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Gastric Cancer: The Basics

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What is the stomach?

Gastric cancer is cancer of the stomach. The stomach is the organ that holds and stores food. It is located just underneath (deep to) the lower portion of the rib cage on the left side. It is connected to the mouth and throat by the esophagus. The stomach contains acid and is quite muscular. Due to the motion of the stomach and the acid, quite a bit of digestion takes place in the stomach. The partially digested food is then emptied into the small intestine so that absorption of the nutrients from food can take place.

What is gastric cancer?

The definition of a tumor is a mass of quickly and abnormally growing cells. Tumors can be either benign or malignant. Benign tumors have uncontrolled cell growth, but without any invasion into normal tissues and without any spread. A malignant tumor is called cancer when these tumor cells gain the ability to invade tissues and spread locally as well

as to distant parts of the body. In this sense, gastric cancer occurs when cells in the lining of the stomach grow uncontrollably and form tumors that can invade normal tissues and spread to other parts of the body.

Cancers are described by the types of cells from which they arise. Over 90% of gastric cancers arise from the lining of the stomach. Since this lining has glands, the cancer that comes from it is called adenocarcinoma. Although there are other cancers that can arise in the stomach (lymphomas-from lymph tissue, leiomyosarcoma-from muscle tissue, squamous cell carcinoma-from lining without glands), the vast majority of gastric cancers are adenocarcinomas. Hence, these are the most commonly studied.

Am I at risk for gastric cancer?

In the United States, in 2015, there are expected to be about 24,590 gastric cancers diagnosed, with an estimated 10,720 deaths attributed to this disease. Interestingly, its incidence has drastically decreased since 1930. Although it is presumed that this is due to some sort of dietary or environmental factor(s), the exact reason behind this decrease is not known. One theory is that the advent of refrigeration led to decreased use of nitrites, "smoking" of foods, and other such forms of food preservation. Gastric cancer is approximately twice as common in men and more common in Blacks than Caucasians. It is rare to see gastric cancer before the age of 40, and its incidence increases with age. There are two types of gastric cancer, the intestinal type and the diffuse type. This is determined by the pathologist, with the diffuse type carrying a worse prognosis.

Although gastric cancer has greatly decreased in the United States, on a worldwide scale its incidence is still high, and it is the second leading cause of cancer death worldwide, behind lung cancer. Its highest incidence is in East Asia (e.g.-Japan, China), presumably because of a diet consisting of heavily smoked, salted, and pickled foods. Interestingly, first generation immigrants from these countries have a decreased incidence of stomach cancer after moving to the United States, but it is still higher than the general American population. However, the incidence greatly declines in second and third generation Japanese and Chinese immigrants to the United States, pointing to the fact that there does not appear to be an inherently genetic component in Eastern Asians' risk to develop gastric cancer, but rather an environmental component.

As mentioned above, diets heavily salted, smoked, or pickled are associated with an increased risk of disease, while diets rich in fruits, vegetables, and dietary fiber are associated with a decreased risk of gastric cancer. The incidence of gastric cancers also increases with decreasing socioeconomic status, likely due to a number of social, occupational, and cultural factors. Tobacco use has also been associated with an increase in gastric cancers. There does not appear to be a link with alcohol consumption.

There does appear to be a genetic link in some cases of gastric cancer (5-10% of cases). There are some genetic diseases such as hereditary nonpolyposis colorectal cancer (<http://www.oncolink.org/types/article.cfm?aid=135&id=7017&c=122>), familial adenomatous polyposis, and Peutz Jeghers syndrome which all predispose to gastric cancer. It also appears that people with blood type A are at increased risk for gastric cancer for an unknown reason.

Hereditary diffuse gastric cancer (HDGC) is an inherited genetic abnormality that is associated with an increased risk of developing gastric cancer. The gene that is abnormal in HDGC is called CDH1 and the abnormality is referred to as a mutation. It is not known how many families carry the CDH1 mutation. Families that have had several cases of gastric cancer, particularly if they are the diffuse type, should consider genetic testing and screening options.

Studies have also linked infection with *Helicobacter pylori* with gastric cancer. *H. pylori* is associated with gastric ulcers and chronic atrophic gastritis, which may explain the higher incidence of gastric cancer in patients infected with *H. pylori*. However, the exact role of *H. pylori* in the development of gastric cancer remains unclear. It is theorized that *H. pylori* causes a gastritis or inflammation of the stomach, which can lead to a loss of secretory cells in the stomach, also known as atrophic gastritis. It is believed that this process of atrophy can lead to gastric cancer. *H. pylori* has also been linked to lymphomas of the stomach.

