

STOMACH 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 Stomach Cancer?

Stomach cancer is a cancer that starts in the stomach. The medical name for stomach cancer is *gastric cancer*.

After food is chewed and swallowed, it enters the *esophagus*, a tube-shaped organ that carries food through the neck and chest. The esophagus joins the stomach just beneath the *diaphragm* (the breathing muscle under the lungs). The stomach is a sack-like organ that holds food and begins the digestive process by secreting gastric juice. The food and gastric juice are mixed into a thick fluid called *chyme*, which is then emptied into the first part of the small intestine called the *duodenum*.

In nonmedical conversation, the word "stomach" is often used to refer to the area of the body between the chest and the pelvic area. For instance, some patients with diseases of the appendix, small intestine, colon (large intestine), or gallbladder may say they have a "stomach ache." The medical term for this area is *abdomen*. And, doctors would describe this symptom as "abdominal pain."

This point is also very important in considering cancers. The stomach is only one of many organs in the abdomen in which cancers may develop. It is important not to confuse stomach cancer with cancers of the colon (large intestine), liver, pancreas, small intestine, or gallbladder, because these cancers may have different symptoms, a different *prognosis* (the outlook for chances of survival) and different treatments.

The stomach is divided into five different sections. The upper portion (closest to the esophagus) of the stomach is the *proximal* stomach. Some cells of this area of the stomach produce acid and *pepsin* (a digestive enzyme), the ingredients of the gastric juice that help digest food. The lower portion (closest to the intestine) is the *distal* stomach. This area includes the *antrum*, where the food is mixed with gastric juice, and the *pylorus*, which acts as a valve to control emptying of the stomach contents into the small intestine.

The stomach has two curves which form its upper and lower borders. They are called the *lesser and greater curves*, respectively. Other organs next to the stomach include the colon, liver, spleen, small intestine, and pancreas.

Cancer can develop in any of the five sections of the stomach. Cancers beginning in these different sections may produce different symptoms and tend to have different outcomes. The location can also affect some of the treatment options that are available.

Stomach cancers are believed to develop slowly over many years. Before a true cancer develops, there are usually precancerous changes that occur in the lining of the stomach. These early changes rarely produce symptoms and therefore often go undetected.

If left untreated, stomach cancers can spread by several different means. They can grow through the wall of the stomach and involve the nearby organs. They can also spread through the bloodstream or lymph system to form distant colonies of cancer called *metastasis*.

Approximately 90% to 95% of the *malignant* (cancerous) tumors of the stomach are *adenocarcinomas*. The terms stomach cancer or gastric cancer almost always refer to adenocarcinoma of the stomach. This cancer develops from the cells that form the inner lining of the stomach called the *epithelium*.

The following are other, less common tumors that are found in the stomach:

- *Lymphoma*: These are cancers of the immune system tissue that is sometimes found in the wall of the stomach. They account for about 4% of cancers in the stomach. Prognosis and treatment depend on whether the cancer is an aggressive lymphoma or an indolent (slowly growing) lymphoma of mucosa-associated lymphoid tissue (MALT).
- *Gastric stromal tumors*: These tumors develop from the muscle or connective tissue of the stomach wall. Some are benign; others are malignant (cancerous). The malignant stomach tumors are also called *gastric sarcomas* and make up about 2% of cancers starting in the stomach.
- *Carcinoid tumors*: These are tumors of hormone-producing cells of the stomach. Most of these do not spread to other organs. Carcinoid tumors account for about 3% of cancers starting in the stomach.

The treatment and outlook of these rarer types of cancers are different from that of adenocarcinoma and are not covered here. Gastrointestinal carcinoid tumors are discussed in a separate document called "Gastrointestinal (Digestive System) Carcinoid Tumors."

The information contained in the rest of this document about stomach cancer refers only to adenocarcinoma of the stomach.

What Are The Key Statistics About Stomach Cancer?

It is estimated that 21,700 Americans (13,400 men and 8,300 women) will be diagnosed with stomach cancer during 2001. There will be an estimated 12,800 (7,400 men and 5,400 women) deaths from this type of cancer in 2000. Most people diagnosed with stomach cancer are in their 60s and 70s.

Stomach cancer is much more common in certain Asian, Central European, Central American, and South American countries, especially Japan, Chile, Costa Rica, Hungary, and Poland. It is the leading cause of cancer death in many of these countries and is a major cause of cancer death worldwide.

In the United States, stomach cancer is now only one-fourth as common as it was in 1930. The reasons for this dramatic decline are not completely known but may be related to increased use of refrigeration for food storage and decreased use of salted and smoked foods.

