Gastrointestinal Carcinoid Tumors

What is cancer?

The body is made up of trillions of living cells. Normal body cells grow, divide into new cells, and die in an orderly fashion. During the early years of a person's life, normal cells divide faster to allow the person to grow. After the person becomes an adult, most cells divide only to replace worn-out or dying cells or to repair injuries.

Cancer begins when cells in a part of the body start to grow out of control. There are many kinds of cancer, but they all start because of out-of-control growth of abnormal cells.

Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells continue to grow and form new, abnormal cells. Cancer cells can also invade (grow into) other tissues, something that normal cells cannot do. Growing out of control and invading other tissues are what makes a cell a cancer cell.

Cells become cancer cells because of damage to DNA. DNA is in every cell and directs all its actions. In a normal cell, when DNA gets damaged the cell either repairs the damage or the cell dies. In cancer cells, the damaged DNA is not repaired, but the cell doesn’t die like it should. Instead, this cell goes on making new cells that the body does not need. These new cells will all have the same damaged DNA as the first cell does.

People can inherit damaged DNA, but most DNA damage is caused by mistakes that happen while the normal cell is reproducing or by something in our environment. Sometimes the cause of the DNA damage is something obvious, like cigarette smoking. But often no clear cause is found.

In most cases the cancer cells form a tumor. Some cancers, like leukemia, rarely form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Cancer cells often travel to other parts of the body, where they begin to grow and form new tumors that replace normal tissue. This process is called metastasis. It happens when the cancer cells get into the bloodstream or lymph vessels of our body.

No matter where a cancer may spread, it is always named for the place where it started. For example, breast cancer that has spread to the liver is still called breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bone is metastatic prostate cancer, not bone cancer.

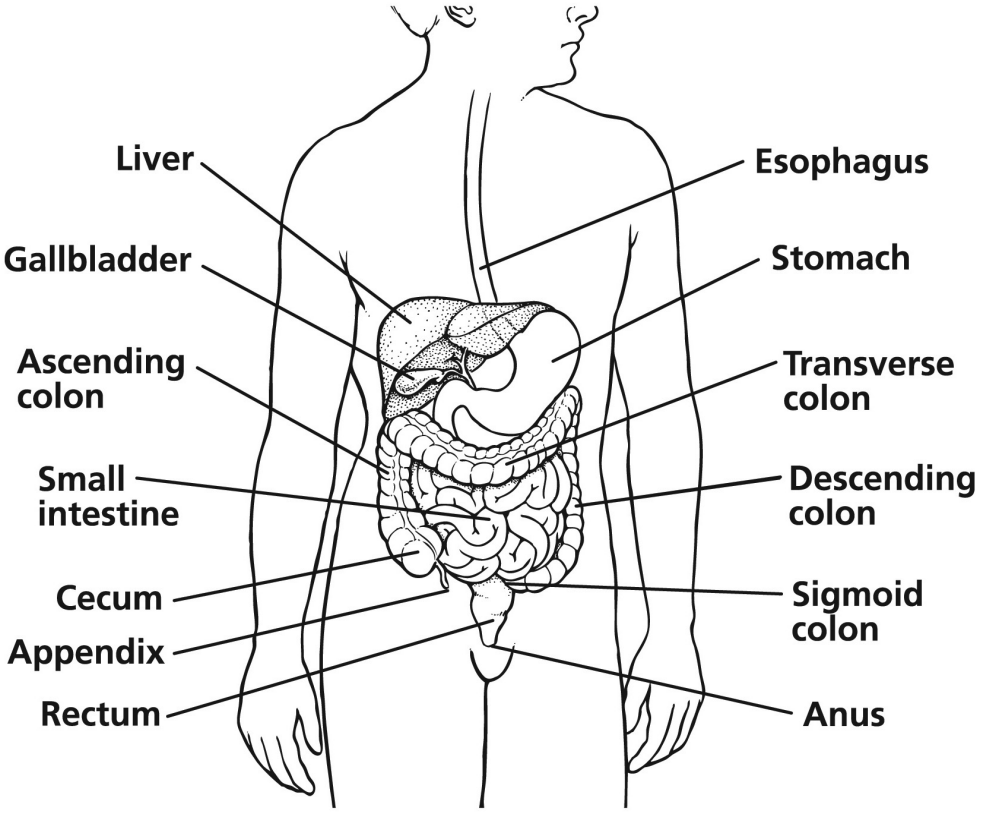
Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

Not all tumors are cancerous. Tumors that aren't cancer are called benign. Benign tumors can cause problems – they can grow very large and press on healthy organs and tissues. But they cannot grow into (invade) other tissues. Because they can't invade, they also can't spread to other parts of the body (metastasize). These tumors are almost never life threatening

What is a gastrointestinal carcinoid tumor?

The gastrointestinal system

The gastrointestinal (GI) system processes food for energy and rids the body of solid waste. It is also known as the *digestive system*. After food is chewed and swallowed, it enters the esophagus. This tube carries food through the neck and chest to the stomach. The esophagus joins the stomach just beneath the diaphragm (the breathing muscle under the lungs). The stomach is a sac-like organ that holds food and begins the digestive process by secreting gastric juice. The food and gastric juices are mixed into a thick fluid, which then empties into the small intestine.



The small intestine continues breaking down food and absorbs most of the nutrients. It is the longest section of the gastrointestinal (GI) tract, measuring more than 20 feet. The small intestine then joins the colon (large intestine). This is a wider, muscular tube about 5 feet long. The appendix is found near the junction of small intestine and colon. The colon absorbs water and mineral nutrients from the food matter and serves as a storage place for waste. The waste left after this process goes into the rectum. From there it passes out of the body through the anus as stool (feces).

The diffuse neuroendocrine system

Carcinoid tumors start from cells of the diffuse neuroendocrine system. This system consists of cells that are like nerve cells in certain ways and like hormone-making endocrine cells in other ways. These cells do not form an actual organ like the adrenal or thyroid glands. Instead, they are scattered throughout other organs like the esophagus, stomach, pancreas, intestines, and lungs. The digestive system is large and has more neuroendocrine cells than any other part of the body. This might be why carcinoid tumors most often start in the digestive system.

Neuroendocrine cells help control the release of digestive juices and how fast food moves in the GI tract. They may also help control the growth of other types of digestive system cells.

Neuroendocrine tumors

Like most cells in the body, GI tract neuroendocrine cells sometimes go through certain changes that cause them to grow too much and form tumors. These tumors are known as *neuroendocrine tumors* (NET) and *neuroendocrine cancers*. In the past, most abnormal growths of neuroendocrine cells were called *carcinoids*. But in 2000, the World Health Organization (WHO) reclassified carcinoids as neuroendocrine tumors and neuroendocrine cancers.

Neuroendocrine tumors are growths that look benign but that might possibly spread to other parts of the body. Neuroendocrine cancers are abnormal growths of neuroendocrine cells which can spread to other parts of the body.

Neuroendocrine cancers (also known as *neuroendocrine carcinomas*) are divided into groups based on the way the cells look under a microscope:

- *Well differentiated* neuroendocrine cancers have cells that do not look very abnormal and are not multiplying rapidly. These tumors tend to be less aggressive, meaning that they tend to grow and spread slowly. Well differentiated neuroendocrine cancers can look identical to benign neuroendocrine tumors when examined under the microscope. Sometimes the only way to know for certain that a mass is a neuroendocrine cancer (and not a benign tumor) is when it spreads to other organs or tissues.
- *Poorly differentiated* cancers have cells that look very abnormal and are multiplying more rapidly. Poorly differentiated cancers tend to be more aggressive, meaning that they grow and spread quickly.
- *Moderately differentiated* cancers have features in between those of well differentiated and poorly differentiated cancers.

Neuroendocrine tumors of the pancreas

Neuroendocrine tumors in the pancreas are known as *islet cell carcinomas* or *pancreatic neuroendocrine tumors.* Islet cell tumors are not the same as carcinoid tumors. They have a different prognosis (course of disease and outlook) and respond differently to treatment. This document does not discuss neuroendocrine tumors, but you can find more information in our document *Pancreatic Cancer*.

Carcinoid tumors

Carcinoid is the term used to describe well to moderately differentiated neuroendocrine tumors in the stomach, intestine, appendix, rectum, and lung. This document does not discuss

carcinoid tumors that start in the lung, but you can find more information in our document *Lung Carcinoid Tumor*.

Neuroendocrine tumors and cancers act like the cells they come from, often releasing certain hormone-like substances into the bloodstream. In most people with carcinoid tumors, the levels of these hormones are not high enough to cause symptoms. But in about 1 person out of 10 with carcinoid tumors, the tumor spreads and grows enough to release high amounts of these hormones. This can cause a set of symptoms known as the *carcinoid syndrome*. Some symptoms of the carcinoid syndrome include flushing (redness of the skin with a feeling of warmth), wheezing, diarrhea, and a fast heartbeat.

Other gastrointestinal tumors

Carcinoids and other neuroendocrine tumors are different from the more common tumors of the GI tract. Most GI tract tumors start from the glandular cells that produce mucus and make up the inner lining of the digestive system. When these tumors are benign, they are called *adenomas.* When these cells develop into cancer, the tumors are known as *adenocarcinomas.* These tumors differ quite a lot from carcinoid tumors in their symptoms, their outlook, and their treatment. For these reasons, it is important to know what type of tumor you have: a neuroendocrine tumor, a neuroendocrine cancer, an adenoma, an adenocarcinoma, some other type of tumor, or a non-cancerous condition. And it is important to understand that neuroendocrine tumors and neuroendocrine cancers are not the same as other, more common types of GI tract tumors. Information about adenocarcinomas of the GI tract can be found in our documents *Esophagus Cancer*, *Stomach Cancer*, *Small Intestine Cancer*, and *Colorectal Cancer*.

In general, neuroendocrine tumors and neuroendocrine cancers grow slower than other cancers in the GI tract. But how they grow and whether or not they spread to other areas varies widely. This depends to some extent on which part of the body the tumor starts in.

What are the key statistics about gastrointestinal carcinoid tumors?

Although the exact number isn’t known, about 8,000 neuroendocrine tumors and cancers that start in the gastrointestinal tract (the stomach, intestine, appendix, colon, or rectum) are diagnosed each year in the United States. These tumors can also start in the lungs (see our document *Lung Carcinoid Tumor* for more information) and the pancreas, although a small number develop in other organs.

The number of carcinoid tumors diagnosed has been increasing for many years. The reason for this is unknown. Some think it may be a byproduct of doing more endoscopy and CT scans to look for something else and finding carcinoid tumors. Since many carcinoids never cause any symptoms, there are probably many people with carcinoid tumors that are never

found. These tumors may only be seen during an autopsy when a person dies of something else, or when someone has surgery or imaging tests for an unrelated condition.

The most common location of gastrointestinal carcinoid tumors is the small intestine, often in the section near the appendix (called the *ileum*). Other common sites include the rectum, the colon (large intestine), the appendix, and the stomach.

The average age of people diagnosed with carcinoid is early 60s. Carcinoid tumors are more common in African Americans than in whites, and are slightly more common in women than men.

What are the risk factors for gastrointestinal carcinoid tumors?

A *risk factor* is anything that affects your chance of getting a disease such as cancer. For example, exposure to strong sunlight is a risk factor for skin cancer, while smoking is a risk factor for cancer of the lung, and several other cancers. But risk factors don't tell us everything. Someone without any known risk factors can still develop cancer. And someone can have a risk factor, but still not get the disease. Only a few risk factors for GI carcinoid tumors are known.

Genetic syndromes

Multiple endocrine neoplasia, type I

This is a rare condition caused by inherited defects in the gene *MEN1*. People with this syndrome have a very high risk of getting tumors of 3 glands: the pituitary, parathyroid, and pancreas. They also have an increased risk of carcinoid tumors. Some studies estimate that inherited mutations of the *MEN1* gene are responsible for about 10% of carcinoid tumors. Most of these are gastric (stomach) carcinoids. Children have a 50/50 chance of inheriting this syndrome from an affected parent.

