

PANCREATIC
CANCER
ACTION
NETWORK[®]

AN OVERVIEW OF PANCREATIC CANCER



A GUIDE TO UNDERSTANDING
A COMPLEX DISEASE

ABOUT THIS BOOKLET

This booklet is a resource for patients and families who want to understand pancreatic cancer. The more information and knowledge you have, the more empowered you can be about decisions associated with a pancreatic cancer diagnosis.

Use this booklet as a reference guide to talk about pancreatic cancer with your healthcare team.

You are your own best advocate. The Pancreatic Cancer Action Network (PanCAN) strongly recommends that you discuss your treatment goals with your healthcare team and know all of your options at every stage of your disease.

And, our PanCAN Patient Services staff is trained in a wide variety of topics relating to pancreatic cancer with the goal of empowering you to be your own best advocate.

Hablamos Español. Contact Patient Services toll-free at 877-2-PANCAN or email patientservices@pancan.org. Our Patient Services Helpline is available Monday – Friday, 7 a.m. – 5 p.m. Pacific Time, for support and information about:



Disease and treatment



Know Your Tumor® precision medicine service



Clinical trials – personalized searches using our comprehensive database



Diet and nutrition



Pain and symptom management



Pancreatic cancer specialists



Support resources

All services are free of charge.

A glossary is provided at the end of this booklet for **bold** words in the booklet's text.

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THE PANCREAS

The **pancreas** is a **gland**, about six inches long, located deep in the **abdomen**. It is shaped like a flat pear and is surrounded by the stomach, **small intestine**, **liver**, **spleen** and **gallbladder**. The wide end of the pancreas is called the head. The middle sections are the neck and body. The thin end of the pancreas is called the tail. Three very important blood vessels, the **superior mesenteric artery**, **superior mesenteric vein** and **portal vein**, cross behind the neck of the pancreas. See anatomical illustration (Figure 1) on the next page.

The pancreas functions as both an **exocrine gland** and an **endocrine gland**. Exocrine cells of the pancreas produce **enzymes** that help with digestion. When food enters the stomach, the pancreas releases enzymes into a system of small ducts that lead to the main **pancreatic duct**. The main pancreatic duct runs the length of the pancreas and carries **pancreatic enzymes** and other secretions, collectively called pancreatic juice.

The main pancreatic duct connects with the **common bile duct**, which carries **bile** from the gallbladder, and together they connect with the **duodenum** at a point called the **ampulla of Vater**. Here, bile and pancreatic enzymes enter the duodenum to aid with the digestion of fats, carbohydrates and proteins.

The endocrine cells of the pancreas produce **hormones**. Hormones are substances that control or regulate specific functions in the body. They are usually made in one part of the body and carried through the blood to take action on another part of the body. The two main pancreatic hormones are **insulin** and **glucagon**. **Islet cells** are endocrine cells within the pancreas that produce and secrete insulin and glucagon into the bloodstream. Insulin lowers blood sugar levels while glucagon raises blood sugar levels. Together, these two main hormones work to maintain the proper level of sugar in the blood.

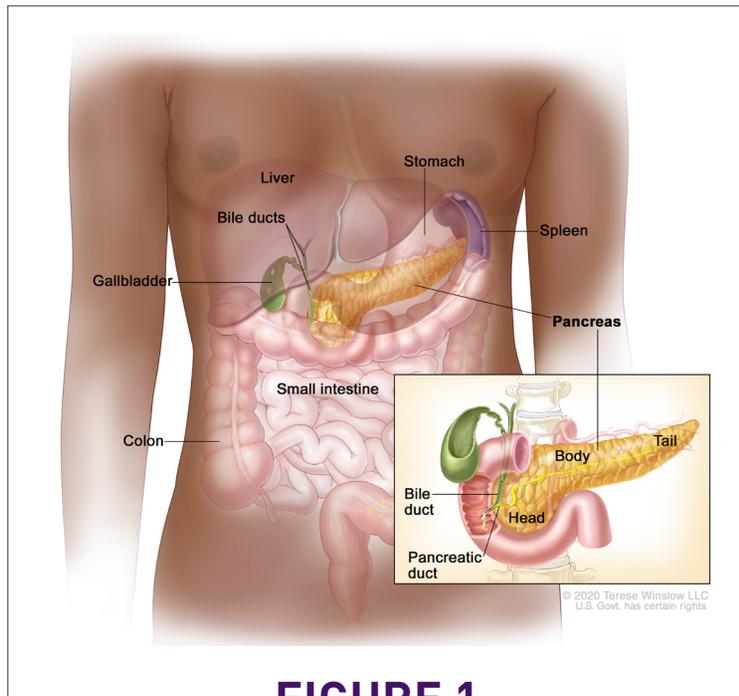


FIGURE 1

The pancreas is located deep in the abdomen and is surrounded by many other organs.

