



Pancreatic Cancer

What is cancer?

The body is made up of trillions of living cells. Normal body cells grow, divide, 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.

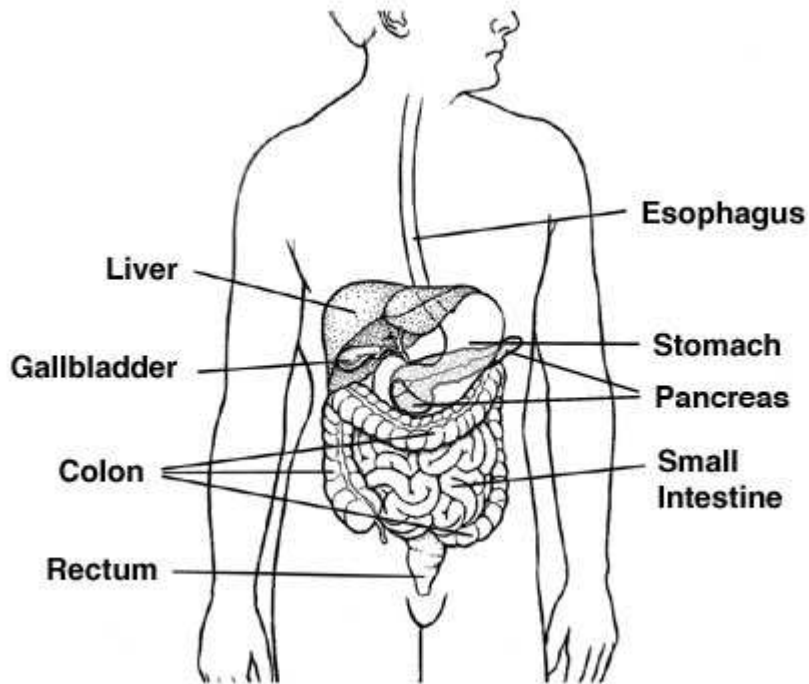
Different types of cancer can behave very differently. For example, lung cancer and breast cancer are very different diseases. They grow at different rates and respond to different treatments. That is why people with cancer need treatment that is aimed at their particular kind of cancer.

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 pancreatic cancer?

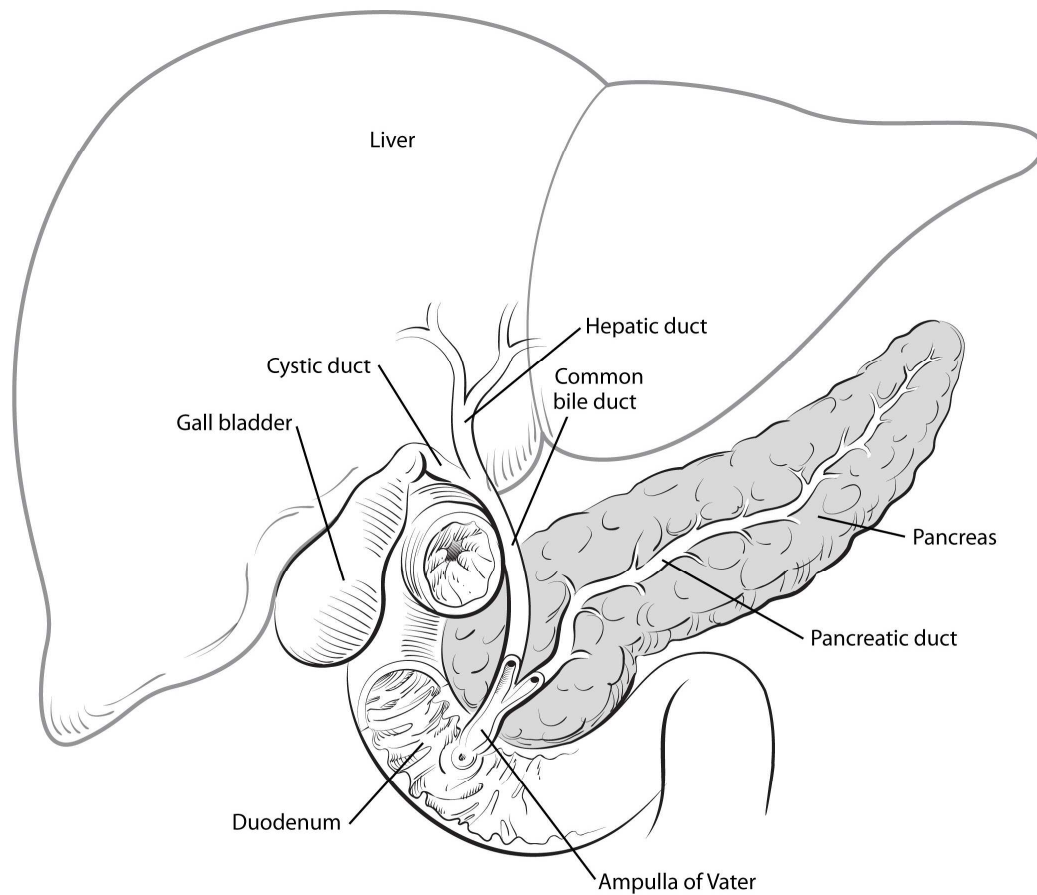
The normal pancreas

The pancreas is an organ located behind the stomach. It is shaped a little bit like a fish with a wide head, a tapering body, and a narrow, pointed tail. It is about 6 inches long but less than 2 inches wide and extends horizontally across the abdomen. The head of the pancreas is on the right side of the abdomen (belly), behind the place where the stomach meets the duodenum (the first part of the small intestine). The body of the pancreas is located behind the stomach and the tail of the pancreas is on the left side of the abdomen next to the spleen.



The pancreas contains 2 different types of glands: exocrine and endocrine.

The *exocrine* glands make pancreatic "juice," which is released into the intestines. This juice contains enzymes that help you digest fats, proteins, and carbohydrates in the food you eat. Without these, some of the food you eat would just pass through your intestines without being absorbed. The enzymes are released into tiny tubes called *ducts*. These tiny ducts merge to form larger ducts that empty into the pancreatic duct. The pancreatic duct merges with the common bile duct (the duct that carries bile from the liver), and empties the pancreatic juice into the duodenum (the first part of the small intestine) at the ampulla of Vater. More than 95% of the cells in the pancreas are exocrine glands and ducts.



A small percentage of the cells in the pancreas are *endocrine* cells. These cells are arranged in small clusters called islets (or *islets of Langerhans*). The islets release important hormones, such as insulin and glucagon, directly into the blood. Insulin reduces the amount of sugar in the blood, while glucagon increases it. Diabetes results from a defect in insulin production.

Types of pancreatic tumors

The exocrine cells and endocrine cells of the pancreas form completely different types of tumors.

Exocrine tumors

Exocrine tumors are by far the most common type of pancreas cancer. When someone says that they have pancreatic cancer, they usually mean an exocrine pancreatic cancer. Benign (non-cancerous) cysts and benign tumors called *cystadenomas* can occur, but most pancreatic exocrine tumors are malignant (cancerous).

An adenocarcinoma is a cancer that starts in gland cells. About 95% of cancers of the exocrine pancreas are adenocarcinomas. These cancers usually begin in the ducts of the pancreas, but they sometimes develop from the cells that make the pancreatic enzymes (acinar cell carcinomas).

Less common types of ductal cancers of the exocrine pancreas include adenosquamous carcinomas, squamous cell carcinomas, and giant cell carcinomas. These types are distinguished from one another based on how they look under the microscope.

The treatment of an exocrine pancreatic cancer is mostly based on the stage of the cancer, not its exact type. The stage of the cancer describes how large the tumor is and how far it has spread. Pancreatic cancer staging is described later in this document.

A special type of cancer, called *ampullary cancer* (or carcinoma of the ampulla of Vater) deserves mention here. The place where the bile duct and pancreatic duct come together and empty into the duodenum is called the *ampulla of Vater*. Cancers that start here are called *ampullary cancers*. These cancers often block the bile duct while they are still small and have not spread far. This blockage causes bile to build up in the body, which leads to yellowing of the skin and eyes (jaundice) and can turn the urine dark. This is an easily recognized sign that something is wrong. This is why ampullary cancers are usually found at an earlier stage than most pancreatic cancers, which means they usually have a better prognosis (outlook) than typical pancreatic cancers.

Ampullary cancers are included with pancreatic cancer in this document because their treatments are very similar.

Endocrine tumors

Tumors of the endocrine pancreas are uncommon. As a group, they are known as *pancreatic neuroendocrine tumors (NETs)*, or sometimes as *islet cell tumors*. There are several subtypes of islet cell tumors. Each is named according to the type of hormone-making cell it starts in:

- *Insulinomas* come from cells that make insulin.
- *Glucagonomas* come from cells that make glucagon.
- *Gastrinomas* come from cells that make gastrin.
- *Somatostatinomas* come from cells that make somatostatin.
- *VIPomas* come from cells that make vasoactive intestinal peptide (VIP).
- *PPomas* come from cells that make pancreatic polypeptide.

Carcinoid tumors are another type of pancreatic NET. These tumors often make serotonin (also called *5-HT*) or its precursor, *5-HTP*.

About half of pancreatic NETs make hormones that are released into the blood and so are called functioning tumors. Tumors that do not make hormones are called *non-functioning*.

Islet cell tumors can be benign or malignant. Benign tumors are called *pancreatic neuroendocrine tumors*, while malignant tumors are called *pancreatic neuroendocrine cancers or carcinomas*. Malignant and benign tumors can look very similar under the microscope, so it isn't always clear at the time of diagnosis whether or not a NET is cancer. Sometimes the diagnosis only becomes clear when the tumor has spread outside of the pancreas.

Pancreatic neuroendocrine cancers make up less than 4% of all pancreatic cancers diagnosed. Treatment and prognosis depend on the specific tumor type and the stage (extent) of the tumor but the prognosis is generally better than that of pancreatic exocrine cancers. The most common types of pancreatic endocrine tumors are gastrinomas and insulinomas. The other types occur very rarely.

It is very important to distinguish between exocrine and endocrine cancers of the pancreas. They have distinct risk factors and causes, have different signs and symptoms, are diagnosed using different tests, are treated in different ways, and have different prognoses. In this document, the term pancreatic neuroendocrine tumor is used for both benign and malignant endocrine pancreatic tumors.

What are the key statistics about pancreatic cancer?