If your family is affected by the MEN1 syndrome, you might want to talk to your doctor about the pros and cons of getting tested for it. Although the gene that causes tumors in people with the MEN1 syndrome has been found, genetic testing for MEN1 is not widely available. Because the results of genetic testing are not always clear cut, it is important that the test is done along with genetic counseling to help you make sense of the results.

Neurofibromatosis type 1

This disease often runs in families and is characterized by many *neurofibromas* (benign tumors that form in nerves under the skin and in other parts of the body).It is caused by

defects in the gene *NF1*. Some people with this condition also develop neuroendocrine tumors of the small intestines.

Other genetic syndromes

Neuroendocrine tumors are also more common among people with tuberous sclerosis complex and von Hippel Lindau disease. Tuberous sclerosis complex can be caused by a defect in the *TSC1* gene or the *TSC2* gene. People with this condition may also develop tumors of the heart, eyes, brain, lungs, and skin. von Hippel Lindau disease is an inherited tendency to develop blood vessel tumors of the brain, spinal cord, or retina, as well as kidney cancer. It is caused by changes in the *VHL* gene.

To find our more on being tested for genetic syndromes, see our document *Genetic Testing: What You Need to Know*.

Race and gender

Carcinoid tumors are more common among African Americans than whites. Outcomes are also not as good for African Americans. Researchers do not yet know why. Carcinoid tumors are also slightly more common in women than men.

Other stomach conditions

People with certain diseases that damage the stomach and reduce the amount of acid it makes have a greater risk of developing stomach carcinoid tumors, but their risk for carcinoid tumors of other organs is not affected.

Factors with uncertain or unproven effects

Smoking

Smoking may double the risk of getting a carcinoid tumor of the small intestine, according to a recent European study. But further research is needed to confirm this.

Diet

The risk of developing GI carcinoid tumors does not appear to be increased or decreased by any specific foods.

Do we know what causes gastrointestinal carcinoid tumors?

Researchers have made great progress in understanding how certain changes in DNA can cause normal cells to become cancerous. DNA is the chemical in each cell that carries our genes − the instructions for how our cells function. We look like our parents because they are the source of our DNA. But DNA affects more than the way we look. Some genes have instructions for controlling when our cells grow and divide. Certain genes that make cells divide are called *oncogenes*. Others that slow down cell division or cause cells to die at the right time are called *tumor suppressor genes*. Cancers can be caused by DNA mutations (defects) that turn on oncogenes or turn off tumor suppressor genes.

Mutations of 2 tumor suppressor genes are responsible for many inherited cases of neuroendocrine tumors and neuroendocrine cancers. Most inherited cases are due to changes in the *MEN1* gene. A smaller number are caused by inherited changes in the *NF1* gene.

Most cases of neuroendocrine tumors and neuroendocrine cancers are caused by sporadic mutations of oncogenes or tumor suppressor genes. Mutations are called *sporadic* if they occur after a person is born, rather than having been inherited. The mutations that cause carcinoid tumors often affect the *MEN1* gene, the same gene that is responsible for most familial neuroendocrine tumors and neuroendocrine cancers. In many other types of cancer, researchers have shown that these acquired mutations are the result of cancer-causing chemicals in our environment, diet, or tobacco smoke. Relatively little is known, however, about factors that cause new mutations in genes that lead to neuroendocrine tumors and neuroendocrine cancers.

Doctors do know that carcinoid tumors start out very small and grow slowly. When patients have parts of their stomach or small intestine removed to treat other diseases, taking a close look under the microscope often shows small groups of neuroendocrine cells that look like tiny carcinoids. Researchers still do not know why some stay small but others grow large enough to cause symptoms.

Can gastrointestinal carcinoid tumors be prevented?

At this time, there is no known way to prevent gastrointestinal carcinoid tumors. Since smoking might increase the risk of carcinoid tumors of the small intestine, not starting or quitting smoking may reduce the risk for this disease.

Can gastrointestinal carcinoid tumors be found early?

Because carcinoid tumors usually grow and spread slowly, about half of all gastrointestinal carcinoid tumors are found in an early or localized stage, usually before they cause any problems.

Carcinoid tumors often are found incidentally (by accident). These tumors aren't causing any symptoms but are found when tests are done for other diseases. They may also be found when parts of the gastrointestinal system are removed to treat other diseases.

For example, a person with stomach pain or bleeding may have a test called an *upper endoscopy* to look for an ulcer. In this test, the doctor looks at the stomach lining through a flexible lighted tube. During this test, the doctor may notice a small bump in the stomach wall that turns out to be a carcinoid tumor.

Sometimes during colorectal cancer screening, a routine *sigmoidoscopy* or *colonoscopy* (looking at the large bowel through a flexible lighted tube) will incidentally find a small carcinoid tumor.

Sometimes when the appendix is removed (to treat appendicitis or as part of a larger operation), a small carcinoid is found at the tip. This happens in about 1 of every 300 people who have appendix surgery done for other diseases. In most of these cases, the carcinoid was too small to have caused any symptoms.

Signs and symptoms of gastrointestinal carcinoid tumors

As mentioned in the last section, gastrointestinal (GI) carcinoids often do not cause any symptoms and may be found when looking for causes of other problems. But some do cause symptoms that may lead to their diagnosis.

Symptoms by location of the tumor

The symptoms a person develops from a GI carcinoid tumor often depend on where it is located.

The appendix

People with tumors/cancers in their appendix often don’t have symptoms. If it is discovered, it is often when they have their appendix removed during an operation for some other problem. Sometimes, the tumor blocks the opening between the appendix and the rest of the

intestine and causes appendicitis. This leads to symptoms like nausea, vomiting, and abdominal (belly) pain.

The small intestine or colon

If the tumor/cancer starts in the small intestine, it can sometimes kink or block the intestines, causing abdominal pain. This pain can be mild and last for a couple of years or more before the carcinoid tumor is found. A tumor usually needs to grow fairly large before it blocks (obstructs) the intestine. When that happens, patients have severe abdominal pain, nausea and vomiting.

Sometimes, a carcinoid can cause intestinal bleeding. This can lead to *anemia* (too few red blood cells) with fatigue and shortness of breath. These same problems can also happen with carcinoid tumors that start in the colon.

The rectum

Rectal carcinoid tumors are often found during routine exams, even though they can cause pain and bleeding from the rectum.

The stomach

Carcinoid tumors that develop in the stomach usually grow slowly and often do not cause symptoms. They are sometimes found during an exam of the stomach by an endoscopy looking for other things (endoscopy is described later in this section). Some can cause symptoms such as the carcinoid syndrome.

Signs and symptoms caused by hormone production by carcinoid tumors

Carcinoid tumors can release hormones into the bloodstream. This can create different problems depending on which hormones are released.

Carcinoid syndrome

About 1 out of 10 carcinoid tumors release enough hormone-like substances into the bloodstream to cause the symptoms of carcinoid syndrome. These symptoms include:

- Facial flushing (redness and warm feeling)
- Severe diarrhea
- Wheezing
- Fast heartbeat

Many patients find that these symptoms are triggered by factors such as stress, heavy exercise, and drinking alcohol. Over a long time, these hormone-like substances can damage heart valves, causing shortness of breath, weakness, and a heart murmur (an abnormal heart sound).

Not all GI neuroendocrine tumors/cancers can cause the carcinoid syndrome. For example, rectal carcinoids usually do not make the hormone-like substances that cause these symptoms.

Most cases of carcinoid syndrome occur only after the cancer has already spread to other parts of the body. Normally, blood coming from the GI tract first flows through the liver, where substances made by GI carcinoid tumors are broken down before they can reach the rest of the body. This prevents carcinoid symptoms. But if the neuroendocrine cancer spreads outside the intestine (such as to the liver or lungs), the substances it makes can enter the main bloodstream and reach other parts of the body, where it can cause symptoms.

Cushing's syndrome

Some neuroendocrine tumors/cancers may produce ACTH (adrenocorticotropic hormone), a substance that causes the adrenal glands to make too much cortisol. This can cause *Cushing's syndrome*, with symptoms of:

- Weight gain
- Muscle weakness
- High blood sugar (even diabetes)
- High blood pressure
- Increased body and facial hair
- Bump of fat on back of neck
- Skin changes like stretch marks (called *striae*)

Most GI carcinoids grow slowly and produce vague symptoms that are more often caused by something else. When trying to figure out what's going on, doctors and patients are likely to explore other, more common possible causes first. This can delay a diagnosis, sometimes even for several years.

How are gastrointestinal carcinoid tumors diagnosed?

If you have symptoms of a gastrointestinal carcinoid tumor, you should see a doctor. He or she will take a history and examine you. If the doctor suspects some type of tumor or cancer, he or she will order some tests.

Medical history and physical exam

In taking a medical history, the doctor asks questions about the patient's general health, lifestyle habits, symptoms, and risk factors. The doctor also will probably ask about symptoms of the carcinoid syndrome, as well as symptoms that might be caused by a mass (tumor) in the stomach, intestines, or rectum.

Some patients with neuroendocrine tumors/cancers also have cancers or benign tumors of other organs, so doctors may ask about symptoms that might suggest other tumors are present. A thorough physical exam will provide information about signs of neuroendocrine tumors/cancers and other health problems. The doctor may pay special attention to the abdomen, looking for a tumor mass or enlarged liver.

If your medical history and physical exam give the doctor reason to suspect you might have a GI carcinoid, some tests will be ordered to find out if the disease is present.

Imaging tests

Your doctor may order one or more types of imaging tests to help determine the cause of your symptoms.

Barium x-ray

These studies use a barium-containing solution that coats the lining of the esophagus, stomach, and intestines. The coating of barium helps show up abnormalities of the lining of these organs. This type of study is often useful in diagnosing some GI carcinoid tumors. It is least effective in finding small intestine carcinoids. Barium studies can be used to examine the upper or lower parts of the digestive system. You will probably not be able to eat or drink anything (other than water) the night before the test. If the colon is being examined, you may need to take laxatives and/or enemas to cleanse the bowel the night before or the morning of these exams.

Barium swallow: This test is used to examine the lining of the esophagus. The patient drinks a barium solution which coats the lining of the esophagus. Then x-ray pictures are taken.

Upper GI series: This test is used to examine the lining of the stomach and the first part of the small intestine. The patient swallows the barium solution, and then may be moved around

a bit so that it coats the inside of the stomach. Then, over time, it will leave the stomach and coat the first part of the small intestine. More x-rays can be taken over the next few hours as the barium travels through the rest of the small intestine. This is called a *small bowel follow-through.*

Enteroclysis: This is another way to look at the small intestine. In this test, a thin tube is passed from the mouth or nose down through the stomach to the start of the small intestine. Barium contrast is sent through the tube, along with a substance that creates more air in the intestines, causing them to expand. X-rays of the intestines are then taken. This test may be quicker and give clearer images of the small intestine than a small bowel follow-through, but the use of a tube to give the barium makes it more uncomfortable.

Barium enema: This test (also known as a *lower GI series*) is used to look at the inner surface of the large intestine. The barium solution is given as an enema (through the anus) while the patient is lying on the x-ray table. When the colon is about half full of barium, the patient rolls over so the barium spreads throughout the colon. Then x-rays are taken. After the barium is put in the colon, air may be blown in to help spread the barium toward the bowel wall and better coat the inner surface. This is called an *air contrast* (or *double contrast*) *barium enema.* X-rays are then taken.

Barium x-rays are used less these days than in the past. In many cases they are being replaced by endoscopy, where the doctor actually looks into the esophagus, stomach, or colon with a narrow fiber optic scope.

Computed tomography(CT) scan

A CT (or CAT) scan can help tell if your cancer has spread into lymph nodes or other organs such as your liver.

The CT scan uses x-rays to produce detailed cross-sectional images of your body. Instead of taking one picture, like a regular x-ray, a CT scanner takes many pictures as it rotates around you. A computer then combines these into images that look like slices of the part of your body that is being studied.

Before any pictures are taken, you might be asked to drink 1 to 2 pints of a liquid called *oral contrast*. This helps outline the intestine so that certain areas are not mistaken for tumors. You might also receive an IV (intravenous) line through which a different kind of contrast dye (IV contrast) is injected. This helps better outline structures in your body. The injection can cause some flushing (redness and warm feeling that may last hours to days). A few people are allergic to the dye and get hives. Rarely, more serious reactions like trouble breathing and low blood pressure can occur. Medicine can be given to prevent and treat allergic reactions. Be sure to tell the doctor if you have ever had a reaction to any contrast material used for x-rays.