UNDERSTANDING CANCER

Cancer begins within one cell in the body. Cells are the body's basic units of life. Each cell carries **genetic** information in the form of **deoxyribonucleic acid (DNA)**. DNA provides the necessary instructions for the proper growth and function of each cell within the body.

Normally, cells divide to form new cells as the body needs them. When cells grow old, they die and new cells take their place. Sometimes this process breaks down due to a **mutation** in the cell's DNA. A mutation can be inherited or acquired in the course of a lifetime. A mutation may cause new cells to form when the body does not need them or may prevent old cells from dying. The extra cells may form a mass of tissue called a tumor. Tumors can be **benign** or **malignant**.

Benign tumors are made up of abnormal cells that do not have the ability to invade other parts of the body or spread to other organs. If a benign tumor is big enough, its size and weight can cause problems, as it can put pressure on nearby blood vessels, nerves or organs.

Malignant tumors are called cancer and are characterized by uncontrolled cell division and the ability to invade nearby and distant tissues and organs. Cancer cells can break away (**metastasize**) from the original cancer site (**primary tumor**) and form new tumors in other parts of the body.

PANCREATIC CANCER

Pancreatic cancer begins when abnormal cells within the pancreas grow out of control and form a tumor.

When pancreatic cancer spreads (metastasizes) outside the pancreas, it forms **secondary tumors** (metastases) in other tissues or organs. Common sites for secondary pancreatic tumors include the **lymph nodes**, liver, **peritoneum** and lungs. Because the cancer cells in these other locations originated in the pancreas, they are still considered and treated as pancreatic cancer.

Pancreatic tumors are classified into two groups according to the type of cell in which they start – exocrine and neuroendocrine (endocrine) tumors.

PANCREATIC EXOCRINE TUMORS

About 93% of pancreatic cancers are classified as exocrine tumors. These tumors start in the exocrine cells of the pancreas. The following list describes the most common pancreatic exocrine tumors.

Adenocarcinoma

Adenocarcinoma is the most common type of pancreatic cancer. It accounts for about 90% of all pancreatic cancers. It begins in the cells lining the pancreatic duct.

Acinar Cell Carcinoma

Acinar cell carcinoma is a very rare form of pancreatic cancer. Some tumors may cause excessive production of pancreatic lipase, the **enzyme** secreted to digest fats. Pancreatic lipase levels can be measured in the blood.

Intraductal Papillary-Mucinous Neoplasm (IPMN)

An IPMN is a cystic tumor that grows from the main pancreatic duct or from side branches of the duct. The tumor may appear as a finger-like (papillary) projection into the duct. An IPMN may be benign at the time of diagnosis. However, it has a risk of progressing to malignancy. This risk is high when the IPMN originates in the main pancreatic duct.

Mucinous Cystic Neoplasm

Mucinous cystic **neoplasm** with an invasive adenocarcinoma is a rare, cancerous tumor. It is a **cyst** filled with thick fluid. It is like an IPMN but is in just one part of the pancreas, usually the body or tail. These tumors are mostly in women. Mucinous cystic neoplasms can be benign if there is no invasive component.

There are other rare types of exocrine pancreatic tumors not discussed in this booklet. For information about other types of exocrine pancreatic tumors, contact PanCAN Patient Services.

PANCREATIC NEUROENDOCRINE TUMORS (PNETS)

Pancreatic neuroendocrine tumors (pancreatic NETs or PNETs) account for about 7% of all pancreatic tumors. They may be benign or malignant and they tend to grow slower than exocrine tumors. They develop from the abnormal growth of endocrine (hormone-producing) cells in the pancreas called islet cells. This is why these tumors are sometimes referred to as “islet cell tumors.”

Islet cells produce hormones including insulin, glucagon and somatostatin. Insulin and glucagon are the two main pancreatic hormones. Insulin lowers blood sugar levels, while glucagon raises blood sugar levels. Together, these two main hormones work to maintain the proper level of sugar in the blood. Somatostatin regulates the levels of a variety of other hormones in the blood.

Pancreatic neuroendocrine tumors are either functional (produce hormones) or nonfunctional (do not produce hormones).

Functional neuroendocrine tumors cause the pancreas to overproduce hormones, which causes hormone-related **symptoms**. The majority of PNETs are nonfunctional tumors. Nonfunctional tumors do not produce any hormones, so they do not cause any hormone-related symptoms. As a result, these tumors are typically diagnosed once the tumor is advanced and is causing symptoms such as pain or **jaundice**.

The following list describes the different types of pancreatic neuroendocrine tumors classified by the hormones that they produce.