The overall 5-year survival rate of all stages of stomach cancer combined is about 21%. The *prognosis* (the outlook for chances of survival) for patients with early-stage stomach cancer is much better, but depends on the location of the cancer. The 5-year survival rate for early stage cancers of the *proximal* stomach (the upper portion of the stomach closest to the esophagus) is about 10% to 15%. For early stage cancers in the *distal* stomach (the lower portion of the stomach closest to the intestines), the 5-year survival rate is 50%. Unfortunately, only about 10% to 20% of patients with stomach cancer in the United States are diagnosed at an early stage. It is important to remember that these statistics are averages. The outlook for any individual patient cannot be predicted with certainty, and many people survive much longer than would be expected based on the stage of their cancer.

The 5-year survival rate refers to the percent of patients who live at least 5 years after their cancer is diagnosed. Many of these patients live much longer than 5 years after diagnosis, and 5-year rates are used to produce a standard way of discussing prognosis. 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.

What Are The Risk Factors For Stomach Cancer?

A *risk factor* is anything that increases a person's chance of getting a disease such as cancer. Different cancers have different risk factors. For example, smoking is a risk factor for lung, larynx, mouth, and many other cancers. Unprotected exposure to sunlight is a risk factor for skin cancer. Scientists have found several risk factors that make a person more likely to develop stomach cancer:

Helicobacter pylori infection: Long-term infection of the stomach with this bacterium may lead to *chronic atrophic gastritis* (inflammation and damage to the inner layer of the stomach), a possible precancerous change of the lining of the stomach. Patients with adenocarcinoma of the stomach have a higher rate of infection than people without this cancer. Helicobacter infection is also associated with some types of lymphoma of the stomach. But the vast majority of people who carry this bacterium in their stomachs never develop cancer.

Dietary causes: An increased risk of stomach cancer is associated with diets containing large amounts of smoked foods, salted fish and meat, certain foods high in starch that are also low in fiber, and pickled vegetables. On the other hand, eating whole grain products, fresh fruits and vegetables that contain vitamins A and C appears to lower the risk of stomach cancer. Nitrates and nitrites are substances commonly found in cured meats, some drinking water, and certain vegetables. They can be converted by certain bacteria, such as *Helicobacter pylori*, into compounds that have been found to cause stomach cancer in animals.

Tobacco and alcohol abuse: These habits can increase stomach cancer risk, particularly for cancers of the *proximal* stomach (the upper portion of the stomach closest to the esophagus).

Previous stomach surgery: Stomach cancers are more likely to develop in people who have had part of their stomach removed to treat noncancerous diseases such as ulcers. This may be because there are more nitrite-producing bacteria present. Also, acid production goes down after ulcer surgery, and there may be *reflux* (backup) of bile from the small intestine into the stomach. The risk continues to increase for as long as 15 to 20 years after surgery, and those patients who underwent a *Billroth II* operation are at higher risk.

Pernicious anemia: Certain cells in the stomach lining normally produce a substance essential for absorbing vitamin B12 from foods. If enough of this substance is not present, a vitamin B12 deficiency results, leading to problems in producing enough red blood cells (*anemia*). In addition to anemia, there is a slightly increased risk of stomach cancer for patients with this disease. However, because the risk seems to be very small, screening of these patients for stomach cancer is not recommended.

Menetrier's disease: This is also called *hypertrophic gastropathy* and is a condition of large folds in the stomach associated with changes in the stomach lining and low acid production. Because this disease is very rare, the exact risk of stomach cancer is not known.

Being male: Stomach cancer is about twice as common in men than in women.

Aging: There is a sharp increase in stomach cancer after the age of 50. Most people diagnosed with stomach cancer are in their 60's and 70's.

Blood group A: Blood groups refer to certain *antigens* (chemicals recognized by the immune system) that are normally present on red blood cells and some other types of cells. These groups are important in matching blood for transfusions. For unknown reasons, people with blood group A have a higher risk of developing stomach cancer.

Familial cancer syndromes: *Hereditary nonpolyposis colon cancer* (Lynch Syndrome or HNPCC) and *Familial Adenomatous Polyposis* are inherited genetic disorders. They cause a greatly increased risk of developing colorectal cancer and a slightly increased risk of stomach cancer in family members affected by these inherited gene mutations.

Family history of stomach cancer: People with several close blood relatives who have had stomach cancer are more likely to develop this disease.

Stomach polyps: *Polyps* are small bumps or larger mushroom-like growths of the lining of the stomach. Most types of polyps (like *hyperplastic* polyps or *inflammatory* polyps) do not increase a person's risk of stomach cancer but *adenomatous* polyps sometimes develop into *gastric* (stomach) cancers.

Do We Know What Causes Stomach Cancer?

While there are many known risk factors for stomach cancer, it is not known exactly how all of these factors cause cells of the stomach lining to become cancerous. This is the subject of ongoing research.