A CT scanner has been described as a large donut, with a narrow table in the middle opening. You will need to lie still on the table while the scan is being done. CT scans take longer than

regular x-rays and you might feel a bit confined by the ring while the pictures are being taken.

CT scans can also be used to guide a biopsy needle precisely into a suspected area of cancer spread. For a CT-guided needle biopsy, the patient remains on the CT scanning table, while a doctor moves a biopsy needle in the body toward the location of the mass. CT scans are repeated until the doctor is sure that the needle is in the mass. A fine-needle biopsy sample (tiny fragment of tissue) or a core-needle biopsy sample (a thin cylinder of tissue about ½-inch long and less than $^{1}/_{8}$-inch in diameter) is removed and looked at under a microscope.

Magnetic resonance imaging (MRI) scan

MRI scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed by the body and then released in a pattern formed by the type of tissue and by certain diseases. A computer translates the pattern into a detailed image of parts of the body. Like a CT scanner, this produces cross-sectional slices of the body. An MRI can produce slices that are parallel with the length of your body. As with a CT scan, a contrast material might be injected into a vein, but it is not needed as often.

MRI scans take longer than CT scans, often up to an hour. You may have to lie inside a narrow tube which may feel confining and can upset people with a fear of enclosed spaces. Special, "open" MRI machine can help with this if needed, although the images may not be as sharp in some cases. The MRI machine makes loud buzzing noises, but some places provide headphones to help block the sound.

Radionuclide scans

Scans using small amounts of radioactivity and special cameras can be helpful in looking for carcinoid tumors. They can help determine the extent of the tumor, as well as help locate it if doctors aren't sure where it is in the body.

Somatostatin receptor scintigraphy (OctreoScan®): This is the scan most often used to look for carcinoid tumors. For this scan, a radioactive substance called indium-111 is bound to a hormone-like substance called *octreotide.* When a small amount of this combined substance is injected into a vein, it travels through the blood and the octreotide causes it to attach to proteins on carcinoid cells. About 4 hours after the injection, a special camera can be used to show where the radioactivity has collected in the body. More scans may be done over the next few days as well.

I-131 MIBG scan: This is another test that can be used to find carcinoid tumors, but it is used less often than the OctreoScan. This test uses a chemical called *MIBG* which has radioactive iodine (I-131) attached. This substance is injected into a vein, and the body is scanned several hours or days later with a special camera to look for areas that picked up the radioactivity. These would most likely be carcinoid tumors, although other kinds of neuroendocrine tumors will also pick up this chemical.

Positron emission tomography (PET) scan

A PET scan is another imaging test that uses low levels of radioactivity to look for tumors. PET scans usually use a form of radiolabeled glucose (sugar) to find tumors. But to look for neuroendocrine tumors/cancers, a special type of PET scan is done, using a radioactive form of 5-hydroxytryptophan (5-HTP). This chemical is injected into the bloodstream, then spreads through the body and is taken up and used by carcinoid cells. After about an hour, a special camera is used to find the areas of radioactivity. Some doctors have found this type of PET scan to be more accurate than CT scans for detecting spread of disease. However, this type of PET scan is not available in every hospital (even hospitals that have a PET scanner).

You can read more about these and other kinds of tests in our document *Imaging (Radiology) Tests*.

Endoscopy

These tests use a flexible lighted tube (endoscope) with a video camera on the end. The camera is connected to a monitor, which lets the doctor see any masses in the lining of the digestive organs clearly. If abnormal areas are found, small pieces of tissue can be removed through the endoscope (biopsy). The tissue can be looked at under the microscope to find out if cancer is present and what kind of cancer it is.

Upper endoscopy

This test is also known as *esophogogastroduodenoscopy* or *EGD*. The endoscope is passed down through the mouth to show the esophagus, stomach, and first part of the small bowel.

An upper endoscopy may be done in a hospital outpatient department, in a clinic, or in a doctor's office. It usually takes 15 to 30 minutes, and most patients are given intravenous medicine to make them feel relaxed and sleepy. If you are sedated for the procedure, you will need someone to take you home (not just a cab).

Colonoscopy

This test is also called *lower endoscopy*. A special endoscope known as a colonoscope is inserted through the anus up into the colon. Using the colonoscope, the doctor will be able to see the lining of the entire rectum and colon. For a clear view though, the colon must be completely cleaned out before the test. This often means drinking a large volume of a laxative solution the night before the exam (and then spending much of the night on the toilet). Sometimes an enema is also needed just before the procedure to make sure the bowels are empty.

You will be given intravenous medicine to make you feel relaxed and sleepy during the procedure. A colonoscopy can be done in a hospital outpatient department, in a clinic, or in a

doctor's office. It usually takes 15 to 30 minutes, although it may take longer if a tumor is seen and/or a biopsy is taken. Because you will be sedated for the procedure, you will need someone to take you home (not just a cab).

Proctoscopy

Proctoscopy may be used to look for a rectal tumor. This involves using a shorter, rigid, hollow tube (a proctoscope), which is about 10 inches long and about 1 inch in diameter and may have a light on the end of it. The doctor coats the proctoscope with a lubricant and then gently pushes it into the anus and rectum. By shining a light into this tube, the doctor has a clear view of the lining of the rectum and anus. This test usually requires that you take laxatives or have an enema beforehand to make sure the bowels are empty.

Capsule endoscopy

Unfortunately, neither upper nor lower endoscopy can reach all areas of the small intestine, where many carcinoid tumors begin. A technique known as *capsule endoscopy* may help in some cases. This test doesn't really use an endoscope. Instead, the patient swallows a capsule (about the size of a large vitamin pill) that contains a light source and a very small camera. Like any other pill, the capsule goes through the stomach and into the small intestine. As it travels (usually over a period of about 8 hours), it takes thousands of pictures. These images are transmitted electronically to a device worn around the person's waist, while he or she goes on with normal daily activities. The pictures can then be downloaded onto a computer, where the doctor can watch them as a video. The capsule passes out of the body during a normal bowel movement and is discarded.

Double balloon enteroscopy

This is another way to look at the small intestine. The small intestine is too long (20 feet) and has too many curves to be examined well with regular endoscopy. This method gets around these problems by using a special endoscope that is made up of 2 tubes, one inside the other. First the inner tube, which is an endoscope, goes forward about a foot, and then a balloon at its end is inflated to anchor it. Then the outer tube goes forward to near the end of the inner tube and it is then anchored in place with a balloon. This process keeps being repeated over and over, letting the doctor see the intestine a foot at a time. This procedure is done after the patient is given drugs to make him or her sleepy and may be even done under general anesthesia (where the patient is asleep). The main advantage of this test over capsule endoscopy is that the doctor can take a biopsy if something abnormal is seen. As with other tests that are done under sedation, you will need someone to take you home after this procedure (not just a cab).

Endoscopic ultrasound (EUS)

This test uses an endoscope with a small ultrasound probe on the end. This probe releases sound waves and then detects the echoes that bounce off tissues of the digestive tract wall. A computer then translates the pattern of echoes into an image of the wall of the esophagus, stomach, intestine, or rectum. Putting the ultrasound probe on the end of an endoscope lets it get very close to the tumor. Because the probe is close to the area being studied, it can make very detailed pictures. EUS can be used to see how deeply a tumor has grown into the wall of the esophagus, stomach, intestine, or rectum. Endoscopic ultrasound can also help see if certain lymph nodes are enlarged and help a doctor guide a needle into lymph node, tumor, or other suspicious area to do a biopsy. You will be sedated for this test, so you will need someone to take you home (not just a cab).

You can find out more about these tests and others in our document *Endoscopy*.

Biopsy

Even if an imaging test finds a mass, it cannot tell if the mass is a carcinoid tumor, some other type of tumor or cancer, or an area of infection. The only way to know for sure is to remove cells from the abnormal area and look at them under a microscope. This procedure is called a *biopsy*.

There are several ways to take a sample from a gastrointestinal tumor. One way is through the endoscope. When a tumor is found, the doctor can use biopsy forceps (pincers or tongs) through the tube to take a small sample of it. Another way to sample a tumor is with a CT-guided needle biopsy, as described in the section on CT scans.

Bleeding after a biopsy of a GI carcinoid cancer is a rare but potentially serious problem. If serious bleeding occurs, doctors can sometimes inject drugs into the tumor to constrict blood vessels and slow or stop bleeding.

In rare cases, neither endoscopic biopsy nor a CT-guided needle biopsy will be able to get enough tissue to identify the type of tumor. This is sometimes the case with tumors in the small intestine. In such cases, surgery may be needed to remove a tissue sample.

You can find out more about biopsies and how they are tested in our document *Testing Biopsy and Cytology Specimens for Cancer*.

Blood and urine tests

Blood and urine tests can be very helpful in diagnosing carcinoid syndrome in patients who have symptoms that might be caused by it.

Many carcinoid tumors, especially those in the small intestine, make serotonin (also called *5-HT*). It is probably the cause of at least some of the symptoms of carcinoid syndrome. The

body breaks it down into 5-hydroxyindoleactic acid (5-HIAA), which is released into the urine. A commonly used test to look for carcinoid syndrome measures the levels of 5-HIAA in a urine sample collected over 24 hours. Measuring the serotonin levels in the blood may also give useful information. These tests can help diagnose many (but not all) carcinoid tumors. Sometimes, the tumors are small and don't release enough serotonin for a positive test result.

In other cases, the tumors do not make much serotonin, but they do make its precursor, 5-HTP, which can be converted to serotonin in the urine. In patients with these tumors, the blood serotonin level may be normal, but the urine levels of serotonin and 5-HTP are high.

Some foods, including bananas, plantains, kiwi, certain nuts, avocado, tomatoes, and eggplant, contain a lot of serotonin and can raise 5-HIAA levels in the urine. Medicines, including cough syrup and acetaminophen (Tylenol), can also affect the results. Ask your doctor what you should avoid before having urine or blood tests for carcinoids.

Other commonly used tests to look for carcinoids can include blood tests for chromogranin A (CgA), neuron-specific enolase (NSE), substance P, and gastrin. Medicines that lower stomach acid called proton-pump inhibitors (such as omeprazole/Prilosec®, lansoprazole/Prevacid®, esomeprazole/Nexium®, and many others) can make CgA and gastrin levels high even when carcinoid tumors aren’t present. If you take any of these medicines, talk to your doctor about what you need to avoid before having these blood tests. Depending on the tumor’s location and your symptoms, your doctor might do other blood tests as well.

Some of these tests can also be used to show how well treatment is working, since the levels of these substances tend to go down as tumors shrink.

How are gastrointestinal carcinoid tumors staged?

Staging — or determining the stage of disease — is the process of finding out if the tumor has spread, and if it has, how far. To help stage the tumor, doctors might use several types of imaging, endoscopy, or other tests described in the previous section, "How are gastrointestinal carcinoid tumors diagnosed?"

The stage of the tumor, along with the place it started, tells us about the prognosis (outlook) for someone with a gastrointestinal (GI) carcinoid tumor. These 2 factors also help the doctor decide what treatment to recommend.

Localized, regional, and distant stages

GI carcinoid tumors/cancers can start in several different locations, and until recently there had been no standard system for describing their spread. In the past, many doctors simply

divided GI carcinoid tumors into 3 general stages: localized, regional spread, and distant spread. This approach was fairly easy to understand and could be useful when choosing among treatment options. It might not be possible to tell a benign tumor from a cancer when it is localized because the cells can look the same under the microscope. Any tumor that spreads, though, is a cancer (by definition).

Localized

The cancer has not spread beyond the wall of the organ it started in (for example, the stomach, intestine, or rectum).

Regional spread

The cancer has either spread to nearby lymph nodes or it has grown through the wall of the organ where it started to grow into nearby tissues such as fat, ligaments, and muscle (or both).

Distant spread

The cancer has spread to tissues or organs that are not near the organ where the cancer started (such as the liver, bones, or lungs).