Gastrinoma (Zollinger-Ellison Syndrome)

Gastrinomas produce **gastrin**. When this tumor is inherited as part of a genetic syndrome called Multiple Endocrine Neoplasia Type 1 (MEN1) (see next page), multiple tumors may be found in the head of the pancreas and/or the duodenum. Most gastrinomas are associated with a relatively high risk of being cancerous.

Glucagonoma

Glucagonomas produce glucagon. They are commonly found in the tail of the pancreas. They are usually large, and most are cancerous.

Insulinoma

Insulinomas produce insulin. They are the most common type of functional pancreatic neuroendocrine tumor. They tend to be small and hard to diagnose. Most of them are non-cancerous.

Somatostatinoma

Somatostatinomas produce somatostatin. They are extremely rare and usually very large. They can occur anywhere in the pancreas and in the duodenum. Most somatostatinomas are associated with a relatively high risk of being cancerous.

VIPoma (Verner-Morrison Syndrome)

VIPomas produce vasoactive intestinal peptide (VIP). Two-thirds of VIPomas are found in women. The syndrome is also known as Watery Diarrhea and Hypokalemia Achlorhydria (WDHA) Syndrome.

Nonfunctional Islet Cell Tumor

Nonfunctional islet cell tumors are usually cancerous. They are hard to detect.

Multiple Endocrine Neoplasia Type-1 (MEN1)

MEN1 (also known as Wermer Syndrome) is a **hereditary** syndrome that causes multiple tumors in the **parathyroid glands**, pituitary glands, and the pancreas. The syndrome is suspected when tumors are found in at least two of the three endocrine glands mentioned above. About 30-75% of people with MEN1 will develop pancreatic neuroendocrine tumors. Gastrinomas are the most common pancreatic neuroendocrine tumors in individuals with MEN1. The second most common are insulinomas. The tumors in the pancreas may be malignant and generally appear in individuals in their 30s or 40s.

This booklet does not provide comprehensive information on pancreatic neuroendocrine tumors (PNETs). For more information, contact PanCAN Patient Services and request the *Diagnosing Pancreatic Neuroendocrine Tumors* and *Pancreatic Neuroendocrine Tumors* fact sheets.

SYMPTOMS OF PANCREATIC CANCER

Pancreatic cancer is sometimes called a “silent” disease because symptoms are rarely present in its early stages. Many patients have advanced disease by the time it becomes noticeable to the patient and doctors. If symptoms are present, they are often vague. Patients may experience different symptoms depending on the location, type and **stage** of the cancer. Symptoms that commonly lead to diagnosis include jaundice, abdominal and/or back pain, new onset **diabetes**, unexplained weight loss and loss of appetite. A person with advanced pancreatic cancer may also experience **ascites** (fluid in the abdomen) and **blood clots**. Symptoms such as fatigue, weakness, digestive difficulties and depression may occur at any time.

Common symptoms associated with pancreatic cancer are described below. If someone experiences one or more of the symptoms mentioned in this section, it does not mean that they have pancreatic cancer. There are other common medical problems or conditions that may also cause these or similar symptoms. Anyone experiencing these symptoms should consult with a doctor.

PAIN

Pain in the upper abdomen or mid-back may be caused by the tumor pushing against or invading nerves or organs located near the pancreas. Pain can also result if the tumor blocks

the digestive tract. Treatment, including pain medications and procedures such as a **celiac plexus block**, can be important in managing pancreatic cancer pain. Many pain medications lead to **constipation**, which could make the pain worse. A doctor can prescribe medications to avoid constipation.

JAUNDICE

It is common for people with pancreatic cancer to experience jaundice. Jaundice is a yellowing of the skin and eyes caused by excess **bilirubin** (a component of bile) in the blood. A tumor in the head of the pancreas can cause narrowing of the bile duct and block the bile flowing from the gallbladder into the small intestine. Blockage of the bile duct causes a buildup of bilirubin. People with jaundice may also experience itchiness of the skin, abnormally dark urine and light or clay-colored stools. If surgery to remove the tumor is possible, this can provide relief. In some cases, a biliary bypass surgery may be performed to bypass the blocked bile duct (see page 41). Otherwise, the jaundice is commonly treated by inserting a **stent** to keep the bile duct open (see page 41).

DIGESTIVE DIFFICULTIES

Common digestive difficulties associated with pancreatic cancer include poor appetite, indigestion, nausea and vomiting. These symptoms may be caused by the tumor invading or pressing against the duodenum, which may block food from passing through the intestine. They can also be caused by a blockage of the pancreatic duct or by changes in the amount of pancreatic enzymes produced. Various changes in diet, pancreatic enzyme products and other treatments can help to alleviate many of these symptoms.

