Pancreatic Cancer

What is cancer?

The body is made up of trillions of living cells. Normal body cells grow, divide to make new cells, and die in an orderly way. During the early years of a person's life, normal cells divide faster to allow the person to grow. Once 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. In most cases the cancer cells form a tumor. Cancer cells can also invade (grow into) other tissues, something that normal cells can't 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 is 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 abnormal cell does.

People can inherit damaged DNA, but most often the 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.

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 named (and treated) based on the place where it started. For example, breast cancer that has spread to the liver is still breast cancer, not liver cancer. Likewise, prostate cancer that has spread to the bones is still prostate cancer, not bone cancer.

Different types of cancer can behave very differently. 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.

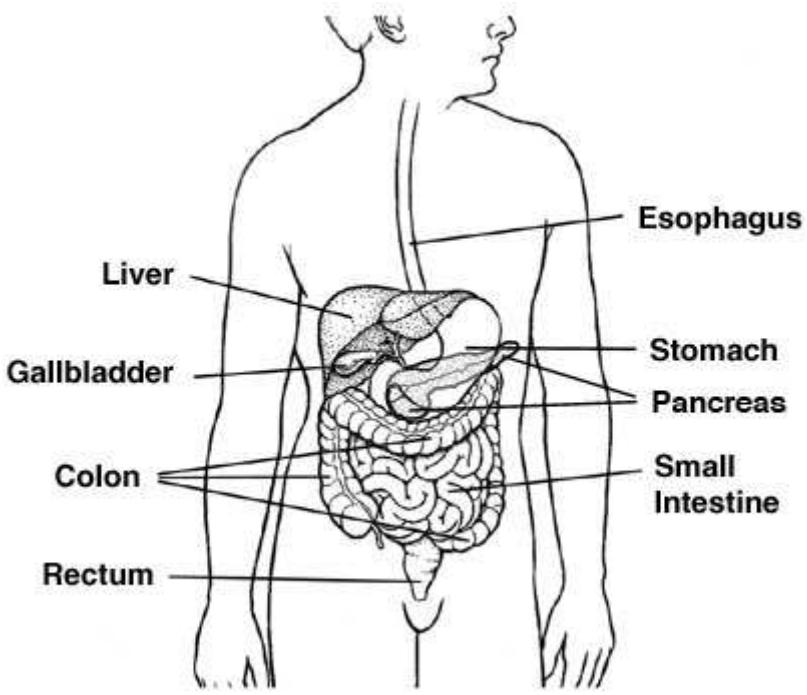
Not all tumors are cancerous. Tumors that aren't cancer are called *benign*. Benign tumors can cause problems – they can grow large and press on healthy organs and tissues. But they can't grow into (invade) other tissues. Because they can't invade, they also can't spread to other parts of the body (metastasize). These tumors are rarely life threatening.

What is pancreatic cancer?

To understand pancreatic cancer, it helps to know about the pancreas and what it does.

The normal pancreas

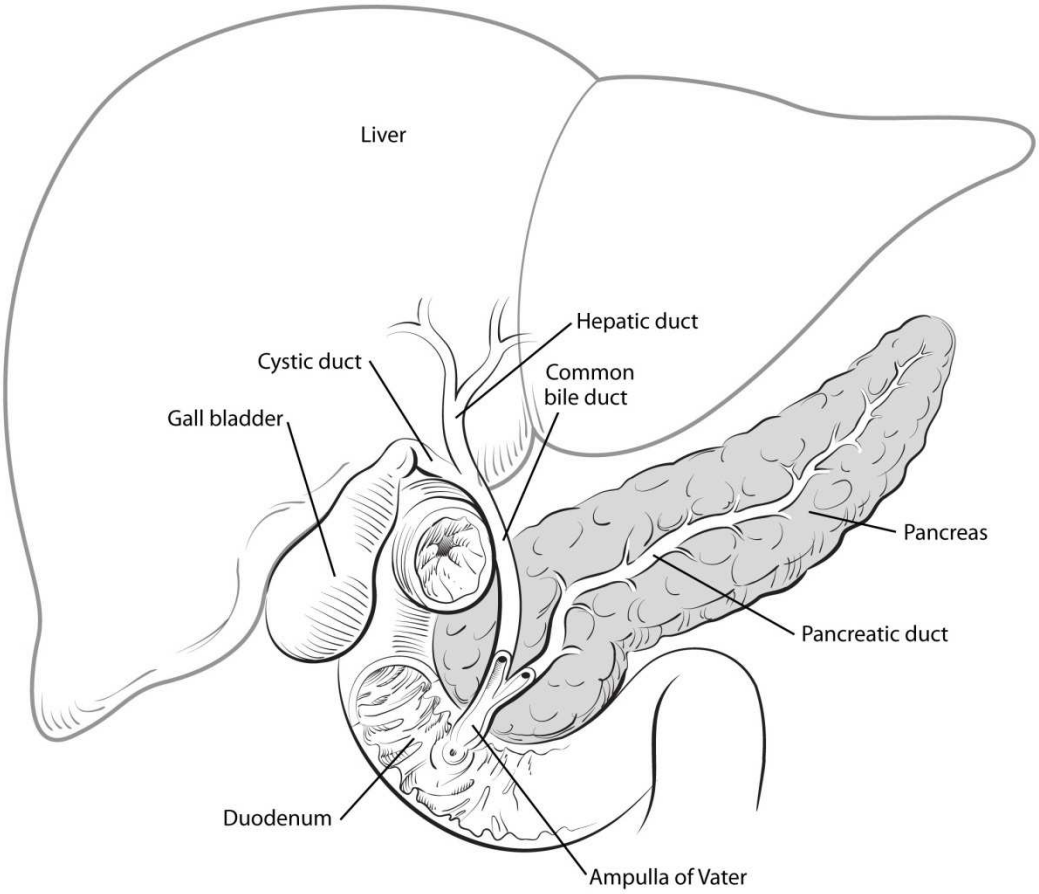
The pancreas is an organ located behind the stomach. It is shaped a little bit like a fish with a wide head, a tapering body, and a narrow, pointed tail. In adults it is about 6 inches long but less than 2 inches wide. The head of the pancreas is on the right side of the abdomen (belly), behind where the stomach meets the duodenum (the first part of the small intestine). The body of the pancreas is 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 the food you eat. Without these, some of the food 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, which 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 in the exocrine glands and ducts.



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

Benign and precancerous growths in the pancreas

Not all growths in the pancreas are cancer. Some growths are simply benign (not cancer), while others might become cancer over time if left untreated (known as *precancers*). Because people are getting imaging tests such as CT scans more often than in the past

(for a number of reasons), these types of pancreatic growths are now being found more often.

Serous cystic neoplasms (SCNs) (also known as *serous cystadenomas*) are tumors that have sacs (cysts) filled with watery fluid. SCNs are almost always benign, and most don't need to be treated unless they grow large or cause symptoms.

Mucinous cystic neoplasms (MCNs) (also known as *mucinous cystadenomas*) are slow-growing tumors that have cysts filled with a jelly-like substance called *mucin*. These tumors usually start in the body or tail of the pancreas. While they are not cancer, some of them can progress to cancer over time if not treated. Whether these tumors need to be removed or can just be followed closely over time depends on several factors, such as their size, rate of growth, how they look on imaging tests, and if they are causing symptoms.

Intraductal papillary mucinous neoplasms (IPMNs) are benign tumors that grow in the pancreatic ducts. Like MCNs, these tumors make mucin, and they can sometimes become cancer over time if not treated. Some IPMNs can just be followed closely over time, but as with MCNs, some might need to be removed with surgery if they have concerning features.

Pancreatic cancers

The exocrine cells and endocrine cells of the pancreas form different types of tumors. It's 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 outlooks.

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.

Pancreatic adenocarcinoma: 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 sometimes they develop from the cells that make the pancreatic enzymes, in which case they are called *acinar cell carcinomas*.

Less common types of cancers: Other cancers of the exocrine pancreas include adenosquamous carcinomas, squamous cell carcinomas, signet ring cell carcinomas, undifferentiated carcinomas, and undifferentiated carcinomas with giant cells. These types are distinguished from one another based on how they look under the microscope.

Solid pseudopapillary neoplasms (SPNs): These are rare, slow-growing tumors that almost always occur in young women. Even though these tumors tend to grow slowly, they can sometimes spread to other parts of the body, so they are best treated with surgery. The outlook for people with these tumors is usually very good.

Ampullary cancer (carcinoma of the ampulla of Vater): This cancer starts in the ampulla of Vater, which is where the bile duct and pancreatic duct come together and empty into the small intestine. Ampullary cancers aren't technically pancreatic cancers, but they are included in this document because their treatments are very similar.

Ampullary 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 urine dark. Because of this, these cancers are usually found at an earlier stage than most pancreatic cancers, and they usually have a better prognosis (outlook) than typical pancreatic cancers.

Endocrine tumors

Tumors of the endocrine pancreas are uncommon, making up less than 4% of all pancreatic cancers. As a group, they are sometimes known as *pancreatic neuroendocrine tumors (NETs)* or *islet cell tumors*.

Pancreatic NETs can be benign or malignant (cancer). Benign and malignant tumors can look alike under a microscope, so it isn't always clear whether or not a pancreatic NET is cancer. Sometimes the diagnosis only becomes clear when the tumor spreads outside of the pancreas.

There are many types of pancreatic NETs.

Functioning tumors: About half of pancreatic NETs make hormones that are released into the blood and cause symptoms. These are called *functioning* tumors. Each one is named for the type of hormone-making cell it starts in.

- **Gastrinomas** come from cells that make gastrin. About half of gastrinomas are cancers.
- **Insulinomas** come from cells that make insulin. Most insulinomas are benign (not cancers).
- **Glucagonomas** come from cells that make glucagon. Most glucagonomas are cancers.
- **Somatostatinomas** come from cells that make somatostatin. Most somatostatinomas are cancers.
- **VIPomas** come from cells that make vasoactive intestinal peptide (VIP). Most VIPomas are cancers.
- **PPomas** come from cells that make pancreatic polypeptide. Most PPomas are cancers.

The most common types of functioning NETs are gastrinomas and insulinomas. The other types occur very rarely.

Non-functioning tumors: These tumors don't make enough excess hormones to cause symptoms. They are more likely to be cancer than functioning tumors. Because they don't make excess hormones that cause symptoms, they can often grow quite large before they are found.

Carcinoid tumors: These are another type of NET that rarely can start in the pancreas, although they are much more common in other parts of the digestive system. These tumors often make serotonin (also called 5-*HT*) or its precursor, 5-HTP.

The treatment and outlook for pancreatic NETs depend on the specific tumor type and the stage (extent) of the tumor, but the outlook is generally better than that of pancreatic exocrine cancers.

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 2015:

- About 48,960 people (24,840 men and 24,120 women) will be diagnosed with pancreatic cancer.
- About 40,560 people (20,710 men and 19,850 women) will die of pancreatic cancer

Rates of pancreatic cancer have been fairly stable over the past several years.