There are several changes that can occur in the lining of the stomach that are thought to be precancerous. One of these conditions is *atrophic gastritis*. This is a condition where the normal glands of the stomach are either decreased or absent. There is a variable degree of inflammation (the stomach cells are damaged by cells of the patient's immune system), and this is often due to *Helicobacter pylori* infection. It is not known exactly why this condition progresses to cancer.

Another change in the lining of the stomach which may also be precancerous is *intestinal metaplasia*. This is a condition where the normal lining of the stomach is replaced with cells that closely resemble the cells that usually line the intestine. People with this condition usually have *chronic atrophic gastritis* as well. How and why this change occurs and progresses to stomach cancer is not well understood.

Recent research has provided some clues to how stomach cancers form. For instance, *Helicobacter pylori* bacteria, particularly certain strains or subtypes, can convert some of the chemicals in high-risk foods into cancer-causing chemicals that produce *mutations* (changes) of a cell's DNA in the stomach lining. This is why certain foods increase a person's risk for stomach cancer. On the other hand, some of the foods that lower stomach cancer risk contain vitamins and other chemicals that can deactivate substances that damage a cell's DNA.

During the past few years, scientists have made great progress in understanding how certain changes in DNA can cause normal stomach cells to grow abnormally and form cancers. 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 cells grow and divide. Certain genes that promote cell division are called *oncogenes*. Others that slow down cell division or cause cells to die at the appropriate time 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.

Some people with certain types of cancer have DNA mutations they inherited from a parent. These inherited DNA changes in certain genes may increase a person's risk of developing cancer. *Familial adenomatous polyposis (FAP)* and *hereditary nonpolyposis colon cancer (HNPCC)* are two conditions caused by inherited gene mutations. Both greatly increase a person's risk of developing colorectal cancer but, to a lesser degree, can also contribute to the development of stomach cancer. Changes in a tumor suppressor gene called APC are responsible for *familial adenomatous polyposis (FAP)*. People with these conditions have a change in this gene resulting in an incomplete and ineffective tumor suppressor protein. This causes growth of many benign

(noncancerous) polyps in the colon and other parts of the digestive system. Over time, cancer will nearly always develop in one or more of these colon polyps and may also develop in the stomach. A defective DNA repair mechanism is responsible for *hereditary nonpolyposis colon cancer (HNPCC)*. Cells must make a new copy of their DNA each time they divide. Occasional errors are made in copying the DNA code. Fortunately, cells have DNA repair enzymes that act like proofreaders or "spell checkers" in a word processing program. But, mutations in certain DNA repair enzyme genes allow DNA errors to persist without correction. If these errors affect growth-regulating genes, cancers may develop in the colon, stomach, uterus, or other organs.

DNA mutations related to stomach cancer are usually *acquired* (develop during a person's life) rather than having been inherited before birth. Acquired mutations that may cause stomach cancer might result from cancer-causing chemicals in some foods. Changes of certain oncogenes or tumor suppressor genes may make some stomach cancers more likely to grow and spread more rapidly than others. Current research in this field is aimed at developing tests that can detect stomach cancers at an early stage by recognizing their DNA changes. Other researchers are working on gene therapy strategies for repairing or replacing these mutated genes in order to stop the abnormal growth and spread of the cancer cells.

Can Stomach Cancer Be Prevented?

Even though the exact cause of stomach cancer is not completely known, it is still possible to prevent many stomach cancers.

The dramatic decline of stomach cancer over the last 60 years is thought to be a result of people reducing many of the known dietary risk factors. This includes greater use of refrigeration for food storage rather than preservation of foods by salting, pickling, and smoking. To reduce the risk, people should avoid diets that are high in smoked and pickled foods and salted meats and fish.

A diet high in fresh fruits and vegetables can also lower stomach cancer risk. The American Cancer Society recommends choosing most foods from plant sources. This includes fruits, vegetables, breads, cereals, pasta, rice, and beans.

Tobacco and alcohol use can increase the risk of cancers of the *proximal* stomach (the upper portion of the stomach closest to the esophagus). These cancers tend to be particularly hard to treat successfully. The American Cancer Society recommends limiting the use of alcoholic beverages, if you drink at all. Tobacco use increases the risk for many types of cancer and is responsible for about one-third of all cancer deaths in the United States. If you don't use tobacco, don't start. If you already do, call your health care provider or the American Cancer Society for advice about quitting.

It is not yet known if people without symptoms who have chronic infection of their stomach lining with the bacteria *Helicobacter pylori* should be treated for this infection. This issue is a topic of current research.

Although avoiding risk factors whenever possible can lower a person's stomach cancer risk, it cannot guarantee protection from this disease. Particularly in countries where stomach cancer is common, early detection may be the best way to improve the chance of successful treatment and reduce the number of deaths caused by the disease.

Can Stomach Cancer Be Found Early?