Pernicious anemia, an autoimmune disease where the stomach does not produce stomach acid, has also been linked to gastric cancer. Drugs which cause a decrease in stomach acid production have not been linked to an increased risk of gastric cancer.

It should be noted that, although these risk factors are listed above, the majority of gastric cancers develop without any one obvious predisposing cause. In other words, there is no extremely strong cause effect relationship with any risk factor, in contrast, for example, to that between smoking and lung cancer.

How can I prevent gastric cancer?

Because there is no one risk factor directly associated with gastric cancer, there is no strict lifestyle change that can greatly decrease a person's risk of developing gastric cancer. However, eating a "Western" type diet, without heavily smoked or salted foods and rich in fruits and vegetables will likely decrease a person's risk. Also, smoking cessation (<https://www.oncolink.org/risk/index.cfm?c=21>) will likely decrease gastric cancer risk (though smoking should be stopped for numerous other health reasons). Some have advocated the consumption of foods with high level of antioxidants and vitamin C to prevent gastric cancers, though this has not been definitively proven. Since *H. pylori* infections have been linked to the development of gastric cancers, the quick treatment of *H. pylori* infections may decrease the numbers of gastric cancers, though whether treating *H. Pylori* actually reduces the risk of gastric cancer remains controversial. The decision to treat *H. pylori* should be discussed with your physician.

What screening tests are available?

There are no established programs for primary prevention of gastric cancer in the United States. There are no plans to initiate a screening program in the United States, simply because the incidence of gastric cancer is fairly low, and thus the yield from gastric cancer screening would be far too low to approach cost-effectiveness. A few populations may be exceptions (e.g.-patients with known atrophic gastritis, a chronic inflammation of the stomach lining), but overall screening for gastric cancer in the United States would likely cause more problems than it would solve (i.e. a lot of false positives, or false alarms). Currently, screening for *H. Pylori* is not recommended for areas with a relatively low incidence of gastric cancer, such as in the United States.

In Japan, where gastric cancer is much more prevalent, screening programs have been successful and in place for more than 50 years. A variety of tests have been used in these screening programs, with the ability to accurately identify gastric cancers in over 90% of patients who actually have it. These tests include double-contrast barium radiographs (so-call "upper GIs" or "barium swallows") and upper endoscopies. An upper endoscopy (or an "EGD") is a test done using a camera at the end of a long tube that is placed down the patient's throat, into the stomach, by the gastroenterologist. The physician performing the EGD is able to directly visualize the stomach. Many abnormalities can be detected with an EGD-most importantly, ulcers and cancers. Patients are sedated during the procedure, so discomfort is kept to a minimum.

More recently, studies have verified the use of a blood test that could be used to screen for gastric cancer. This analyzes the presence of enzymes in the blood called the serum pepsinogen I/II ratio, which is low in patients at risk for atrophic gastritis and gastric cancer. However, this is still in the early stage of testing and needs to be verified. Patients who have an identified HDGC mutation CDH1, should have a screening EGD.

What are the signs of gastric cancer?

The symptoms of gastric cancer are often nonspecific, and the majority of people will unfortunately present with advanced disease. The vast majority of gastric cancer patients present with vague complaints such as upper abdominal discomfort or indigestion, loss of appetite, occasional vomiting, belching, or decreased ability to eat a large meal. Additional symptoms are unexplained weight loss, fatigue and weakness, with or without anemia. Again, these symptoms are vague. These symptoms are often the exact symptoms that patients experience when they have peptic ulcer disease or gastritis. Therefore, patients may be treated for benign diseases, such as ulcers, before the cancer diagnosis is made. This is not incorrect management, as gastritis and peptic ulcer disease are much more common than gastric cancer. However, if symptoms persist or do not respond to treatment, further evaluation should be done.

Other symptoms, such as vomiting blood or problems with swallowing, are less common, but should be investigated without delay. Advanced disease can present with palpable lymph nodes (able to be felt by the healthcare provider) with masses in the area of the belly button, the underarms, or the clavicle. People with advanced disease may also present with abdominal swelling.

How is gastric cancer diagnosed and staged?

How is gastric cancer diagnosed and staged?

Diagnosis

Upper EGD, is routinely used for the initial diagnosis and staging of patients with gastric cancer. Using endoscopy, the diagnosis can be obtained in over 95% of cases. Many times, ultrasound during endoscopy is used to attempt to identify how deep into the wall of the stomach the cancer has penetrated. In addition, ultrasound can identify spread to lymph nodes in many cases. Depth of wall invasion and presence of lymph node spread are two very important components of treatment, as the surgeon uses this information to determine if surgery is a treatment option.