The American Cancer Society's most recent estimates for pancreatic cancer in the United States are for 2012:

- About 43,920 people (22,090 men and 21,830 women) will be diagnosed with pancreatic cancer.
- About 37,390 people (18,850 men and 18,540 women) will die of pancreatic cancer

Since 2004, rates of pancreatic cancer have increased about 1.5% per year.

The lifetime risk of developing pancreatic cancer is about 1 in 71 (1.41%). This is about the same for men and women. A person's risk may be altered by certain risk factors (listed in the next section).

What are the risk factors for pancreatic cancer?

A risk factor is anything that affects your chance of getting a disease such as cancer. Different cancers have different risk factors. Some risk factors, like smoking, can be changed. Others, like a person's age or family history, can't be changed. But risk factors don't tell us everything. Having a risk factor, or even several risk factors, does not mean that you will get the disease. And many people who get the disease may not have had any known risk factors.

Researchers have found several factors that affect a person's chance of getting cancer of the pancreas. Most of these are risk factors for exocrine pancreatic cancer.

Age

The risk of developing pancreatic cancer increases as people age. Almost all patients are older than 45. Nearly 90% are older than 55 and more than 70% are older than 65. The average age at the time of diagnosis is 72.

Gender

Men are slightly more likely to develop pancreatic cancer than women. This may be due, at least in part, to increased tobacco use in men. The difference in pancreatic cancer risk was more pronounced in the past (when tobacco use was much more common among men than women), but the gap has closed in recent years.

Race

African Americans are more likely to develop pancreatic cancer than whites. The reasons for this are not clear, but it may be due in part to higher rates of smoking and diabetes in men and being overweight in women.

Cigarette smoking

The risk of getting pancreatic cancer is 2 to 3 times higher among smokers. Scientists think this may be due to cancer-causing chemicals in cigarette smoke that enter the blood and damage the pancreas. About 20% to 30% of exocrine pancreatic cancer cases are thought to be caused by cigarette smoking.

People who use smokeless tobacco are also more likely to get exocrine pancreatic cancer.

Obesity and physical activity

Very overweight (obese) people are more likely to develop exocrine pancreatic cancer, as are people who don't get much physical activity. Exercise lowers the risk of this cancer.

Diabetes

Exocrine pancreatic cancer is more common in people with this disease. The reason for this link is not known. Most of the risk is found in people with type 2 diabetes. This type of diabetes most often starts in adulthood. It is often related to being overweight or obese. It is not clear if people with type 1 (juvenile) diabetes have a higher than average risk. In some patients, though, the cancer seems to have caused the diabetes (not the other way around).

Chronic pancreatitis

Chronic pancreatitis is a long-term inflammation of the pancreas. This condition is linked with an increased risk of pancreatic cancer, but most patients with pancreatitis never develop pancreatic cancer. The link between chronic pancreatitis and pancreatic cancer is strongest in smokers.

A small number of cases of chronic pancreatitis appear to be due to an inherited gene mutation (see "Family history"). People with this inherited form of chronic pancreatitis seem to have a high lifetime risk for developing pancreatic cancer (about 40% to 75%).

Cirrhosis of the liver

Cirrhosis is a scarring of the liver. It develops in people with liver damage from things like hepatitis and alcohol use. People with cirrhosis seem to have an increased risk of pancreatic cancer.

Occupational exposure

Heavy exposure at work to certain pesticides, dyes, and chemicals used in metal refining may increase the risk of developing pancreatic cancer.

Family history

Pancreatic cancer seems to run in some families. In some of these families, the high risk is due to an inherited syndrome (explained in the next section, "Genetic syndromes"). In other families, the gene causing the increased risk of pancreatic cancer is not known.

Genetic syndromes

Inherited gene mutations are abnormal copies of certain genes that can be passed from parent to child. These abnormal genes may cause as many as 10% of pancreatic cancers and can cause other problems as well. Examples of the genetic syndromes that can cause exocrine pancreatic cancer include:

- **Hereditary breast and ovarian cancer syndrome**, caused by mutations in the gene *BRCA2*
- **Familial melanoma**, caused by mutations in the gene *p16*
- **Familial pancreatitis**, caused by mutations in the gene *PRSS1*
- **Hereditary non-polyposis colorectal cancer (HNPCC)**, most often caused by a defect in either the gene *MLH1* or the gene *MSH2*. At least 5 other genes can also cause HNPCC: *MLH3*, *MSH6*, *TGBR2*, *PMS1*, and *PMS2*. This disorder is also known as Lynch syndrome.

- **Peutz-Jeghers syndrome (PJS)**, caused by defects in the gene *STK11*. This syndrome is also linked with polyps in the digestive tract and several other cancers
- **Von Hippel-Lindau syndrome**, caused by mutations in the gene *VHL*, can lead to an increased risk of pancreatic cancer and carcinoma of the ampulla of Vater

Pancreatic neuroendocrine tumors and cancers can also be caused by a genetic syndrome, such as:

- **Neurofibromatosis, type 1**, which is caused by mutations in the gene *NF1*. This syndrome leads to an increased risk of many tumors, including somatostatinomas.
- **Multiple endocrine neoplasia, type 1**, caused by mutations in the gene *MEN1*, leads to an increased risk of tumors of the parathyroid gland, the pituitary gland, and the islet cells of the pancreas.

Scientists have found the genes that cause the syndromes listed above and they can be recognized by genetic testing. For more information on genetic testing, see the section, “Can pancreatic cancer be found early?”

Stomach problems

Infection of the stomach with the ulcer-causing bacteria *Helicobacter pylori* (*H. pylori*) may increase the risk of getting pancreatic cancer. Some researchers believe that excess stomach acid may also increase the risk.

Diet

Some studies linked pancreatic cancer and diets high in fat, or those that include a lot of red meat, pork, and processed meat (such as sausage and bacon). Others have found that diets high in fruits and vegetables may help reduce the risk of pancreatic cancer. But not all studies have found such links, and the exact role of diet in relation to pancreatic cancer is still being studied.

Coffee

Some older studies have suggested that drinking coffee might increase the risk of pancreatic cancer, but more recent studies have not confirmed this.

Alcohol

Most studies have not found a link between alcohol use and pancreatic cancer. But heavy alcohol use can raise the risk of diabetes, liver cirrhosis, and chronic pancreatitis, which are all risk factors for pancreatic cancer.

Do we know what causes pancreatic cancer?

Scientists still do not know exactly what causes most cases of pancreatic cancer, but they have found several risk factors that can make a person more likely to get this disease. Recent research has shown that some of these risk factors affect the DNA of cells in the pancreas, which can result in abnormal cell growth and may cause tumors to form.

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 contain instructions for controlling when our cells grow and divide. Certain genes that promote cell division are called *oncogenes*. Others that slow down cell division 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.

Several cancer family syndromes have been found in which inherited DNA mutations cause a very high risk of developing certain cancers. In some of these, there is an increased risk of getting pancreatic cancer. Researchers have characterized many of these DNA changes in the past few years. (See the section, “What are the risk factors for pancreatic cancer?”)

Most often, DNA mutations of oncogenes or tumor suppressor genes related to cancers of the pancreas occur after you are born, rather than having been inherited. These acquired mutations may result from cancer-causing chemicals in our environment, diet, or tobacco smoke. Sometimes they occur for no apparent reason.

Often, the DNA changes seen in sporadic (non-inherited) cases of pancreatic cancer are the same as those seen in inherited cases. For example, most sporadic cases of exocrine pancreatic cancer have changes in the p16 gene. This is why scientists are studying inherited cases closely to learn more about what causes pancreatic cancer. Some specific DNA abnormalities recently discovered in pancreatic cancer are discussed in the section, “What's new in pancreatic cancer research and treatment?”

Can pancreatic cancer be prevented?

There are no established guidelines for preventing pancreatic cancer. For now, the best approach is to avoid pancreatic cancer risk factors whenever possible.

Cigarette smoking is the most important avoidable risk factor for pancreatic cancer. It is responsible for 20% to 30% of pancreatic cancers. Tobacco use also increases the risk of many other cancers such as cancers of the lung, mouth, larynx (voice box), esophagus, kidney, bladder, and some other organs. If you smoke and want help quitting, please talk to your doctor or call the American Cancer Society at 1-800-227-2345.

Maintaining a healthy weight, eating well, and exercising are also important. The American Cancer Society recommends choosing foods and beverages in amounts that

help achieve and maintain a healthy weight. Eat a healthy diet, with an emphasis on plant foods. This includes eating at least 2½ cups of vegetables and fruits every day. Choosing whole-grain breads, pastas, and cereals instead of refined grains, and eating fish, poultry, or beans instead of processed meat and red meat may also help lower your risk of cancer, as well as some other diseases.

Can pancreatic cancer be found early?

One reason for the often poor outlook for people with exocrine pancreatic cancer is that very few of these cancers are found early. The pancreas is located deep inside the body, so early tumors cannot be seen or felt by health care providers during routine physical exams. Patients usually have no symptoms until the cancer has spread to other organs. Right now, there are no blood tests to find early cancers of the pancreas. Doctors are looking to see if something called *endoscopic ultrasound* can be useful in screening people with a high risk of pancreatic cancer.

Blood tests

A substance called CA 19-9 is released into the blood by exocrine pancreatic cancer cells and can be detected by blood tests. But by the time blood levels are high enough to be consistently detected by available methods, the cancer is no longer in its early stages. This is why the test is not recommended for routine screening of people without symptoms or a known diagnosis of cancer. The CA 19-9 test is sometimes used during treatment to see if the therapy is working or after treatment to see if the cancer has recurred (come back).

Another substance, carcinoembryonic antigen (CEA), can help detect advanced pancreatic cancer in some people. But it isn't sensitive enough to find the cancer early and is not recommended as a screening test.

Genetic testing

Inherited DNA changes are thought to cause as many as 10% of pancreatic cancers. Because these inherited cases are sometimes linked with other cancers, determining whether a patient's relatives have an increased risk is not simple. Talking to someone with experience in hereditary cancer syndromes such as a genetic counselor, geneticist, or an oncologist (doctor who specializes in caring for people who have cancer) is often helpful.

The American Cancer Society strongly recommends that any person considering genetic testing talk with a genetic counselor, nurse, or doctor qualified to interpret and explain the test results before they proceed with testing. It is important for people to understand and carefully weigh the benefits and risks of genetic testing before these tests are done. For more information, see our document, *Genetic Testing: What You Need to Know*.