In countries such as Japan where stomach cancer is about 5 times more common than in the United States, mass screening of the population has helped find many cases at an early, curable stage and has reduced the number of people who die of this disease. However, studies in the United States have not found mass screening for stomach cancer to be useful because this disease is so uncommon. On the other hand, people with certain stomach cancer risk factors may benefit from screening. If you have any questions about your stomach cancer risk or about benefits of screening, ask your doctor.

Because mass screening for stomach cancer is not done in the United States, most people with this disease are diagnosed when certain signs and symptoms indicate the need for further medical testing.

Signs and Symptoms of Stomach Cancer

Unfortunately, patients who have stomach cancer rarely have symptoms in the early stages of the disease. This is one of the reasons why stomach cancer is so difficult to detect early. The signs and symptoms of stomach cancer include:

- Unintended weight loss and lack of appetite
- Abdominal pain
- Vague discomfort in the abdomen, usually above the *umbilicus* (navel)
- A sense of fullness in the upper abdomen, just below the chest bone after eating a small meal. Doctors call this *early satiety*.
- Heartburn, indigestion, or ulcer-type symptoms
- Nausea
- Vomiting, with or without blood
- Swelling of the abdomen due to accumulation of fluid and cancer cells. Doctors call this *malignant ascites*.

Some of these symptoms can occur with noncancerous conditions such as a stomach virus or with other types of cancer. However, people who have any of these problems that persist for a long time should check with their doctor, especially if they are over 50 years old or have stomach cancer risk factors.

Since symptoms of stomach cancer often do not appear until the disease is advanced, only about 10% to 20% of stomach cancers in the United States are found in the early stages, before they have spread to other areas of the body.

Tests for Detection of Stomach Cancer

In the United States, there are three procedures commonly used when people have certain risk factors for gastric cancer or when signs and symptoms of this disease are present.

Upper endoscopy: While the patient is sedated, a doctor puts a slender, flexible, lighted tube called an *endoscope* down the throat. This instrument allows the doctor to view the lining of the esophagus, stomach, and first part of the small intestine. If abnormalities are noted, *biopsies* (tissue samples) can be taken. Small (less than 1/8 inch) tissue samples can be removed using instruments operated through the endoscope. The tissue samples are examined under a microscope to see if cancer is present and, if so, what type of cancer. This test is easily tolerated by almost all patients.

Barium upper GI radiographs: Patients having this test drink a barium-containing solution that coats the lining of the esophagus, stomach, and first portion of the small intestine. The radiologist then takes multiple x-ray pictures. The coating of barium helps in finding abnormalities of the lining of these organs. For the identification of early gastric cancers, a "double contrast" technique is commonly used. Air is pumped into the stomach after the barium solution.

When viewed through an endoscope, gastric cancer can appear as an ulcer, a polypoid or protruding mass, or as a flat, thickened area of mucosa, known as linitis plastica. The latter condition is more difficult to recognize in its earliest stages because only a biopsy of a suspicious area will result in the diagnosis.

Endoscopic Ultrasound: This is a new technique in which a special instrument is used in patients undergoing upper endoscopy. For this test, the endoscope has a small ultrasound probe on the end. This probe releases high frequency sound waves and then detects the sound wave echoes that bounce off tissue of the stomach wall. A computer then translates the pattern of echoes into an image of the stomach wall. This test is usually only available at specialized centers. It is used to estimate how far cancer has spread into the wall of the stomach, into nearby tissues, and to nearby lymph nodes.

How Is Stomach Cancer Diagnosed?

If there is a reason to suspect you may have stomach cancer, the doctor will use one or more methods to find out if the disease is really present.

A **complete medical history** is an interview in which the doctor asks questions about risk factors and symptoms.

A **physical examination** provides information about signs of gastric cancer and other health problems.

A **barium upper GI radiograph** may be done. See the section, "Can Stomach Cancer be Found Early?" for more details.

Upper endoscopy with biopsies is essential for establishing a diagnosis. See the section "Can Stomach Cancer be Found Early?" for additional details.

Endoscopic ultrasound may be used to help determine the extent of the cancer. Refer to the section "Can Stomach Cancer be Found Early?" for additional details.

Laboratory studies may include a blood test called a complete blood count (CBC) to look for anemia and a fecal occult blood test, which looks for microscopic amounts of blood in *stool* (feces).

The doctor may recommend other tests and procedures as well.

How Is Stomach Cancer Staged?

Staging is a process that tells the doctor how widespread a cancer may be. It will show if the cancer has spread and how far. The treatment and *prognosis* (the outlook for chances of survival) for stomach cancer depend, to a large extent, on the patient's stage at diagnosis.