Other procedures are needed to determine the stage of the disease. CT scans (<http://www.oncolink.org/treatment/article.cfm?c=248&aid=723&id=492>) ("CAT scans") of the abdomen and chest are done, not only to rule out spread to distant organs, like the liver and lungs, but also to determine the spread to lymph nodes close to the stomach that could not be identified by ultrasound. Other tests to rule out abdominal spread of disease outside of the stomach itself are PET scans (<http://www.oncolink.org/treatment/article.cfm?c=209&aid=778&id=581>), which use radioactive solutions to identify tumors, and laparoscopy.

Laparoscopy is a surgical procedure that involves puncturing the abdominal cavity with a fiber optic camera and directly viewing the organs and tissues in the area of the stomach, the entire abdominal cavity, and the lining of the abdomen (omentum and peritoneum). A sample of abdominal fluid can be sent to cytology/pathology to check for cancer cells in the fluid. (Learn more about your pathology report (<http://www.oncolink.org/treatment/article.cfm?id=7138&aid=7138>).

Other, more routine tests done before treatment include blood screening tests, to insure that overall blood counts are within normal limits, to check for anemia and that a patient's liver and kidneys are functioning properly.

All of these tests are important to determine the extent of the disease, which allows the disease to be staged. The stage provides a guideline for the optimal treatment of the gastric cancer.

How does gastric cancer spread?

Before the staging systems are introduced, here is some background on how cancers grow and spread, and therefore become more advanced in stage.

Cancers cause problems because they spread and can disrupt the functioning of normal organs. One way gastric cancer can spread is by local extension to invade through the stomach wall and into adjacent structures. These surrounding structures include the soft tissues and fat surrounding the stomach as well as other organs such as the spleen, pancreas, large intestine, small intestine, liver, and large blood vessels.

Gastric cancer can also spread by accessing the lymphatic system. The lymphatic circulation is a complete circulation system in the body (somewhat like the blood circulatory system) that drains into various lymph nodes. When cancer cells access this lymphatic circulation, they can travel to lymph nodes and start new sites of cancer. This is called lymphatic spread. Gastric cancers have a propensity to undergo lymphatic spread because there are many small lymphatic vessels contained within the stomach wall. The first lymph nodes that cancer cells spread to are the "perigastric" nodes along the sides of the stomach itself. They can then spread to lymph nodes adjacent to the liver, spleen, pancreas, and aorta.

Gastric cancers can also spread through the bloodstream. Cancer cells gain access to distant organs via the bloodstream and the tumors that arise from these cells are called metastases. Because of the stomach's blood supply, the most common organ it spreads to is the liver, though tumors can also spread to the lung or other organs less commonly.

A fourth way gastric cancer can spread is throughout the entire abdomen, the so-called peritoneal cavity. Although rare, once cancer cells grow outside of the stomach itself, there is nothing stopping cells from spreading to any surface in the entire abdominal cavity.

Staging

The staging of a cancer basically describes how much it has grown before the diagnosis is made, documenting the extent of disease. Unfortunately, gastric cancer often presents as a more advanced disease because of lack of early diagnosis, due mainly to the vague associated symptoms. The TNM system is used to describe many types of cancers. It has three components: T-describing the extent of the "primary" tumor (the tumor in the stomach itself); N-describing the spread to the lymph nodes; M-describing the spread to other organs (i.e.-metastases).

The "T" stage is as follows:

- Tx- Primary tumor cannot be assessed
- Tis-"in-situ cancer" - intraepithelial tumor without invasion of the lamina propria (stomach wall)
- T0- No evidence of primary tumor
- T1-tumor invades into only the superficial portions of the stomach wall (lamina propria, muscularis mucosa and submucosa)
- T1b: invades submucosa
- T2-tumor invades into muscular layers of the stomach wall (muscularis propria)
- T3-tumor extends through the stomach wall into the subserosal connective tissue without invasion of the visceral peritoneum or adjacent structures
- T4-tumor extends outside the stomach wall and invades the visceral peritoneum or adjacent structures (Spleen, transverse colon, liver, diaphragm, pancreas, abdominal wall, adrenal glands, kidney, small intestine, and retroperitoneum)
- T4a – invades serosa (visceral peritoneum) T4b- invades the adjacent structures

The "N" stage is as follows:

- Nx- Number of lymph nodes cannot be assessed
- N0-no spread to lymph nodes
- N1-tumor spread to 1-2 lymph nodes
- N2-tumor spread to 3-6 lymph nodes
- N3-tumor spread to more than 6 lymph nodes
- N3a: spread to 7-15 lymph nodes
- N3b: spread to 16 or more lymph nodes

The "M" stage is as follows:

- M0-no tumor spread to other organs
- M1-tumor spread to other organs

The overall stage is based on a combination of these T, N, and M parameters:

- Stage 0 - Tis N0M0
- Stage IA-T1N0M0
- Stage IB-T1N1M0 or T2N0M0
- Stage IIA-T1N2M0 or T2N1M0 or T3N0M0
- Stage IIB-T1N3M0 or T2N2M0 or T3N1M0 or T4aN0M0
- Stage IIC- T4aN3M0, T4bN3M0, T4bN2M0
- Stage IIIA-T2N2M0 or T2N2M0 or T4aN1M0

- Stage IIIA- T4N3M0 or T3N2M0 or T4aN1M0
- Stage IIIB - T4bN0M0 or T4bN1M0 or T4aN2M0 or T3N3M0
- Stage IV- any T, any N, M1

Though complicated, this staging system help physicians determine the extent of the cancer, and therefore make treatment decisions regarding a patient's cancer. The stage of cancer, or extent of disease, is based on information gathered through various tests done as the diagnosis and work-up of the cancer is being performed.

What are the treatments for gastric cancer?

Currently, all curative treatments for gastric cancer involve surgery (surgical resection of the cancer). The smallest amount of surgery that is possible while still taking out all of the cancer is what is normally performed. Generally, tumors that are localized to the part of the stomach closest to the esophagus (proximal stomach) are treated with a gastrectomy (removal of the entire stomach). A partial gastrectomy is the removal of only a portion of the stomach, in contrast to a total gastrectomy, which is done when the tumor is larger. Partial gastrectomies may be appropriate for those tumors located further from the esophagus, in the distal portion of the stomach. For partial gastrectomy, the surgical margin around the gastric cancer needs to be 5 cm, i.e., there needs to be 5 cm of normal stomach tissue around the tumor in the portion of the stomach removed. Disease involving the entire stomach is also an indication for a total gastrectomy. The surgeon removes the cancer with an adequate margin of healthy tissue and the surrounding lymph nodes. How extensive of a lymph node dissection to perform is controversial, with contradictory data from the United States compared with Japan. However, it is import that an experienced surgeon performs the dissection as it is a difficult surgery. Obviously, when the stomach or a portion of the stomach is removed, the two ends must be rejoined. This is done by various procedures, all attempting to eliminate as many of the side effects of the surgery as possible, such as inability to eat larger meals and the so-called "dumping syndrome." Dumping syndrome results from the stomach being removed and the result of the small intestine filling too rapidly with undigested food. Symptoms include nausea, vomiting, bloating, diarrhea, and even shortness of breath. These symptoms can usually be managed with dietary modifications.

Although surgery is always required for curative treatment, it is often not enough to achieve cure in many cases. The majority of cases of early gastric cancer are cured by surgery alone. However, in most patients with more advanced cases of gastric cancer, such as those with positive lymph nodes or tumors which have invaded the deep layers of the stomach or beyond, the cancer will come back if only surgery is done. Up to two-thirds of these patients recur, with cancer coming back in their lymph nodes or other organs. To combat this, radiation therapy and chemotherapy are recommended for many patients. It is felt that any patient with stage IB or higher gastric cancer (involvement of deeper portions of the stomach wall or any lymph nodes involved with cancer) will benefit from additional therapy with concurrent radiation and chemotherapy.

Radiation therapy (<http://www.oncolink.org/treatment/article.cfm?c=154&aid=586&id=322>) makes the use of high energy x-rays to kill cancer cells. It does this by damaging the DNA in tumor cells. Normal cells in our body can repair radiation damage much quicker than tumor cells, so while tumor cells are killed by radiation, many normal cells are not. This is the basis for the use of radiation therapy in cancer treatment. Radiation is delivered using large machines that produce the high energy x-rays. After radiation oncologists set up the radiation fields ("radiation fields" are the areas of the body that will be treated by radiation), treatment is begun. Radiation is given 5 days a week for approximately 5 weeks at a radiation treatment center. The treatment takes just a few minutes each day and is completely painless. The typical radiation field used in the treatment of gastric cancer includes portions of the upper abdomen. In other words, it is designed to kill tumor cells in the area that the surgery was performed. Typical side effects include nausea and vomiting (though this should be less of a problem since the stomach has already been removed) and diarrhea.