The AJCC TNM system

Modern staging of GI carcinoid tumors/cancers uses a system created by the American Joint Committee on Cancer (AJCC) that is known as the *TNM system*. The TNM system for staging has 3 key pieces of information:

- T describes the size of the primary tumor, measured in centimeters (cm), and whether the cancer has spread to organs next to the tumor.
- N describes the extent of spread to nearby (regional) lymph nodes.
- M indicates whether the cancer has metastasized (spread) to other organs of the body.

Numbers or letters appear after *T*, *N*, and *M* to provide more details about each of these factors:

- The numbers 0 through 4 indicate increasing severity.
- The letter X means "cannot be assessed" because the information is not available.
- The letters "is" mean "carcinoma in situ," or the tumor is contained within the top layer of cells and has not yet reached deeper layers of tissue.

The T categories for GI carcinoid cancers differ depending on where the cancer starts, but the N and M categories are the same. Once the T, N, and M categories for a tumor are known, the information is combined to determine the overall stage. This process is known as stage grouping.

T categories for carcinoid tumors of the stomach

The T category describes how far down through the stomach layers the cancer has grown. The wall of the stomach is made of 5 layers. From innermost to outermost, they are:

- **Mucosa:** This innermost layer is where stomach acid and digestive enzymes are made. The mucosa has 3 parts: epithelial cells which lie on top of a layer of connective tissue (the lamina propria), which is on top of a thin layer of muscle (the muscularis mucosa).
- **Submucosa:** This is a supporting layer under the mucosa.
- **Muscularis:** This is a layer of muscle that moves and mixes the stomach contents.
- **Subserosa and serosa:** These are the two outermost layers. They act as wrapping layers for the stomach.

TX: Primary (main) tumor cannot be assessed due to incomplete information.

T0: The primary tumor cannot be found.

Tis: The tumor is less than 0.5 mm (about half the width of a grain of rice) and the cancer cells are found only in the top layer of cells of the stomach lining. This is also known as carcinoma in situ or severe dysplasia.

T1: The tumor has grown from the top layer of cells and into deeper layers, such as the lamina propria or the submucosa. The tumor is 1 cm (less than half of an inch) or less.

T2: Either:

- The tumor has grown into the lamina propria or submucosa (or both) and is greater than 1 cm.

  OR

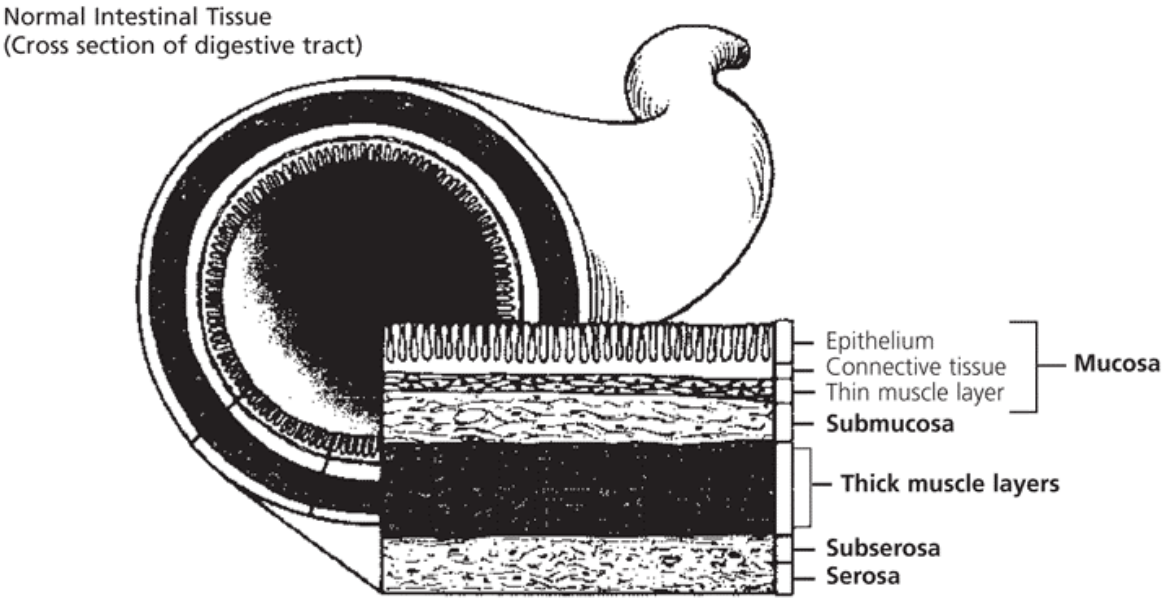
- The tumor has grown through the lamina propria and submucosa and into the main muscle layer of the stomach (called the *muscularis propria*).

T3: The tumor has grown through the muscularis propria and into the subserosa.

T4: The tumor has grown into the serosa (the outer layer of tissue covering the stomach, also called the visceral peritoneum) or into nearby organs or structures.

T categories for carcinoid tumors of the small intestine

T categories of small intestine cancer describe the extent of spread through the layers that form its wall.



The layers of the intestine (from innermost to outermost) are:

- **Mucosa:** This is the innermost layer of the intestine. It has 3 parts: the top layer of cells (called the epithelium), a thin layer of connective tissue (called the lamina propria), and a thin layer of muscle.
- **Submucosa:** This is the fibrous tissue that lies beneath the mucosa.
- **Thick muscle layers (muscularis propria):** This layer of muscle contracts to force the contents of the intestines along the tract.
- **Subserosa and serosa:** These are the thin outermost layers of connective tissue that cover the small intestine. The serosa is also known as the *visceral peritoneum*.

TX: Primary (main) tumor cannot be assessed.

T0: The primary tumor cannot be found.

T1: The tumor has grown from the top layer of cells and into deeper layers, such as the lamina propria or the submucosa. The tumor is 1 cm (less than half of an inch) or less.

T2: Either:

- The tumor has grown into the lamina propria or submucosa (or both) and is greater than 1 cm.

OR

- The tumor has grown through the lamina propria and submucosa and into the main muscle layer of the colon (called the muscularis propria).

T3: The tumor has grown through the muscularis propria and into the subserosa, the pancreas, and/or the retroperitoneum (the area in back of the abdomen).

T4: The tumor has grown into the serosa (the outer layer of tissue covering the intestine, also called the visceral peritoneum) or into nearby organs.

T categories for carcinoid tumors of the colon or rectum

T categories for carcinoid tumors of the colon and rectum cancer describe the extent of spread through the layers that form its wall. These layers are similar to those found in the wall of the small intestine (see above). From innermost to outermost, they are:

- **Mucosa:** This is the innermost layer of the intestine. It has 3 parts: the top layer of cells (called the *epithelium*), a thin layer of connective tissue (called the *lamina propria*), and a thin layer of muscle.
- **Submucosa:** This is the fibrous tissue beneath the mucosa.
- **Thick muscle layers (muscularis propria):** This layer of muscle contracts to force the contents of the intestines along the tract.
- **Subserosa and serosa:** These are the thin outermost layers of connective tissue that cover the large intestine. The serosa is also known as the *visceral peritoneum*.

TX: Primary (main) tumor cannot be assessed due to incomplete information.

T0: The primary tumor cannot be found.

T1: The tumor has grown from the top layer of cells and into deeper layers, such as the lamina propria or the submucosa. The tumor is 2cm (about 4/5 of an inch) or less.

T1a: The tumor is less than 1 cm across (1 cm is less than half an inch).

T1b: The tumor is 1 to 2 cm across.

T2: Either:

- The tumor has grown into the lamina propria or submucosa (or both) and is greater than 2 cm.

OR

- The tumor has grown through the lamina propria and submucosa and into the main muscle layer of the colon (called the *muscularis propria*).

T3: The tumor has grown through the muscularis propria and into the subserosa or other tissue around the colon or rectum.

T4: The tumor has grown through the wall of the colon (or rectum) and into the serosa (also called peritoneum) and/or into nearby organs.

T categories for carcinoid tumors of the appendix

TX: Primary (main) tumor cannot be assessed.

T0: No signs of a primary tumor.

T1: The tumor is no more than 2 cm (2 cm is about 4/5 of an inch) across.

- **T1a:** The tumor is no more than 1 cm across (1 cm is a little less than half an inch).
- **T1b:** The tumor is larger than 1 cm but not larger than 2 cm across.

T2: Either:

- The tumor is larger than 2 cm but not larger than 4 cm.

  OR

- The tumor has grown into the cecum (the first part of the large intestine).

T3: Either:

- The tumor is larger than 4 cm.

  OR

- The tumor has grown into the ileum (the last part of the small intestine).

T4: The tumor has grown into nearby organs or tissues (such as the abdominal wall).

N categories for GI carcinoid tumors/cancers

NX: The cancer has spread to nearby (regional) lymph nodes and cannot be assessed.

N0: The cancer has not spread to nearby lymph nodes.

N1: The cancer has spread to nearby lymph nodes.

M categories for GI carcinoid tumors/cancers

M0: The cancer has not spread (metastasized) to distant organs or structures.

M1: The cancer has spread (metastasized) to distant organs or structures (such as the liver, lungs, bones, *etc*).

Stage groupings for carcinoid of the stomach

Stage 0: Tis, N0, M0: Carcinoma in situ: the tumor is less than 0.5 mm (and the cancer cells are found only in the top layer of cells of the stomach lining (Tis). The cancer has not spread to nearby lymph nodes (N0) or to distant sites (M0).

Stage I: T1, N0, M0: The tumor is 1 cm or less in size and has grown from the top layer of cells and into deeper layers, such as the lamina propria or the submucosa (T1). The cancer has not spread to nearby lymph nodes (N0) or to distant sites (M0).

Stage IIA: T2, N0, M0: Either the tumor has grown into the lamina propria or submucosa (or both) and is greater than 1 cm in size; OR the tumor has grown into the main muscle layer of the stomach (called the *muscularis propria*) (T2). The cancer has not spread to nearby lymph nodes (N0) or to distant sites (M0).

Stage IIB: T3, N0, M0: The tumor has grown through the muscularis propria and into the subserosa (T3). The cancer has not spread to nearby lymph nodes (N0) or to distant sites (M0).

Stage IIIA: T4, N0, M0: The tumor has grown into the outer layer of tissue covering the stomach (the serosa or visceral peritoneum) or into nearby organs or structures. The cancer has not spread to nearby lymph nodes (N0) or to distant sites (M0).

Stage IIIB: any T, N1, M0: The tumor can be any size and may or may not have grown into nearby structures (any T). It has spread to nearby lymph nodes (N1), but not to distant sites (M0).

Stage IV: any T, any N, M1: The tumor can be any size and may or may not have grown into nearby structures (any T). It may or may not have spread to nearby lymph nodes (any N). The cancer has spread to distant sites (most often the liver).

Stage groupings for carcinoid of the small intestine

Stage I: T1, N0, M0: The tumor is 1 cm or less and has grown from the top layer of cells and into deeper layers, such as the lamina propria or the submucosa (T1). The cancer has not spread to nearby lymph nodes (N0) or to distant sites (M0).

Stage IIA: T2, N0, M0: Either the tumor has grown into the lamina propria or submucosa (or both) and is greater than 1 cm; OR the tumor has grown into the main muscle layer of the intestine (called the muscularis propria) (T2). The cancer has not spread to nearby lymph nodes (N0) or to distant sites (M0).

Stage IIB: T3, N0, M0: The tumor has grown through the muscularis propria and into the subserosa (T3). The cancer has not spread to nearby lymph nodes (N0) or to distant sites (M0).

Stage IIIA: T4, N0, M0: The tumor has grown into the outer layer of tissue covering the intestine (the serosa or visceral peritoneum) or into nearby organs or structures. The cancer has not spread to nearby lymph nodes (N0) or to distant sites (M0).

Stage IIIB: any T, N1, M0: The tumor can be any size and may or may not have grown into nearby structures (any T). It has spread to nearby lymph nodes (N1), but not to distant sites (M0).

Stage IV: any T, any N, M1: The tumor can be any size and may or may not have grown into nearby structures (any T). It may or may not have spread to nearby lymph nodes (any N). The cancer has spread to distant sites (most often the liver).