For people in families at high risk of pancreatic cancer, there are newer tests for detecting early pancreatic cancer that may help. One of these is called *endoscopic ultrasound* (see

the section, “How is pancreatic cancer diagnosed?”). This test is not used to screen the general public but might be used for someone with a strong family history of pancreatic cancer. Using endoscopic ultrasound, doctors have been able to find early, treatable pancreatic cancers in some members of high-risk families. In addition, interested families may wish to participate in ongoing research studies aimed at investigating the genetic factors and possible role of screening methods in those with a family history of the disease.

How is pancreatic cancer diagnosed?

If one or more of the signs and symptoms described here is present, certain exams and tests may be done to find out whether they are caused by pancreatic cancer or by some other disease.

Signs and symptoms of exocrine pancreatic cancer

Jaundice

Jaundice is yellowing of the eyes and skin caused by the buildup of bilirubin in the body. Bilirubin is a dark yellow-brown substance that is made in the liver. Normally, the liver excretes bilirubin into bile. Bile goes through the common bile duct into the intestines, eventually leaving the body in the stool. When the common bile duct becomes blocked, bile can't reach the intestines, and the level of bilirubin builds up. At least half of all people with pancreatic cancer and in all people with ampullary cancer have jaundice.

Cancers that begin in the head of the pancreas are near the common bile duct. These cancers can compress the duct while they are still fairly small. This can lead to jaundice, which may allow these tumors to be found in an early stage. But cancers that begin in the body or tail of the pancreas do not compress the duct until they have spread through the pancreas. By this time, the cancer may have also spread beyond the pancreas.

When pancreatic cancer spreads, it often goes to the liver. This can also lead to jaundice.

Sometimes, the first sign of jaundice is darkening of the urine from bilirubin. As bilirubin levels in the blood increase, the urine becomes brown in color.

If the bile duct is blocked, bile (and bilirubin) can't get through to the bowel. When this happens, a person may notice their stools becoming lighter in color.

When bilirubin builds up in the skin, it turns yellow and starts to itch.

Cancer is not the most common cause of jaundice. Other causes, such as gallstones, hepatitis, and other liver diseases, are much more common.

Abdominal or back pain

Pain in the abdomen or back is common in advanced pancreatic cancer. Cancers that start in the body or tail of the pancreas may grow fairly large and start to compress on other nearby organs, causing pain. The cancer may also spread to the nerves surrounding the pancreas, which often causes back pain. The pain may be constant or it may come and go. Of course, pancreatic cancer is not a common cause of pain in the abdomen or back. It is more often caused by a non-cancerous disease or even another type of cancer.

Weight loss and poor appetite

Unintended or unexpected weight loss is very common in patients with pancreatic cancer. These people also complain of being very tired and having little or no appetite.

Digestive problems

If cancer blocks the release of the pancreatic juice into the intestine, a person may not be able to digest fatty foods. The undigested fat may cause stools to be unusually pale, bulky, greasy, and to float in the toilet. The cancer may also wrap around the far end of the stomach and partly block it. This can cause nausea, vomiting, and pain that tend to be worse after eating.

Gallbladder enlargement

If the cancer blocks the bile duct, bile can build up in the gallbladder, which then becomes enlarged. This can sometimes be felt by a doctor during a physical exam. It can also be detected by imaging studies.

Blood clots or fatty tissue abnormalities

Sometimes, the first clue that there is a pancreatic cancer is the development of a blood clot in a large vein, often a vein in the leg. This is called a *deep venous thrombosis* or DVT. Sometimes a clot breaks off and travels to the lungs, making it hard to get enough air. A blood clot in the lungs is called a *pulmonary embolism* or PE. Still, having a blood clot does not usually mean that you have cancer. Most blood clots are caused by other things.

Another pancreatic cancer clue is the development of uneven texture of the fatty tissue underneath the skin. This is caused by the release of the pancreatic enzymes that digest fat.

Diabetes

Rarely, exocrine cancers of the pancreas cause diabetes (high blood sugar) because they destroy the insulin-making cells. More often, there are slight problems with sugar metabolism that do not cause symptoms of diabetes but can still be recognized by certain blood tests.

Signs and symptoms of pancreatic neuroendocrine tumors

Most of the signs and symptoms of pancreatic neuroendocrine tumors (NETs) are caused by the excess hormones that the tumors release into the bloodstream. Different types of tumors make different hormones.

Gastrinomas

These tumors make gastrin, a hormone that tells the stomach to make more acid. Too much gastrin causes a condition known as *Zollinger-Ellison syndrome*. The excess gastrin causes the stomach to make too much acid. This leads to stomach ulcers, which can cause pain, nausea, and a decreased appetite. If the ulcer is severe, it may start bleeding. If the bleeding is mild, it may lead to anemia (low red blood cell counts). This can cause symptoms like feeling very tired and being short of breath when you exercise. If the bleeding is more severe, it can cause the stool to become black and tarry. Severe bleeding can itself be life-threatening. The ulcers in patients with gastrinomas can be hard to treat, requiring high doses of anti-ulcer medication to heal. Patients need to stay on these drugs for a long time, because the ulcers tend to come back again if treatment is stopped.

When the stomach makes too much acid it can be released into the small intestine. There it can damage the cells of the intestinal lining and break down digestive enzymes before they have a chance to digest food. This can cause diarrhea and weight loss.

Most gastrinomas are cancers.

Glucagonomas

These tumors make glucagon, a hormone that increases glucose levels in the blood. Excess glucagon can cause the blood sugar to go up, sometimes leading to diabetes. Patients also have problems with diarrhea, weight loss, and malnutrition. The nutrition problems can lead to symptoms like irritation of the tongue (*glossitis*) and the corners of the mouth (*angular cheilosis*). Most of the symptoms that can be caused by a glucagonoma are mild and more often are found to be caused by something else.

The symptom that brings most people with glucagonomas to their doctor is a rash called *necrolytic migratory erythema*. It is a red rash with swelling and blisters and it often travels place to place on the skin. It is the most distinctive feature of a glucagonoma.

Most glucagonomas are cancers.

Insulinomas

These tumors make insulin, which lowers blood glucose levels. Too much insulin leads to low blood sugar (*hypoglycemia*), with symptoms like weakness, confusion, sweating, and rapid heart beat. When blood sugar gets very low, it can lead to the patient passing out or even going into a coma and having seizures. These symptoms improve if the patient gets glucose (sugar) — either by mouth (as food) or as an injection into the vein (IV).

Most insulinomas are benign (not cancers).

Somatostatinomas

These tumors make somatostatin, which helps regulate other hormones. Symptoms of this type of tumor include diarrhea, diabetes, and gallbladder problems. The problems with the gallbladder can lead to abdominal pain, nausea, poor appetite, and jaundice (yellowing of the skin and eyes). Since symptoms of a somatostatinoma tend to be mild and are more often caused by other things, these tumors tend to be diagnosed at an advanced stage.

Most somatostatinomas are cancers. Often, they are not found until they spread to the liver, when they cause problems like jaundice and pain.

VIPomas

These tumors make a substance called vasoactive intestinal peptide (VIP). Too much VIP can lead to problems with diarrhea and low blood levels of potassium. Patients also have low levels of acid in their stomachs, leading to problems digesting food. They may also have high blood glucose levels. The diarrhea may be mild at first, but gets worse over time. By the time they are diagnosed, most patients have severe, watery diarrhea, with as many as 20 bowel movements per day.

Most VIPomas are cancers.

PPomas

These tumors make pancreatic polypeptide, which helps regulate both the exocrine and endocrine pancreas. They cause problems with abdominal pain and an enlarged liver. Some patients also get watery diarrhea.

Most PPomas are cancers.

Carcinoid tumors

These tumors often make serotonin or its precursor 5-HTP. When a pancreatic tumor makes these substances, they first travel to the liver. The liver breaks down these substances before they can reach the rest of the body and cause problems. This is why carcinoid tumors may not cause symptoms until they spread outside the pancreas. When they do, it is most often to the liver. When that happens, the hormones can be released from the cancer cells directly into the blood leaving the liver. This can cause something called the *carcinoid syndrome*, with symptoms including: flushing (skin turning red with a warm feeling), diarrhea, wheezing, and a rapid heart rate. These symptoms often occur in episodes, and between episodes the patient may feel fine.

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).

Non-functioning tumors

These tumors do not make hormones, so they do not cause symptoms in early stages. Most of these are cancers and start to cause problems as they get larger or spread outside the pancreas.

Symptoms caused by the cancer spreading

When pancreatic NETs spread, they most often spread to the liver. This can cause the liver to enlarge, which can cause pain and a poor appetite. It can also interfere with the liver function, sometimes leading to jaundice (yellowing of the skin and eyes) and abnormal lab tests.

Although these cancers often first spread to the liver, they can go on to spread to other organs and tissues. The symptoms depend on where the cancer is growing. For example, cancer spread to the lungs can cause problems breathing and a cough. Spread to bones can cause pain in those bones.

Tests to diagnose pancreatic cancer

History and physical exam

A thorough medical history will be taken to check for any pancreatic cancer risk factors, and to get information about pain (how long it has been present, its severity, its location, and what makes it worse or better), appetite, weight loss, tiredness, and other symptoms.

A thorough physical exam will focus mostly on the abdomen to check for any masses or fluid buildup. The skin and the white part of the eyes will be checked for jaundice (yellowing). Cancers that block the bile duct may also cause the gallbladder to become enlarged, which can sometimes be felt on physical exam. Pancreatic cancer may spread to the liver, causing it to enlarge.

The cancer can also spread to lymph nodes above the collarbone and other locations. These areas will be looked at carefully for swelling that might indicate spread of a cancer.

Imaging tests

Computed tomography (CT, CAT) scan

The CT scan is an x-ray procedure that produces detailed cross-sectional images of your body. Instead of taking one picture, like a standard x-ray, a CT scanner takes many pictures as it rotates around you. A computer then combines these pictures into images that resemble slices of the part of your body being studied.

Before the scan, the patient may be asked to drink a contrast solution and/or get an intravenous (IV) injection of a contrast dye to better outline abnormal areas in the body.

The patient may need an IV line through which the contrast dye is injected. The injection can cause some flushing (a feeling of warmth, especially in the face). Some people are allergic to the dye and get hives or a flushed feeling or, rarely, have more serious reactions like trouble breathing and low blood pressure. Be sure to tell the doctor if you have any allergies or have ever had a reaction to any contrast material used for x-rays. Medicine can be given to prevent and treat allergic reactions.