Pancreatic cancer accounts for about 3% of all cancers in the US, and accounts for about 7% of cancer deaths.

The average lifetime risk of developing pancreatic cancer is about 1 in 67 (1.5%). A person's risk may be altered by certain risk factors (listed in the next section).

For statistics related to survival, see the section "Pancreatic cancer survival by stage."

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 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 have few or no known risk factors.

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

Risk factors that can be changed

Tobacco use

Smoking is one of the most important risk factors for pancreatic cancer. The risk of getting pancreatic cancer is about twice as high among smokers compared to those who have never smoked. 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. Cigar and pipe smoking also increase risk, as does the use of smokeless tobacco products.

Overweight and obesity

Being overweight is a risk factor for pancreatic cancer. Very overweight (obese) people are about 20% more likely to develop pancreatic cancer.

Carrying extra weight around the waistline may be a risk factor even in people who are not very overweight.

Workplace exposure to certain chemicals

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

Risk factors that can’t be changed

Age

The risk of developing pancreatic cancer increases as people age. Almost all patients are older than 45. About two-thirds are at least 65 years old. The average age at the time of diagnosis is 71.

Gender

Men are about 30% more likely to develop pancreatic cancer than women. This may be due, at least in part, to higher tobacco use in men, which raises pancreatic cancer risk (see above). 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 having higher rates of other risk factors for pancreatic cancer, such as diabetes, smoking in men, and being overweight in women.

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 below). In other families, the gene causing the increased risk is not known.

Genetic syndromes

Inherited gene changes (mutations) 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/CDKN2A*
- Familial pancreatitis, caused by mutations in the gene *PRSS1*
- Hereditary non-polyposis colorectal cancer (HNPCC), also known as *Lynch syndrome*, most often caused by a defect in the genes *MLH1* or *MSH2*. Changes in other genes can also cause HNPCC, such as *MLH3, MSH6, TGBR2, PMS1,* and *PMS2.*
- 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*. It 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 genetic syndromes, 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 I (MEN1), caused by mutations in the gene *MEN1*. This syndrome leads to an increased risk of tumors of the parathyroid gland, the pituitary gland, and the islet cells of the pancreas.

Changes in the genes that cause these syndromes can be recognized by genetic testing. For more information on genetic testing, see the section “Can pancreatic cancer be found early?”

Diabetes

Pancreatic cancer is more common in people who have diabetes. The reason for this is not known. Most of the risk is found in people with type 2 diabetes. This type of diabetes

most often starts in adulthood and is often related to being overweight or obese. It’s not clear if people with type 1 (juvenile) diabetes have a higher risk.

In some people, though, the cancer seems to have caused the diabetes (not the other way around). This can happen when cancer spreads through the pancreas and damages enough of the insulin-making cells to cause diabetes.

Chronic pancreatitis

Chronic pancreatitis is a long-term inflammation of the pancreas. This condition is linked with an increased risk of pancreatic cancer (especially in smokers), but most people with pancreatitis never develop pancreatic cancer.

A small number of cases of chronic pancreatitis are due to an inherited gene mutation. People with this inherited (familial) form of pancreatitis have a high lifetime risk for developing pancreatic cancer.

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.

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 might also increase the risk.

Factors with unclear effect on risk

Diet

Some studies linked pancreatic cancer and diets 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.

Physical inactivity

Some research has suggested that lack of physical activity might increase pancreatic cancer risk. But not all studies have found this.

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

Some studies have shown a link between heavy alcohol intake and pancreatic cancer. This link is still not certain, but heavy alcohol use can lead to conditions such as chronic pancreatitis and cirrhosis, which are known to increase pancreatic cancer risk.

Do we know what causes pancreatic cancer?

Scientists don't know exactly what causes most pancreatic cancers, but they have found several risk factors that can make a person more likely to get this disease. 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.

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 control when our cells grow, divide into new cells, and die. Certain genes that help cells grow, divide, and stay alive 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.

Inherited gene mutations

Certain *inherited* DNA changes can lead to conditions running in some families that increase the risk of pancreatic cancer. These syndromes, which cause a small portion of all pancreatic cancers, were described in the section "What are the risk factors for pancreatic cancer?".

Acquired gene mutations

Most often, DNA mutations of genes related to cancers of the pancreas occur after you are born, rather than having been inherited. These *acquired* mutations sometimes result from exposure to cancer-causing chemicals (like those found in tobacco smoke). But often what causes these changes is not known. Many gene changes are probably just random events that sometimes happen inside a cell, without having an outside cause.

Some of the DNA changes often seen in sporadic (non-inherited) cases of pancreatic cancer are the same as those seen in inherited cases, while others are different. For example, many sporadic cases of exocrine pancreatic cancer have changes in the *p16* and *TP53* genes, which can also be seen in some genetic syndromes. But many pancreatic

cancers also have changes in genes such as *KRAS*, *BRAF*, and *DPC4* (*SMAD4*), which are not part of inherited syndromes. Other gene changes can also be found in pancreatic cancers, although often it's not clear what has caused these changes.

Can pancreatic cancer be prevented?

The cause of many pancreatic cancers is not known, so there is no sure way to prevent it. But there are some ways you might be able to reduce your risk of this disease.

Smoking is the most important avoidable risk factor for pancreatic cancer. It is responsible for 20% to 30% of pancreatic cancers. Quitting smoking helps lower risk. If you smoke and want help quitting, please talk to your doctor or call the American Cancer Society at 1-800-227-2345.

Getting to and staying at a healthy weight might also help lower your risk. While the effects of getting physical activity and eating well on pancreatic cancer risk are not as clear, both of these can help you stay at a healthy weight. 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 at least 2½ cups of vegetables and fruits every day. Choose whole-grain breads, pastas, and cereals instead of refined grains, and eat fish, poultry, or beans instead of processed meat and red meat. For more, see the *American Cancer Society Guidelines on Nutrition and Physical Activity for Cancer Prevention*.

Finally, avoiding workplace exposure to harmful substances such as certain pesticides and other chemicals may reduce your risk for pancreatic cancer.

Can pancreatic cancer be found early?

Pancreatic cancer is hard to find early. The pancreas is deep inside the body, so early tumors can't be seen or felt by health care providers during routine physical exams. Patients usually have no symptoms until the cancer has already spread to other organs.

Screening tests or exams are used to look for a disease in people who have no symptoms (and who have not had that disease before). At this time, no major professional groups recommend routine screening for pancreatic cancer in people who are at average risk. This is because no screening test has been shown to lower the risk of dying from this cancer.

Sometimes when a person has pancreatic cancer, the levels of certain proteins in the blood go up. These proteins, called *tumor markers*, can be detected with blood tests. The tumor markers CA 19-9 and carcinoembryonic antigen (CEA) are the ones most closely tied to pancreatic cancer. But these proteins don't always go up when a person has pancreatic cancer, and even if they do, the cancer is often already advanced by the time this happens. Sometimes levels of these tumor markers can go up even when a person doesn't have pancreatic cancer. For these reasons, blood tests aren't used to screen for pancreatic cancer, although a doctor might still order these tests if a person has symptoms

that might suggest pancreatic cancer. These tests are more often used in people already diagnosed with pancreatic cancer to help tell if treatment is working or if the cancer is progressing (see “How is pancreatic cancer diagnosed?”).

Genetic testing for people who might be at increased risk

Some people might be at increased risk of pancreatic cancer because of a family history of the disease (or a family history of certain other cancers). Knowing whether or not you are at increased risk can help you and your doctor decide if you should have tests to look for pancreatic cancer early, when it might be easier to treat (see below).

Inherited DNA changes are thought to cause as many as 10% of pancreatic cancers. Some of these changes can be tested for. But determining whether someone has 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 treats people with cancer) is often helpful.

The American Cancer Society strongly recommends that anyone 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’s important to understand what the tests can − and can’t − tell you, and what any results would mean. Genetic tests look for the gene mutations in your DNA that cause inherited conditions. The tests are used to diagnose these inherited conditions, not pancreatic cancer itself. Your risk may be increased if you have one of these conditions, but it does not mean that you have (or definitely will get) pancreatic cancer. For more information, see our document *Genetic Testing: What You Need to Know*.

Testing for pancreatic cancer in people at high risk

For people in families at high risk of pancreatic cancer, newer tests for detecting early pancreatic cancer 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 it might be used for someone with a strong family history of pancreatic cancer or with a known genetic syndrome that increases their risk. Doctors have been able to find early, treatable pancreatic cancers in some members of high-risk families with this test.

Doctors are also studying other new tests to try to find pancreatic cancer early. Interested families may wish to take part in studies of the possible role of screening in those with a family history of the disease.

Signs and symptoms of pancreatic cancer

The symptoms of exocrine and endocrine pancreatic cancers are often different, so they are described separately.

Having one or more of the symptoms below does not mean you have pancreatic cancer. In fact, many of these symptoms are more likely to be caused by other conditions. Still, if

you have any of these symptoms, it's important to have them checked by a doctor so that the cause can be found and treated, if needed.

Signs and symptoms of exocrine pancreatic cancer

Early pancreatic cancers often do not cause any signs or symptoms. By the time they do cause symptoms, they have often already grown through the pancreas or spread beyond it.

Jaundice and related symptoms

Jaundice is yellowing of the eyes and skin. Most people with pancreatic cancer (and virtually all people with ampullary cancer) will have jaundice as one of their first symptoms.

Jaundice is caused by the buildup of bilirubin, a dark yellow-brown substance made in the liver. Normally, the liver excretes bilirubin as part of a liquid called *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 in the body builds up.

Cancers that start in the head of the pancreas are near the common bile duct. These cancers can press on the duct and cause jaundice while they are still fairly small, which may allow these tumors to be found at an early stage. But cancers that start in the body or tail of the pancreas don't press on the duct until they have spread through the pancreas. By this time, the cancer has often spread beyond the pancreas as well.

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

Dark urine: 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.

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

Itchy skin: When bilirubin builds up in the skin, it can start to itch as well as turning yellow.

Pancreatic 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 (belly) or back is common in pancreatic cancer. Cancers that start in the body or tail of the pancreas can grow fairly large and start to press on other nearby organs, causing pain. The cancer may also spread to the nerves surrounding the pancreas, which often causes back pain. Of course, pain in the abdomen or back is fairly common and is most often caused by something other than pancreatic cancer.

Weight loss and poor appetite

Unintended weight loss is very common in people with pancreatic cancer. These people often have little or no appetite.

Digestive problems

Pale, greasy stools: If cancer blocks the release of the pancreatic juice into the intestine, a person might not be able to digest fatty foods. The undigested fat can cause stools to be unusually pale, bulky, greasy, and to float in the toilet.

Nausea and vomiting: If the cancer presses on the far end of the stomach it can partly block it, making it hard for food to get through. 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 (as a large lump under the right ribcage) during a physical exam. It can also be detected by imaging tests.

Blood clots

Sometimes, the first clue that someone has pancreatic cancer is the development of a blood clot in a large vein, often in the leg. This is called a *deep venous thrombosis* or DVT. Symptoms can include pain, swelling, redness, and warmth in the affected leg. Sometimes a piece of the clot can break off and travel to the lungs, which might make it hard to breathe or cause chest pain. 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.