UNEXPLAINED WEIGHT LOSS

Weight loss is a common problem in patients with pancreatic cancer. The weight loss can be associated with treatment or the cancer itself. Cancer-induced weight loss (also known as **cancer cachexia**) is a complex problem that affects the way calories and protein are used by the body. Cancer cachexia can cause the body to burn more calories than usual, break down muscle and decrease appetite. A person may also notice a change in appetite or desire for certain foods.

CHANGES IN STOOLS

Many patients with pancreatic cancer experience **diarrhea**, constipation or both. Diarrhea consisting of loose, watery, oily or foul-smelling stools is a common problem that can be caused by insufficient amounts of pancreatic enzymes in the intestines. This leads to malabsorption as undigested food passes quickly through the digestive tract. Constipation is also a common problem, particularly in patients taking pain medications. These medications slow the passage of food through the intestines. If the digestive system works too slowly, it can cause stools to become dry, hard and difficult to pass. Changes in diet and additional medications may be necessary to eliminate or reduce the severity of these symptoms.

BLOOD CLOTS

Deep vein thrombosis (DVT) is a potentially serious condition in which blood clots form in the veins, usually in the legs. Cancer causes changes in the blood that can increase the likelihood of forming clots. Blood clots may go unnoticed and cause no symptoms. However, they are often associated with swelling, pain and tenderness in the affected area. Swelling in only one leg is often a sign of DVT. A fragment of the clot may break loose and travel to the lungs, causing damage to the lung tissue from the sudden decrease in blood supply. This is

called a pulmonary embolism and is a serious condition. DVT is commonly treated with anticoagulant drugs that thin the blood and prevent existing clots from getting larger and new clots from forming.

DEPRESSION

Depression may be more common in pancreatic cancer patients than those with other cancers. It is important for patients to know depression is a treatable condition. Depression may be treated with prescription medications and/or professional counseling. Studies have shown that the best approach for treating depression is a combination of both methods. Some of the signs of depression include loss of interest or pleasure in daily life activities, loss of appetite, difficulty making decisions and concentrating, insomnia, decreased energy, excessive sleeping, feelings of worthlessness, hopelessness or guilt, and negative thoughts and behaviors. It is common for a person who has been diagnosed with pancreatic cancer to feel sad, anxious, and angry. However, if these symptoms happen regularly, continue for an extended period, or keep coming back, they may be a sign of depression.

DIABETES

Diabetes is a condition in which the body does not make, or properly use, a pancreatic hormone called insulin. Insulin helps the body use glucose (sugar) efficiently. Normally, insulin allows glucose to enter cells and be used for energy. In the case of diabetes, either the body does not produce enough insulin or the amount that is produced is not fully effective. Research studies suggest that a sudden onset of type 2 diabetes in people age 50 or older may be an early symptom of pancreatic cancer, especially in those who have a low **body**

mass index (BMI), experience continuous weight loss or do not have a family history of diabetes. A sudden change in blood sugar levels in diabetics who previously had well-controlled diabetes may also be a sign of pancreatic cancer.

Changes in diet, and sometimes insulin therapy, are necessary to control blood sugar levels in people with diabetes.

ASCITES

Ascites is the abnormal accumulation of fluid in the abdomen. This extra fluid causes the belly to become swollen and distended. Ascites may be present at any time during the pancreatic cancer journey but is especially common in patients with advanced metastatic pancreatic cancer. The spread of cancer to the abdominal lining (peritoneum) can result in irritation that causes fluid buildup. As the amount of fluid increases, discomfort, difficulty breathing, nausea and decreased appetite may occur. Treatment with water pills, called **diuretics**, may slow the buildup of fluid. Ascites can also be managed by draining the fluid through a procedure called **paracentesis**.

For more detailed information on pain and symptom management and dietary issues related to pancreatic cancer, contact Patient Services and request copies of the educational booklets, *Diet and Nutrition: Nutritional Concerns with Pancreatic Cancer* and *Supportive Care: Quality of Life and Practical Care in Pancreatic Cancer*.

SYMPTOMS RELATED TO PANCREATIC NEUROENDOCRINE TUMORS

Pancreatic neuroendocrine tumors may cause the pancreas to overproduce hormones, such as insulin, glucagon or somatostatin. High levels of these hormones in the blood result in symptoms such as weight loss, nausea, vomiting, muscle weakness and skin rash. Pancreatic neuroendocrine tumors that do not produce hormones may cause symptoms such as jaundice or pain.

For more information about the symptoms of pancreatic neuroendocrine tumors, contact Patient Services and ask for the fact sheet *Symptoms Specific to Pancreatic Neuroendocrine Tumors (pNETs)*.

