian tube on the opposite side are not taken out. On the other hand, if future pregnancy is not important to you, the uterus, both ovaries, and both fallopian tubes may be removed.

If cancer involves both ovaries (stage IB), both ovaries and both fallopian tubes will be removed. Sometimes by removing a part of one ovary, the patient can maintain her ovarian function. Consultation with a gynecologic oncologist is advised in these cases. The uterus may be removed if childbearing is complete. However, the uterus can be left to allow future pregnancy through the use of in-vitro fertilization. If cancer has spread beyond the ovaries (stage IC and higher) the involved ovary and tube will be removed and debulking may be done (removing as much cancer as possible without damaging or removing essential organs).

**Stage IA dysgerminoma:** If careful staging has found that 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 chemotherapy after surgery. This approach requires close follow-up so that any recurrence can be found early and treated. The advantage of this approach is that the majority of patients in this stage will not have recurrence of their cancer and will not need to have any chemotherapy.

**Grade 1 immature teratoma:** A grade 1 immature teratoma is composed mostly of noncancerous tissue, with only a few cancerous areas seen under the microscope which are *immature* (looking 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, without chemotherapy after surgery. If there are implants (tumor deposits) outside of the ovary, but under a microscope they appear mature (resemble adult tissues), no chemotherapy is needed.

**Recurrent or persistent germ cell tumors:** Recurrent tumors are those that reappear after initial treatment. Persistent tumors are those that never disappeared even after treatment. For either of these types of ovarian cancer, a clinical trial for new treatments may provide important advantages. Ask your cancer care team for information on suitable clinical trials for your type of cancer.

Treatment for recurrent or persistent germ cell tumors may include chemotherapy or, rarely, radiation therapy. In chemotherapy, a combination of drugs is used, sometimes referred to as

VIP, including vinblastine, ifosfamide, and cisplatin (Platinol). BEP chemotherapy may be used if the patient has never received this combination of drugs.

### **Treatment for Stromal Tumors of the Ovary**

Stromal tumors start from connective tissue cells, which hold the ovary together and produce hormones. Cells of stromal tumors often produce the estrogen and progesterone (female hormones). Less often, they produce androgens (male hormones). Epithelial and germ cell tumors are more common than stromal tumors. Most stromal tumors are benign (noncancerous) and are treated by surgical removal of the ovary containing the tumor. Malignant (cancerous) stromal tumors are less common. They are initially treated by removing the cancerous ovary as completely as possible. If the other ovary is enlarged, it will be biopsied.

These cancers may come back years later. Even so, their prognosis is still quite good because they grow so slowly. There are no standard chemotherapy regimens for treating recurrent stromal cancer. Some of the drugs used are vincristine, cisplatin, doxorubicin (Adriamycin), and cyclophosphamide. Radiation therapy may also be used.

### **What Should You Ask Your Physician 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 cancer do I have?
- Has my cancer spread beyond the ovaries?
- What is the cell type, microscopic grade, and stage of my cancer? What does that mean in my case?
- What treatments are appropriate for me? What do you recommend? Why?
- What are the risks or side effects that I should expect?
- What are the chances my cancer will recur (come back) with the treatment programs 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, based on my cancer as you view it?
- Will I need a wig?
- 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 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?**

During and after treatment you may be able to hasten your recovery and improve your quality of life by taking an active role. Learn about the benefits and disadvantages of each of your treatment options, and ask questions of your cancer care team if there is anything you do not understand. Learn about and look out for side effects of treatment, and report these promptly to your cancer care team so that they can take steps to minimize them and shorten their duration.

Remember that your body is as unique as your personality and your fingerprints. Although understanding your cancer's stage and learning about the effectiveness of your treatment options can help predict what health problems you may face, no one can say precisely how you will respond to cancer or its treatment.

You may have special strengths such as a history of excellent nutrition and physical activity, a strong family support system, or a deep faith, and these strengths may make a difference in how you respond to cancer. In fact, behavioral scientists have recently found that some people who took advantage of a social support system, such as a cancer support group, survived with a better quality of life. There are also experienced professionals in mental health services, social work services, and pastoral services who may assist you in coping with your illness.