Fatty tissue abnormalities

Some people with pancreatic cancer develop an uneven texture of the fatty tissue underneath the skin. This is caused by the release of the pancreatic enzymes that digest fat.

Diabetes

Rarely, pancreatic cancers cause diabetes (high blood sugar) because they destroy the insulin-making cells. Symptoms can include feeling thirsty and hungry, and having to urinate often. More often, there are small changes in blood sugar levels that don’t cause symptoms of diabetes but can still be detected with blood tests.

Signs and symptoms of pancreatic neuroendocrine tumors

Pancreatic neuroendocrine tumors (NETs) often release excess hormones into the bloodstream. Different types of tumors make different hormones, which lead to different symptoms.

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*, in which the stomach makes too much acid. This leads to stomach ulcers, which can cause pain, nausea, and loss of appetite. Severe ulcers can start bleeding. If the bleeding is mild, it can lead to anemia (too few red blood cells), which can cause symptoms like feeling tired and being short of breath. If the bleeding is more severe, it can make stool black and tarry. Severe bleeding can itself be life-threatening.

If the stomach acid reaches the small intestine, 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.

Glucagonomas

These tumors make glucagon, a hormone that increases glucose levels in the blood. Most of the symptoms that can be caused by a glucagonoma are mild and more often are found to be caused by something else.

Excess glucagon can raise blood sugar, sometimes leading to diabetes. This can cause symptoms such as feeling thirsty and hungry, and having to urinate often.

People with these tumors also often 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*).

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 that often travels place to place on the skin. It is the most distinctive feature of a glucagonoma.

Insulinomas

These tumors make insulin, which lowers blood glucose levels. Too much insulin leads to low blood sugar (*hypoglycemia*), which can cause symptoms like weakness, confusion, sweating, and rapid heartbeat. When blood sugar gets very low, it can lead to a person passing out or even going into a coma and having seizures.

Somatostatinomas

These tumors make somatostatin, which helps regulate other hormones. Symptoms of this type of tumor can include diarrhea, gallbladder problems, and symptoms of diabetes

(feeling thirsty and hungry, and having to urinate often). The problems with the gallbladder can lead to belly pain, nausea, poor appetite, and jaundice (yellowing of the skin and eyes).

The early symptoms of a somatostatinoma tend to be mild and are more often caused by other things, so these tumors tend to be diagnosed at an advanced stage. 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. This may be mild at first, but gets worse over time. By the time they are diagnosed, most people have severe, watery diarrhea, with many bowel movements each day.

People with these tumors also tend to have low levels of acid in their stomachs, leading to problems digesting food. They may also have high blood sugar levels.

PPomas

These tumors make pancreatic polypeptide (PP), which helps regulate both the exocrine and endocrine pancreas. They can cause problems such as belly pain and an enlarged liver. Some patients also get watery diarrhea.

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 these substances down before they can reach the rest of the body and cause problems. Because of this, carcinoid tumors often don’t cause symptoms until they spread outside the pancreas.

When these tumors do spread, it is most often to the liver. There, the cancer cells can release hormones directly into the blood leaving the liver. This can cause 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, between which the person may feel fine.

Over a long time, the hormone-like substances released by these tumors can damage heart valves, causing shortness of breath, weakness, and a heart murmur (an abnormal heart sound).

Non-functioning neuroendocrine tumors

These tumors don’t make excess hormones, so they don’t cause symptoms in early stages and often grow quite large before they are found. Most of these are cancers and start to cause problems as they get larger or spread outside the pancreas. Symptoms can be like those from exocrine pancreas cancers, including jaundice (yellowing of the eyes and skin), belly pain, and weight loss.

Symptoms caused by the cancer spreading

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

Although these cancers often spread to the liver first, 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 shortness of breath or a cough. Spread to bones can cause pain in those bones.

How is pancreatic cancer diagnosed?

If a person has signs and symptoms that might be caused by pancreatic cancer, certain exams and tests will be done to find the cause. If cancer is found, further tests will then be done to help determine the extent (stage) of the cancer.

Medical history and physical exam

Your doctor will ask about your medical history to check for any pancreatic cancer risk factors, and to learn more about any symptoms you are having, such as pain, changes in appetite, weight loss, and tiredness.

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

Pancreatic cancer can also spread to lymph nodes above the collarbone and other locations. These areas will be looked at carefully for lumps or swelling that might mean cancer spread.

If the results of the exam are abnormal, your doctor will probably order tests to help find the problem. You might also be referred to a gastroenterologist (a doctor who treats digestive system diseases) for further tests and treatment.

Imaging tests

Imaging tests use x-rays, magnetic fields, sound waves, or radioactive substances to create pictures of the inside of your body. Imaging tests might be done for a number of reasons both before and after a diagnosis of pancreatic cancer, including:

- To look for suspicious areas that might be cancer
- To learn if and how far cancer has spread

- To help determine if treatment is working
- To look for signs of cancer coming back after treatment

Computed tomography (CT) scan

The CT scan uses x-rays to produce detailed cross-sectional images of your body. CT scans are often used to diagnose pancreatic cancer because they can show the pancreas fairly clearly. They can also help show if cancer has spread to organs near the pancreas, as well as to lymph nodes and distant organs. A CT scan can help determine if surgery might be a good treatment option.

A CT scanner has been described as a large donut, with a narrow table that slides in and out of the middle opening. You will need to lie still on the table while the scan is being done. CT scans take longer than regular x-rays, and you might feel a bit confined by the ring while the pictures are being taken. 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 an image of a slice of your body.

Before the test, you might be asked to drink 1 to 2 pints of a liquid called *oral contrast*. This helps outline the intestine so that certain areas are not mistaken for tumors. You might also receive an IV line through which a different kind of contrast dye (IV contrast) is injected. This helps better outline structures such as blood vessels in your body.

The injection can cause some flushing (redness and warm feeling). Some people are allergic to the dye and get hives 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.

If your doctor suspects you might have pancreatic cancer, you may have one set of CT scans of your abdomen taken before you get IV contrast. Other sets of scans may then be taken over the next several minutes as the contrast passes through the pancreas and other parts of the body. These sets of scans together are known as a *multiphase CT scan* or a *pancreatic protocol CT scan*.

CT-guided needle biopsy: CT scans can also be used to guide a biopsy needle into a suspected pancreatic tumor. But if a needle biopsy is needed, most doctors prefer to use endoscopic ultrasound (described below) to guide the needle into place.

For this procedure, you remain on the CT scanning table while the doctor advances a biopsy needle through the skin and toward the tumor. CT scans are repeated until the needle is within the mass. A needle biopsy sample is then removed to be 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. A contrast material might be injected just as with CT scans, but this is used less often.

Most doctors prefer to look at the pancreas with CT scans, but an MRI can also be done.

Special types of MRI scans can also be used in people who might have pancreatic cancer:

- **MR cholangiopancreatography (MRCP)**, which can be used to look at the pancreatic and bile ducts, is described below in the section on cholangiopancreatography.
- **MR angiography (MRA)**, which looks at blood vessels, is mentioned below in the section on angiography.

MRI scans take longer than CT scans – often up to an hour – and are a little more uncomfortable. 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.

Ultrasound

Ultrasound tests use sound waves to create images of organs such as the pancreas.

Abdominal ultrasound: For this test, a wand-shaped probe called a *transducer* is moved over the skin of the abdomen. It gives off sound waves and detects the echoes as they bounce off 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 doctors tell some types of pancreatic tumors from one another.

If it’s not clear what might be causing a person’s abdominal symptoms, an ultrasound might be the first test done because it is easy to do and it doesn’t expose a person to radiation. But if signs and symptoms are more likely to be caused by pancreatic cancer, a CT scan is often more useful for looking at the pancreas than an ultrasound.

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 (EUS): This test is more accurate than abdominal ultrasound and can be very helpful in diagnosing pancreatic cancer. This test is done with a small ultrasound probe on the tip of an endoscope — a thin, flexible tube that doctors use to look at the inside of the digestive tract.

For this test, you will first be sedated (given medicine to make you sleepy). The probe is then passed through your mouth or nose, down through the esophagus and stomach, and into the first part of the small intestine. It is then pointed toward the pancreas, which is next to the small intestine. The probe on the tip of the endoscope can get very close to the pancreas, so 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, a small, hollow needle can be passed down the endoscope to get biopsy samples of it during this procedure.

Cholangiopancreatography

A cholangiopancreatogram is an imaging test that looks at the pancreatic and bile ducts to see if they are blocked, narrowed, or dilated. These tests can help show if someone might have a pancreatic tumor that is blocking a duct. They can also be used to help plan surgery. The test can be done in different ways, each of which has pros and cons.

Endoscopic retrograde cholangiopancreatography (ERCP): For this test, an endoscope (a thin, flexible tube with a tiny video camera on the end) is passed down the throat, through the esophagus and stomach, and into the first part of the small intestine. This is usually done while you are sedated (given medicine to make you sleepy).

The doctor can see through the endoscope to find the ampulla of Vater (where the common bile duct empties into the small intestine). The doctor guides a catheter (a very small tube) through the tip of the endoscope and into the common bile duct. A small amount of dye (contrast material) is then injected into the common bile duct, and x-rays are taken. This dye outlines the bile and pancreatic ducts. 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).

ERCP can also be used to place a stent (small tube) into a bile or pancreatic 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 for pancreatic cancer” section.

Magnetic resonance cholangiopancreatography (MRCP): This is a non-invasive way to look at the pancreatic and bile ducts using the same type of machine used for standard MRI scans. It does not require an infusion of a contrast agent and is not invasive, unlike ERCP. Because it is non-invasive, doctors often use MRCP if the purpose of the test is just to look at the pancreatic and bile ducts. But this test can’t be used to get biopsy samples of tumors or to place stents in ducts.

Percutaneous transhepatic cholangiography (PTC): In this procedure, the doctor places a thin, hollow needle through the skin of the belly and into a bile duct within the liver. A contrast dye is then injected through the needle, and x-rays are taken as it passes through the bile and pancreatic ducts. As with ERCP, this approach can also be used to take fluid or tissue samples or to place a stent into a duct to help keep it open. Because it is more invasive (and might cause more pain), PTC is not usually used unless ERCP has already been tried or can’t be done for some reason.

Somatostatin receptor scintigraphy (SRS)

This test, also known as *OctreoScan,* can be very helpful in diagnosing pancreatic neuroendocrine tumors (NETs). It uses a hormone-like substance called *octreotide* that is

bound to a radioactive substance (indium-111). Octreotide attaches to proteins on the tumor cells of many NETs, but it is less helpful in finding insulinomas.

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

This scan can help diagnose NETs, but it can also help decide on treatment. NETs that show up on SRS scans will often stop growing if treated with 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. The amount of radioactivity used is very low and will pass out of the body over the next day or so. Because cancer cells in the body grow 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 sometimes used to look for spread from exocrine pancreatic cancers, but because NETs grow slowly, they do not show up well on PET scans.