DIAGNOSIS AND STAGING

Diagnosing pancreatic cancer can be difficult for several reasons. First, the pancreas is located deep in the abdomen between the stomach and the back, so it is difficult for a doctor to see or feel the tumor during a physical exam. Additionally, the symptoms of pancreatic cancer are not always obvious and usually develop gradually. If a person has symptoms that suggest pancreatic cancer, a variety of tests may be performed to make an accurate diagnosis. However, there is no standard diagnostic test for pancreatic cancer, which further complicates the diagnosing process.

Generally, the doctor will begin by asking about medical and family history and will perform a physical exam. The doctor will examine the patient's body, including skin and eyes, and press on the abdomen to check for changes in the area near the pancreas, liver and gallbladder. Blood, urine and stool tests may be ordered. A pancreatic tumor can only be seen on an imaging study such as a computed tomography (CT) scan or with magnetic resonance imaging (MRI).

Below are some of the tests used to diagnose and monitor people with pancreatic cancer.

IMAGING TESTS

Imaging studies provide visual information about the pancreas and surrounding tissues. These tests are very important in diagnosing and monitoring pancreatic cancer. Many of the commonly used imaging studies are described in this section.



Computed Axial Tomography (CAT or CT) Scan

A CT scan takes detailed images of the body. During a CT scan, the patient lies very still on a table while the scanner (a donut-shaped machine) rotates around the body and takes cross-sectional, x-ray images. Each rotation provides a picture of a thin slice of the organ, and a computer combines all of the pictures and creates a three-dimensional image of the body.

CT images show bones, blood vessels, muscles and organs. When a CT scan is used with an oral or **intravenous (IV)** contrast substance, it may show small tumors of the pancreas and whether the cancer has spread. A CT scan that examines the blood vessels of the pancreas, called angiography, can provide detailed information about the relationship between the tumor and blood vessels. This information is important for the doctor to determine whether or not the cancer is operable.

Radiologists have developed specific CT techniques called “pancreatic protocols” that give high-resolution (clear and detailed) images of the pancreas, liver and key blood vessels. This is the preferred type of CT scan for diagnosing pancreatic cancer. However, a high-quality CT scan may be sufficient if a pancreatic protocol CT is not available.

Reasons for Use and Other Considerations

A CT scan is one of the most common imaging procedures used to create three-dimensional images of the body. Doctors usually order CT scans when they suspect that an individual has pancreatic cancer. The images often help determine if the tumor can be surgically removed.

A very small percentage of patients are allergic to contrast substances, in which case other imaging tests must be used.

CT scans use x-rays, a form of radiation. Repeated exposure to radiation may be a concern when CT is used for screening and surveillance. Patients must discuss the risks and benefits with their healthcare team.



Magnetic Resonance Imaging (MRI)

MRI scans use radio waves and powerful magnets to take images of organs and structures inside the body by measuring their energy. Similar to a CT scan, an MRI takes several pictures of thin slices of the organ while the patient lies on a table. Then, a computer combines all of the images and creates a three-dimensional image of the body.

A pancreas protocol MRI can aid in the staging of pancreatic cancer, especially when tumors are not visible on a CT scan or when patients are allergic to contrast substances used in CT scans.

Reasons for Use and Other Considerations

MRI is often used for people who are allergic to the substance needed for CT scans because a different type of contrast substance is typically used. Also, MRI scans do not involve exposure to radiation.

MRI scans take longer than CT scans. During a traditional MRI, a patient is required to lie motionless in a long cylinder. Patients who are claustrophobic may need to take a drug to calm their anxiety before entering this type of MRI scanner. There is a different type of MRI scanner called “open MRI.” In this type, the sides of the machine are open. This may be helpful for patients who are fearful of being in a closed space.

In addition, an MRCP can be performed at the time of the MRI for patients who need specific imaging of the bile and pancreatic ducts.

Magnetic Resonance Cholangiopancreatography (MRCP)

MRCP is a special type of MRI. It uses computer software that specifically images pancreatic and bile ducts, which are often the site of tumors. Fluid naturally present in the ducts serves as a contrast substance. MRCP is an excellent tool for visualizing pancreatic cysts and blockages in the ducts. An MRCP can be done at the same time as an MRI.

Reasons for Use and Other Considerations

MRCP provides a similar picture to ERCP (see next page), but without the risks of an invasive procedure. MRCP may be used in place of ERCP to diagnose pancreatic cancer if a stent placement is not required.

Jaundice or abnormal liver function can also be caused by other conditions such as bile duct stones, tumors in the small intestine or a type of pancreatic tumor called intraductal papillary mucinous neoplasm (IPMN) (see page 5). MRCP may be used to diagnose these conditions.

Positron Emission Tomography (PET) Scan

PET scans produce images based on the **metabolic** activity level in cells.