Chemotherapy (<http://www.oncolink.org/treatment/article.cfm?c=142&aid=582&id=319>) is defined as drugs that are used to kill tumor cells. The large advantage in using chemotherapy is that, it travels through the entire body. Hence, if some tumor cells have spread outside of what surgery or radiation can treat, they can potentially be killed by chemotherapy. Similar to radiation, some normal cells are damaged during treatment, resulting in side effects. The standard chemotherapy used in the treatment of gastric cancer is called 5-FU (<http://www.oncolink.org/treatment/article.cfm?c=2&id=172&aid=465>) (fluorouracil), coupled with another drug called leucovorin. This type of chemotherapy is delivered through the vein. Sometimes chemotherapy and radiation are used prior to surgery. Other chemotherapy agents used to treat gastric cancer include: epirubicin (<http://www.oncolink.org/treatment/article.cfm?c=2&id=313&aid=576>), cisplatin (<http://www.oncolink.org/treatment/article.cfm?c=2&id=117&aid=455>), paclitaxel (<http://www.oncolink.org/treatment/article.cfm?c=2&id=145&aid=430>), oxaliplatin (<http://www.oncolink.org/treatment/article.cfm?c=2&id=203&aid=354>), and 5-fluorouracil. About 20% of gastric cancers overproduce a protein called HER-2; in such cases the addition of Herceptin (<http://www.oncolink.org/treatment/article.cfm?c=2&id=343&aid=608>), a biological agent, to chemotherapy has been shown to improve survival for patients with advanced disease. Ramucirumab (<http://www.oncolink.org/treatment/article.cfm?c=2&id=7048&aid=7048>) is a therapy that targets vascular endothelial growth factor receptor (VEGF), which works by preventing growth of the blood supply to the tumor.

The biology of stomach cancer is key to developing new treatment for gastric cancer. Areas of research include evaluating the role of immunotherapy and investigating the role of epidermal growth factor receptors (EGFR) and angiogenesis inhibitors.

Follow-up testing for gastric cancer

Once someone completes treatment for gastric cancer (including surgery +/- radiation and chemotherapy), he or she needs to be closely followed by the oncology team. This close follow-up is required for a couple of reasons. First, to evaluate the patient for side effects related to their treatment. This includes ensuring that the patient has no vomiting or diarrhea and has healed from surgery. Symptoms of "dumping syndrome" may need to be addressed with dietary modifications. In addition, because of the removal of the stomach or a portion of the stomach, gastric cancer patients are prone to a certain type of anemia, resulting from not having enough vitamin B-12. This will be monitored for the patient's entire life, as this anemia does not usually occur until years after the surgery.

The other major reason a patient needs to be followed closely is to make sure their cancer does not recur. Recurrence can be detected using physical exam, repeat, periodic endoscopies, and CT scans. The National Comprehensive Cancer Network guidelines (NCCN) recommend follow up every 3 to 6 months following initial treatment for two years then every 6 months for years 3-5. Labs and imaging studies are done as indicated. Patients do need to be monitored for nutritional deficiencies, especially if they have had surgery.

After treatment, talk with your oncology team about receiving a survivorship care plan, which can help you manage the transition to survivorship and learn about long-term concerns and life after cancer. You can create a care plan on OncoLink (<http://www.livestrongcareplan.org/>).

Resources for Further Reading

Gastric Cancer Foundation (<http://www.gastriccancer.org/>)

GCF serves as a comprehensive resource for anyone with stomach cancer, their family, friends or caregivers – after a new diagnosis, during treatment and post-treatment. Also operates a Gastric Cancer Registry to assist in research.

No Stomach for Cancer (<http://www.nostomachforcancer.org/>)

Empowering families by providing information on stomach cancer and a community of support.

Debbie's Dream Foundation: Curing Stomach Cancer (<http://www.debbiesdream.org/>)

Raising awareness, funding research, and supporting patients through education, an online community and a clinical trials matching service.

National Institute of Health Medline Plus Stomach Cancer (<http://www.nlm.nih.gov/medlineplus/stomachcancer.html>)

Provides information on treatment and research, much of it in Spanish.

Hereditary Diffuse Gastric Cancer (<http://www.cancer.net/cancer-types/hereditary-diffuse-gastric-cancer>) - From cancer.net

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National Cancer Institute Dictionary of Cancer Terms

Find easy-to-understand definitions of terms related to cancer and medicine.



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