Special machines can do both a PET and CT scan at the same time (known as a *PET/CT scan*). This lets the doctor compare areas of higher radioactivity on the PET scan with the more detailed appearance of that area on the CT scan. This test can help determine the stage (extent) of the cancer. It might be especially useful for spotting exocrine cancer that has spread beyond the pancreas and wouldn't be treatable by surgery.

Angiography

This is an x-ray test that looks at blood vessels. A small amount of contrast material is injected into an artery to outline the blood vessels, and 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 if the cancer can be removed completely without damaging vital blood vessels and helps them plan the operation.

Angiography can also be used to look for pancreatic NETs 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.

X-ray angiography can be an uncomfortable procedure because the doctor 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.

Angiography can also be done with a CT scanner (CT angiography) or an MRI scanner (MR angiography). These techniques are now used more often because they can give information about the blood vessels in or near the pancreas without the need for a catheter in the artery. You might still need an IV line so that a contrast dye can be injected into the bloodstream during the imaging.

Blood tests

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

Blood tests for exocrine pancreatic cancers

Liver function tests: Jaundice (yellowing of the skin and eyes) is often one of the first signs of pancreatic cancer, but it can have many causes other than cancer. Doctors often get blood tests to assess liver function in people with jaundice to help determine its cause.

For example, blood tests that look at levels of different kinds of bilirubin (a chemical made by the liver) can help tell whether a patient's jaundice is caused by disease in the liver itself or by a blockage of bile flow (from a gallstone, a tumor, or other disease).

Tumor markers: Tumor markers are substances that can sometimes be found in the blood when cancer is present. Two tumor markers may be helpful in pancreatic cancer:

- *CA 19-9* is a substance often released into the blood by exocrine pancreatic cancer cells, although it often can't be detected until the cancer is already advanced.
- *Carcinoembryonic antigen* (CEA) is another tumor marker that might help find advanced pancreatic cancer in some people, but it is not used as often as CA 19-9.

Neither of these tumor marker tests is accurate enough to tell for sure whether or not someone has pancreatic cancer. Levels of these tumor markers are not high in all people with pancreatic cancer, and some people who don't have pancreatic cancer might have high levels of these markers for other reasons. Still, these tests can sometimes be helpful, along with other tests, in figuring out if someone has cancer.

In people already known to have pancreatic cancer and who have high CA19-9 or CEA levels, these levels can be followed over time to help tell how well treatment is working. If all of the cancer has been removed, these tests can also be done to look for the cancer coming back.

Other blood tests: Other tests can help evaluate a person's general health (such as kidney and bone marrow function). These tests can help determine if they'll be able to withstand the stress of a major operation.

Blood tests for pancreatic neuroendocrine tumors

Blood tests looking at the levels of certain pancreatic hormones can often 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 of low blood sugar. 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 (vasoactive intestinal peptide) can be measured in blood to help 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 tumors that don't make excess hormones (non-functioning tumors).

People with heartburn or ulcers who are taking medicines known as *proton pump inhibitors*, such as omeprazole (Prilosec®), esomeprazole (Nexium®), lansoprazole (Prevacid®), often need to stop taking them for a week before having these tests. This is because these medicines can falsely raise gastrin and CgA levels.

Measurement of gastrin levels is most useful when combined with a test that measures the amount of acid in the stomach. This 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.

Carcinoid tumors: For carcinoids, 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-hydroxyindoleactic 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, avocado, tomatoes, and eggplant. 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 common tests to look for carcinoids include blood tests for chromogranin A (CgA), neuron-specific enolase (NSE), substance P, and gastrin. As noted above, medicines called proton-pump inhibitors, which lower stomach acid, can raise CgA and gastrin levels even in people without carcinoid tumors. If you take one of these medicines, talk to your doctor about what you need to avoid before having these blood tests.

Depending on where the tumor might be located and the patient's symptoms, doctors might do other blood tests as well.

Biopsy

A person's medical history, physical exam, and imaging test results may strongly suggest pancreatic cancer, but usually 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*. Biopsies can be done in different ways.

Percutaneous (through the skin) biopsy: For this test, a doctor inserts a thin, hollow needle through the skin over the abdomen and into the pancreas to remove a small piece of a tumor. This is known as a *fine needle aspiration* (FNA). The doctor guides the needle into place using images from ultrasound or CT scans.

Endoscopic biopsy: Doctors can also biopsy a tumor during an endoscopy. The doctor passes an endoscope (a thin, flexible, tube with a small video camera on the end) down the throat and into the small intestine near the pancreas. At this point, the doctor can either use endoscopic ultrasound (EUS) to pass a needle into the tumor or endoscopic retrograde cholangiopancreatography (ERCP) to remove cells from the bile or pancreatic ducts. These tests are described in more detail above. You will be sedated (made sleepy) for these tests, but general anesthesia (being put into a deep sleep) is not usually needed. Major side effects from these types of biopsies are rare.

Surgical biopsy: Surgical biopsies are now done less often than in the past. They can be useful if the surgeon is concerned the cancer has spread beyond the pancreas and wants to look at (and possibly biopsy) other organs in the abdomen.

The most common way to do a surgical biopsy is to use *laparoscopy* (sometimes called *keyhole surgery*). You will be sedated or asleep for this procedure. The surgeon makes several small incisions (cuts) in the abdomen and inserts small telescope-like instruments. One of these has a small video camera on the end to let the surgeon see inside the abdomen. The surgeon can look at the pancreas and other organs for tumors and take biopsy samples of abnormal areas.

In the past, surgeons often used a *laparotomy* (a large incision through the skin into the wall of the abdomen) to examine internal organs and take biopsies. But this type of surgery requires a longer recovery and is now rarely used.

Some people might not need a biopsy

Rarely, the doctor might not do a biopsy on someone who has a tumor in the pancreas if imaging tests show the tumor is very likely to be cancer and if it looks like surgery can remove all of it. Instead, the doctor will proceed with surgery, at which time the tumor cells can be looked at to confirm the diagnosis. 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.

See our document *Testing Biopsy and Cytology Specimens for Cancer* to learn more about different types of biopsies, how the samples are tested in the lab for disease diagnosis, and what the results will tell you.

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. Pancreatic cancer is staged based on the results of exams, imaging tests, endoscopies, and biopsies, which are described in "How is pancreatic cancer diagnosed?"

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

A staging system is a standard way for doctors to sum up how far a cancer has spread. The main system used stage cancers of the pancreas is the American Joint Committee on Cancer (AJCC) TNM system. The TNM system is based on 3 key pieces of information:

- **T** describes the size of the main (primary) **tumor** and whether it has grown outside the pancreas and into 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.

T categories

TX: The main tumor cannot be assessed.

T0: No evidence of a primary tumor.

Tis: Carcinoma in situ (the tumor is confined to the top layers of pancreatic duct cells). (Very few pancreatic tumors are found at this stage.)

T1: The cancer is still within the pancreas and is 2 centimeters (cm) (about ¾ inch) or less across.

T2: The cancer is still within the pancreas but is larger than 2 cm across.

T3: The cancer has grown outside the pancreas into nearby surrounding tissues but not into major blood vessels or nerves.

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

N categories

NX: Nearby (regional) lymph nodes cannot be assessed.

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

N1: The cancer has spread to nearby 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: The cancer has spread to distant lymph nodes or to distant organs.

Stage grouping for pancreatic cancer

Once the T, N, and M categories have been determined, this information is combined to assign an overall stage of 0, I, II, III, or IV (sometimes followed by a letter). This process 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 2 cm across or smaller (T1). It has not spread to nearby lymph nodes (N0) or distant sites (M0).

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

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

Stage IIB (T1-3, N1, M0): The tumor is either confined to the pancreas or growing outside the pancreas but not into major blood vessels or nerves (T1-T3). It has spread to nearby lymph nodes (N1) but not to distant sites (M0).

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

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

Other prognostic factors

Although not formally part of the TNM system, other factors are also important in determining prognosis (outlook).

Tumor grade: The *grade* of the cancer (how abnormal the cells look under the microscope) is listed on a scale from G1 to G3 (or sometimes G1 to G4), with G1 cancers looking the most like normal cells and having the best outlook.

The details of grading are a little different for exocrine cancers and NETs. For NETs, measures of how many of the cells seem to be dividing is an important part of grading. This can be determined by counting mitoses (cells that have started to split into two new cells) under a microscope or with a Ki-67 test that recognizes cells that are almost ready to start splitting.

Extent of resection: For patients who have surgery, another important factor is the *extent of the resection* — whether or not all of the tumor is removed:

- **R0:** All visible and microscopic tumor was removed.
- **R1:** All visible tumor was removed, but lab tests of the removed specimen show that some small areas of cancer were probably left behind.
- **R2:** Some visible tumor could not be removed.

Resectable versus unresectable pancreatic cancer

The AJCC staging system provides a detailed summary of how far the cancer has spread. But for treatment purposes, doctors use a simpler staging system, which divides cancers into groups based on whether or not they can likely be removed (resected) with surgery. These groups are called *resectable*, *borderline resectable*, and *unresectable* (either *locally advanced* or *metastatic*).

These terms are used more often to describe exocrine pancreatic cancers than pancreatic neuroendocrine tumors.

Resectable

If the cancer is only in the pancreas (or has spread just beyond it) and the surgeon believes the entire tumor can be removed, it is called *resectable*. (In general, this would include most stage IA, IB, and IIA cancers in the TNM system.)

It’s important to note that some cancers might appear to be resectable based on imaging tests such as CT scans, but once the surgeon starts the operation it might become clear that not all of the cancer can be removed. If this happens, only a sample of the cancer may be removed to confirm the diagnosis (if a biopsy hasn’t been done already), and the rest of the planned operation will be stopped to help avoid the risk of major side effects.

Borderline resectable

This term is used to describe some cancers that might have just reached nearby blood vessels, but which the doctors feel might still be removed completely with surgery. This would include some stage III cancers in the TNM system.

Unresectable

These cancers can't be removed entirely by surgery.

Locally advanced: If the cancer has not yet spread to distant organs but it still can't be removed completely with surgery, it is called *locally advanced.* Often the reason the cancer can't be removed is because it has grown into or surrounded nearby major blood vessels. (In general, this would include stage IIB and most III cancers in the TNM system.)

Surgery to try to remove these tumors would be very unlikely to be helpful and could still have major side effects. Some type of surgery might still be done, but it would be a less involved operation with the goal of relieving symptoms or problems like a blocked bile duct or intestinal tract, not of curing the cancer.

Metastatic: If the cancer has spread to distant organs, it is called *metastatic*. These cancers can't be removed completely. Surgery might 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 people 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 of these people live much longer than 5 years. Also, people with pancreatic cancer can die of other things. The rates below, called *observed survival rates*, don't take that into account.

The numbers below are among the most current available. 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 better 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 can't predict what will happen with any particular person. Many other factors can affect a person's outlook, such as their age and overall health and how well the cancer responds to treatment. Your doctor can tell you how the numbers below apply to you, as he or she knows your situation best.

Exocrine pancreatic cancer

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.