The most common PET imaging study is FDG-PET. For this procedure, a small amount of radioactive glucose called fluorodeoxyglucose (FDG) is injected into the patient’s body to measure the metabolic function of cancer cells. The FDG is allowed to circulate for 45–60 minutes as the patient rests. Cancer cells are more metabolically active than normal cells and use more FDG than most normal cells. The PET scanner tracks and records the signals given off by the FDG, and a computer turns these signals into whole-body images that show the areas where cancer cells may be present. Because cancer cells use more FDG, they appear brighter on computer images.

Reasons for Use and Other Considerations

PET scans may help differentiate between benign and malignant pancreatic tumors. They may also help detect the spread of pancreatic cancer to other parts of the body. PET may be used when changes such as abnormal liver growths or enlarged lymph nodes are noted on other scans. **Pancreatitis** or infections can give false positives on PET scans. Therefore, a positive PET scan does not always mean that a person has pancreatic cancer. The opposite is also true — a negative PET scan does not always mean that a person does not have pancreatic cancer.

PET is often used together with CT scans to get a more complete image. New scanners can do a combined PET-CT scan. Studies are still underway to determine the usefulness of PET scans in pancreatic cancer. PET-CT is not a substitute for high-quality, contrast-enhanced CT scans. However, they may be used in addition to CT in high-risk patients.

Endoscopic Retrograde Cholangiopancreatography (ERCP)

During an ERCP, an endoscope (a thin, lighted tube) is guided through the patient's mouth into the stomach and the duodenum. A narrower tube, called a **catheter**, is inserted through the endoscope and into the bile and pancreatic ducts from the small intestine. A contrast substance is injected through the catheter into these ducts and an x-ray picture is taken. These pictures show whether the ducts are narrowed or blocked by a tumor or other condition.

An ERCP can also be used to treat jaundice caused by a blockage of the bile duct. ERCP is generally performed to evaluate or treat jaundice and blocked pancreatic or bile ducts. During the ERCP, a stent can be placed (see page 41) into the blocked duct to keep it open and allow bile to flow.

Biopsies (samples of the tumor) can also be obtained during an ERCP (see page 22).

Reasons for Use and Other Considerations

ERCP is an outpatient procedure usually performed in a hospital endoscopy unit or **ambulatory surgery center**. Patients are given a sedative to help them relax and an anesthetic drug to block pain.

Complications from ERCP are uncommon. Approximately 5-7% of patients experience inflammation of the pancreas, called pancreatitis. Often the pancreatitis is mild, but serious pancreatitis can occur. **Gastrointestinal** bleeding, tearing from the endoscope, allergic reactions to **anesthesia** and infection are other rare complications of ERCP. Sometimes patients are admitted to the hospital for one night of observation after the ERCP procedure.

Endoscopic Ultrasound (EUS)

During an EUS, an endoscope (a thin, lighted tube) with a small ultrasound probe built into the tip is passed through the patient's mouth into the stomach and the duodenum. The ultrasound probe

is used to obtain immediate, detailed images of the pancreas, bile duct and digestive tract. An EUS allows a doctor to determine the size and location of a tumor in the pancreas and whether the tumor has spread to nearby lymph nodes or invaded nearby blood vessels or other structures.

During this procedure, a thin needle that does not cause pain can also be passed through the endoscope into the tumor to obtain tissue samples. This is a type of **biopsy** called "fine-needle aspiration," or FNA (see page 22). Cells collected from the biopsy are examined with a microscope to see if they are cancerous.

Reasons for Use and Other Considerations

EUS is an outpatient procedure usually performed in a hospital endoscopy unit or ambulatory surgery center. Patients are given a sedative to help them relax and an anesthetic drug to block pain. EUS is one of the most common imaging procedures used to diagnose pancreatic cancer. It is often the best procedure to obtain samples of a tumor to make a definitive diagnosis of pancreatic cancer. EUS may be able to find small pancreatic masses that have not been detected by CT or MRI scans but are suspected by the doctor as a result of symptoms and/or blood test results. Studies show that EUS is equal to or better than CT scans in detecting early pancreatic cancer.

Studies using EUS to screen people at higher risk for developing pancreatic cancer are underway. EUS may have the ability to detect early abnormal changes in the pancreas in these individuals.

Complications of EUS are very rare, but they include infection of a pancreatic cyst, pancreatitis, gastrointestinal bleeding and reactions to anesthesia medications.

Laparoscopy

Diagnostic laparoscopy is a minimally-invasive surgery that allows a surgeon to directly view the abdominal organs to determine if a pancreatic tumor has spread to other organs or structures.

During laparoscopy, the surgeon makes a small cut in the abdomen and inserts a tube with a small camera. The camera allows the surgeon to see the inside of the abdomen. In some cases, other small instruments may be inserted to help move organs or structures to allow the surgeon to see the area more clearly.