The system most often used to stage stomach cancer in the United States is the American Joint Commission on Cancer (AJCC) TNM system. **T** stands for features of tumor (how far it has spread within the stomach and to nearby organs), **N** stands for spread to lymph nodes (bean-sized collections of immune system cells that fight infections and cancers), and **M** is for *metastasis* (spread) to distant organs. In TNM staging, information about the tumor, lymph nodes, and metastasis is combined by a process called *stage grouping*. The stage is described by a number in Roman numerals from 0 to IV.

Stage 0: This is cancer in its earliest stage. It has not progressed beyond the layer of cells that line the stomach (*epithelium*). This stage is also known as *carcinoma in situ* which means the cancer cells have not spread beyond the layer in which they started.

Stage IA: The cancer has spread under the epithelium into one or more of the nearby layers such as the *lamina propria*, *muscularis mucosae*, or the *submucosa*. However, it has not grown into the main muscle layer of the stomach called the *muscularis propria*. The cancer has not spread to any lymph nodes.

Stage IB: There are 2 combinations of T and N features that are assigned to this stage.

- The cancer has spread into the main muscle layer of the stomach wall and may have spread into but not beyond the *subserosa* (outermost layer of the stomach). It has not spread to any nearby tissues or organs and has not spread to any lymph nodes.

- The cancer has spread under the epithelium into the *lamina propria*, *muscularis mucosae*, or the *submucosa* but it has not grown into the main muscle layer of the stomach called the *muscularis propria*. It has spread to between one and six lymph nodes near the stomach.

Stage II: There are 3 combinations of T and N features that are assigned to this stage.

- The cancer has spread under the epithelium into the lamina propria, muscularis mucosae, or the submucosa but it has not grown into the main muscle layer of the stomach called the *muscularis propria*. It has spread to between seven and fifteen lymph nodes near the stomach.
- The cancer has spread into the *muscularis propria* (the main muscle layer of the stomach wall) and may have spread into but not beyond the *subserosa* (outermost layer of the stomach). It has not spread to any nearby tissues or organs. It has spread to between one and six lymph nodes near the stomach.
- The cancer has spread completely through the *muscularis propria* (the main muscle layer of the stomach wall) and the *subserosa* (outermost layer of the stomach). But, it has not spread to any nearby tissues or organs. It has not spread to any lymph nodes.

Stage IIIA: There are 3 combinations of T and N features that are assigned to this stage.

- The cancer has spread into the *muscularis propria* (the main muscle layer of the stomach wall) and may have spread into but not beyond the *subserosa* (outermost layer of the stomach). It has not spread to any nearby tissues or organs. It has spread to between seven and fifteen lymph nodes near the stomach.
- The cancer has spread completely through the *muscularis propria* (the main muscle layer of the stomach wall) and the *subserosa* (outermost layer of the stomach). But, it has not spread to any nearby tissues or organs. It has spread to between one and six lymph nodes near the stomach.
- The cancer has spread completely through the stomach wall into other nearby organs such as the spleen, liver, intestines, kidneys, pancreas, etc. It has not spread to any lymph nodes.

Stage IIIB: There is one of T and N features that is assigned to this stage.

- The cancer has spread completely through the *muscularis propria* (the main muscle layer of the stomach wall) and the *subserosa* (outermost layer of the stomach). But, it has not spread to any nearby tissues or organs. It has spread to between seven and fifteen lymph nodes near the stomach.

Stage IV: There are several combinations of T, N, and M features that are assigned to this stage.

- The cancer has spread completely through the stomach wall into other nearby organs such as the spleen, liver, intestines, kidneys, pancreas, etc. It has spread to between one and six lymph nodes near the stomach.
- The cancer has spread under the epithelium into the *lamina propria*, *muscularis mucosae*, or the *submucosa* but it has not grown into the main muscle layer of the stomach called the *muscularis propria*. It has spread to more than fifteen lymph nodes near the stomach.
- The cancer has spread into the *muscularis propria* (the main muscle layer of the stomach wall) and may have spread into but not beyond the *subserosa* (outermost layer of the stomach). It has not spread to any nearby tissues or organs. It has spread to more than fifteen lymph nodes near the stomach.
- The cancer has spread completely through the *muscularis propria* (the main muscle layer of the stomach wall) and the *subserosa* (outermost layer of the stomach). But, it has not spread to any nearby tissues or organs. It has spread to more than fifteen lymph nodes near the stomach.
- The cancer has spread completely through the stomach wall into other nearby organs such as the spleen, liver, intestines, kidneys, pancreas, etc. It has spread to between seven and fifteen lymph nodes near the stomach.
- The cancer has spread completely through the stomach wall into other nearby organs such as the spleen, liver, intestines, kidneys, pancreas, etc. It has spread to more than fifteen lymph nodes near the stomach.
- The cancer may have any extent of growth within the stomach and nearby lymph nodes, and has metastasized (spread) through the lymphatic system or blood stream to distant organs. Distant organ spread includes lymph nodes that are not near the stomach, and distant organs such as the bones, lungs, or brain. Spread through the bloodstream to the liver that has led to one or more tumor nodules inside the liver is considered distant spread. In contrast, spread beyond the stomach wall with growth into (and possibly, through) the surface of the liver is considered extensive local spread.