CT scans take longer than regular x-rays. You need to lie still on a table while they are being done. During the test, the table slides in and out of the scanner, a ring-shaped machine that completely surrounds the table. You might feel a bit confined by the ring in when the pictures are being taken.

CT scans are often used to diagnose pancreatic cancer and are helpful in staging the cancer (determining the extent of its spread). CT scans show the pancreas fairly clearly and often can confirm the location of the cancer. CT scans can also show the organs near the pancreas, as well as lymph nodes and distant organs where the cancer might have spread. The CT scan can help determine whether surgery is a good treatment option.

CT scans can also be used to guide a biopsy needle precisely into a suspected area of spread. For this procedure, called a *CT-guided needle biopsy*, the patient remains on the CT scanning table as a radiologist advances a biopsy needle toward the location of the mass. CT scans are repeated until the doctors are sure that the needle is within the mass. A biopsy sample is then removed and looked at under a microscope.

Magnetic resonance imaging (MRI)

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 body tissue and by certain diseases. A computer translates the pattern into a detailed image of parts of the body. Not only does this produce cross-sectional slices of the body like a CT scanner, it also produces slices that are parallel with the length of the body. A contrast material might be injected just as with CT scans, this but is used less often.

Most doctors prefer CT scans to look at the pancreas, but an MRI may sometimes provide more information. MRI scans are also particularly helpful in looking at the brain and spinal cord.

MRI scans take longer than CT scans, often up to an hour. You may have to lie inside a narrow tube, which is confining and can be distressing to some people. Newer, more open MRI machines may be another option. The MRI machine makes loud buzzing and clicking noises that you might find disturbing. Some places give you headphones or earplugs to help block this noise out.

Somatostatin receptor scintigraphy

Somatostatin receptor scintigraphy (SRS), also known as *OctreoScan*, can be very helpful in diagnosing pancreatic neuroendocrine tumors. It uses a hormone-like substance called

octreotide that has been bound to a radioactive substance (indium-111). Octreotide attaches to proteins on the tumor cells of many NETs.

A small amount of this substance is injected into a vein. It travels through the blood and is attracted to neuroendocrine tumors. About 4 hours after the injection, a special camera can be used to show where the radioactivity has collected in the body. Additional scans may be done on the following few days as well.

This scan can help diagnose a NET, but it can also help decide on a treatment. If a NET shows up on a SRS scan, it often means that the tumor will stop growing if treated with a drug called octreotide.

Positron emission tomography (PET) scan

For a PET scan, a form of radioactive sugar (known as *fluorodeoxyglucose* or *FDG*) is injected into the blood. Because cancer cells in the body are growing quickly, they absorb large amounts of the radioactive sugar. After about an hour, you will be moved onto a table in the PET scanner. You lie on the table for about 30 minutes while a special camera creates a picture of areas of radioactivity in the body. The picture is not finely detailed like a CT or MRI scan, but it can provide helpful information about your whole body.

This test is useful to look for spread from exocrine pancreatic cancers, but because NETs grow slowly, they do not show up well on PET.

PET/CT scans combine a CT scan and a PET scan to even better pinpoint the tumor. This test may be especially useful for spotting exocrine cancer that has spread beyond the pancreas and wouldn't be treatable by surgery. It may be a useful test for staging the cancer. It may even be able to spot early cancers.

Ultrasonography (ultrasound or US)

Ultrasound uses sound waves to produce images of internal organs such as the pancreas. For an abdominal ultrasound, a wand-shaped probe called a *transducer* is placed on the skin of the abdomen. It emits sound waves and detects the echoes as they bounce off internal organs. The pattern of echoes is processed by a computer to produce an image on a screen.

The echoes made by most pancreatic tumors differ from those of normal pancreas tissue. Different echo patterns can help distinguish some types of pancreatic tumors from one another.

If signs and symptoms indicate that a pancreatic cancer is likely, a CT scan is often more useful than ultrasound for an accurate diagnosis. But if it's not clear whether certain other diseases may account for the patient's signs or symptoms, ultrasound may be done. Ultrasound is also commonly used to look at the liver, and may be used if someone has symptoms (like jaundice) that point to a liver problem.

Endoscopic ultrasound is more accurate than abdominal ultrasound and is probably the best way to diagnose pancreatic cancer. This test is done with an ultrasound probe that is attached to an endoscope — a thin, lighted, flexible, fiber optic tube — that doctors use to look at the inside of the intestinal tract. Patients are first sedated (given medicine to make them sleepy). The probe is then passed through the mouth or nose, through the esophagus (the tube that connects the mouth to the stomach) and stomach, and into the first part of the small intestine. The probe can then be pointed toward the pancreas, which sits next to the small intestine. The probe is on the tip of the endoscope, so it can get very close to where the tumor is to take pictures. This is a very good way to look at the pancreas. It is better than CT scans for spotting small tumors. If a tumor is seen, it can be biopsied during this procedure.

Endoscopic retrograde cholangiopancreatography (ERCP)

For this procedure, an endoscope (a thin, lighted, flexible tube) is passed down the patient's throat, through the esophagus and stomach, and into the first part of the small intestine. The doctor can see through the endoscope to find the ampulla of Vater (where the common bile duct connects to the small intestine). The doctor guides a catheter (a very small tube) from the end of the endoscope into the common bile duct. A small amount of dye (contrast material) is then injected through the tube into the common bile duct and x-rays are taken. This dye outlines the bile duct and pancreatic duct. The x-ray images can show narrowing or blockage in these ducts that might be due to pancreatic cancer. The doctor doing this test can also put a small brush through the tube to remove cells for a biopsy (to view under a microscope to see whether or not they look like cancer). This procedure is usually done while the patient is sedated (given medicine to make them sleepy).

ERCP can also be used to place a stent (small tube) into the bile duct to keep it open if a nearby tumor is pressing on it. This is described in more detail in the section on palliative surgery in the “Surgery” section.

Angiography

This is an x-ray procedure that looks at blood vessels. A small amount of contrast material is injected into an artery to outline the blood vessels, then x-rays are taken.

Angiography can show if blood flow in a particular area is blocked or compressed by a tumor. It can also show any abnormal blood vessels (feeding the cancer) in the area. This test can be useful in finding out if a pancreatic cancer has grown through the walls of certain blood vessels. Mainly, it helps surgeons decide whether the cancer can be completely removed without damaging vital blood vessels and helps them plan the operation.

Angiography can also be used to look for pancreatic neuroendocrine tumors that are too small to be seen on other imaging tests. These tumors cause the body to make more blood vessels to "feed" the tumor. These extra blood vessels can be seen on angiography.

Angiography can be an uncomfortable procedure because the radiologist who performs it has to put a small catheter into the artery leading to the pancreas. Usually the catheter is put into an artery in your inner thigh and threaded up to the pancreas. A local anesthetic is often used to numb the area before inserting the catheter. Then the dye is injected quickly to outline all the vessels while the x-rays are being taken.

Blood tests

Several types of blood tests may be used to help diagnose pancreatic cancer or to help determine treatment options if it is found.

Blood tests that look at levels of different kinds of bilirubin (a chemical made by the liver) are useful in deciding whether a patient's jaundice is caused by liver disease or a blockage (by a gallstone, a tumor, or other disease) of bile flow.

Elevated blood levels of the tumor markers CA 19-9 and carcinoembryonic antigen (CEA) may point to a diagnosis of exocrine pancreatic cancer, but these tests aren't always accurate (see the section, "Can pancreatic cancer be found early?").

Other blood tests can help evaluate a patient's general state of health (such as liver, kidney, and bone marrow function). These tests can also help determine whether they'll be able to withstand the stress of a major operation.

Pancreatic neuroendocrine tumors

Blood tests looking at the levels of certain pancreatic hormones can help diagnose pancreatic neuroendocrine tumors (NETs). For insulinomas, insulin, glucose, and C-peptide levels are measured while the patient is fasting (not eating or drinking). (C-peptide is a by-product of insulin production). Blood is drawn every 6 to 8 hours until the patient starts having symptoms. The diagnosis of an insulinoma is made when there is low blood glucose with high levels of insulin and C-peptide.

Other pancreatic hormones, such as gastrin, glucagon, somatostatin, pancreatic polypeptide, and VIP can be measured in blood samples and can be used to diagnose pancreatic NETs. Measuring the level of a substance called chromogranin-A (CgA) can be very helpful. This level goes up in most cases of pancreatic NETs — even the non-functioning tumors.

Gastrin levels go up in patients who are taking a common type of anti-ulcer medication known as *proton pump inhibitors*. Examples of these drugs include omeprazole (Prilosec[®]), esomeprazole (Nexium[®]), lansoprazole (Prevacid[®]), and many others. These medicines are commonly used to treat people with stomach pain and heartburn. A patient must be off any proton pump inhibitors for at least a week before measuring a gastrin level, so that the drug doesn't falsely increase the gastrin level. Gastrin levels are most useful when combined with a test that measures the amount of acid in the stomach. That is because low acid levels can lead to high gastrin levels. When a gastrinoma is present, high gastrin levels are seen along with high acid levels.

For carcinoid tumors, a blood test may be done to look for serotonin, which is made by many of these tumors. The body breaks serotonin down into 5-hydroxyindoleacetic acid (5-HIAA), and releases it into the urine. A test commonly used to look for carcinoid syndrome measures the levels of 5-HIAA in a urine sample collected over 24 hours. This test can help diagnose many (but not all) carcinoid tumors.

Sometimes, 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. Eating foods that contain a lot of serotonin can raise 5-HIAA levels in the urine. Such foods include, bananas, plantains, kiwi, certain nuts, and avocado. Medicines, including cough syrup and acetaminophen (Tylenol), can also affect the results. These substances should be avoided before urine and blood testing 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. Depending on where the tumor might be located and the patient's symptoms, doctors may do other blood tests as well.

Biopsy

A patient's history, physical exam, and imaging test results may strongly suggest pancreatic cancer, but the only way to be sure is to remove a small sample of tumor and look at it under the microscope. This procedure is called a *biopsy*.

There are several types of biopsies. The procedure used most often to diagnose pancreatic cancer is called a *fine needle aspiration (FNA) biopsy*. For this test, a doctor inserts a thin needle through the skin and into the pancreas. The doctor uses CT scan images or endoscopic ultrasonography to view the position of the needle and make sure that it is in the tumor.