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

In general, people who can be treated with surgery survive longer, while those not treated with surgery don't fare as well.

Pancreatic neuroendocrine tumors 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.

Stage	5-year observed survival rate
Stage I	61%
Stage II	52%
Stage III	41%
Stage IV	16%

In this database, the overall 5-year survival rate for people who were *not* able to have their tumors removed by surgery was 16%.

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

After the cancer is found and staged, your cancer care team will discuss treatment options with you. It is important that you take time to think about your choices. You will want to weigh the benefits of each treatment option against the possible risks and side effects. In choosing a treatment plan, two of the main factors to consider are whether or not the cancer can be removed (resected) with surgery and your overall health.

The main types of treatment for pancreatic cancer are:

- Surgery
- Ablative techniques
- Radiation therapy
- Chemotherapy and other drugs

Pain control is also an important part of treatment for many patients.

Depending on the type and stage of the cancer, some of these treatments may be combined.

Doctors on your cancer treatment team might include:

- A surgeon: a doctor who uses surgery to treat cancers or other problems
- An endocrinologist: a doctor who treats diseases in glands that secrete hormones
- A radiation oncologist: a doctor who uses radiation to treat cancer
- A medical oncologist: a doctor who uses chemotherapy and other medicines to treat cancer

Many other specialists might be part of your treatment team as well, including physician assistants, nurse practitioners, nurses, psychologists, social workers, nutritionists, and other health professionals. See *Health Professionals Associated With Cancer Care* for more on this.

It is important to discuss all of your treatment options, including their goals and possible side effects, with your doctors to help make the decision that best fits your needs. It's also very important to ask questions if there is anything you're not sure about. You can find some good questions to ask in the section "What should you ask your doctor about pancreatic cancer?"

The next few sections describe the different types of treatment for pancreatic cancer. This is followed by a discussion of the most common treatments for pancreatic cancer by stage.

Surgery for pancreatic cancer

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

- **Potentially curative surgery** is used when the results of exams and 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 removed completely. This surgery is done to relieve symptoms or to prevent certain complications like a blocked bile duct or intestine, but it is not meant to try to cure the cancer.

Several studies have shown that removing only part of the cancer does not help patients live longer, so potentially curative surgery is only done if the surgeon thinks all of the cancer can be removed. Even then, this is one of the most difficult operations a surgeon can do. It is also one of the hardest for patients. It can cause complications and take several weeks to recover from. Patients need to weigh the potential benefits and risks of such surgery carefully.

Potentially curative surgery

Fewer than 1 in 5 pancreatic cancers appear to be confined to the pancreas at the time of diagnosis. Even then, not all of these cancers turn out to be truly resectable once the surgery is started. Sometimes once the surgeon starts the operation it becomes clear that the cancer has grown too far to be removed completely. If this happens, the operation may be stopped, or the surgeon might continue with a smaller operation with a goal of relieving or preventing symptoms (see "Palliative surgery" below). This is because the planned operation would be very unlikely to cure the cancer and could still lead to major side effects. It would also lengthen the recovery time, which could delay other treatments.

Surgery offers the only realistic chance to cure exocrine pancreatic cancer, but it doesn't always lead to a cure. Even if all visible cancer is removed, often some cancer cells have already spread to other parts of the body. These cells can eventually grow into new tumors, which can be very hard to treat.

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

Curative surgery is done mainly to treat cancers in the head of the pancreas. Because these cancers are near the bile duct, they often cause jaundice, which allows them to be 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.

Three procedures can be 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 is also sometimes used to treat pancreatic NETs.

During this operation, the surgeon removes the head of the pancreas and sometimes the body of the pancreas as well. Nearby structures such as part of the small intestine, part of the bile duct, the gallbladder, lymph nodes near the pancreas, and sometimes part of the stomach are also removed. The remaining bile duct and pancreas are then attached to the small intestine so that bile and digestive enzymes can enter the small intestine. The pieces of the small intestine (or the stomach and small intestine) are then reattached as well so that food can pass through the digestive tract.

Most often, this operation is done through a large incision (cut) down the middle of the belly. Some doctors at major cancer centers also do the operation laparoscopically, which is sometimes known as "keyhole surgery" (see "What's new in pancreatic cancer research and treatment?").

A Whipple procedure is a complex operation that requires a lot of skill and experience. It carries a relatively high risk of complications that can sometimes be life threatening. When the operation is done in small hospitals or by doctors with less experience, as many as 15% of patients may die as a result of surgical complications. In contrast, when the operation is done in cancer centers by surgeons experienced in the procedure, less than 5% of patients die as a direct result of surgery.

For patients to have the best outcomes, they should be treated by a surgeon who does many of these operations and have the surgery at a hospital where many of them are done. In general, people having this type of surgery do better when it is done at a hospital that does at least 15 to 20 Whipple procedures per year.

Still, even in the best of hands, many patients suffer complications from the surgery. These can include:

- Leaking from the various connections among organs that the surgeon has to make
- Infections
- Bleeding
- Trouble with the stomach emptying itself after eating

Other, longer-term complications can include weight loss, trouble digesting some foods, changes in bowel habits, and diabetes in some people.

Distal pancreatectomy: In this operation, the surgeon 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 to treat PNETs 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.

The spleen helps the body fight infections, so if it's removed you'll be at increased risk of infection with certain bacteria. To help with this, doctors recommend that patients get certain vaccines before this surgery.

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 and other hormones that help maintain blood sugar levels. These people develop diabetes, which can be hard to manage because they are totally dependent on insulin shots. People who have had this surgery also need to take pancreatic enzyme pills to help them digest certain foods.

Your doctor will recommend certain vaccines before this operation because the spleen will be removed.

Palliative surgery

If the cancer has spread too far to be removed completely, any surgery being considered would be palliative (intended to relieve or prevent symptoms). Because pancreatic cancer can progress quickly, most doctors do not advise major surgery for palliation, especially for people who are in poor health.

Sometimes surgery might begin with the hope it will cure the patient, but the surgeon discovers this is not possible. In this case, the surgeon might continue the operation as a palliative procedure (bypass surgery) 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 can cause pain and digestive problems because bile can't get into the intestine. The bile chemicals will also build up in the body. This can cause jaundice, nausea, vomiting, and other problems.

There are 2 main options for relieving bile duct blockage.

Stent placement: The most common approach to relieving a blocked bile duct does not involve actual surgery. Instead, a stent (small tube, usually made of metal) is placed inside the duct to keep it open. This is usually done through an endoscope (a long, flexible tube) while the patient is sedated. Often this is part of an endoscopic retrograde cholangiopancreatography (ERCP). The doctor passes the endoscope down the 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 can also be placed through the skin during a percutaneous transhepatic cholangiography (PTC). (These tests are described in the section "How is pancreatic cancer diagnosed?")

The stent 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 or replaced. Larger stents can also be used to keep parts of the small intestine open if they are in danger of being blocked from the cancer.

Stents can also be placed to help relieve jaundice before curative surgery is done (typically a couple of weeks later). This helps lower the risk of complications from the surgery.

Bypass surgery: In people who are healthy enough, another option for relieving a blocked bile duct is surgery to reroute the flow of bile from the common bile duct directly into the small intestine, bypassing the pancreas. This typically requires a large incision in the abdomen, from which it can take weeks to recover. Sometimes it can be done through several small cuts made in the abdomen using special long surgical tools. (This is known as *laparoscopic* or *keyhole surgery*.)

Having a stent placed is often easier and the recovery is much shorter, which is why this is done more often than bypass surgery. But surgery can have some advantages, such as:

- It can often give longer-lasting relief than a stent, which might need to be cleaned out or replaced.
- It might be an option if a stent can't be placed for some reason.
- During surgery, 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 caused by the cancer. (Pancreatic cancer often causes pain if it reaches these nerves.)

Still, a biliary bypass can be a major operation, so it is important that you are healthy enough to withstand it and that you talk with your doctor about the possible benefits and risks before you have the surgery.

Sometimes, the end of the stomach is disconnected from the duodenum (the first part of the small intestine) and attached farther down the small intestine during this surgery as well. (This is known as a *gastric bypass*.) 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 sometimes help avoid a second operation.

Surgery to treat pancreatic neuroendocrine tumors

Along with the surgeries described above, some less extensive procedures may be used to remove pancreatic NETs.

Often laparoscopy is done first to better locate the tumor and see how far it has spread. For this procedure, the surgeon makes a few small incisions (cuts) in the abdomen and inserts thin, telescope-like instruments. One of these has a small video camera on the end to let the surgeon see inside the abdomen. The surgeon can look at the pancreas and other organs for tumors and take biopsy samples of abnormal areas.

Sometimes if the pancreatic 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 and some other pancreatic NETs may also be treated with enucleation, but sometimes the duodenum (the first part of the small intestine) is removed as well. Larger gastrinomas and other types of pancreatic NETs often require a pancreaticoduodenectomy (Whipple procedure) 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 to the liver (the most common site of spread) or the lungs. Removing metastases can improve symptoms and prolong life in patients with pancreatic NETs. In rare cases, a liver transplant might be used to treat pancreatic NETs that have spread to the liver.

For more general information about surgery as a treatment for cancer, see our document *Understanding Cancer Surgery: A Guide for Patients and Families*.

Ablation or embolization treatments for pancreatic cancer

These treatments are different ways of destroying tumors, rather than removing them with surgery. They can sometimes be used to help treat pancreatic cancer that has spread to other sites, especially the liver. But these treatments are very unlikely to cure cancers

on their own. They are more likely to be used to help prevent or relieve cancer symptoms, and are often used along with other types of treatment.

- **Pancreatic neuroendocrine tumors (NETs):** When these tumors have spread to other sites, these treatments can often improve symptoms and help people live longer.
- **Exocrine pancreas cancers:** These treatments are used much less often for exocrine cancers (which account for most pancreatic cancers), but they might sometimes be used to treat areas of spread when there are only a few of them.

Ablative treatments

Ablation refers to treatments that destroy tumors, usually with extreme heat or cold. This type of treatment typically does not require a hospital stay. There are different kinds of ablative treatments:

Radiofrequency ablation (RFA): This procedure uses high-energy radio waves for treatment. The doctor inserts a thin, needle-like probe into the tumor. A high-frequency current is then passed through the tip of the probe, which heats the tumor and destroys the cancer cells. This treatment is used mainly for small tumors.

Microwave thermotherapy: This procedure is similar to RFA, except microwaves are used to heat and destroy the abnormal tissue.

Cryosurgery (cryoablation): This procedure destroys a tumor by freezing it using a thin metal probe. The probe is guided into the tumor, and very cold gasses are passed through the probe to freeze the tumor, killing the cancer cells. This method can be used to treat larger tumors than the other ablation techniques, but it sometimes requires general anesthesia (where you are deeply asleep and not able to feel pain).

Side effects of ablation treatments: Possible side effects after ablation therapy include abdominal pain, infection, and bleeding inside the body. Serious complications are uncommon, but they are possible.

Embolization

During embolization, the doctor injects substances into an artery to try to block the blood flow to cancer cells, causing them to die. This can sometimes be used for tumors that are too large to be treated with ablation. This type of treatment typically does not require a hospital stay.