If you have any questions about your stage, ask your doctor to explain the extent of your disease. Remember that the stage of a stomach cancer is the most important factor in considering treatment options and in predicting outlook for survival.

How Is Stomach Cancer Treated?

No matter what stage of stomach cancer you have, treatment is available. The choice of treatment you receive depends on many factors. The location and the *stage* (extent of spread) of the tumor are very important, of course. But in creating your treatment plan, you and your cancer care team will also take your age, general state of health, and personal preferences into account.

The three main treatments for stomach cancer are surgery, chemotherapy, and radiation therapy.

Often the best approach involves using two or more of these treatment methods. Your recovery is one goal of your cancer care team. If a cure is not possible, treatment is aimed at relieving symptoms, such as pain or bleeding. It is important that you understand the goal of your treatment, whether to cure or to *palliate* (relieve symptoms), prior to starting treatment.

Surgery

Depending on the type and stage of stomach cancer, surgery may be used to remove the cancer and part or all of the stomach.

Currently, surgery is the only way to cure stomach cancer. If a patient has a stage 0, I, II, or III cancer, and is able to tolerate an operation, an attempt should be made to treat the cancer by completely removing it. Even when the cancer is too widespread to be completely removed by surgery, most patients are helped by an operation to control bleeding or to prevent the flow of food through the stomach from being blocked. This type of surgery is called *palliative surgery*, meaning that it relieves or prevents symptoms but it is not expected to cure the cancer.

The particular operation performed usually depends on what part of the stomach is involved (proximal or distal) and how much cancer is in the surrounding tissue. There are three primary types:

Distal subtotal gastrectomy: This operation removes the distal part of the stomach (lower portion of the stomach closest to the intestines). Sometimes the first part of the small intestine (the *duodenum*) is also removed.

Proximal subtotal gastrectomy: This operation removes the proximal parts of the stomach (upper portion of the stomach closest to the esophagus). The nearby end of the esophagus may also be removed.

Total gastrectomy: This operation removes the entire stomach.

Usually in curative resections (operations intended to cure the cancer by completely removing it), the nearby lymph nodes and some of the *omentum* (fatty tissue in the abdomen) are removed. Lymph nodes are bean-sized collections of immune system tissue that are important in fighting infections and cancers. Stomach cancer often spreads to lymph nodes. The *omentum* is an area of fatty tissue near the stomach and intestines. The spleen is a collection of immune system cells and tissues that filter the blood to remove worn-out blood cells. It is located next to the stomach. If a cancer has extended beyond the stomach to the spleen, the spleen is usually removed together with the stomach, lymph nodes, and omentum.

Possible complications of stomach surgery include excessive bleeding, blood clots, and damage to nearby organs such as the gallbladder and pancreas during the operation. Rarely, the connections between the ends of the stomach and esophagus or small intestine may not hold together completely. During the 1950s, the risk of fatal complications after surgery for stomach

cancer was nearly 10%. Thanks to improvement in surgical techniques, the rate had dropped to approximately 1% to 2%. Possible side effects include abdominal pain, heartburn, and vitamin deficiencies. The stomach is important in helping the body absorb certain vitamins. If certain parts of the stomach are removed, doctors routinely prescribe vitamin supplements, some of which can be taken only by injection. Changes in the diet are often necessary after a partial or total gastrectomy (surgery to remove all or part of the stomach). Smaller, more frequent meals are often recommended for these patients by their doctors.

Chemotherapy

Chemotherapy uses anticancer drugs that are given most commonly in a vein or by mouth. These drugs enter the bloodstream and reach all areas of the body, making this treatment useful for cancer that has *metastasized* (spread) to organs beyond the stomach. Chemotherapy may be given as the primary (main) treatment for stomach cancer that has spread to distant organs. Chemotherapy is being studied as an *adjuvant* (treatment in addition to surgery) or as a *neoadjuvant* (before surgery) therapy. Studies completed so far have found that chemotherapy may help relieve symptoms for some patients, especially those with *metastases* (cancer that has spread from the primary tumor to other areas of the body). There is some evidence that chemotherapy (alone or together with radiation therapy) may delay cancer recurrence and extend the lifespan of people with less advanced stomach cancer, especially if their cancer could not be removed completely by surgery.