Stage groupings for carcinoid of the colon and rectum

Stage I: T1, N0, M0: The tumor is 2 cm (about 4/5 of an inch) or less and has grown into the lamina propria and may have grown into the submucosa. The cancer has not spread to nearby lymph nodes (N0) or to distant sites (M0).

Stage IIA: T2, N0, M0: Either the tumor has grown into the lamina propria or submucosa (or both) and is greater than 2 cm; OR the tumor has grown into the main muscle layer of the colon (called the *muscularis propria*). The cancer has not spread to nearby lymph nodes (N0) or to distant sites (M0).

Stage IIB: T3, N0, M0: The tumor has grown through the muscularis propria and into the subserosa or other tissue around the colon or rectum. The cancer has not spread to nearby lymph nodes (N0) or to distant sites (M0).

Stage IIIA: T4, N0, M0: The tumor has grown through the wall of the colon (or rectum) and into the serosa (also called *peritoneum*) and/or into nearby organs. The cancer has not spread to nearby lymph nodes (N0) or to distant sites (M0).

Stage IIIB: any T, N1, M0: The tumor can be any size and may or may not have grown into nearby structures (any T). It has spread to nearby lymph nodes (N1), but not to distant sites (M0).

Stage IV: any T, any N, M1: The tumor can be any size and may or may not have grown into nearby structures (any T). It may or may not have spread to nearby lymph nodes (any N). The cancer has spread to distant sites (most often the liver).

Stage groupings for carcinoid tumors of the appendix

Stage I: T1, N0, M0: The tumor is no more than 2 cm. The cancer has not spread to nearby lymph nodes (N0) or to distant sites (M0).

Stage II: T2 or T3, N0, M0: The tumor is either larger than 2 cm or it has grown into the cecum (T2) or ileum (T3). The cancer has not spread to nearby lymph nodes (N0) or to distant sites (M0).

Stage III: Either:

T4, N0, M0: The tumor has grown into nearby organs or tissues. The cancer has not spread to nearby lymph nodes (N0) or to distant sites (M0).

OR

Any T, N1, M0: The tumor can be any size and may or may not have grown into nearby structures (any T). It has spread to nearby lymph nodes (N1), but not to distant sites (M0).

Stage IV: Any T, any N, M1: The tumor can be any size and may or may not have grown into nearby structures (any T). It may or may not have spread to nearby lymph nodes (any N). The cancer has spread to distant sites (most often the liver).

Survival rates for gastrointestinal carcinoid tumors

Survival rates are often used by doctors as a standard way of discussing a person's prognosis (outlook). Some patients with cancer may want to know the survival statistics for people in similar situations, while others may not find the numbers helpful, or may even not want to know them. If you decide that you do not want to know them, stop reading here and skip to the next section.

The 5-year survival rate refers to the percentage of patients who live at least 5 years after their cancer is diagnosed. Of course, many people live much longer than 5 years (and many are cured). Also, people who have this cancer can die from something else. These survival rates, called *observed* survival rates, do not take this into account.

To get 5-year survival rates, doctors have to look at people who were treated at least 5 years ago. Improvements in treatment since then may result in a more favorable outlook for people now being diagnosed with carcinoid tumors and cancers.

Survival rates are often based on previous outcomes of large numbers of people who had the disease, but they cannot predict what will happen in any particular person's case. Many other factors may affect a person's outlook, such as treatment received, the grade of the tumor and its growth rate, and the patient's age and health. Your doctor can tell you how the numbers below may apply to you, as he or she is familiar with the aspects of your situation.

Most GI carcinoid tumors are found while they are still localized, but this does vary based on the organ they start in. Tumors of the stomach, duodenum (the first part of the small intestine), appendix, and rectum are likely to be found before they have spread. In contrast, many tumors of other parts of the small intestine (the jejunum/ileum) and the colon (including the cecum) have already spread to nearby tissues or lymph nodes or to distant sites when they are first diagnosed.

The following 5-year survival rates are based on people diagnosed with carcinoid (well and moderately differentiated neuroendocrine tumors) between 1988 and 2004:

5-year observed survival rates

Site	Localized	Regional	Distant
Stomach	73%	65%	25%
Duodenum	68%	55%	46%
Jejunum/ileum	65%	71%*	54%
Cecum	68%	71%*	54%
Appendix	88%	78%	25%
Colon	85%	46%	14%
Rectum	90%	62%	24%

*These numbers are correct as written (the 5-year survival for regional stage is slightly better than for localized stage)

How are gastrointestinal carcinoid tumors treated?

This information represents the views of the doctors and nurses serving on the American Cancer Society's Cancer Information Database Editorial Board. These views are based on their interpretation of studies published in medical journals, as well as their own professional experience.

The treatment information in this document is not official policy of the Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor.

Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask him or her questions about your treatment options.

General approach to treatment

Once a gastrointestinal (GI) carcinoid tumor is found and staged, the cancer care team will discuss your treatment options with you. Depending on your situation, you may have different types of doctors on your treatment team. These doctors may include:

- A surgeon: a doctor who treats diseases with surgery.
- A radiation oncologist: a doctor who treats cancer with radiation therapy.

- A medical oncologist: a doctor who treats cancer with medicines such as chemotherapy.
- A gastroenterologist: a doctor who specializes in diagnosing and treating diseases of the digestive system.
- An endocrinologist: a doctor who specializes in the diagnosis and treatment of diseases related to hormones

Many other specialists may be involved in your care as well, including nurse practitioners, nurses, nutrition specialists, social workers, and other health professionals.

The main types of treatment for GI carcinoid tumors are:

- Surgery
- Chemotherapy
- Radiation

In some cases, doctors may recommend combining more than one of these treatments. It is important to discuss all of your treatment options, including their goals and possible side effects, with your doctors to help make the decision that best fits your needs. Some of the factors that will influence your treatment options for a GI carcinoid tumor are:

- Its size and location
- Whether it has spread to lymph nodes, liver, bones, or other organs
- Whether you have any other serious medical conditions
- Whether the tumor is causing bothersome symptoms

Take your time and think about all of your options when you make this important decision. It is often a good idea to get a second opinion. A second opinion may give you more information and help you feel more confident about the treatment plan you choose. It’s also very important to ask questions if there is anything you’re not sure about. You can find some good questions to ask in the section “What should you ask your doctor about gastrointestinal carcinoid tumors?”

The first part of this section describes the various types of treatments used for GI carcinoid tumors. This is followed by a description of the most common approaches used to treat them based on their stage and primary site.

Surgery for gastrointestinal carcinoid tumors

Most GI carcinoid tumors can be cured by surgery alone. The type of operation will depend on a number of factors, including the size and location of the tumor, whether the person has any other serious diseases, and whether the tumor is causing the carcinoid syndrome.

Surgeons often try to cure localized carcinoid tumors by removing them completely, which is usually successful. The options for GI carcinoid tumors that have spread locally or distantly are more complex. Because most carcinoid tumors grow very slowly and some do not cause any symptoms, completely removing all metastatic carcinoid tumors may not always be needed. In some patients, surgery to remove all visible cancer is the best option. This is particularly true if removing most of the cancer will reduce the level of hormone-like substances causing symptoms.

Several types of operations may be used to treat GI carcinoid tumors. Some of these remove the primary tumor (where the cancer started), while others remove or destroy cancer spread (metastases) in other organs.

Fulguration (electrofulguration)

This treatment destroys a tumor by heating it with electric current. It is sometimes used for small rectal carcinoid tumors, which can be reached fairly easily.

Endoscopic mucosal resection

In this procedure, the cancer is removed through an endoscope. This is most often used to treat small carcinoid tumors of the stomach and duodenum (the first part of the small intestine) and it can be used to remove small carcinoid tumors of the rectum.

Local excision

This operation removes the primary tumor and some normal tissue around it. The edges of the defect are then sewn together. This usually doesn’t cause any prolonged problem with eating or bowel movements. This operation may be done for small carcinoid tumors (no larger than 2 cm, or a little less than an inch).

Carcinoid tumors are sometimes removed during an operation for some other reason. This often occurs with carcinoid tumors of the appendix. When the appendix is removed (for some other reason), it is examined after surgery, and sometimes a carcinoid tumor is found. Most doctors believe that if the tumor is small — 2 cm or less — removing the appendix (appendectomy) is curative and no other surgery is needed. If the tumor is larger than 2 cm, more surgery may be needed.

Rectal carcinoid tumors may be excised (taken out) through the anus, without cutting the skin. Other GI carcinoid tumors can sometimes be locally excised through an endoscope but usually it is done through an incision (cut) in the skin.

More extensive surgeries

For larger tumors, a larger incision (cut) is needed to remove the tumor along with nearby tissues. This also gives the surgeon the chance to see whether the tumor has grown into other

tissues in the abdomen (belly). If it has, the surgeon may be able to remove the areas of cancer spread.

Partial gastrectomy: In this operation, part of the stomach is removed. If the upper part is removed, sometimes part of the esophagus is removed as well. If the lower part of the stomach is removed, sometimes the first part of the small intestine (the duodenum) is also taken. Nearby lymph nodes are also removed. This operation is also known as a *subtotal gastrectomy*.

Small bowel resection: This is an operation to remove a piece of the small intestine (also called the *small bowel*). When it is used to treat a small bowel carcinoid, this surgery includes removing the tumor and some of the small bowel around it (called a *wide margin resection*), plus removing nearby (regional) lymph nodes and the supporting connective tissue (called the *mesentery*) that contains lymph nodes and vessels that carry blood to and from the intestine. Tumors in the terminal ileum (the last part of the small bowel) may require removing the right side of the colon (hemicolectomy).

Pancreaticoduodenectomy (*Whipple procedure*): This operation is most often used to treat pancreatic cancer, but it is also used to treat cancers of the duodenum. It removes the duodenum, part of the pancreas, nearby lymph nodes and part of the stomach. The gallbladder and part of the common bile duct are removed and the remaining bile duct is attached to the small intestine so that bile from the liver can continue to enter the small intestine. This is a complex operation that requires a lot of skill and experience. It carries a relatively high risk of complications that could even be fatal.

Segmental colon resection or hemicolectomy: This operation removes between ⅓ and ½ of the colon, as well as the nearby mesentery (the layers of tissue that hold and connect the intestines), which includes blood vessels and lymph nodes.

Low anterior resection: This operation can be used for some tumors in the upper part of the rectum. It removes some of the rectum and the remaining ends are sewn together. This does not have much effect on digestive function.

Abdominoperineal (AP) resection: This surgery is done for large or very invasive cancers in the lower part of the rectum. It removes the anus, rectum, and lower part of the colon. After this operation, the end of the colon is connected to an opening on the skin on the abdomen (called a *colostomy*). A bag attached over this opening collects stool (feces) as it leaves the body. (For more information, see our document *Colostomy: A Guide*).

For more information on surgery for treating cancer, see our document *Understanding Cancer Surgery: A Guide for Patients and Families*.

Treatment for liver metastases

The liver is a common site of spread for GI carcinoid tumors. Treating cancer spread to the liver can help with symptoms and can even help some people live longer.

Ablation

These methods are often useful in destroying carcinoids that have spread to the liver, especially if their number or location makes removing them difficult or impossible. CT scan images are used to guide a needle precisely into the tumor deposits. The cells can then be destroyed by:

- **Cryotherapy (cryoablation):** Injecting liquid nitrogen through the needle to kill the carcinoid cells by freezing.
- **Radiofrequency ablation:** Using high-energy radio waves released from the end of the needle, which destroy the cancer cells with heat.
- **Percutaneous ethanol injection:** Injecting concentrated alcohol through the needle kills the cancer cells.

Embolization

Another approach that can be useful in shrinking these tumors is hepatic artery embolization. In this procedure a catheter (a thin, flexible tube) is put into an artery through a small cut in the inner thigh and threaded up into the hepatic artery in the liver. Once the catheter is in place, tiny particles are injected into a branch of the hepatic artery, which cuts off the tumor's blood supply. This is also known as trans-arterial embolization (or TAE).