Doctors can also biopsy the tumor by using the endoscopic ultrasound to place the needle directly through the wall of the duodenum into the tumor. In either case, small tissue samples can be removed through the needle. The main advantages of the test are that the patient does not need general anesthesia (is not "asleep") during the test, and major side effects are rare.

In the past, surgical biopsies were performed more commonly. This type of biopsy requires a *laparotomy* (a large incision through the skin into the wall of the abdomen to examine internal organs). Areas that look or feel abnormal can be sampled by removing a small portion of tissue with a scalpel or a needle. The surgeon may use a thin needle (as in a fine needle aspiration biopsy). More commonly, surgeons use a wider needle that removes a cylindrical core of tissue about 1/2 inch long and less than 1/8 inch in diameter (called a *core needle biopsy*). The main drawback of this type of biopsy is that the patient must have general anesthesia and remain in the hospital for a period of time to recover.

Laparotomy is now rarely recommended. Doctors prefer to use *laparoscopy* (sometimes called *keyhole surgery*) as a way of looking at and perhaps taking a piece of the pancreas

with a biopsy. Patients are sedated or asleep for this procedure. The surgeon makes several small incisions in the abdomen and inserts small telescope-like instruments into the abdominal cavity. One of these is usually connected to a video monitor. The surgeon can see the abdomen, how big the tumor is, and whether it has spread and may take tissue samples as well.

The doctor may not do a biopsy on someone who has a tumor in the pancreas that looks like cancer (based on imaging tests) if it looks like surgery can remove all of the cancer. Instead, the doctor will proceed with surgery. If the doctor finds during surgery that the cancer has spread too far to be removed completely, only a sample of the cancer may be removed to confirm the diagnosis, and the rest of the planned operation will be stopped.

If treatment (such as chemotherapy or radiation) is planned before surgery, a biopsy is needed first to be sure of the diagnosis.

How is pancreatic cancer staged?

The stage of a pancreatic cancer (extent of disease at diagnosis) is the most important factor in choosing treatment options and predicting a patient's outlook. The tests described above (see the section, "How is pancreatic cancer diagnosed?") are the ones used to determine the stage of the cancer.

The American Joint Committee on Cancer (AJCC) TNM staging system

A staging system is a standardized way in which the cancer care team describes the extent that a cancer has spread. The main system used to describe the stages of cancers of the pancreas is the American Joint Committee on Cancer (AJCC) TNM system. The TNM system for staging contains 3 key pieces of information:

- **T** describes the size of the primary tumor(s), measured in centimeters (cm), and whether the cancer has spread within the pancreas or to nearby organs.
- **N** describes the spread to nearby (regional) lymph nodes.
- **M** indicates whether the cancer has metastasized (spread) to other organs of the body. (The most common sites of pancreatic cancer spread are the liver, lungs, and the peritoneum - the space around the digestive organs.)

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," which means the tumor is contained within the top layers of pancreatic duct cells and has not yet invaded deeper layers of tissue.

T categories

TX: The main tumor cannot be assessed.

T0: No evidence of a primary tumor.

Tis: Carcinoma in situ (very few tumors are found at this stage)

T1: The cancer has not spread beyond the pancreas and is smaller than 2 cm (about $\frac{3}{4}$ inch) across.

T2: The cancer has not spread beyond the pancreas but is larger than 2 cm across.

T3: The cancer has spread from the pancreas to surrounding tissues near the pancreas but not to major blood vessels or nerves.

T4: The cancer has extended further beyond the pancreas into nearby large blood vessels or nerves.

N categories

NX: Regional lymph nodes cannot be assessed.

N0: Regional lymph nodes (lymph nodes near the pancreas) are not involved.

N1: Cancer has spread to regional lymph nodes.

M categories

M0: The cancer has not spread to distant lymph nodes (other than those near the pancreas) or to distant organs such as the liver, lungs, brain, etc.

M1: Distant metastasis is present.

Stage grouping for pancreatic cancer

After the T, N, and M categories of the cancer have been determined, this information is combined to assign a stage, which is expressed in Roman numerals I through IV. The process of assigning a stage number based on TNM stages is called *stage grouping*.

Stage 0 (Tis, N0, M0): The tumor is confined to the top layers of pancreatic duct cells and has not invaded deeper tissues. It has not spread outside of the pancreas. These tumors are sometimes referred to as *pancreatic carcinoma in situ* or *pancreatic intraepithelial neoplasia III (PanIn III)*.

Stage IA (T1, N0, M0): The tumor is confined to the pancreas and is less than 2 cm in size. It has not spread to nearby lymph nodes or distant sites.

Stage IB (T2, N0, M0): The tumor is confined to the pancreas and is larger than 2 cm in size. It has not spread to nearby lymph nodes or distant sites.

Stage IIA (T3, N0, M0): The tumor is growing outside the pancreas but not into large blood vessels. It has not spread to nearby lymph nodes or distant sites.

Stage IIB (T1-3, N1, M0): The tumor is either confined to the pancreas or growing outside the pancreas but not into nearby large blood vessels or major nerves. It has spread to nearby lymph nodes but not distant sites.

Stage III (T4, Any N, M0): The tumor is growing outside the pancreas into nearby large blood vessels or major nerves. It may or may not have spread to nearby lymph nodes. It has not spread to distant sites.

Stage IV (Any T, Any N, M1): The cancer has spread to distant sites.

Other factors

Although not formally part of the TNM system, other factors are also important in determining prognosis (outlook). The *grade* of the cancer (how abnormal the cells look under the microscope) is sometimes listed on a scale from G1 to G4, with G1 cancers looking the most like normal cells and having the best outlook.

For patients who have surgery, another important factor is the *extent of the resection* — whether or not all of the tumor is removed. This is sometimes listed on a scale from R0 (where all visible and microscopic tumor was removed) to R2 (where some visible tumor could not be removed).

Terms commonly used to describe pancreatic cancer

From a practical standpoint, how far the cancer has spread often can't be determined accurately without surgery. That's why doctors use a simpler staging system, which divides cancers into groups based on whether or not it is likely they can be removed surgically. These groups are called *resectable*, *locally advanced* (unresectable), and *metastatic*. These terms can be used to describe both exocrine and endocrine pancreatic cancers.

Resectable

If the cancer is only in the pancreas (or has spread just beyond it) and the surgeon can remove the entire tumor, it is called *resectable*.

Locally advanced (unresectable)

If the cancer has not yet spread to distant organs but it still can't be completely removed with surgery, it is called *locally advanced*. Often the reason the cancer can't be removed is because too much of it is present in nearby blood vessels. Since the cancer cannot be removed entirely by surgery, it is also called *unresectable*. For these tumors, surgery would only be done to relieve symptoms or problems like a blocked bile duct or intestinal tract.

Metastatic

When the cancer has spread to distant organs, it is called metastatic. Surgery may still be done, but the goal would be to relieve symptoms, not to cure the cancer.

Pancreatic cancer survival by stage

Survival rates are often used by doctors as a standard way of discussing a person's prognosis (outlook). Some patients with pancreatic 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 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).

In order 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 cancer of the pancreas.

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 can affect a person's outlook, such as the patient's overall health, what treatments are given, and how well the cancer responds to treatment. Your doctor can tell you how the numbers below may apply to you, as he or she is familiar with the aspects of your particular situation.

The numbers below come from the National Cancer Data Base and are based on people diagnosed with exocrine cancer of the pancreas between 1992 and 1998.

Exocrine pancreatic cancer

Stage	5-year survival
Stage IA:	14%
Stage IB	12%
Stage IIA	7%
Stage IIB	5%
Stage III	3%
Stage IV	1%

In general, those treated with surgery survived longer, while those not treated with surgery fared worse. However, only about 1 one of every 6 patients was treated with surgery.

For pancreatic neuroendocrine tumors, survival statistics by stage are only available for patients treated with surgery. These numbers come from the National Cancer Data Base and are based on patients diagnosed between 1985 and 2004.

Pancreatic neuroendocrine tumors treated with surgery

Stage	5- year survival
Stage I	61%
Stage II	52%
Stage III	41%
Stage IV	15%

How is pancreatic cancer 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 treatment information

The 3 main types of treatment for exocrine pancreatic cancer are surgery, radiation therapy, and chemotherapy. Depending on the stage of the cancer, some of these treatments may be combined. Pancreatic endocrine tumors are also treated with these 3 types of therapy. In addition, drugs (besides chemotherapy) can be helpful.

Pancreatic cancer surgery

There are 2 general types of surgery used for pancreatic cancer:

- Potentially curative surgery is used when imaging tests suggest that it is possible to remove all the cancer.
- Palliative surgery may be done if imaging tests show that the tumor is too widespread to be completely removed. This is done to relieve symptoms or to prevent certain complications like a blocked bile duct or intestinal tract.

Several studies have shown that removing only part of the cancer does not help patients live longer. Pancreatic cancer surgery is one of the most difficult operations a surgeon can do. It is also one of the hardest for patients to undergo. There may be complications and it may take several weeks for patients to recover. Patients need to weigh the potential benefits and risks of such surgery carefully.

Potentially curative surgery

Most curative surgery is designed to treat cancers at the head of the pancreas. Because these cancers are near the bile duct, some of them cause jaundice and are found early enough to be removed. Surgeries for other parts of the pancreas are mentioned below, but these are only done when it's possible to remove all of the cancer.

There are 3 procedures used to remove tumors of the pancreas:

Pancreaticoduodenectomy (Whipple procedure): This is the most common operation to remove a cancer of the exocrine pancreas. It removes the head of the pancreas and sometimes the body of the pancreas as well. Part of the stomach, small intestine, and lymph nodes near the pancreas are also removed. 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 much skill and experience. It carries a relatively high risk of complications that may even be fatal. When the operation is done in small hospitals or by doctors with less experience, more than 15% of patients may die as a result of surgical complications. In contrast, when this operation is performed in cancer centers by surgeons experienced in the procedure, less than 5% of patients die as a direct result of complications from surgery. Still, even in the best of hands, many patients suffer complications from the surgery. These can include:

- Leaking from the various connections that the surgeon has to make

- Infections
- Bleeding
- Trouble with the stomach emptying itself after eating

For patients to have the best outcomes, they should be treated by a surgeon who does many of these operations and have the operation at a hospital where many of them are done. In general, people having this type of surgery do better when it is performed at a hospital that does at least 20 Whipple procedures per year.