You can also help in your own recovery from cancer by making healthy lifestyle choices. If you use tobacco, stop now. Quitting will improve your overall health and the full return of the sense of smell may help you enjoy a healthy diet during recovery. If you use alcohol, limit how much you drink. Have no more than one or two drinks per day. Good nutrition can help you get better after treatment. Eat a nutritious and balanced diet, with plenty of fruits, vegetables, and whole grain foods. Ask your cancer care team if you could benefit from a special diet -- they may have specific recommendations for people who have had radiation therapy, chemotherapy or surgery.

If you are in treatment for cancer, be aware of the battle that is going on in your body. Radiation therapy and chemotherapy add to the fatigue caused by the disease itself. Give your body all the rest it needs so that you will feel better as time goes on. Exercise once you feel rested enough. Ask your cancer care team whether your cancer or its treatments might limit your exercise program or other activities.

Surgery and radiation therapy may sometimes affect a person's feelings about their body, and may lead to specific physical problems that affect sexuality. Your cancer care team can help with these issues, so don't hesitate to share your concerns.

A cancer diagnosis and its treatment are major life challenges, with an impact on you and everyone who cares for you. Before you get to the point where you feel overwhelmed, consider attending a meeting of a local support group. If you need individual assistance in other ways, contact your hospital's social service department or the American Cancer Society for help in contacting counselors or other services.

For years after treatment ends, regular follow-up exams will be very important for you. These can detect *recurrence* (the cancer coming back). Be sure to tell your doctor about any new or persistent symptoms to right away. Follow-up usually includes a careful general physical exam and blood tests for tumor markers (that help recognize recurrence) and for liver function (to help detect spread to the liver). 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 in follow-up of women with epithelial ovarian cancers. For women with germ cell tumors, blood tests for alpha-fetoprotein (AFP) and/or human chorionic gonadotropin (HCG) are done. Imaging studies such as chest x-rays, CT scans, and ultrasound may also be done if symptoms or other test results suggest a recurrence.

## **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 to how these genes normally work and how disrupting their action can lead to cancer. This information is expected to eventually lead to new drugs for preventing and treating familial ovarian cancer.

For the present, 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 the extent to which BRCA1 and BRCA2 gene mutations increase ovarian cancer risk have been applied to 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 removed in order to prevent a cancer from developing. 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.

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

**Early Detection:** Accurate methods for the early detection of ovarian cancer could have a great impact on the cure rate. Researchers are testing new approaches to screening, and a national repository for blood and tissue samples from ovarian cancer patients is being established to aid in these studies.

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

Studies continue to assess the value of laparoscopy in surgical staging with the intention of avoiding laparotomy (surgery through an abdominal incision) in some cases and minimizing the recovery period after surgery. New combinations that include recently developed drugs such as topotecan and gemcitabine are being tested. Monoclonal antibody drugs that are designed to

block oncogene products (such as the HER-2 protein) and slow cancer cell growth are being studied in clinical trials.

Another area of investigation involves giving very high doses of standard anticancer drugs, and then "rescuing" the woman from the side effects with infusions of her own stem cells (immature blood cells that may be taken from the bone marrow or removed from the bloodstream by using a special filtering process). The bone marrow or peripheral (circulating) blood stem cells are removed before high doses of chemotherapy are administered and are returned to the woman after the high-dose treatment is complete. In that way, the side effect of suppressed blood cell production is overcome. This is an extremely high-risk, experimental procedure because, for the time, the woman is without her normal supply of blood cells and is very vulnerable to infection. It is also a costly procedure that is not available in many community hospitals and may not be covered by all health care plans. Because bone marrow/stem cell transplantation is considered experimental, a woman seeking this treatment should do so in a clinical trial.

Early studies of gene therapy are in progress. Defective tumor suppressor genes are known to promote abnormal growth and spread of ovarian cancer cells. Researchers are testing ways to package normal genes into viruses. The viruses are then modified to infect cancer cells, replace the normal genes and restore normal growth control. Another gene therapy strategy is to target new viral genes in cancer cells. Cancer cells containing the viral gene would then become susceptible to killing by antiviral drugs that do not harm the normal cells.

A variety of immunotherapy strategies intended to boost the immune system's ability to destroy ovarian cancer cells are being tested. One approach is the use of cytokines (protein-like substances that activate immune system cells). Several of these substances such as *interferon*, *interleukins* and *tumor necrosis factor* are being tested. Another approach is to develop tumor vaccines that program the immune system to better recognize cancer cells. Also, antibodies that specifically recognize and attack ovarian cancer cells are being developed. Perhaps some or all of these approaches along with chemotherapy will lead to more cures of this disease.