There are 3 main types of embolization:

Arterial embolization: This is also known as trans-arterial embolization (or TAE). In this procedure a catheter (a thin, flexible tube) is put into an artery through a small cut in the inner thigh and threaded up into the artery feeding the tumor. A dye is usually injected into the blood at this time to help the doctor monitor the path of the catheter with angiography, a special type of x-ray. Once the catheter is in place, small particles are injected into the artery to plug it up.

Chemoembolization: This approach, also known as trans-arterial chemoembolization (or TACE) combines embolization with chemotherapy. Most often, this is done by using tiny beads that give off a chemotherapy drug for the embolization. TACE can also be done by giving chemotherapy through the catheter directly into the artery, then plugging up the artery.

Radioembolization: This technique combines embolization with radiation therapy. In the United States, this is done by injecting small radioactive beads (called *microspheres*) into the artery. Once infused, the beads lodge in the blood vessels near the tumor, where they give off small amounts of radiation to the tumor site for several days. The radiation travels a very short distance, so its effects are limited mainly to the tumor.

Side effects of embolization: Possible complications after embolization include abdominal pain, fever, nausea, infection, and blood clots in nearby blood vessels. Serious complications are not common, but they can happen.

Radiation therapy for pancreatic cancer

Radiation therapy uses high-energy x-rays (or particles) to kill cancer cells. It can be helpful in treating some exocrine pancreatic cancers. Pancreatic neuroendocrine tumors (NETs) don't respond well to radiation, 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. It may also be used to treat these tumors in the form of radioembolization, which was discussed in the section "Ablation or embolization treatments for pancreatic cancer."

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.

Radiation can be used in different situations for exocrine pancreas cancers:

- If surgery is planned, a person may get radiation before surgery (*preoperative* or *neoadjuvant* treatment) or after surgery (*postoperative* or *adjuvant* treatment). The radiation is typically given along with chemotherapy, which is together known as *chemoradiation* or *chemoradiotherapy.* Preoperative treatment is often preferred because postoperative treatment often has to be delayed for several weeks while the person recovers from surgery. Treatment right after surgery can interfere with wound healing.

- Radiation therapy (combined with chemotherapy) may be used in people whose cancers have grown beyond the pancreas and can't be removed by surgery (locally advanced/unresectable cancers).

- Radiation is sometimes used to help relieve symptoms such as pain in people with advanced cancers or in people who aren't healthy enough have other treatments like surgery.

Before your treatment starts, the radiation team will take careful measurements to determine the correct angles for aiming the radiation beams and the proper dose of radiation. Radiation therapy is much like getting an x-ray, but the radiation is stronger. The procedure itself is painless. Each treatment lasts only a few minutes, although the setup time – getting you into place for treatment – usually takes longer. Most often, radiation treatments are given 5 days a week for several weeks.

Possible side effects

Some of the common side effects of radiation therapy include:

- Skin changes (like a sunburn) in areas getting radiation
- 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.

For more general information about radiation therapy, please see the "Radiation Therapy" section of our website or our document *Understanding Radiation Therapy: A Guide for Patients and Families*.

Chemotherapy and other drugs for pancreatic cancer

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

Chemotherapy for exocrine pancreatic cancer

Chemo may be used at any stage of pancreatic cancer:

- Chemo can be given before surgery (sometimes along with radiation) to try to shrink the tumor. This is known as *neoadjuvant* treatment.
- Chemo can be used after surgery (sometimes along with radiation) to try to kill any cancer cells that have been left behind (but can't be seen). This type of treatment, called *adjuvant* treatment, lowers the chance that the cancer will come back later.

- Chemo is commonly used when the cancer is advanced and can't be removed completely with surgery.

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

Many different chemo drugs can be used to treat pancreatic cancer, including:

- Gemcitabine (Gemzar®)
- 5-fluorouracil (5-FU)
- Irinotecan (Camptosar®)
- Oxaliplatin (Eloxatin®)
- Albumin-bound paclitaxel (Abraxane®)
- Capecitabine (Xeloda®)
- Cisplatin
- Paclitaxel (Taxol®)
- Docetaxel (Taxotere®)

In people who are healthy enough, 2 or more drugs are usually given together. For people who are not healthy enough for combined treatments, a single drug (usually gemcitabine, 5-FU, or capecitabine) can be used.

Doctors give chemo in cycles, with each period of treatment followed by a rest period to allow the body time to recover. Each chemo cycle typically lasts for a few weeks.

Possible side effects

Chemo drugs attack cells that are dividing quickly, which is why they work against cancer cells. But other cells in the body, such as those in the bone marrow (where new blood cells are made), the lining of the mouth and intestines, and the hair follicles, also divide quickly. These cells are also likely to be affected by chemo. 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 or constipation

Because chemo can damage 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 too few red blood cells)

Many of the chemo drugs used for pancreatic cancer can cause diarrhea.

Other side effects can occur depending on what chemo drugs are used. For example:

- Drugs such as cisplatin, oxaliplatin, and albumin-bound paclitaxel 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.
- 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.

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

For more information about chemo, please see the Chemotherapy section of our website, or our document *A Guide to Chemotherapy*.

Targeted therapy for exocrine pancreatic cancers

As researchers have learned more about the changes in cells that cause cancer, they have developed newer drugs that specifically target these changes. These targeted drugs work differently from standard chemo drugs. Sometimes they work when standard chemo drugs don't, and they often have different (and less severe) side effects. (See "What's new in pancreatic cancer research and treatment?" for more information.)

Erlotinib (Tarceva®) is a drug that targets a protein on the surface of cancer cells called *EGFR*, which normally prompts cancer cells to grow. This drug can help some patients with advanced pancreatic cancer. People given erlotinib combined with the chemo drug gemcitabine tend to do slightly better than those who get 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

Chemo is not often very helpful in treating these tumors, so it isn't often used. As with exocrine pancreatic cancers, when chemo is used it often includes a combination of 2 or more drugs.

The most commonly used drugs for pancreatic NETs are doxorubicin (Adriamycin®) and streptozocin. Sometimes a special form of doxorubicin known as *liposomal doxorubicin* (Doxil®) has been used instead of the regular drug. In this form, the drug is dissolved in fat droplets, which allows it to be given with less serious side effects.

Other chemo drugs that might be 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

Some targeted drugs can be helpful in treating advanced pancreatic NETs.

Sunitinib (Sutent®) attacks both blood vessel growth and other targets that help cancer cells grow. In advanced pancreatic NETs, it has been shown to slow tumor growth and help patients live longer. This drug is taken as pills once a day. 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.

Everolimus (Afinitor®) works by blocking a cell protein known as *mTOR*, which normally helps cells grow and divide. This drug has been shown to slow tumor growth, but it's not yet clear if it helps patients live longer. Everolimus is a pill taken once a day. Common side effects of this drug include mouth sores, 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.

Other drugs for treating pancreatic neuroendocrine tumors

Other types of drugs are sometimes useful in treating people with pancreatic NETs as well.

Somatostatin analogs: Drugs that are chemically related to somatostatin, a natural hormone in the body, can be very helpful for some patients with pancreatic NETs. They stop tumors from releasing hormones into the bloodstream, which can often relieve symptoms and help patients feel better. They also seem to help slow the growth of some tumors. These drugs 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).

These drugs can help reduce diarrhea in patients with VIPomas, glucagonomas, and somatostatinomas, and can also help the rash of glucagonomas.

The main side effects are pain at the site of the injection, and rarely, stomach cramps, nausea, vomiting, headaches, dizziness, and fatigue. These drugs can also cause sludge to build up in the gallbladder, which can lead to gallstones. They can also make the body resistant to the action of insulin, which can raise blood sugar levels and make pre-existing diabetes harder to control. These drugs are not often used in treating insulinomas, because the effects on the release of other hormones can cause worse problems with blood sugars.

Octreotide (Sandostatin®) was the first somatostatin analog to become available. 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.

Lanreotide (Somatuline® Depot), a newer somatostatin analog, is given as an injection under the skin about once a month. It has been shown to help slow the growth of pancreatic NETs.

Pasireotide (Signifor®, Signifor® LAR), another newer somatostatin, is injected either twice a day or about once a month. This drug is also being studied for use in pancreatic NETs.

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

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

To learn more about a drug mentioned in this section, or any specific drug you're taking for cancer, call us at 1-800-227-2345 or visit our Cancer Drug Guide online.

Pain control in pancreatic cancer

Pain can be a major problem for people with pancreatic cancer, especially the exocrine type. These cancers can invade and press on nerves near the pancreas, which can cause pain in the abdomen (belly) or back.

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.

Pain medicines

For most patients, treatment with morphine or similar drugs (opiates) can help control the pain. Many people are worried about these drugs because they fear becoming addicted, but studies have shown that the risk of this is low if the patient takes the drug for pain as directed by the doctor.

Pain medicines work best when they are taken on a regular 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 opioids are in pill form and only need be taken once or twice a day. There is even a long-acting form of the drug fentanyl that is applied as a patch every 3 days.

Common side effects of these drugs are nausea and feeling sleepy, which often get better over time. Constipation is a common side effect that does not get better on its own, so it needs to be treated. Most people on these drugs need to take laxatives daily.

Other treatments

Sometimes certain procedures might be needed to treat pain. For example, cutting or injecting alcohol into some of the nerves near the pancreas that carry pain sensations can improve pain and allow you to use lower doses of pain medicines. If you are having surgery for some reason (such as to remove the cancer or relieve bile duct blockage), this can be done as part of the same operation.

This can also be done as a separate procedure. For example, the doctor might do a *nerve block* by injecting the nerves near the pancreas with either an anesthetic or a medicine that destroys the nerves. This can be done either by passing a needle through the skin or by using an endoscope (a long, flexible tube that is passed down the mouth and past the stomach).

Treating the cancer with chemotherapy and/or radiation therapy can also sometimes relieve pain by shrinking the size of the cancer.

For more information on pain and what can be done about it, see our document *Guide to Controlling Cancer Pain*. A list of some other documents on this topic can be found in the “Additional resources for pancreatic cancer” section.

Clinical trials for pancreatic cancer

You may have had to make a lot of decisions since you’ve been told you have pancreatic 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 pancreatic 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 learn more about promising new treatments or procedures.

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

If you would like to learn more about clinical trials that might be right for you, 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 studies that meet your medical needs. You can reach this service at 1-800-303-5691 or on our website at www.cancer.org/clinicaltrials. You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials website at www.cancer.gov/clinicaltrials.

You must meet certain requirements to take part in any clinical trial. If you do qualify for a clinical trial, you decide whether or not to enter (enroll in) it.

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

Complementary and alternative therapies for pancreatic cancer

When you have pancreatic 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 social media groups and websites might offer ideas for what might help you. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

What exactly are complementary and alternative therapies?