At the time of diagnosis, only about 10% of cancers of the pancreas appear to be contained entirely within the pancreas. Only about half of these turn out to be truly resectable once the surgery is started. Although surgery offers the only real chance to cure exocrine pancreatic cancer, it doesn't always lead to a cure. Even if all the visible tumor is removed, often some cancer cells have already spread to other parts of the body. These cells eventually grow into new tumors and cause many problems — even death. This is why the cancer comes back later in most patients who had surgery that appeared to completely remove a cancer of the exocrine pancreas.

Long-term success rates for pancreatic neuroendocrine tumors are often much better. These tumors are more likely to be cured with surgery.

Distal pancreatectomy: This operation removes only the tail of the pancreas or the tail and a portion of the body of the pancreas. The spleen is usually removed as well. This operation is used more often with islet cell tumors found in the tail and body of the pancreas. It is seldom used to treat cancers of the exocrine pancreas because these tumors have usually already spread by the time they are found.

Total pancreatectomy: This operation was once used for tumors in the body or head of the pancreas. It removes the entire pancreas and the spleen. It is now seldom used to treat exocrine cancers of the pancreas because there doesn't seem to be an advantage in removing the whole pancreas. It is possible to live without a pancreas. But when the entire pancreas is removed, people are left without any islet cells, the cells that make insulin. These people develop diabetes, which can be hard to manage because they become totally dependent on insulin.

Palliative surgery

If the cancer has spread too far to be completely removed, any surgery being considered would be palliative (intended to relieve or prevent symptoms). Because pancreatic cancer can progress quickly, most doctors do not advise surgery for palliation. However, sometimes surgery may begin with the hope it will cure the patient, but the surgeon discovers this is not possible. In this case, the surgeon may continue the operation as a palliative procedure to relieve or prevent symptoms.

Cancers growing in the head of the pancreas can block the common bile duct as it passes through this part of the pancreas. This may cause pain and digestive problems because

the bile can't get into the intestine. The bile chemicals will build up in the body. There are 2 options for relieving bile duct blockage.

Surgery can reroute the flow of bile from the common bile duct directly into the small intestine, bypassing the pancreas. This requires a large incision in the abdomen, and it may take weeks to completely recover. One advantage is that during this procedure, the surgeon may be able to cut the nerves leading to the pancreas or inject them with alcohol. This may reduce or get rid of any pain that may be caused by the cancer.

Sometimes, the stomach connection to the duodenum (the first part of the small intestine) is rerouted at this time as well. Often, late in the course of pancreatic cancer, the duodenum becomes blocked by cancer, which can cause pain and vomiting that requires surgery. Bypassing the duodenum before this happens can help avoid a second operation.

A second approach to relieving a blocked bile duct does not involve surgery. Instead, a stent (small tube) is placed in the duct to keep it open. This is usually done through an endoscope (a long, flexible tube) while the patient is sedated. The doctor passes the endoscope down the patient's throat and all the way into the small intestine. The doctor can then insert the stent into the bile duct through the endoscope. The stent, which is usually made of metal, helps keep the bile duct open and resists compression from the surrounding cancer. After several months, the stent may become clogged and may need to be cleared. Larger stents are also used to keep the duodenum (or other parts of the small intestine) open if it is in danger of being blocked.

In general, the use of endoscopically placed stents has replaced surgery to relieve bile duct obstruction. Stents can also be placed before surgery to relieve jaundice before the pancreas is removed.

Surgery to treat pancreatic neuroendocrine tumors and cancers

In addition to the procedures described above, some less extensive procedures may be used to remove pancreatic neuroendocrine tumors (NETs). Often laparoscopy is done first to better locate the tumor and see how far it has spread.

Sometimes if the tumor is small, just the tumor itself is removed. This is called *enucleation*. This operation may be done using a laparoscope, so that only a few small incisions are needed. This operation may be all that is needed to treat an insulinoma, since this type of tumor is often benign.

Small gastrinomas (tumors 2 inches or less) may also be treated with enucleation, but sometimes the duodenum (the first part of the small intestine) is removed as well. Larger gastrinomas may require a pancreaticoduodenectomy or a distal pancreatectomy, depending on the location of the tumor.

The lymph nodes around the pancreas are also removed in some cases so that they can be checked for signs of cancer spread.

Surgery may be used to remove metastases if a pancreatic NET has spread. This can be used when it has spread to the liver (the most common site of spread) and the lungs.

Removing metastases can improve symptoms and prolong life in patients with pancreatic NETs. In rare cases, liver transplantation may be used to treat pancreatic NETs that have spread to the liver.

Ablative techniques for pancreatic cancer

When a pancreatic neuroendocrine tumor has spread to other sites, the metastases can be removed by surgery and by other techniques as well. By treating metastases, symptoms can improve and the patient may live longer. These techniques are most often used to treat cancer that has spread to the liver. Sometimes these treatments are also used to treat areas of metastases from pancreatic exocrine cancer when there are only a few of them.

Radiofrequency ablation: Radiofrequency ablation (RFA) uses radio waves to heat and destroy tissues, such as areas of cancer spread.

Microwave thermotherapy: In this procedure, microwaves are used to heat and destroy the abnormal tissue.

Cryosurgery: In cryosurgery, a probe is inserted into the tumor which freezes the tissue with liquid nitrogen or liquid carbon dioxide. The area being frozen is destroyed. This technique is also known as *cryoablation*.

Embolization: For an embolization procedure, a catheter is used to find the artery feeding the tumor. Then a substance is injected into the blood vessel, cutting off the blood supply to the tumor. This kills the tumor. The substance injected can be tiny beads (called *microspheres*). This procedure is also known as *transarterial embolization* or TAE. Sometimes radioactive beads are used to deliver radiation to the tumor. When the catheter for TAE is also used to inject chemotherapy drugs it is called *transarterial chemoembolization* or TACE.

Radiation therapy for pancreatic cancer

Radiation therapy uses high-energy x-rays (or particles) to kill cancer cells. It can be helpful in treating exocrine pancreatic cancer. Pancreatic neuroendocrine tumors (NETs) don't respond well to radiation, and so it is rarely used to treat these tumors. Radiation is sometimes used to treat pancreatic NETs that have spread to the bone and are causing pain.

External beam radiation therapy is the type of radiation therapy most often used in treating cancers of the exocrine pancreas. This treatment focuses the radiation on the cancer from a machine outside the body. Having this type of radiation therapy is like having an x-ray, except that each treatment lasts longer, and the patient usually receives 5 treatments per week over a period of weeks or months.

Patients may receive preoperative (before surgery) or postoperative (after surgery) treatment. If surgery is planned, preoperative treatment is often preferred because postoperative treatment often has to be delayed for several weeks while the patient recovers from surgery. Treatment right after surgery can interfere with wound healing.

Radiation therapy combined with chemotherapy (called *chemoradiation* or *chemoradiotherapy*) may be used in patients whose exocrine pancreatic tumors are too widespread to be removed by surgery. It is also sometimes used after surgery, to help keep the cancer from coming back.

Some of the common side effects of radiation therapy include:

- Mild skin changes (like a sunburn)
- Nausea and vomiting
- Diarrhea
- Fatigue
- Poor appetite
- Weight loss

Radiation can also lower blood counts and can increase the risk of serious infection.

Usually these effects go away a few weeks after the treatment is complete. When radiation is given with chemotherapy the side effects are often worse. Ask your doctor what side effects to expect and how to prevent or relieve them.

Chemotherapy for pancreatic cancer

Chemotherapy (chemo) uses anti-cancer drugs injected into a vein or given by mouth. These drugs enter the bloodstream and reach all areas of the body, making this treatment potentially useful for cancers that have metastasized (spread) beyond the organ they started in.

Chemotherapy for exocrine pancreatic cancer

Chemo may be used at any stage of pancreatic cancer. It is commonly used when the cancer is advanced and can't be removed completely with surgery. Chemo may also be used after the cancer has been removed with surgery to try to kill any cancer cells that may have been left behind (but can't be seen). This type of treatment is called *adjuvant* treatment. This lowers the chance that the cancer will come back later. Chemo can also be given before surgery to try to shrink the tumor. This is known as *neoadjuvant* treatment.

When chemo is given along with radiation, it can help the radiation work better. This, known as *chemoradiation* or *chemoradiotherapy*, has more severe side effects.

Gemcitabine (Gemzar[®]) is the chemotherapy drug used most often to treat pancreatic cancer. Another commonly used drug is 5-fluorouracil (5-FU).

Sometimes, other drugs may be used along with gemcitabine or 5-FU, such as cisplatin, irinotecan (Camptosar[®], CPT-11), paclitaxel (Taxol[®]), docetaxel (Taxotere[®]), capecitabine (Xeloda[®]), or oxaliplatin (Eloxitan[®]).

Chemotherapy drugs kill cancer cells but also damage some normal cells. This can lead to side effects, which depend on the type of drugs, the amount taken, and the length of treatment. Common short-term side effects include:

- Nausea and vomiting
- Loss of appetite
- Hair loss
- Mouth sores
- Diarrhea

Because chemotherapy can damage the bone marrow, where new blood cells are made, blood cell counts might become low. This can result in:

- Increased chance of infection (from a shortage of white blood cells)
- Bleeding or bruising after minor cuts or injuries (from a shortage of platelets)
- Fatigue and shortness of breath (from low red blood cell counts)

Many of the chemotherapy drugs used for pancreatic cancer can cause diarrhea. Other side effects can occur depending on what chemo drugs are used. For example, cisplatin can cause kidney damage (called *nephropathy*). Doctors try to prevent this problem by giving the patient lots of fluid before and after the drug is given. Both cisplatin and oxaliplatin can cause nerve damage (called *neuropathy*). This can lead to symptoms of numbness, tingling, or even pain in the hands and feet. For a day or so after treatment, oxaliplatin can cause nerve pain that gets worse with exposure to cold. This often causes pain when swallowing that is worse when trying to swallow cold foods or liquids. If you will be getting chemo, ask your cancer care team about the drugs being used and what side effects to expect.

Most side effects disappear once treatment is stopped. If you do have side effects, there are treatments that can help reduce them or make them go away. For example, drugs can be given to prevent or reduce nausea and vomiting.

Targeted therapy for exocrine pancreatic cancers

As researchers have learned more about the gene changes in cells that cause cancer, they have been able to develop newer drugs that specifically target these changes. These drugs are often referred to as *targeted therapy*. They work differently from standard chemotherapy drugs and often have different (and less severe) side effects. (See “What's new in pancreatic cancer research and treatment?” for more information.)

