About Ovarian Cancer

Overview and Types

If you have been diagnosed with ovarian cancer or are worried about it, you likely have a lot of questions. Learning some basics is a good place to start.

- What Is Ovarian Cancer?

Research and Statistics

See the latest estimates for new cases of ovarian cancer and deaths in the US and what research is currently being done.

- Key Statistics for Ovarian Cancer
- What's New in Ovarian Cancer Research and Treatment?

What Is Ovarian Cancer?

Cancer starts when cells in the body begin to grow out of control. Cells in nearly any part of the body can become cancer, and can spread to other areas of the body. To learn more about how cancers start and spread, see What Is 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 can be more concerning 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.

- References

See all references for Ovarian Cancer

Last Medical Review: August 5, 2014 Last Revised: February 4, 2016

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Key Statistics for Ovarian Cancer

The American Cancer Society estimates for ovarian cancer in the United States for 2018 are:

- About 22,240 women will receive a new diagnosis of ovarian cancer.
- About 14,070 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 79. Her lifetime chance of dying from ovarian cancer is about 1 in 108. (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.

Visit the American Cancer Society’s Cancer Statistics Center for more key statistics.

- References

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Last Medical Review: August 5, 2014 Last Revised: January 5, 2018

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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 \textit{BRCA1} and \textit{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 \textit{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 \textit{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 \textit{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.

\textbf{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 \textit{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 buildup (ascites) that can occur when cancer is present.

- References
  See all references for Ovarian Cancer

Last Medical Review: August 5, 2014 Last Revised: February 4, 2016

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