Trans-arterial chemoembolization (or TACE) combines embolization with chemotherapy. Most often, this is done by using tiny beads for the embolization that give off a chemotherapy drug. TACE can also be done by giving chemotherapy through the catheter directly into the artery, then plugging up the artery. (See the "Chemotherapy for gastrointestinal carcinoid tumors" section.)

Radioembolization combines embolization with radiation. In the United States, this is done by injecting small radioactive beads (called *microspheres*) into the hepatic artery. Once infused, the beads lodge in the blood vessels near the tumor, where they give off small amounts of radiation to the tumor site for several days. This is discussed in more detail in the section about radiation therapy.

Liver resection

In this operation, one or more pieces of the liver that contain areas of cancer spread are removed. When it is not possible to remove all areas of cancer spread, surgery may still be done to remove as much tumor as is possible. This is sometimes called *cytoreductive surgery*. If enough tumor can be removed, the surgery can help reduce symptoms of carcinoid syndrome. Removing liver metastases may help some people with carcinoid tumors to live longer, but more than 9 out of 10 people who have this surgery develop new liver metastases within 10 years.

Liver transplant

This operation removes the liver and puts a liver (or a piece of a liver) from someone else in its place. It is rarely used to treat neuroendocrine cancers that have only spread to the liver after the primary tumor has been completely cut out. It is generally only an option for people who are young and otherwise healthy. Although this is a very difficult treatment to go through, it can be curative and should be considered if you are young. For more information on liver transplants see the American Cancer Society document *Liver Cancer*.

Chemotherapy for gastrointestinal carcinoid tumors

Chemotherapy (chemo) uses anti-cancer drugs that are injected into a vein or a muscle or taken by mouth to kill cancer cells. These drugs enter the bloodstream and reach all areas of the body, making this treatment useful for some types of cancers that have spread to other organs.

Unfortunately, carcinoid tumors often do not respond well to chemo. Because of this, chemo generally is used only for tumors that have spread to other organs, are causing severe symptoms, and have not responded to other medicines.

Some of the chemo drugs used to treat GI carcinoid include:

- Capecitabine (Xeloda®)
- 5-fluorouracil (5-FU)
- Doxorubicin (Adriamycin®)
- Etoposide (VP-16)
- Dacarbazine (DTIC)
- Streptozocin
- Temozolomide
- Cisplatin
- Cyclophosphamide (Cytoxan®)

Some tumors, especially “high-grade” tumors, may be treated with more than one drug. For these, combinations of etoposide plus carboplatin or temozolomide plus capecitabine may be used.

Chemo drugs kill cancer cells but also damage some normal cells, which can cause some side effects. Side effects depend on the type of drugs, the amount taken, and the length of treatment. Short-term side effects might include:

- Nausea and vomiting

- Loss of appetite
- Hair loss
- Mouth sores
- Low blood counts

Because chemo can damage the blood-making cells of the bone marrow, you may have low blood cell counts. This can result in:

- Increased risk of infection (from too few white blood cells)
- Bleeding or bruising after minor cuts or injuries (from a shortage of blood platelets)
- Fatigue or shortness of breath (from too few red blood cells)

Most side effects go away a short time after treatment. Often medicines can help prevent or minimize many of the side effects. For example, your doctor can prescribe drugs to help prevent or reduce nausea and vomiting.

Intra-arterial therapy and chemoembolization

Normally, chemo drugs enter the bloodstream and can travel throughout the body. When carcinoid cancer has spread to the liver, it is sometimes treated by directly injecting the chemo drug into the hepatic artery, which supplies blood to parts of the liver. This exposes the liver tumors to high doses of the drug but limits exposing the rest of the body. This lets patients avoid some side effects. Sometimes the chemo drug is injected together with a material that plugs up the artery (an approach called *chemoembolization*). When the arteries leading to them are blocked, the tumors become starved for nutrients and oxygen and many die off.

For more information on chemo, see the “Chemotherapy” section of our website, or our document *A Guide to Chemotherapy*.

Other drugs for treating carcinoid tumors

Several medicines can help control the symptoms of carcinoid syndrome in patients with metastatic neuroendocrine cancers.

Octreotide (Sandostatin®) is an agent chemically related to a natural hormone, somatostatin. It is very helpful in treating flushing, diarrhea, and wheezing from carcinoid syndrome. While this drug rarely shrinks carcinoid tumors, it may slow or stop their growth. Although this is not curative, it can prolong life. The main side effects are pain at the site of the injection and − rarely − stomach cramps, nausea, vomiting, headaches, dizziness, and fatigue. Octreotide causes sludging (thickening or crystallizing) of bile in the gallbladder which can

lead to gallstones (cholelithiasis). It can also result in insulin resistance that can make pre-existing diabetes more difficult to control.

This drug comes in a short-acting version that is given 2 to 4 times a day. It is also available as a long-acting injection (Sandostatin LAR) given only once a month, which may help patients more than the short-acting version.

Octreotide is also sometimes given to prevent and treat problems caused by the release of serotonin or other hormones when patients with carcinoid tumors have surgery.

Lanreotide (Somatuline®) is a drug that works like octreotide that can also be used to control symptoms caused by carcinoid tumors. It is given as an injection once a month.

A newer drug, pasireotide (Signifor®), is more helpful in treating the symptoms of Cushing's syndrome.

Interferons are natural substances that normally activate the body's immune system. They also slow the growth of tumor cells. Interferon-alfa is sometimes helpful in shrinking or slowing the growth of metastatic neuroendocrine cancers and improving symptoms of carcinoid syndrome. Its usefulness is sometimes limited by its flu-like side effects, which may be severe. The drug is given by injection.

Cyproheptadine is an antihistamine that can help relieve some of the symptoms of carcinoid syndrome.

Other medicines are also available to control specific symptoms. Please ask your doctor about these, or describe your symptoms and ask about medicines to control them.

Radiation therapy for gastrointestinal carcinoid tumors

External beam radiation therapy

In this form of radiation therapy, a beam of high-energy rays (or particles) is used to kill cancer cells. A machine aims this beam at a specific part of the body. This is the type of radiation used most often for most types of GI cancers. It is like having a regular x-ray except it takes longer and uses much higher amounts of radiation. Patients typically have treatments for 5 days a week for several weeks.

Unfortunately, this type of radiation therapy is not very effective against most GI carcinoid tumors. It is used mainly to treat pain from cancers that have spread to the bones or other parts of the body. Although surgery is the first option for most carcinoid cancers, those who can't have surgery might choose radiation therapy.

The main side effects of GI radiation therapy are tiredness (fatigue), nausea, vomiting, diarrhea, and mild, sunburn-like skin changes.

Radioembolization

This technique combines embolization with radiation therapy and is used to treat liver metastases. Embolization reduces blood flow to the cancer cells by blocking the artery feeding the area of the liver containing the tumor. This artery is a branch of the hepatic artery, the artery that feeds the liver. Blood flow is blocked (or reduced) by injecting materials that plug up the artery. Most of the healthy liver cells will not be affected because they get their blood supply from another blood vessel (the portal vein).

In this procedure a catheter is put into an artery in the inner thigh and threaded up into the liver. A dye is usually injected into the bloodstream at the same time to allow the doctor to monitor the path of the catheter via angiography, a special type of x-ray. Once the catheter is in place, small particles called *microspheres* are injected into the artery to plug it up.

In radioembolization, microspheres that are attached to a radioactive element called *yttrium-90* (or *90Y*) are used (some brand names for these beads include TheraSphere® and SIR-Spheres®). After they are injected, the beads travel in the liver blood vessels until they get stuck in small blood vessels near the tumor. There they give off radioactivity for a short while, killing tumor cells. The radiation travels a very short distance, so its effects are limited mainly to the tumor.

Radiopharmaceuticals

In this form of radiation therapy, a drug is linked to a radioactive element. The drug travels throughout the body, attaches to the cancer cells, and gives off radiation to kill them. This type of treatment has been used for a long time to treat some cancers, but is now also being used to treat carcinoid tumors. One option is to use I-131 MIBG in higher doses than are normally used to image carcinoid tumors (see “Imaging tests” in the section “How are gastrointestinal carcinoid tumors diagnosed?” Treatment using I-131 MIBG is available in Europe, but is not available in the United States.

Another radiopharmaceutical being studied is a drug like octreotide called *edotreotide* labeled with the element yittrium. This is discussed in more detail in the section “What's new in gastrointestinal carcinoid tumor research and treatment?”

For more information on radiation therapy, see the “Radiation Therapy” section of our website, our or document *Understanding Radiation Therapy: A Guide for Patients and Families*.

Clinical trials for gastrointestinal carcinoid tumors

You may have had to make a lot of decisions since you've been told you have cancer. One of the most important decisions you will make is choosing which treatment is best for you. You might have heard about clinical trials being done for your type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you.

Clinical trials are carefully controlled research studies that are done with patients who volunteer for them. They are done to get a closer look at promising new treatments or procedures.

If you would like to take part in a clinical trial, you should start by asking your doctor if your clinic or hospital conducts clinical trials. You can also call our clinical trials matching service for a list of clinical trials that meet your medical needs. You can reach this service at 1-800-303-5691 or on our website at www.cancer.org/clinicaltrials. You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll-free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at www.cancer.gov/clinicaltrials.

There are requirements you must meet to take part in any clinical trial. If you do qualify for a clinical trial, it is up to you whether or not to enter (enroll in) it.

Clinical trials are one way to get state-of-the art cancer treatment. They are the only way for doctors to learn better methods to treat cancer. Still, they are not right for everyone.

You can get a lot more information on clinical trials in our document called *Clinical Trials: What You Need to Know*.

Complementary and alternative therapies for gastrointestinal carcinoid tumors

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that your doctor hasn't mentioned. Everyone from friends and family to Internet groups and websites offer ideas for what might help you. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

What exactly are complementary and alternative therapies?

Not everyone uses these terms the same way, and they are used to refer to many different methods, so it can be confusing. We use *complementary* to refer to treatments that are used *along with* your regular medical care. *Alternative* treatments are used *instead of* a doctor's medical treatment.

Complementary methods: Most complementary treatment methods are not offered as cures for cancer. Mainly, they are used to help you feel better. Some methods that are used along with regular treatment are meditation to reduce stress, acupuncture to help relieve pain, or peppermint tea to relieve nausea. Some complementary methods are known to help, while others have not been tested. Some have been proven not be helpful, and a few have even been found harmful.

Alternative treatments: Alternative treatments may be offered as cancer cures. These treatments have not been proven safe and effective in clinical trials. Some of these methods may pose danger, or have life-threatening side effects. But the biggest danger in most cases is that you may lose the chance to be helped by standard medical treatment. Delays or interruptions in your medical treatments may give the cancer more time to grow and make it less likely that treatment will help.

Finding out more

It is easy to see why people with cancer think about alternative methods. You want to do all you can to fight the cancer, and the idea of a treatment with few or no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or they may no longer be working. But the truth is that most of these alternative methods have not been tested and proven to work in treating cancer.

As you consider your options, here are 3 important steps you can take:

- Look for "red flags" that suggest fraud. Does the method promise to cure all or most cancers? Are you told not to have regular medical treatments? Is the treatment a "secret" that requires you to visit certain providers or travel to another country?
- Talk to your doctor or nurse about any method you are thinking about using.
- Contact us at 1-800-227-2345 to learn more about complementary and alternative methods in general and to find out about the specific methods you are looking at. You can also learn more in the “Complementary and Alternative Medicine” section of our website.

The choice is yours

Decisions about how to treat or manage your cancer are always yours to make. If you want to use a non-standard treatment, learn all you can about the method and talk to your doctor about it. With good information and the support of your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

Treatment of gastrointestinal carcinoid tumors by stage

Localized disease

A tumor is localized when it is found only in the organ where it started. Treatment of localized carcinoid tumors is based mostly on their size. Experts sometimes disagree on the

exact size for making treatment decisions, and there are some sizes where it has not been determined exactly what treatment is best.

Stomach

Carcinoid tumors of the stomach are divided into 3 groups based the level of a hormone called *gastrin* and the amount of acid in the stomach (measured before surgery). Certain conditions linked to high gastrin levels are also linked to getting many carcinoid tumors of the stomach. Patients with these conditions who have stomach carcinoid tumors are treated differently from patients without these conditions.