A pill called *erlotinib* (Tarceva[®]) has helped some patients with advanced pancreatic cancer. Erlotinib targets a protein on the surface of cancer cells called EGFR, which normally prompts cancer cells to grow. When combined with gemcitabine, it has been shown to work slightly better than gemcitabine alone. Some people may benefit more

from this combination than others. Common side effects of erlotinib include an acne-like rash, diarrhea, loss of appetite, and feeling tired.

Chemotherapy for pancreatic neuroendocrine tumors

Chemotherapy (chemo) is not often very helpful in treating these tumors, so it isn't often used. When chemo is used the preferred drugs are doxorubicin (Adriamycin[®]) and streptozocin. Recently, a special form of doxorubicin known as *liposomal doxorubicin* (Doxil[®]) has been used instead of the regular drug. In the newer form, the drug is dissolved in fat droplets, which allows it to be given with less serious side effects. Other chemo drugs that have been helpful in treating these tumors include fluorouracil (5-FU), dacarbazine (DTIC), and temozolomide (Temodar[®]). Some recent studies have found that combining temozolomide with thalidomide or with capecitabine (Xeloda) can be helpful.

Targeted therapy for pancreatic neuroendocrine tumors

The drug sunitinib (Sutent[®]) attacks both blood vessel growth and other targets that stimulate cancer cell growth. When used to treat patients with pancreatic neuroendocrine tumors (NETs) with spread outside of the pancreas, it has been shown to slow tumor growth and help patients live longer. This drug comes in pill form that is taken once a day to treat pancreatic NETs. The most common side effects are nausea, diarrhea, changes in skin or hair color, mouth sores, weakness, and low blood cell counts. Other possible effects include tiredness, high blood pressure, heart problems, bleeding, hand-foot syndrome (redness, pain, and skin peeling of the palms of the hands and the soles of the feet), and low thyroid hormone levels. This drug is approved by the FDA to treat pancreatic NETs that cannot be removed with surgery or have spread outside the pancreas.

Everolimus (Afinitor[®]) works by blocking a cell protein known as *mTOR*, which normally promotes cell growth and division. When used to treat patients with pancreatic NETs with spread outside of the pancreas, it has been shown to slow tumor growth. It's not yet clear if this drug helps patients live longer. Everolimus is a pill that is taken once a day to treat pancreatic NETs. Common side effects of this drug include mouth sores, an increased risk of infections, nausea, loss of appetite, diarrhea, skin rash, feeling tired or weak, fluid buildup (usually in the legs), and increases in blood sugar and cholesterol levels. A less common but serious side effect is damage to the lungs, which can cause shortness of breath or other problems. This drug is approved by the FDA to treat pancreatic NETs that cannot be removed with surgery or have spread outside the pancreas.

Other drugs for treating pancreatic neuroendocrine tumors

Somatostatin analogs: Octreotide (Sandostatin[®]) is an agent chemically related to a natural hormone, somatostatin. It is very helpful for some patients with pancreatic endocrine tumors. It can stop the tumor from releasing its hormone into the blood stream. This reduces symptoms and helps patients feel better. This drug can be expected to help anyone with a tumor that can be seen on somatostatin receptor scintigraphy (see

“Imaging tests” in the “How is pancreatic cancer diagnosed?” section). Octreotide can help reduce diarrhea in patients with VIPomas, glucagonomas, and somatostatinomas. It also helps the rash of glucagonomas. This drug may even stop tumors from growing. 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 of bile in the gallbladder which can lead to gallstones. It can also make the body resistant to the action of insulin, making pre-existing diabetes more difficult to control. This drug is not very helpful in treating insulinomas, because its effects on the release of other hormones can cause worse problems with blood sugars.

The standard version of octreotide is short-acting and is given as an injection 2 to 4 times a day. This drug is also available in a long-acting form (called Sandostatin LAR Depot) that only needs to be given once a month, which may help patients more than the short-acting version. A similar drug, lanreotide (Somatuline[®] Depot), is also available. It is also given as an injection once a month. A newer drug called *pasireotide* is currently being studied.

Diazoxide is a drug that can block insulin release from the pancreas. It can be used to prevent low blood sugars (hypoglycemia) in patients with insulinomas. This drug is often used to normalize blood glucose levels before surgery, to make the operation safer for the patient.

Proton pump inhibitors block acid secretion from the stomach. These drugs often need to be taken in higher than usual doses, but are very helpful in preventing ulcers in patients with gastrinomas. Examples of these drugs include omeprazole (Prilosec), esomeprazole (Nexium), lansoprazole (Prevacid), and others.

Clinical trials for pancreatic cancer

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 may 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 Web site 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*. You can read it on our Web site or call our toll-free number (1-800-227-2345) and have it sent to you.

Complementary and alternative therapies for pancreatic cancer

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 Web sites 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 to 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 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.

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.

Treating pancreatic cancer by stage

It is hard to stage pancreatic cancer accurately using imaging tests. Doctors must do their best to decide before surgery whether there is a good chance the cancer can be completely removed. Surgeons usually consider an exocrine pancreatic cancer *resectable* (completely removable by surgery) if it is staged as T1, T2, or T3. That means it doesn't extend far beyond the pancreas, especially into nearby large blood vessels (T4). There is no accurate way to assess the tumor's spread to the lymph nodes before surgery.

Exocrine pancreatic cancer

Resectable: If imaging tests show a reasonable chance of completely removing the cancer, surgery should be done if possible, as it is the only chance to cure this disease. Based on where the cancer started, either a pancreaticoduodenectomy (Whipple procedure) or a distal pancreatectomy is usually used.

Unfortunately, even when surgery has removed all of the tumor that can be seen, the cancer often comes back. Studies have shown that giving chemotherapy (chemo) after surgery can delay the cancer's return by about 6 months. It may also help some patients live longer. Either gemcitabine (Gemzar) or 5-FU can be used for this. It is not yet clear if adding radiation to chemo would result in more of a benefit.

Some patients are given chemo, either alone or with radiation therapy (chemoradiation), before surgery. Some centers prefer giving chemo before surgery because the recovery after surgery is often long, which can delay or even prevent its use. But it is not yet clear that this approach is better than giving the treatment after surgery.

Locally advanced: Locally advanced cancers of the pancreas are those in which the tumor in the pancreas has grown into nearby blood vessels and other tissues, but have not spread to the liver or distant organs and tissues. These tumors have grown too far to be completely removed by surgery. Several studies have shown that only removing part of

the cancer does not help patients live longer. Therefore, surgery in these cancers is used mainly to relieve bile duct blockage or to bypass a blocked intestine caused by the cancer pressing on other organs.

The standard treatment options for locally advanced cancers are chemo and/or chemoradiation. Sometimes, this treatment will shrink the cancer enough to allow it to be removed completely with surgery. This treatment may help some patients live longer even if the cancer doesn't shrink enough to be able to be removed. When radiation is given, the chemo drug can be either gemcitabine or 5-FU. Giving chemo and radiation together may work better to shrink the cancer, but this combination has more side effects and can be harder to take than either treatment alone.

Metastatic (widespread): Pancreatic cancers often first spread within the abdomen (belly) and to the liver. They can also spread to the lungs, bone, and brain.

These cancers have spread too much to be removed by surgery or treated by radiation therapy alone. Even when imaging tests show that the spread is only to one area of the body, it has to be assumed that small groups of cancer cells (too small to be seen on imaging tests) are already present in other organs of the body.

One standard treatment for advanced pancreatic cancer is chemotherapy with gemcitabine. It can shrink the cancer and help patients live longer. People who get this treatment also seem to have fewer symptoms related to their cancer.

Adding other drugs to gemcitabine may improve the chance the tumors will shrink and may help people live longer. So far, only erlotinib (Tarceva) and capecitabine (Xeloda) have been shown to help some patients live longer when given along with gemcitabine. Overall, the benefit of giving erlotinib along with gemcitabine was very small (patients lived about 2 weeks longer). Erlotinib doesn't seem to help all patients, so experts are trying to find a way to figure out who should get the drug and who try something else. Capecitabine also only seemed to help some of the people who received it with gemcitabine. Most doctors give chemo with gemcitabine for pancreatic cancer, and consider adding another drug on a case-by-case basis.

Another option that may help patients live longer is a combination of chemo drugs called FOLFIRINOX. This consists of 4 drugs: 5-FU, leucovorin, irinotecan, and oxaliplatin. In one study, this treatment helped patients live longer than gemcitabine, but had more severe side effects, so it's not for everyone. Also, there have been recent problems getting a supply of leucovorin, because of a nationwide shortage of this drug. This has limited the ability of doctors to give FOLFIRINOX.

Because the treatments now available don't work well for most patients, people may want to think about taking part in a clinical trial involving chemotherapy combinations (with or without radiation therapy) and new targeted therapies.

Recurrent cancer: 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 liver, lungs, or bone). When pancreatic exocrine cancer recurs, it is essentially

treated the same way as metastatic cancer, and is likely to include chemotherapy if the patient can tolerate it.

Cancer of the ampulla of Vater

The ampulla of Vater is the area where the pancreatic duct and the common bile duct empty into the duodenum (the first part of the small intestine). Cancer at this site can start in the pancreatic duct, the duodenum, or the common bile duct. Surgery with pancreaticoduodenectomy (Whipple procedure) is often successful as cancer treatment with a 5-year survival rate of 30% to 50%. More advanced ampullary cancers are treated like pancreatic cancer. In many patients, ampullary cancer cannot be distinguished from pancreatic cancer until surgery has been done. Post-operative chemoradiotherapy is often recommended for patients who have had a successful resection of ampullary carcinoma.

Pancreatic neuroendocrine tumors

Resectable: If the tumor is resectable, it will be removed by surgery. The procedure used depends on the type of tumor, its size, and its location in the pancreas. Laparoscopy may be done before resection to better locate and stage the tumor. Surgery can range from as little as enucleation to as much as a pancreatoduodenectomy (Whipple procedure). Lymph nodes are often removed to check for tumor spread.

Before any surgery, medicines are often given to control the symptoms caused by the tumor. For gastrinomas, drugs to block stomach acid are used (like proton pump inhibitors). Often, people with insulinomas are treated with diazoxide to keep the blood sugar from getting too low. If the tumor was visible on somatostatin receptor scintigraphy, octreotide (Somatostatin) may be used to control any symptoms.

After surgery, the patient will be watched closely for signs that the cancer may have come back or spread.