Reasons for Use and Other Considerations

Laparoscopy is a surgical procedure performed under general anesthesia, meaning the patient is completely asleep during this procedure. Laparoscopic exploration may be used if it is unclear whether the pancreatic tumor has spread throughout the abdomen. If the tumor has not spread, the surgeon may then remove the tumor by making a larger incision in the abdomen.

Because the laparoscopic incision is so small, recovery time from laparoscopy is generally short. Complications are rare, but they include allergic reactions to anesthesia and infection.

BIOPSY

Imaging tests are important in diagnosing pancreatic cancer, but they cannot determine with 100% certainty if an abnormal mass or tumor is actually cancer, or the type of cancer. The doctor must obtain and analyze a tissue sample (biopsy) of the tumor in order to determine the exact diagnosis. A **pathologist** looks at tissue samples of the tumor under a microscope to determine if cancer cells are present. The shape, size and arrangement of the cancer cells may help determine the type of pancreatic cancer. However, not all biopsies provide a conclusive (definite) result.

The most common procedure to obtain samples of a pancreatic tumor is called Fine-Needle Aspiration (FNA).

An FNA can be performed by inserting a needle through the abdomen or by inserting an endoscope (a thin, lighted tube) down the patient's throat and passing a needle through the endoscope to the pancreas.

The procedure that inserts a needle through the abdomen is called a "percutaneous FNA." During this procedure, a numbing substance and a cleaning solution are applied on the skin. Then, a thin needle is inserted through the abdominal wall and directed into the pancreas to obtain cells from the tumor. The doctor uses the image from a CT scan or ultrasound to guide placement of the needle.

The procedure that uses an endoscope to collect tumor samples is called EUS-guided FNA. This procedure is performed during an endoscopic ultrasound (EUS) (see page 20). This process involves imaging the tumor with ultrasound, passing the needle through an endoscope (which is inserted down the patient's throat), and directing the needle to the pancreas through the stomach or duodenum. Unlike percutaneous FNA, there is no discomfort with this procedure. EUS-guided FNA, performed by a specially trained and experienced doctor, is the most accurate biopsy method for the pancreas, in most circumstances.

Other biopsy methods, such as a brush biopsy or forceps biopsy, can be performed during an ERCP (see page 20). In a brush biopsy, a small brush is passed through the endoscope to rub off cells from the bile duct or pancreatic duct. The chance of getting a diagnosis of pancreatic cancer with ERCP brushings is generally lower than with other methods.

In a forceps biopsy, forceps (tongs) are passed through the endoscope to grasp and extract a small piece of the tumor.

A core needle biopsy can also be performed percutaneously (more common) or during an EUS (rare). In a core needle biopsy, a small cylinder of tissue (core) is removed, as opposed to the small amount of cells removed through FNA. Some institutions and clinical trials attempt core needle biopsies so that biomarker testing of tumor tissue (see page 52) can be performed on the sample.

Lastly, a tumor sample can also be taken during surgery.

Sometimes, the needle or brush used in the biopsy procedure may miss its target, which could lead to a noncancerous diagnosis even when cancer cells are present in the pancreas. Because treatment for pancreatic cancer depends on the specific type of pancreatic cancer, it is generally recommended to have a conclusive diagnosis before starting chemotherapy and/or radiation. However, in some cases, if the tumor is surgically **resectable** and other tests and symptoms indicate pancreatic cancer, the surgeon may elect to proceed with surgery even if the biopsy is inconclusive.

BLOOD TESTS

There are blood tests commercially available that can detect pancreatic exocrine tumors. The blood tests may detect DNA released from cancer cells, the immune system's response to the tumor or other blood-based biomarkers, like CA 19-9 (see below). While blood tests may signify the possible presence of the disease, they cannot lead to a definitive pancreatic cancer diagnosis. Additional tests, like imaging and biopsies, are necessary to confirm the diagnosis. A person with pancreatic cancer may have elevated levels of bilirubin and liver enzymes in the blood if the tumor blocks the bile duct. High levels of certain hormones in the blood may be a sign of a rare pancreatic neuroendocrine tumor, such as insulinoma or gastrinoma (see page 6).

After diagnosis, there are two types of blood tests that can monitor the progress of a pancreatic tumor.

CA 19-9

The CA 19-9 Radioimmunoassay (RIA) is a blood test that measures the level of tumor-associated **antigens** found in the blood. CA 19-9 antigens are substances released by some pancreatic tumor cells.