Type 1: Patients with high gastrin levels but low levels of stomach acid are said to have type 1 tumors. These carcinoid tumors tend to be small, but there may be many of them. The tumors don't tend to grow into the deeper layers of the stomach or spread to other organs or tissues, and are often treated by removing them completely through an endoscope. The other option is to watch the tumors closely (by doing repeat endoscopy), and only removing them if they start growing.

Type 2: Patients who have high gastrin levels and high stomach acid levels are said to have type 2 tumors. Like type 1 tumors they are often small and there may be more than one at a time. Type 2 tumors also don't tend to grow into deeper layers of the stomach or spread to other organs. Small tumors can be watched closely without treatment, removed through endoscopy, or treated with a medicine like octreotide that will lower both gastrin and stomach acid. For tumors larger than 2 cm (slightly less than an inch), just watching the tumor closely isn't usually an option. These tumors need to be removed, either through an endoscope or in a regular operation through an incision in the abdomen that removes the tumor and some surrounding stomach tissue.

Type 3: Patients who don't have high gastrin levels (and have normal levels of stomach acid) are said to have type 3 tumors. There is usually only one tumor, and the tumor tends to grow into deeper layers of the stomach or even spread to nearby lymph nodes or other organs (like the liver). If the tumor is small, endoscopic surgery may still be an option. More, often, though, more extensive surgery is needed. Often, a piece of the stomach is removed (a partial gastrectomy) along with nearby lymph nodes.

Small intestine

Some small tumors in the duodenum (the first part of the small intestine) can often be removed through the endoscope (endoscopic resection). Depending on the size of the tumor and whether it is growing into nearby tissues, other options include surgery to remove the tumor (local excision), removing all or part of the duodenum with nearby lymph nodes, and removing the duodenum and part of the pancreas (a pancreatoduodenectomy).

For tumors in other parts of the small intestine, treatment is either local excision for small tumors or small bowel resection (removal of a piece of intestine as well as some surrounding blood vessels and lymph nodes) for larger tumors.

Large intestine (other than appendix and rectum)

The usual treatment is hemicolectomy (removal of a section of colon along with nearby lymph nodes and blood vessels). Because many patients have more than one carcinoid tumor, the surgeon will often check the rest of the colon for other tumors during surgery. For very small tumors, sometimes the tumor can be removed without surgery using a colonoscope.

Appendix

Most often, an appendectomy (surgical removal of the appendix) is the only treatment needed for carcinoid tumors that are 2 cm (a little less than an inch) or smaller. Still, other factors, such as the way the tumor cells look under the microscope, the patient's age, general health, and the patient's degree of worry about the possibility of the cancer coming back, might also be used to determine whether more treatment is needed.

Tumors larger than 2 cm are more likely to have already spread to nearby tissues and lymph nodes, so for these tumors more extensive surgery is usually recommended. This means removal of about a third of the colon next to the appendix (a hemicolectomy), along with nearby blood vessels and lymph nodes. This procedure may not be recommended for people who are older or have other serious health problems (especially if these problems make surgery more risky), because the benefit may not outweigh the risks.

Rectum

Doctors check how deep the cancer is growing into the wall of the rectum before surgery by using endoscopic ultrasound (discussed in the section about diagnosis). Most rectal carcinoid tumors that are smaller than 2 cm (slightly less than an inch) can be removed through an endoscope or local excision through the anus.

For rectal carcinoid tumors between 1 and 2 cm, the best approach depends on how deeply the carcinoid tumor has grown into the wall of the rectum, as well as other details of each patient's medical situation. If the tumor has grown into the thick muscle layer of the rectum (the muscularis propria) or deeper, it needs to be treated like it is a larger tumor.

Carcinoid tumors larger than 2 cm (and those that have grown deep into the wall of the rectum) have a higher risk of growing and spreading, so they are removed by the same operations used for adenocarcinomas (the usual type of rectal cancer). This operation is a low anterior resection if the carcinoid is in the upper part of the rectum. If the lower part is involved, abdominoperineal (AP) resection and colostomy are used.

Regional spread

Regional spread means that the cancer has either spread to nearby lymph nodes or it has grown through the wall of the organ where it started and has invaded nearby tissues such as fat, ligaments, and muscle.

If possible, the primary (main) tumor and any areas of cancer spread should all be removed by surgery. Nearby lymph nodes should be removed and checked for signs of cancer spread. This provides the best chance of cure. If this can't be done, surgery should remove as much cancer as possible without causing severe side effects. Surgery should also be done to relieve symptoms such as intestinal blockage caused by the local growth of cancer. For example, surgery to redirect stool around a blocked area of intestine can be done by connecting adjacent areas of the intestine.

Distant spread

A cure in this situation is not usually possible, although treatment is not always needed right away, depending on how quickly the tumors are growing. The goal of surgery in this situation is to relieve symptoms and slow the course of the disease. For example, removing or bypassing areas blocked by cancer growth can relieve some symptoms. If distant metastases are not causing symptoms, treatment may not be needed, although chemotherapy or interferon-alfa may help delay symptoms in some patients. If the cancer has spread to the liver, even when it isn’t causing symptoms, some doctors recommend treatment with octreotide because it may slow tumor growth.

If carcinoid syndrome is causing bothersome symptoms, treatment options include chemotherapy, immunotherapy, treatment with octreotide (Sandostatin), or removing the metastatic tumors. If metastatic tumors cannot be removed by surgery without causing severe side effects, ablative methods can be used to destroy as much of the tumors as possible. These methods, used mostly for liver metastases, include chemoembolization, radioembolization, radiofrequency ablation, cryotherapy, and alcohol injection. Patients should also be advised to avoid alcoholic drinks, stress, strenuous exercise, spicy foods, and certain medicines that can make the symptoms of carcinoid syndrome worse.

Recurrent carcinoid tumors

Cancer is called *recurrent* when it come backs after treatment. Recurrence can be local (in or near the same place it started) or distant (spread to organs such as the lungs or bone). Patients with recurrent carcinoid tumors are treated with surgery to remove all signs of tumor whenever possible. This provides the best chance for a good long-term outcome. If surgery is not possible, the treatments described in the “Distant spread” section may be helpful.

Carcinoid heart disease

The substances released into the blood by some carcinoid tumors can damage the heart. Early symptoms are fatigue and shortness of breath. Eventually, patients get fluid in their legs and even their abdomen. The major cause is damage to the valves of the heart. Doctors can usually make the diagnosis by listening to the heart and by an ultrasound exam of the heart called an *echocardiogram*.

The main treatment is with octreotide to block the cancer's secretion of the toxic substances. Drugs (diuretics) to strengthen the heartbeat and to get rid of fluid can also help. In some instances, heart surgery may be needed to replace the damaged valves.

More treatment information about gastrointestinal carcinoid tumors

For more details on treatment options − including some that may not be addressed in this document − the National Comprehensive Cancer Network (NCCN) and the National Cancer Institute (NCI) are good sources of information.

The NCCN, made up of experts from many of the nation's leading cancer centers, develops cancer treatment guidelines for doctors to use when treating patients. Those are available on the NCCN website (www.nccn.org).

The NCI provides treatment guidelines via its telephone information center (1-800-4-CANCER) and its website (www.cancer.gov). Detailed guidelines intended for use by cancer care professionals are also available on www.cancer.gov.

What should you ask your doctor about gastrointestinal carcinoid tumors?

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 you might think they are. For instance, consider these questions:

- What kind of carcinoid tumor/cancer do I have?
- What is the stage of my carcinoid tumor/cancer and what does that mean to me?
- What are my treatment choices?
- What do you recommend and why?
- Based on what you've learned about my tumor/cancer, what is my prognosis (outlook)?

- What risks or side effects are there to the treatments you suggest?
- How will treatment affect my daily activities?
- What are the chances my tumor/cancer will recur with these treatments?
- What should I do to be ready for treatment?

In addition to these sample questions, you might 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 might want to ask about second opinions or if you qualify for any clinical trials.

What happens after treatment for gastrointestinal carcinoid tumors?

For some people with gastrointestinal (GI) carcinoid tumor, treatment may remove or destroy the cancer. Completing treatment can be both stressful and exciting. You may be relieved to finish treatment, but find it hard not to worry about cancer coming back. (When cancer comes back after treatment, it is called *recurrence*.) This is a very common concern in people who have had cancer.

It may take a while before your fears lessen. But it may help to know that many cancer survivors have learned to live with this uncertainty and are leading full lives. Our document *Living With Uncertainty: The Fear of Cancer Recurrence* gives more detailed information on this.

For other people, the cancer may never go away completely. These people may stay on drug therapy or get regular treatments with chemotherapy, radiation therapy, or other therapies to try to help keep the cancer in check. Learning to live with cancer that does not go away can be difficult and very stressful. It has its own type of uncertainty. Our document *When Cancer Doesn't Go Away* talks more about this.

Follow-up care

When treatment ends, your doctors will still want to watch you closely. It is very important to go to all of your follow-up appointments. During these visits, your doctors will ask questions about any problems you may have and may do exams and lab tests or x-rays and scans to look for signs of cancer or treatment side effects. Almost any cancer treatment can have side effects. Some may last for a few weeks to months, but others can last the rest of your life. This is the time for you to talk to your cancer care team about any changes or problems you notice and any questions or concerns you have.

Doctors often advise most people who have had their GI carcinoid tumors completely removed to return after about 3 to 12 months for a complete physical exam and imaging tests

to look for any signs of recurrence. Blood and or urine tests may be helpful for some patients. Further visits may be recommended every 6 to 12 months after that. For small rectal tumors, proctoscopy is often recommended 6 and 12 months after treatment. Small tumors of the appendix, when adequately treated, usually don't require close follow-up, as they are very unlikely to recur. Repeat upper endoscopy every 6 to 12 months is usually recommended for patients with stomach carcinoids who have high gastrin levels. Your doctor may follow one of these schedules, but he or she might have reasons to recommend a different schedule as well.

It is important to keep your health insurance. Tests and doctor visits cost a lot, and even though no one wants to think about their cancer coming back, this could happen.

Should your cancer come back, our document *When Your Cancer Comes Back: Cancer Recurrence* can give you information on how to manage and cope with this phase of your treatment.

Seeing a new doctor

At some point after your cancer diagnosis and treatment, you may find yourself seeing a new doctor who does not know anything about your medical history. It is important that you be able to give your new doctor the details of your diagnosis and treatment. Make sure you have the following information handy:

- A copy of your pathology report(s) from any biopsies or surgeries
- If you had surgery, a copy of your operative report(s)
- If you were in the hospital, a copy of the discharge summary that doctors prepare when patients are sent home
- If you were treated with radiation (including radiopharmacueticals), a copy of your treatment summary
- Since some drugs can have long-term side effects, a list of your drugs, drug doses, and when you took them
- Copies of your imaging tests (these can often be put on a DVD)
- Copies of your lab results

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

Lifestyle changes after treatment of gastrointestinal carcinoid tumors

You can't change the fact that you have had cancer. What you can change is how you live the rest of your life – making choices to help you stay healthy and feel as well as you can. This can be a time to look at your life in new ways. Maybe you are thinking about how to improve your health over the long term. Some people even start during cancer treatment.

Making healthier choices

For many people, a diagnosis of cancer helps them focus on their health in ways they may not have thought much about in the past. Are there things you could do that might make you healthier? Maybe you could try to eat better or get more exercise. Maybe you could cut down on alcohol, or give up tobacco. Even things like keeping your stress level under control may help. Now is a good time to think about making changes that can have positive effects for the rest of your life. You will feel better and you will also be healthier.

You can start by working on those things that worry you most. Get help with those that are harder for you. For instance, if you are thinking about quitting smoking and need help, call the American Cancer Society at 1-800-227-2345. This tobacco cessation and coaching service can help increase your chances of quitting for good.

Eating better

Eating right can be hard for anyone, but it can get even tougher during and after cancer treatment. Treatment may change your sense of taste. Nausea can be a problem. You may not feel like eating and lose weight when you don't want to. Or you may have gained weight that you can't seem to lose. All of these things can be very frustrating.