Unresectable: Pancreatic NETs are generally slow growing so lab tests and imaging are used to monitor the patient and look for signs of tumor growth. Many patients with cancers that have spread outside the pancreas benefit from treating symptoms like diarrhea or hormone problems with drugs like octreotide, diazoxide, and proton pump inhibitors. Often, chemo or targeted therapy is delayed until the patient is having symptoms that can't be controlled with other drugs or has signs of tumor growth on scans. When treatment is started, either sunitinib (Sutent) or everolimus (Afinitor) may be used. Surgery or ablative techniques may also be used to treat metastases in the liver.

More treatment information for pancreatic cancer

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 Web site (www.nccn.org).

The NCI provides treatment guidelines via its telephone information center (1-800-4-CANCER) and its Web site (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 pancreatic cancer?

It is important to have frank, open discussions with your cancer care team. They want to answer all of your questions, no matter how minor they might seem to you. For instance, consider these questions:

- What kind of pancreatic cancer do I have?
- Has my cancer spread beyond the primary site?
- What is the stage of my cancer? Is it resectable?
- What treatment choices do I have?
- What do you recommend and why?
- What risks or side effects are there to the treatments you suggest?
- How would treatment affect my daily activities?
- How is treatment likely to help in my case?
- How much experience do you have with this type of treatment?
- How experienced is the hospital in treating people with this cancer?
- Should I be referred to a cancer center for treatment?
- Should I think about taking part in a clinical trial?
- Based on what you've learned about my cancer, how long do you think I'll survive?
- What should I do to be ready for treatment?

Along with these sample questions, be sure to write down some of your own. For instance, you may want to ask about getting a second opinion.

What happens after treatment for pancreatic cancer?

For some people with pancreatic cancer, treatment may remove or destroy the cancer. Completing treatment can be both stressful and exciting. You will be relieved to finish treatment, yet it is hard not to worry about cancer coming back. (When cancer returns, it is called recurrence.) This is a very common concern among those 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 living full lives. Our document, *Living With Uncertainty: The Fear of Cancer Recurrence*, gives more detailed information on this.

For most people with pancreatic exocrine cancer (and some patients with pancreatic neuroendocrine tumors), the cancer never goes away completely. These people may 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.

After your cancer treatment is finished, you will probably need to still see your cancer doctor for many years. So, ask what kind of follow-up schedule you can expect.

It is important to keep health insurance. Tests and doctor visits cost a lot, and even though no one wants to think of 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.

Nutrition

People with exocrine pancreatic cancer often lose their appetite and suffer weight loss and weakness. These symptoms may be caused by treatment or by the cancer itself. When possible, people are often advised to try to eat high-energy foods as well as supplements. Many patients need to take pancreatic enzymes in pill form in order to help digest food so that it can be absorbed. A nutritionist may be able to help with this. In some cases the

doctors may put a feeding tube into the stomach to improve nutrition and energy levels. This is usually temporary.

Pain

Pain in the abdomen or back can be a major problem for people with exocrine pancreatic cancer. Treatment is available to help relieve this pain. If you are having any pain, please be sure to tell your doctor or nurse right away. Pain is easier to treat if the treatment is started when you first have it. You and your doctor or nurse can talk about the best ways to treat your pain. A pain specialist can also help develop a treatment plan.

There are proven ways to relieve pain from pancreatic cancer. This can be done with a combination of medicines or in some cases, endoscopy or surgery. For example, cutting some of the nerves that carry pain sensations or injecting alcohol into these nerves can provide relief. Often, if the cancer is being removed, these nerves will be cut or treated during the same operation. For most patients, treatment with morphine or other similar medicines (opioid agents) will reduce the pain considerably. Pain medicines work best when they are given regularly on a schedule. They do not work as well if they are only used when the pain becomes severe. Several long-acting forms of morphine and other opioid agents need only be given once or twice a day. Chemotherapy and/or radiation therapy to the pancreas can also sometimes relieve pain by shrinking the size of the cancer.

For more detailed information on pain and what can be done about it, see our document, *Pain Control: A Guide for Those With Cancer and Their Loved Ones*.

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 this information handy:

- A copy of your pathology report(s) from any biopsy or surgery
- If you had surgery, a copy of your operative report(s)
- If you were hospitalized, a copy of the discharge summary that every doctor prepares when patients are sent home from the hospital
- If you had chemotherapy (or were given other drugs such as targeted therapy), a list of the drugs, drug doses, and when you took them

It is also helpful if you have copies of your lab results and imaging tests (these can often be put on a DVD).

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

Lifestyle changes after pancreatic cancer

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 the 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.

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.

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 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, please see *Fatigue in People With Cancer* and *Anemia in People With Cancer*.)

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.

How does having pancreatic cancer 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.

If treatment for pancreatic cancer 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.

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.

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.

What's new in pancreatic cancer research and treatment?

Research into the causes, diagnosis, and treatment of pancreatic cancer is under way in many medical centers throughout the world.

Genetics and early detection

Scientists are learning more about some of the changes in DNA that cause cells in the pancreas to become cancerous. Inherited changes in genes such as BRCA2, p16, and the genes responsible for hereditary non-polyposis colorectal cancer (HNPCC) can increase a person's risk of developing pancreatic cancer. Researchers are now looking at how these genes may be altered in cases of pancreatic cancer that do not seem to be inherited.

Researchers are also looking at tests for detecting other acquired (not inherited) genetic changes in pancreatic cancer pre-cancerous conditions. One of the most common DNA changes in these conditions affects the K-ras oncogene and alters regulation of cell growth. New diagnostic tests are often able to recognize this change in samples of pancreatic juice collected at the time of ERCP.

For now, imaging tests like endoscopic ultrasound (EUS), ERCP, and genetic tests for changes in certain genes (such as K-ras) are options for people with a strong family history of pancreatic cancer. But these tests are not recommended for widespread testing of people at average risk who do not have any symptoms.

Treatment

The major focus of much research is on finding better treatments for pancreatic cancer. Improving surgery and radiation therapy are major goals, as is determining the best combination of treatments for people with certain stages of cancer.

Chemotherapy

Many clinical trials are testing new combinations of chemotherapy drugs for exocrine pancreatic cancer. Studies have looked to see if combining gemcitabine with other drugs would help patients live longer. Adding cisplatin, docetaxel, or irinotecan doesn't seem to be helpful, but adding capecitabine (Xeloda) does seem to help patients live longer. Also, the combination of gemcitabine, irinotecan, and celecoxib (an arthritis drug) shows promise. Other studies are testing the best ways to combine chemotherapy with radiation therapy or newer targeted therapies.

Targeted therapies

As researchers have learned more about what makes pancreatic cancer cells different from normal cells, they have started to develop newer drugs that should be able exploit these differences by attacking only specific targets. These "targeted therapies" may provide another option for treating pancreatic cancer. They may prove to be useful along with, or instead of, current treatment regimens. In general, they seem to have fewer side effects than traditional chemotherapy drugs. Looking for new targets to attack on cancers is an active area of research.

Growth factor inhibitors: Many types of cancer cells, including pancreatic cancer cells, have certain molecules on their surface that help them to grow. These molecules are called growth factor receptors. One example is epidermal growth factor receptor (EGFR). Several drugs that target EGFR are now being studied. One, known as erlotinib (Tarceva), is already approved for use along with gemcitabine.

Anti-angiogenesis factors: All cancers depend on new blood vessels to nourish their growth. To block the growth of these vessels and thereby starve the tumor, scientists have developed anti-angiogenesis drugs. These are being studied in clinical trials and may be used in patients with pancreatic cancer.

Other targeted therapies: Many drugs targeting other aspects of cancer cells are now being studied for use in pancreatic cancer. For example, drugs that target the action of farnesyl transferase, an enzyme that is thought to stimulate the growth of many cancers, are now being tested. Other drugs, such as sunitinib, have several different targets.

Immune therapy

Immune therapies attempt to boost a person's immune system or give them ready-made components of an immune system to attack cancer cells. Some studies of these treatments have shown promising results.

Several pancreatic cancer *vaccines* are now being studied. These vaccines are meant to stimulate a person's own immune system to attack the cancer cells. The patient is given a vaccine that should cause the immune system to recognize some abnormal aspect of pancreatic cancer cells and kill these cells. This might shrink the tumors or help prevent them from coming back after surgery or other treatment.

Another form of immune therapy injects man-made *monoclonal antibodies* into patients. These immune system proteins are made to home in on a specific molecule, such as carcinoembryonic antigen (CEA), which is sometimes found on the surface of pancreatic cancer cells. Toxins or radioactive atoms can be attached to these antibodies, which bring them directly to the tumor cells. The hope is that they will affect cancer cells while leaving normal cells alone. For use in pancreatic cancer, these types of treatments are available only in clinical trials at this time.

Individualization of therapy

Some drugs seem to work better if certain types of mutations can be found in the patient's tumor. For example, erlotinib may work better in patients if their tumors have a particular change in the gene for EGFR. This concept is an area of intense study. There may also be some genetic alterations that affect how well gemcitabine will work in a particular patient. Identifying markers that may predict how well a drug will work before it is given is an important area of research in many types of cancer.

New treatments for pancreatic neuroendocrine cancers

Many pancreatic neuroendocrine tumors have receptors for somatostatin on their cells. These tumors can be treated with octreotide and other drugs like it. A new drug has been developed in which the octreotide has been labeled with radiation. This drug shrunk some tumors and kept others from growing in an early trial. It also helped patients live longer.

Additional resources for pancreatic cancer

More information from your American Cancer Society

The following information may also be helpful to you. These materials may be viewed on our Web site or ordered from our toll-free number, 1-800-227-2345.

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

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

Pain Control: A Guide for Those With Cancer and Their Loved Ones (also available in Spanish)

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

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

The following books are available from the American Cancer Society. Call us at 1-800-227-2345 to ask about costs or to place your order.

American Cancer Society's Guide to Pain Control

Cancer in the Family: Helping Children Cope With a Parent's Illness

Caregiving: A Step-By-Step Resource for Caring for the Person With Cancer at Home

National organizations and Web sites*

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

National Cancer Institute

Toll-free number: 1-800-422-6237 (1-800-4-CANCER)

TTY: 1-800-332-8615

Web site: www.cancer.gov

Pancreatic Cancer Action Network

Toll-free number: 1-877-272-6226

Web site www.pancan.org

Confronting Pancreatic Cancer (Pancreatica)

Web site: www.pancreatica.org

**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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