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

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

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

Finding out more

It is easy to see why people with cancer think about alternative methods. You want to do all you can to fight the cancer, and the idea of a treatment with few or no side effects sounds great. Sometimes medical treatments like chemotherapy can be hard to take, or they may no longer be working. But the truth is that most 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 or see the "Complementary and Alternative Medicine" section of our website 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

Most of the time, the treatment of pancreatic cancer is based on its stage – how far it has spread in the body. But other factors, such as a person's overall health, can also affect treatment options. Talk to your doctor if you have any questions about the treatment plan he or she recommends.

It is hard to stage pancreatic cancer accurately using imaging tests. Doctors do their best to decide before treatment whether there is a good chance the cancer is resectable – that is, if it can be removed completely. But sometimes cancers turn out to have spread farther than was first thought.

Exocrine pancreatic cancer

Resectable: Surgeons usually consider pancreatic cancer to be resectable if it looks like it is still within the pancreas or doesn't extend far beyond the pancreas. Most pancreatic cancers that have reached nearby large blood vessels are not resectable.

If imaging tests show a reasonable chance of removing the cancer completely, surgery is the preferred treatment if possible, as it offers the only realistic chance to cure this

disease. Based on where the cancer started, usually either a Whipple procedure (pancreaticoduodenectomy) or a distal pancreatectomy is used. Sometimes even when a cancer is thought to be resectable, it becomes clear during the surgery that not all of it can be removed. If this happens, continuing the operation might do more harm than good. The surgery might be stopped, or the surgeon might continue with a smaller operation with a goal of relieving or preventing problems such as bile duct blockage.

Even when surgery has removed all of the tumor that can be seen, the cancer often comes back. Giving chemotherapy (chemo), either alone or with radiation therapy (chemoradiation), after surgery (known as *adjuvant treatment*) might help some patients live longer. The chemo drugs most often used are gemcitabine (Gemzar) or 5-FU.

Some patients are given chemo, either alone or with radiation therapy, *before* surgery (known as *neoadjuvant treatment*). Some doctors prefer giving chemo before surgery because the recovery after surgery is often long, which can delay or even prevent its use. Neoadjuvant treatment might also help shrink the tumor, which could make surgery easier. But it is not yet clear that this approach is better than giving the treatment after surgery. Some people who get neoadjuvant treatment might also be given chemo after surgery if they are healthy enough.

Borderline resectable: A small number of pancreatic cancers have reached nearby blood vessels but have not grown deeply into them or surrounded them. These cancers might still be removable by surgery, but the odds of removing all of the cancer are lower, so they are considered *borderline resectable*.

These cancers are often treated first with neoadjuvant chemotherapy (sometimes along with radiation). Imaging tests (and sometimes laparoscopy) are then done to make sure the cancer hasn't grown too much to be removed. As long as it hasn't, surgery is then done to remove it. This might be followed by more chemotherapy.

Another option might be to have surgery as the first treatment, followed by adjuvant chemotherapy (and possibly radiation). If, during the surgery, it becomes clear that not all of the cancer can be removed, continuing the operation might do more harm than good. The surgery might be stopped, or the surgeon might continue with a smaller operation with a goal of relieving or preventing problems such as bile duct blockage.

Locally advanced (unresectable): Locally advanced cancers have grown too far into nearby blood vessels or other tissues to be removed completely by surgery, but have not spread to the liver or distant organs and tissues. Surgery to try to remove these cancers does not help patients live longer. Therefore, if surgery is done in these cancers, it is 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. This treatment may help some patients live longer even if the cancer doesn't shrink. 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. Even when imaging tests show that the spread is only to one other part of the body, it has to be assumed that small groups of cancer cells (too small to be seen on imaging tests) have already reached other organs of the body.

Chemotherapy is the main treatment for these cancers. It can sometimes shrink or slow the growth of these cancers for a time and might help people live longer, but it is not expected to cure the cancer.

Gemcitabine is the drug used most often. It can be used alone (especially for people in poor health), or it can be combined with other drugs like albumin-bound paclitaxel (Abraxane), erlotinib (Tarceva), or capecitabine (Xeloda).

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 (Camptosar), and oxaliplatin (Eloxatin). This treatment might help patients live longer than getting gemcitabine alone, but it can have more severe side effects, so its use is limited to people who are otherwise healthy. There is a nationwide shortage of leucovorin at this time, which can sometimes limit the ability of doctors to give FOLFIRINOX.

Other treatments might also be used to help prevent or relieve symptoms from these cancers. For example, radiation therapy or some type of nerve block might be used to help relieve cancer pain, or a stent might be placed during an endoscopy to help keep the bile duct open.

Because the treatments now available don't work well for many people, you may want to think about taking part in a clinical trial of new drugs or combinations of drugs.

Recurrent cancer: Cancer is called *recurrent* when it come backs after treatment. Recurrence of pancreatic cancer most often occurs first in the liver, but it may also spread to the lungs, bone, or other organs. When pancreatic cancer recurs, it is essentially treated the same way as metastatic cancer. This will likely include chemo if the person can tolerate it. Other treatments such as radiation therapy or stent placement might be used to help prevent or relieve symptoms from the cancer.

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 (known as *ampullary cancer*) can start in the pancreatic duct, the duodenum, or the common bile duct. In many patients, ampullary cancer can't be distinguished from pancreatic cancer until surgery has been done.

These cancers often cause early symptoms such as jaundice, so they are often found while they are still resectable. Surgery with the Whipple procedure is often successful in

treating these early stage cancers. Postoperative chemoradiotherapy is often recommended after surgery.

More advanced ampullary cancers are treated like pancreatic cancer.

Pancreatic neuroendocrine tumors (NETs)

Treatment of pancreatic NETs depends to a large extent on whether they can be removed completely or not. These tumors are more likely to be resectable than exocrine pancreas cancers. Most NETs that have not spread to distant parts of the body are resectable. Even some NETs that have spread might be resectable if they have not spread too far (such as only to a small extent in the liver).

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 (removing just the tumor) to as much as a Whipple procedure (pancreaticoduodenectomy). Lymph nodes are often removed to check for tumor spread.

Before any surgery, medicines are often given to control any symptoms caused by the tumor. Drugs to block stomach acid (like proton pump inhibitors) are used for gastrinomas. 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 (OctreoScan), octreotide (Somatostatin) may be used to control any symptoms.

Surgery alone is all that is needed for many pancreatic NETs, but after surgery, close monitoring is important to look for signs that the cancer may have come back or spread.

Unresectable: These tumors can’t be removed completely with surgery. Pancreatic NETs are often slow growing, so lab and imaging tests are used to monitor the tumor(s) and look for signs of growth.

People with cancers that have spread outside the pancreas often have symptoms like diarrhea or hormone problems. These can often be helped with drugs like octreotide, lanreotide, diazoxide, and proton pump inhibitors. Lanreotide might also slow the growth of the tumor.

If further treatment is needed, chemo or targeted drugs (such as sunitinib or everolimus) might be used, but this is usually delayed until the patient is having symptoms that can’t be controlled with other drugs or has signs of tumor growth on scans. 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. These are available on the NCCN website (www.nccn.org).

The NCI, part of the US National Institutes of Health, provides treatment guidelines by phone (1-800-4-CANCER) and on its website (www.cancer.gov). Detailed information 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 honest, 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 where it started?
- What is the stage of my cancer? Is it resectable?
- Do I need other tests before we can decide on treatment?
- Do I need to see other kinds of doctors?
- How much experience do you have treating this type of cancer?
- Should I get a second opinion? Can you recommend a doctor or cancer center?
- What are my treatment choices?
- What do you recommend and why?
- What is the goal of each treatment?
- How is treatment likely to help me?
- What risks or side effects might I expect? How long are they likely to last?
- Will treatment affect how I eat?
- How would treatment affect my daily activities?
- Should I think about taking part in a clinical trial?
- How soon do I need to start treatment?
- What should I do to be ready for treatment?
- How long will treatment last? What will it be like? Where will it be done?

- What would my options be if the treatment doesn't work or if the cancer comes back?
- Where can I find more information and support?

Along with these sample questions, be sure to write down some of your own. Keep in mind that doctors are not the only ones who can provide you with information. Other health care professionals, such as nurses and social workers, may have the answers to some of your questions. You can find more information about communicating with your health care team in our document *Talking With Your Doctor*.

What happens after treatment for pancreatic cancer?

For some people with pancreatic cancer, treatment can 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 and can be read online.

For most people with pancreatic exocrine cancer (and some people 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 under control and relieve symptoms from it. 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

If you have completed treatment, your doctors will still want to watch you closely. It's very important to go to all of your follow-up appointments. During these visits, your doctors will ask questions about any problems you are having and may do exams and lab or imaging tests to look for signs of cancer or treatment side effects. These tests are described in the section "How is pancreatic cancer diagnosed?"

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. Ask what kind of follow-up schedule you can expect.

It’s also very 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.

If cancer does recur, treatment will depend on where the cancer is, what treatments you’ve had before, and your overall health. 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.

Help with nutrition and pain

Pancreatic cancer often causes weight loss and weakness due to poor nutrition. These symptoms may be caused by treatment or by the cancer itself. A team of doctors and nutritionists can work with you to provide nutritional supplements and information about your individual nutritional needs. This can help you maintain your weight and nutritional intake. Many patients need to take pancreatic enzymes in pill form to help digest food so that it can be absorbed. For serious nutrition problems, the doctor might need to put a feeding tube into the stomach to improve nutrition and energy levels. This is usually temporary. For more information and nutrition tips for during and after cancer treatment, see our document *Nutrition for the Person With Cancer During Treatment: A Guide for Patients and Families.*

There are many ways to control pain caused by pancreatic cancer. If you have pain, tell your cancer care team right away, so they can give you prompt and effective pain management. For more information, see our document *Guide to Controlling Cancer Pain.*

Seeing a new doctor

At some point after your cancer diagnosis and treatment, you may find yourself seeing a new doctor who doesn’t know anything about your medical history. It’s important that you be able to give your new doctor the details of your diagnosis and treatment. Gathering these details during and soon after treatment may be easier than trying to get them at some point in the future. Make sure you have this information handy (and always keep copies for yourself):

- A copy of your pathology report(s) from any biopsy or surgery
- Copies of imaging tests (CT or MRI scans, etc.), which can usually be stored digitally (on a DVD, etc.)
- If you had surgery, a copy of your operative report(s)
- If you stayed in the hospital, a copy of the discharge summary that the doctor prepared when you were sent home
- If you had chemotherapy, targeted therapy, or other drug treatment, a list of the drugs, drug doses, and when you took them

- If you had radiation therapy, a summary of the type and dose of radiation and when and where it was given
- The names and contact information of the doctors who treated your cancer

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're thinking about how to improve your health over the long term. Some people even start during cancer treatment.

Making healthier choices

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

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

Eating better

Eating right can be hard for anyone, but it can get even tougher during and after cancer treatment. This is especially true for cancers of the pancreas (as mentioned in the previous section). The cancer or its treatment may affect your appetite or alter how you digest foods. Nausea can be a problem. You may lose weight when you don't want to. All of these things can be very frustrating.

If treatment causes weight changes or eating problems, do the best you can and keep in mind that these problems may 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 to practice healthy eating habits. 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.