If treatment caused weight changes or eating or taste problems, do the best you can and keep in mind that these problems usually get better over time. You may find it helps to eat small portions every 2 to 3 hours until you feel better. You may also want to ask your cancer team about seeing a dietitian, an expert in nutrition who can give you ideas on how to deal with these treatment side effects.

One of the best things you can do after cancer treatment is put healthy eating habits into place. You may be surprised at the long-term benefits of some simple changes, like increasing the variety of healthy foods you eat. Getting to and staying at a healthy weight, eating a healthy diet, and limiting your alcohol intake may lower your risk for a number of types of cancer, as well as having many other health benefits.

You can get more information in our document *Nutrition and Physical Activity During and After Cancer Treatment: Answers to Common Questions.*

Rest, fatigue, and exercise

Extreme tiredness, called *fatigue*, is very common in people treated for cancer. This is not a normal tiredness, but a bone-weary exhaustion that often doesn't get better with rest. For some people, fatigue lasts a long time after treatment, and can make it hard for them to exercise and do other things they want to do. But exercise can help reduce fatigue. Studies have shown that patients who follow an exercise program tailored to their personal needs feel better physically and emotionally and can cope better, too.

If you were sick and not very active during treatment, it is normal for your fitness, endurance, and muscle strength to decline. Any plan for physical activity should fit your own situation. An older person who has never exercised will not be able to take on the same amount of exercise as a 20-year-old who plays tennis twice a week. If you haven't exercised in a few years, you will have to start slowly – maybe just by taking short walks.

Talk with your health care team before starting anything. Get their opinion about your exercise plans. Then, try to find an exercise buddy so you're not doing it alone. Having family or friends involved when starting a new exercise program can give you that extra boost of support to keep you going when the push just isn't there.

If you are very tired, you will need to balance activity with rest. It is OK to rest when you need to. Sometimes it's really hard for people to allow themselves to rest when they are used to working all day or taking care of a household, but this is not the time to push yourself too hard. Listen to your body and rest when you need to. (For more information on dealing with fatigue and other treatment side effects, please see the “Physical Side Effects” section of our website, or “Additional resources for gastrointestinal carcinoid tumors” to get a list of available information.)

Keep in mind exercise can improve your physical and emotional health.

- It improves your cardiovascular (heart and circulation) fitness.
- Along with a good diet, it will help you get to and stay at a healthy weight.
- It makes your muscles stronger.
- It reduces fatigue and helps you have more energy.
- It can help lower anxiety and depression.
- It can make you feel happier.
- It helps you feel better about yourself.

And long term, we know that getting regular physical activity plays a role in helping to lower the risk of some cancers, as well as having other health benefits. For more on this, see our document *American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention*.

How does treatment for a gastrointestinal carcinoid tumor affect your emotional health?

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

You may find yourself thinking about death and dying. Or maybe you're more aware of the effect the cancer has on your family, friends, and career. You may take a new look at your relationship with those around you. Unexpected issues may also cause concern. For instance, as you feel better and have fewer doctor visits, you will see your health care team less often and have more time on your hands. These changes can make some people anxious.

Almost everyone who has been through cancer can benefit from getting some type of support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, church or spiritual groups, online support communities, or one-on-one counselors. What's best for you depends on your situation and personality. Some people feel safe in peer-support groups or education groups. Others would rather talk in an informal setting, such as church. Others may feel more at ease talking one-on-one with a trusted friend or counselor. Whatever your source of strength or comfort, make sure you have a place to go with your concerns.

The cancer journey can feel very lonely. It is not necessary or good for you to try to deal with everything on your own. And your friends and family may feel shut out if you do not include them. Let them in, and let in anyone else who you feel may help. If you aren’t sure who can help, call your American Cancer Society at 1-800-227-2345 and we can put you in touch with a group or resource that may work for you. You can read our document, *Distress in People With Cancer* or see the “Emotional Side Effects” section of our website for more information.

If treatment of gastrointestinal carcinoid tumor stops working

If cancer keeps growing or comes back after one kind of treatment, it is possible that another treatment plan might still cure the cancer, or at least shrink it enough to help you live longer and feel better. But when a person has tried many different treatments and the cancer has not gotten any better, the cancer tends to become resistant to all treatment. If this happens, it's important to weigh the possible limited benefits of a new treatment against the possible downsides. Everyone has their own way of looking at this.

This is likely to be the hardest part of your battle with cancer − when you have been through many medical treatments and nothing's working anymore. Your doctor may offer you new

options, but at some point you may need to consider that treatment is not likely to improve your health or change your outcome or survival.

If you want to continue to get treatment for as long as you can, you need to think about the odds of treatment having any benefit and how this compares to the possible risks and side effects. In many cases, your doctor can estimate how likely it is the cancer will respond to treatment you are considering. For instance, the doctor may say that more chemo or radiation might have about a 1% chance of working. Some people are still tempted to try this. But it is important to think about and understand your reasons for choosing this plan.

Palliative care

No matter what you decide to do, you need to feel as good as you can. Make sure you are asking for and getting treatment for any symptoms you might have, such as nausea or pain. This type of treatment is called *palliative care*.

Palliative care helps relieve symptoms, but is not expected to cure the disease. It can be given along with cancer treatment, or can even be cancer treatment. The difference is its purpose − the main purpose of palliative care is to improve the quality of your life, or help you feel as good as you can for as long as you can. Sometimes this means using drugs to help with symptoms like pain or nausea. Sometimes, though, the treatments used to control your symptoms are the same as those used to treat cancer. For instance, radiation might be used to help relieve bone pain caused by cancer that has spread to the bones. Or chemo might be used to help shrink a tumor and keep it from blocking the bowels. But this is not the same as treatment to try to cure the cancer.

Hospice care

At some point, you may benefit from hospice care. This is special care that treats the person rather than the disease; it focuses on quality rather than length of life. Most of the time, it is given at home. Your cancer may be causing problems that need to be managed, and hospice focuses on your comfort. You should know that while getting hospice care often means the end of treatments such as chemo and radiation, it doesn't mean you can't have treatment for the problems caused by your cancer or other health conditions. In hospice the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult time. You can learn more about hospice in our document called *Hospice Care*.

Staying hopeful is important, too. Your hope for a cure may not be as bright, but there is still hope for good times with family and friends − times that are filled with happiness and meaning. Pausing at this time in your cancer treatment gives you a chance to refocus on the most important things in your life. Now is the time to do some things you've always wanted to do and to stop doing the things you no longer want to do. Though the cancer may be beyond your control, there are still choices you can make.

You can learn more about the changes that occur when treatment stops working, and about planning ahead for yourself and your family, in our documents *Nearing the End of Life* and *Advance Directives*.

What’s new in gastrointestinal carcinoid tumor research and treatment?

There is always research going on in the field of gastrointestinal (GI) carcinoids. Scientists keep looking for the causes of, ways to prevent, and new approaches to diagnose and treat GI carcinoid tumors.

Genetics

Researchers are looking for the causes of GI carcinoid cancer in the hope that this knowledge can be used to help prevent or treat the disease in the future. A great deal of progress has been made in recent years. For example, scientists have found that changes in the *MEN1* gene (the gene that causes multiple endocrine neoplasia, type 1) are seen in many people with GI carcinoids. Other genetic changes that seem to make tumors more aggressive are now being explored as well.

Diagnosis and staging

Because the outlook and treatment of GI carcinoid tumors/cancers and other cancers of the digestive tract are very different, accurate diagnosis is important. Researchers have made great progress in developing tests that can detect specific substances found in the cells of carcinoid tumors. Most of these tests treat tissue samples with special antibodies produced in the lab. The antibodies are designed to recognize specific substances that appear only in certain types of tumors.

OctreoScan is an imaging test commonly used to look for GI carcinoid cancers in the body. Researchers are now looking at other radionuclide methods to see if they can detect carcinoid tumors early.

Treatment

Surgery is the main treatment option for carcinoid tumors when possible. But better approaches are needed when surgery can't remove all of the tumors. Chemotherapy has had limited success. New chemotherapy drugs and combinations of drugs are being studied, but true advances are likely to come from other approaches.

Targeted therapy

Several newer types of drugs, known as targeted therapies, are now being studied for use against neuroendocrine tumors and cancers. Targeted therapy uses drugs or other substances to identify and attack cancer cells while doing little damage to normal cells. These therapies attack the cancer cells' inner workings − the programming that makes them different from normal, healthy cells. Each type of targeted therapy works differently, but all alter the way a cancer cell grows, divides, repairs itself, or interacts with other cells.

Everolimus (Affinitor®) is a targeted therapy drug that works by blocking a cell protein known as mTOR, which normally promotes cell growth and division. It is approved by the FDA to treat advanced pancreatic neuroendocrine tumors. Because it can be helpful in the treatment of neuroendocrine tumors that start in the pancreas, it was studied to see if it could help patients with GI carcinoids. In one study, adding everolimus to octreotide (Sandostatin) was better than octreotide alone in halting tumor growth.

Bevacizumab (Avastin®) is another type of targeted therapy drug that attacks a tumor's blood supply. It is already being used against some types of cancer and is being studied for carcinoid tumors. Other targeted therapies block the molecules that increase the growth of cancer cells. Some of these (such as erlotinib, temsirolimus, and sorafenib) are used in other types of cancer and are now being tested against carcinoids.

Netazepide is new drug that blocks the hormone gastrin. In early studies of patients who have carcinoid tumors of the stomach and high gastrin levels, this drug helped the tumors shrink. More studies are planned.

Radionuclide scans, such as the I-131 MIBG scan, can be helpful in finding neuroendocrine cancers because they use substances that are attracted to neuroendocrine cells. These substances are attached to slightly radioactive elements so that they can be detected with special cameras. Using higher doses of I-131 MIBG delivers more radiation to the tumor cells and is used in Europe to treat neurendocrine tumors and cancers. But doctors are now studying the use of a form of octreotide (or a similar drug called *edotreotide*) that has been attached to a radioactive form of the element yttrium called *90-Y*. When injected into the body, the drug homes in on the tumor cells, allowing the radiation from the 90-Y to kill them. So far, results have been promising, but this approach is still only available in the United States as a part of a clinical trial.

Additional resources for gastrointestinal carcinoid tumors

More information from your American Cancer Society

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

Living with cancer

Coping With Cancer in Everyday Life (also in Spanish)

Guide to Controlling Cancer Pain (also available in Spanish)

Distress in People With Cancer

Living With Uncertainty: The Fear of Cancer Recurrence

Colostomy: A Guide

Liver Cancer

Pancreatic Cancer

Understanding cancer treatments

Understanding Cancer Surgery: A Guide for Patients and Families (also in Spanish)

A Guide to Chemotherapy (also available in Spanish)

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

Clinical Trials: What You Need to Know

Cancer treatment side effects

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

Nausea and Vomiting

Anemia in People With Cancer

Fatigue in People With Cancer

Cancer that comes back or doesn’t respond to treatment

When Cancer Doesn’t Go Away

When Your Cancer Comes Back: Cancer Recurrence

Advanced or late stage cancer

Advanced Cancer

Nearing the End of Life

Hospice Care

Family communication and caregiver concerns

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

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

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

What It Takes to Be a Caregiver

Your American Cancer Society also has books that you might find helpful. Call us at 1-800-227-2345 or visit our bookstore online at cancer.org/bookstore to find out about costs or to place an order.

National organizations and Web sites*

In addition to the American Cancer Society, other sources of patient information include:

National Cancer Institute
Toll-free number: 1-800-4-CANCER (1-800-422-6237)
Website: www.cancer.gov

> Offers free, accurate, up-to-date information about cancer to patients, their families, and the general public; also helps people find clinical trials in their area

The Carcinoid Cancer Foundation, Inc.
Toll-free number: 1-888-722-3132 or 1-914-683-1001
Website: www.carcinoid.org

> Information on carcinoid, including frequently-asked questions, finding expert doctors, living with carcinoid cancers, and referrals to local support groups

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

No matter who you are, we can help. Contact us anytime, day or night, for information and support. Call us at **1-800-227-2345** or visit www.cancer.org.

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