In order for cancers to grow, blood vessels must develop to nourish the cancer cells. This process is called *angiogenesis*. New drugs are being developed that may be useful in stopping ovarian cancer growth by preventing new blood vessels from forming. Several of these drugs are being tested in clinical trials and trials of new, more potent, antiangiogenesis drugs are expected to begin soon.

## **Additional Resources**

### **National Organizations and Web Sites**

In addition to the American Cancer Society (1-800-ACS-2345), other sources of patient information and support include\*:

Gilda Radner Familial Ovarian Cancer Registry  
Telephone: 1-800-OVARIAN

Internet Address: [rpci.med.buffalo.edu/clinic/gynonc/grnl.html](http://rpci.med.buffalo.edu/clinic/gynonc/grnl.html)

Gilda's Club

Telephone: 212-647-9700

Internet Address: [www.gildasclub.org](http://www.gildasclub.org)

Gynecologic Cancer Foundation

Telephone: 1-800-444-4441

Internet Address: [www.sgo.org/gcf](http://www.sgo.org/gcf)

National Cancer Institute

Telephone 1-800-4-CANCER

Internet Addresses: [www.nci.nih.gov](http://www.nci.nih.gov) and [canceret.nci.nih.gov](http://canceret.nci.nih.gov)

National Coalition for Cancer Survivorship

Telephone: 1-888-650-9127

Internet Address: [www.cansearch.org](http://www.cansearch.org)

National Ovarian Cancer Coalition

Telephone: 1-877-682-6622; 1-888-682-7426 (to order materials)

Internet Address: [www.ovarian.org](http://www.ovarian.org)

Office of Women's Health

Telephone: 1-800-994-WOMAN

Internet Address: [www.4woman.gov](http://www.4woman.gov)

Ovarian Cancer National Alliance

Telephone: 202-331-1332

Internet Address: [www.ovariancancer.org](http://www.ovariancancer.org)

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

### **Additional American Cancer Society Information**

After Diagnosis: A Guide for Patients and Families. (Booklet; Code#9440)

Caregiving: A Step-By-Step Resource for Caring for the Person with Cancer at Home (Book; Code#9422)

Cancer Facts for Women. (Pamphlet; Code #2007)

Caring for the Patient with Cancer at Home. (Booklet; Code#4656)

Runowicz, Carolyn D., Petrek, Jeanne A., and Gansler, Ted S. *Women and Cancer: A Thorough and Compassionate Resource for Patients and their Families*. New York: Villard Books, 1999.

Sexuality and Cancer: For the Women Who Has Cancer and Her Partner. (Booklet; Code#4657)

Understanding Chemotherapy: A Guide for Patients and Families. (Booklet; Code#9458)

Understanding Radiation Therapy: A Guide for Patients and Families. (Booklet; Code#9459)

### **Other Publications\***

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

*A Cancer Survivor's Almanac: Charting Your Journey.* Edited by Barbara Hoffman, JD. National Coalition for Cancer Survivorship. Chronimed Publishing, 1996.

Capossela, Cappy, Warnock, Sheila. *Share the Care: How to Organize a Group for Someone Who Is Seriously Ill.* New York: Simon and Schuster. 1995.

Dollinger, Malin, Rosenbaum, Ernest H., and Cable, Greg. *Everyone's Guide to Cancer Therapy.* Somerville House Books, 1994.

Morra, Marion and Eve Potts. *Choices.* Avon Books, 1994.

Schover, Leslie R. *Sexuality and Fertility after Cancer.* John Wiley and Sons, Inc. 1997

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PDQ database. Ovarian cancer. Bethesda, Md: National Cancer Institute; 2000: Available at [cancernet.nci.nih.gov/Cancer\\_Types/Ovarian\\_Cancer.shtml](http://cancernet.nci.nih.gov/Cancer_Types/Ovarian_Cancer.shtml)

Thigpen JT. Ovaries and Fallopian Tubes. In:Abeloff MD, Armitage JO, Lichter AS, Niederhuber JE. *Clinical Oncology*. Philadelphia, PA. Churchill Livingstone: 2000: 2016-2040

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