For more information, see our document *Nutrition and Physical Activity During and After Cancer Treatment: Answers to Common Questions*.

Rest, fatigue, and exercise

Extreme tiredness, called *fatigue*, is very common in people treated for cancer. This is not a normal tiredness, but a bone-weary exhaustion that often doesn't get better with rest. For some people, fatigue lasts a long time after treatment, and can make it hard for them to be active 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's normal for your fitness, endurance, and muscle strength to decline. Any plan for physical activity should fit your own situation. A person who has never exercised will not be able to take on the same amount of exercise as someone who plays tennis twice a week. If you haven't been active 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 activity 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 learn to balance activity with rest. It's 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 fatigue and other treatment side effects, please see the "Additional resources for pancreatic cancer" section.)

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.

Can I lower the risk of my pancreatic cancer progressing or coming back?

Most people want to know if there are specific lifestyle changes they can make to reduce their risk of their cancer progressing or coming back. Unfortunately, for most cancers there isn't much solid evidence to guide people. This doesn't mean that nothing will help – it's just that for the most part this is an area that hasn't been well studied. Most studies have looked at lifestyle changes as ways of preventing cancer in the first place, not slowing it down or preventing it from coming back.

At this time, not enough is known about pancreatic cancer to say for sure if there are things you can do that will be helpful. Tobacco use has clearly been linked to pancreas cancer, so not smoking may help reduce your risk. We don't know for certain if this will help, but we do know that it can help improve your appetite and overall health. It can also reduce the chance of developing other types of cancer. If you want to quit smoking and need help, call your American Cancer Society at 1-800-227-2345.

Adopting other healthy behaviors such as eating well, getting regular physical activity, and staying at a healthy weight may help as well, but no one knows for sure. However, we do know that these types of changes can have positive effects on your health that can extend beyond your risk of cancer.

So far, no dietary supplements of any kind have been shown to clearly help lower the risk of pancreatic cancer progressing or coming back. Again, this doesn't necessarily mean that none will help, but it's important to understand that none have been proven to do so.

How might having pancreatic cancer affect your emotional health?

During and after treatment, you may find yourself overcome with many different emotions. This happens to a lot of people.

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, you might be stressed by financial concerns resulting from your treatment. You might also see your health care team less often and have more time on your hands. These changes can make some people anxious.

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

If treatment for pancreatic cancer stops working

If cancer keeps growing or comes back after one kind of treatment, it's possible that another treatment plan might still cure the cancer, or at least keep it under control enough to help you live longer and feel better. Clinical trials also might offer chances to try newer treatments that could be helpful. But when a person has tried many different treatments and the cancer has not gotten any better, even newer treatments might no longer be helpful. If this happens, it's important to weigh the possible limited benefits of trying a new treatment against the possible downsides, including treatment side effects. 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 treatments and nothing's working anymore. Your doctor might 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. Your doctor can estimate how likely it is the cancer will respond to treatment you're considering. For instance, the doctor may say that more treatment might have about a 1 in 100 chance of working. Some people are still tempted to try this. But it's important to have realistic expectations if you do choose this plan.

Palliative care

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

Palliative care helps relieve symptoms, but is not expected to cure the disease. It can be given along with cancer treatment, or can even be cancer treatment. The difference is its purpose — the main goal 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

or other treatments might be used to help relieve pain caused by cancer that has spread to nearby nerves. Or a stent might be placed in the intestines to keep them from being blocked by the cancer. But this is not the same as treatment to try to cure the cancer.

Hospice care

At some point, you may benefit from hospice care. This is special care that treats the person rather than the disease; it focuses on quality rather than length of life. Most of the time, it is given at home. Your cancer may be causing problems that need to be managed, and hospice focuses on your comfort. You should know that while getting hospice care often means the end of treatments such as chemo and radiation, it doesn't mean you can't have treatment for the problems caused by the 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 *Hospice Care*.

Staying hopeful is important, too. Your hope for a cure may not be as bright, but there's 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.

To learn more

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

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 and other genes may be altered in pancreatic cancers that do not seem to be inherited. They have discovered that pancreatic cancer does not form suddenly. It develops over many years in a series of steps known as

pancreatic intraepithelial neoplasia or PanIN. In the early steps, such as PanIN 1, there are changes in a small number of genes, and the duct cells of the pancreas do not look very abnormal. In later steps such as PanIN 2 and PanIN 3, there are abnormalities in several genes and the duct cells look more abnormal.

Researchers are using this information to develop tests for detecting acquired (not inherited) gene changes in pancreatic cancer pre-cancerous conditions. One of the most common DNA changes in these conditions affects the *KRAS* oncogene, which affects regulation of cell growth. New diagnostic tests are often able to recognize this change in samples of pancreatic juice collected during an ERCP (endoscopic retrograde cholangiopancreatography).

For now, imaging tests like endoscopic ultrasound (EUS), ERCP, and genetic tests for changes in certain genes (such as *KRAS*) 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.

Surgery

Surgery to remove pancreatic cancer (most often a Whipple procedure) is a long and complex operation that can be hard both for the surgeon and the patient. It often requires a hospital stay of a week or more, at least in part because of the long incision made in the belly.

A newer approach now used at some major medical centers is to do the operation laparoscopically. For this approach, the surgeon makes several small incisions in the belly instead of one large one. Long, thin surgical instruments and a tiny video camera are then inserted through these cuts to do the operation. One advantage of this surgery is that people often recover from it more quickly. But this is still a difficult operation. Surgeons are looking to see how it compares to the standard operation and which patients might be helped the most by it.

Radiation therapy

Some current studies are looking at different ways to give radiation to treat exocrine pancreas cancer. These include intraoperative radiation therapy (in which a single large dose of radiation is given to the pancreas in the operating room at the time of surgery) and proton beam radiation (which uses a special type of radiation that might do less damage to nearby normal cells).

Chemotherapy

Many clinical trials are testing new combinations of chemotherapy drugs for pancreatic cancer. Studies have looked to see if combining gemcitabine with other drugs would help patients live longer. For example, adding capecitabine (Xeloda) to gemcitabine seems to help some patients. The combination of gemcitabine, irinotecan, and celecoxib (an arthritis drug) also 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 developed 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 treatments. In general, they seem to have fewer side effects than traditional chemo 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 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 for patients with pancreatic cancer.

Drugs that target the tumor stroma (supporting tissue): Pancreatic cancer does not always respond well to chemotherapy. This is partly because of the cancer cells themselves, but another reason might be the dense surrounding supportive tissue (*stroma*) in the tumor. The stroma seems to form a barrier that helps protect the cancer cells from the effects of chemo drugs. Researchers are now looking at drugs that attack the stroma directly to help break it down. This might allow chemo or other drugs to be more effective. Some of these types of drugs are now in clinical trials.

Other targeted therapies: Many drugs targeting other aspects of cancer cells are now being studied for use in pancreatic cancer. Some of these drugs, such as sunitinib (Sutent), 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.

Monoclonal antibodies: One form of immune therapy uses injections of man-made *monoclonal antibodies*. 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.

Cancer vaccines: Several types of vaccines for boosting the body's immune response to pancreatic cancer cells are being tested in clinical trials. Unlike vaccines against infections like measles or mumps, these vaccines are designed to help treat, not prevent, pancreatic cancer. One possible advantage of these types of treatments is that they seem to have very limited side effects. At this time, vaccines are available only in clinical trials.

Drugs that target immune system checkpoints: The immune system normally keeps itself from attacking other normal cells in the body by using "checkpoints" – molecules on immune cells that need to be activated (or inactivated) to start an immune response. Cancer cells sometimes find ways to use these checkpoints to avoid being attacked by the immune system. Newer drugs that target these checkpoints have shown a lot of promise in treating some types of cancer, and are now being studied for use in pancreatic cancer.

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 whose tumors have a particular change in the *EGFR* gene. This concept is an area of intense study. There might also be some gene 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 tumors (NETs)

Many pancreatic NETs have receptors for somatostatin on their cells. These tumors can be treated with octreotide and other drugs like it. Newer drugs that use a radioactive form of octreotide have been shown to shrink some tumors and keep others from growing in early studies.

Additional resources for pancreatic cancer

More information from your American Cancer Society

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

Dealing with diagnosis and treatment

Health Professionals Associated With Cancer Care

Talking With Your Doctor (also in Spanish)

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

Coping With Cancer in Everyday Life (also in Spanish)

Nutrition for the Person With Cancer During Treatment: A Guide for Patients and Families (also in Spanish)

Living with cancer

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

Distress in People With Cancer

Guide to Controlling Cancer Pain (also in Spanish)

Anxiety, Fear, and Depression

Living With Uncertainty: The Fear of Cancer Recurrence

When Your Cancer Comes Back: Cancer Recurrence

Family and caregiver concerns

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

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

What It Takes to Be a Caregiver

Insurance and financial issues

In Treatment: Financial Guidance for Cancer Survivors and Their Families (also in Spanish)

Health Insurance and Financial Assistance for the Cancer Patient (also in Spanish)

More on cancer treatments

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

A Guide to Chemotherapy (also in Spanish)

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

Targeted Therapy

Clinical Trials: What You Need to Know

Cancer treatment side effects

Nausea and Vomiting

Anemia in People With Cancer

Fatigue in People With Cancer

Peripheral Neuropathy Caused By Chemotherapy

When treatment isn't working

When Cancer Doesn't Go Away

Nearing the End of Life

Hospice Care

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

National organizations and websites*

Along with the American Cancer Society, other sources of information and support include:

National Cancer Institute (NCI)
Toll-free number: 1-800-422-6237 (1-800-4-CANCER)
TTY: 1-800-332-8615
Website: www.cancer.gov

> Offers a wide variety of free, accurate, up-to-date information about cancer to patients, their families, and the general public; also can help people find clinical trials in their area

Pancreatic Cancer Action Network, Inc.
Toll-free number: 1-877-272-6226
Website www.pancan.org

> Has a “Patient and Liaison Services” (PALS) program which offers information about pancreatic cancer, treatment options, diet and nutrition, specialists and clinical trials specific to pancreatic cancer, and more; also has the PALS Survivor and Caregiver Network through which newly-diagnosed people and families are matched with volunteer survivors and caregivers

Confronting Pancreatic Cancer (Pancreatica)
Website: www.pancreatica.org

> For practical, impartial, understandable information about pancreatic cancer; also has a free phone information and counseling line at 1-800-525-3777 and another free phone service that will put you in contact with a fellow survivor at 1-800-433-0464

Hirshberg Foundation for Pancreatic Cancer Research
Phone number: 1-310-473-5121
Website: www.pancreatic.org

> Provides a variety of types of information, resources, and support to pancreatic cancer patients and their families, including referrals for treatment facilities, second opinions, and doctors across the US

The Lustgarten Foundation for Pancreatic Cancer Research
Toll-free number: 1-866-789-1000
Website: www.lustgarten.org

> Offers a free patient handbook called “Understanding Pancreatic Cancer,” newsletters, and a free quarterly “Ask an Expert” patient information series which includes updates on topics of interest to those with pancreatic cancer

**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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