Chemotherapy for stomach cancer may use one drug such as fluorouracil (5FU), which is often combined with radiation therapy. Or, chemotherapy may use a combination of several anticancer drugs. These combinations, abbreviated by the first letter of the generic or brand names of each drug, include:

- FAM: 5-fluorouracil (5-FU), doxorubicin (Adriamycin), and mitomycin
- FAME: 5-fluorouracil, doxorubicin (Adriamycin), and methyl-CCNU
- FAP: 5-fluorouracil, doxorubicin (Adriamycin), and cisplatin (Platinol)
- FAMTX: 5-fluorouracil (5-FU), doxorubicin (Adriamycin), and methotrexate
- EAP: etoposide, doxorubicin, and cisplatin (Platinol)
- ELF: etoposide, leucovorin, and 5-fluorouracil
- PELF: cisplatin (Platinol), etoposide, leucovorin, and 5-fluorouracil with glutathione and filgrastim (Neupogen), a growth factor to reduce the side effects of chemotherapy on white blood cell production.
- ECF: epirubicin, cisplatin (Platinol), and 5-fluorouracil

Chemotherapy drugs kill cancer cells but also damage some normal cells. Therefore, careful attention must be given to preventing 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, diarrhea, 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 low white blood cells), bleeding or bruising after minor cuts or injuries (due to a low blood platelets), and fatigue and shortness of breath (due to low red blood cell counts).

Most side effects disappear once treatment is stopped. Hair will grow back after treatment ends, although it may look different. It is important to communicate your side effects from chemotherapy to your doctor and/or nurse. 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.

Radiation Therapy

Radiation therapy uses high energy rays or particles to kill cancer cells in a specific area of the body. *External beam radiation therapy* uses radiation delivered from outside the body that is focused on the cancer. This type of radiation therapy is often used to treat *gastric* (stomach) cancer. After surgery, radiation therapy can be used to kill very small remnants of the cancer that cannot be seen and removed during surgery. Some studies suggest that radiation, especially when combined with chemotherapy drugs such as 5-fluorouracil (5-FU), can delay or prevent cancer recurrence after surgery and may help patients to live longer. Radiation therapy can also be used to *palliate* (ease) symptoms of gastric cancer, such as pain, bleeding, and difficulty eating.

Side effects of radiation therapy may include mild skin problems, nausea, vomiting, diarrhea, or fatigue. Often these go away after a short while. Radiation therapy may make the side effects of chemotherapy worse. Talk with your doctor about these side effects since there are ways to relieve them.

Clinical trials

Studies of promising new or experimental treatments in patients are known as clinical trials. 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 anticancer effect by careful measurement of cancer sites which were present at the beginning of the trial. In addition to monitoring patients for a 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 managed?
- 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 (NCI) toll free at 1-800-4-CANCER or visiting the NCI clinical trials website for patients (cancertrials.nci.nih.gov) or health care professionals (cancernet.nci.nih.gov/prot/protsrch.shtml).

Treatment Choices by Type and Stage of Stomach Cancer

Stage 0

Because stage 0 cancers are limited to the lining layer of the stomach and have not invaded the underlying tissue of the stomach, they are treatable by surgery alone. No chemotherapy or radiation therapy is needed. They are usually treated by *gastrectomy* (surgical removal of part or all of the stomach) and *lymphadenectomy* (removal of the nearby lymph nodes).

Stage I

Most patients with stage I stomach cancer have their cancer surgically removed by a total or partial gastrectomy (the complete or partial removal of the stomach), and removal of the *omentum* (fatty tissue in the abdomen) and nearby lymph nodes. No additional therapy is usually required.

Stage II

Surgical removal of all or part of the stomach and an extended lymphadenectomy (removal of more lymph nodes) is the treatment of choice. Clinical trials of *adjuvant* chemotherapy and/or radiation therapy (treatment in addition to surgery) may be tried if the cancer is found to have invaded the outer part of the stomach wall or spread to more than three lymph nodes. Adjuvant therapy may also be recommended if the operation did not remove all of the cancer from the stomach.

Stage III

Patients with this stage should undergo surgery (unless they have other medical conditions that make them too ill for surgery) because up to 15% may be successfully treated. Patients with stage III stomach cancers should be considered for clinical trials of adjuvant chemotherapy and/or radiation therapy, depending on exactly how far their cancer has spread and on the number of lymph nodes involved. Adjuvant therapy may also be recommended if the operation did not remove all the cancer from the stomach.

Stage IV

Because stage IV stomach cancer has spread to distant organs, a cure is not possible. Sometimes surgery to prevent obstruction (blockage) of the stomach and/or intestines or to control bleeding is needed. In some cases, a laser beam directed through the endoscope can vaporize most of the tumor and relieve obstruction without surgery.

Chemotherapy and/or radiation therapy is not expected to cure the cancer but can often help relieve some symptoms. New treatments being tested in clinical trials may benefit some patients. Even if additional treatments to destroy or shrink the cancer are no longer an option, treatments are available to relieve pain and many other symptoms. Patients should not hesitate to tell their cancer care team about any symptoms they experience.

Survival Rate by Stage

The 5-year survival rate is greater than 90% in stages 0 and I gastric cancer, about 50% in stage II disease, 15% or less in stage III cancers, and about 3% in stage IV tumors. Most patients diagnosed with stomach cancer in the United States have stage III or stage IV cancers. It is important to keep in mind that these survival rates are only averages and that the outlook of any individual patient cannot be predicted with great accuracy. Although the stage of a cancer is useful in estimating a patient's outlook, it is not the only factor that influences survival. Some patients survive much longer than doctors would predict by considering their stage only.

What Should You Ask Your Doctor About Stomach Cancer?

As noted earlier, it is important to have honest, open discussions with your cancer care team. They want to answer all of your questions, no matter how trivial they might seem.

For instance, consider these questions:

- What kind of stomach cancer do I have?
- Has my cancer spread beyond the primary site?
- What is the stage of my cancer and what does that mean in my case?
- What treatment choices do I have?
- What do you recommend and why?
- What risks or side effects are there to the treatments you suggest?
- What are the chances of recurrence of my cancer with these treatment plans?
- What should I do to be ready for treatment?
- Based on what you've learned about my cancer, what is my *prognosis* (the outlook for chances of survival)?
- What is the goal of my treatment? To cure or to ease symptoms?

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

What Happens After Treatment For Stomach Cancer?

The cancer care team will recommend a schedule of follow-up physical examinations and tests. Blood tests, such as a complete blood count such and a blood chemistry, and chest x-rays are scheduled regularly. If these tests are abnormal or the patient has new symptoms, upper endoscopy with biopsies and imaging studies, such as CT scans or magnetic resonance imaging, may be done to look for recurrence or metastasis.

It is important for the patient to report any new symptoms or side effects to the doctor right away.

The doctors and other members of the health care team can help refer patients to other organizations for assistance. The American Cancer Society has information and programs to meet various medical, emotional, social, and financial needs of people living with cancer.

What's New In Stomach Cancer Research And Treatment?

There is always research going on in the area of stomach cancer. Scientists are looking for causes and ways to prevent stomach cancer, and doctors are working to improve treatments.

Dietary Risk Factors

Research done over many years has clearly shown that dietary differences are the most important factor in explaining variations in stomach cancer risk around the world. Recent research in countries with relatively low stomach cancer risk has provided some insight into risk factors. One risk factor is a diet high in red meat. Eating red meat more than 13 times per week doubles the risk of stomach cancer. The risk is increased even more if the meat is barbecued and well done.

Chemoprevention

Chemoprevention is the use of natural or man-made chemicals to lower the risk of developing cancer. Two types of chemicals might be useful in preventing stomach cancer: antioxidants and antibiotics.

Antioxidants: Many cancer-causing factors cause chemical changes in cells that form a type of chemical called a "free radical." Free radicals can damage important parts of cells such as genes. Depending on which cell chemicals are damaged and how severe the damage is, the cells may die or they may become cancerous. Antioxidants are a group of nutrients and other chemicals that can destroy free radicals or prevent them from forming. There are ongoing studies looking at the role of micronutrients in the diet, that have an antioxidant effect. These nutrients include

vitamin C, beta-carotene, and vitamin E (alpha-tocopherol). Whether these nutrients will be able to prevent stomach cancer is not yet known.

Antibiotics: Studies are being conducted to see if antibiotic treatment of people who are chronically infected by the bacteria *Helicobacter pylori* will help prevent stomach cancer.

Treatment

Clinical trials are currently in progress to find out whether the addition of chemotherapy and/or radiation therapy after a stomach cancer is removed helps a patient live longer. *Neoadjuvant therapy* (chemotherapy and radiation therapy prior to definitive surgery) is being studied in patients with large cancers. This approach may improve the effectiveness of operations to remove the cancer. New drugs such as paclitaxel (Taxol), irinotecan, aminocamptothecin, and gemcitabine, and new combinations of older drugs are being tested. Very high dose chemotherapy followed by stem cell transplantation is being studied in patients with advanced stomach cancers. Use of high intensity radiation directly aimed at the tumor during surgery is being studied. Other studies are testing even newer approaches to treating stomach cancer. These include vaccines to boost the immune system's ability to fight the cancer and antibodies that target radiation or chemotherapy directly at the cancer cells.

Additional Resources

National Organizations and Web Sites

The following organizations can also provide additional information and resources. *

National Cancer Institute
Telephone: 1-800-4-CANCER
Internet Address: www.nci.nih.gov

National Coalition for Cancer Survivorship
Telephone: 1-888-650-9127
Internet Address: www.cansearch.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)

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

Other Publications*

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

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