The normal range of CA 19-9 in the blood of a healthy individual is 0–37 U/ml (Units per milliliter). CA 19-9 associated antigen levels are elevated in many patients with pancreatic cancer. It is important to note that not every patient with pancreatic cancer will

have an elevated CA 19-9 level. In addition, some non-cancerous conditions, such as gallstones, biliary infection (cholangitis), a blockage of the bile duct (jaundice), pancreatitis, cystic fibrosis and liver disease, can cause high CA 19-9 levels. **For these reasons, the CA 19-9 test cannot be used as a diagnostic or screening test for pancreatic cancer.** After the diagnosis of pancreatic cancer is confirmed, and if the CA 19-9 level was elevated before treatment, the CA 19-9 test may be used to monitor the effectiveness of treatment.

Changes in CA 19-9 levels may help determine if the tumor is growing, remaining stable or getting smaller. In general, gradually rising CA 19-9 values indicate that the tumor is growing. If the values remain the same, then the disease may be stable. Decreasing CA 19-9 values may indicate that treatment is working and that the tumor or amount of cancer in the body is decreasing. A decline in CA 19-9 levels after treatment for pancreatic cancer followed by a rise later may suggest tumor recurrence or progression. The CA 19-9 test helps doctors decide if treatment should be changed or if additional tests or scans are necessary. Doctors will typically look at overall trends in relation to CA 19-9 values, meaning that they will look at the value over time rather than looking at just one individual value.

For more information about CA 19-9 contact Patient Services and request the *CA 19-9* fact sheet.

Carcinoembryonic Antigen (CEA)

The carcinoembryonic antigen (CEA) test is a blood test that measures the level of CEA protein in the blood. The CEA protein is present in developing human embryos but disappears from the blood by birth. It normally remains at undetectable levels throughout adulthood. When CEA does appear in the blood of an adult, it may indicate the presence of cancer, including pancreatic cancer. **However, the test is not used to diagnose pancreatic cancer because the CEA protein is not produced by all pancreatic tumors.** Other tumors, such as colon, breast and

lung cancer, may also cause an elevation in CEA. In addition, other factors, such as smoking, can increase CEA levels in the blood even when no cancer is present. Doctors measure CEA levels in the blood to monitor whether an existing pancreatic tumor is responding to treatment. If a pancreatic tumor produces the CEA protein and surgery is performed to remove the tumor, CEA levels in the blood should return to normal.

GENETIC COUNSELING AND TESTING

All patients diagnosed with pancreatic cancer should undergo genetic testing. Genetic testing looks for specific changes (mutations) in genes that may have been inherited from the patient's mother or father. Genetic testing may reveal mutations that suggest a patient's cancer can be treated with specific therapies. The results can also help inform family members of risk. Testing can be done at diagnosis or later (see pages 60-62).

The Pancreatic Cancer Action Network strongly recommends all pancreatic cancer patients get genetic testing for inherited mutations as soon as possible after diagnosis as well as genetic counseling. A **genetic counselor** is a healthcare professional who assesses a person's risk of developing hereditary (inherited) diseases over time and can help determine which genetic tests may be appropriate. Patients should tell their doctor about family history of cancer, including **melanoma** and cancers of the pancreas, colon or rectum, breast and ovaries, and other digestive diseases, including pancreatitis. The doctor may also refer the patient to a genetic counselor if they are under the age of 50 or of Ashkenazi Jewish ancestry. However, even patients without a family history or suspicion of an inherited mutation should undergo genetic testing. If a relevant mutation is identified, at-risk relatives should be offered genetic counseling and can participate in surveillance programs if they are found to have the mutation and if appropriate. Germline mutations may

also indicate that a specific treatment may work better than for others who do not have the mutation. Contact PanCAN Patient Services to learn about treatment options.

STAGING

Staging is the process the doctor uses to determine the extent of the cancer in the body. After a diagnosis of pancreatic cancer has been made, additional imaging tests and surgery may be required to accurately determine the stage. Knowing the correct stage helps the doctor determine the prognosis and best course of treatment.

There are two ways to describe the stages of pancreatic cancer: stage number or surgical resection category. The stage number indicates the size and location of the cancer. The surgical resection category indicates whether or not the tumor can be surgically removed. Both are determined by the size and location of the primary tumor, the involvement of local lymph nodes and blood vessels and the presence of distant metastases. Metastases are tumors that have spread to other parts of the body. The doctor may use one or both methods to describe the stage. This chart details each stage. Also, see Figures 2-6 on pages 29-31.

	Description	Extent of the Tumor
STAGE IA	Tumor is limited to the pancreas and measures 2 centimeters (cm) or less.	Localized
STAGE IB	Tumor is limited to the pancreas and measures greater than 2 cm but less than 4 cm.	Localized
STAGE IIA	Tumor extends directly beyond the pancreas but does not involve the major local arteries (celiac axis and superior mesenteric artery) or local lymph nodes. Tumor measures greater than 4 cm.	Localized
STAGE IIB	Tumor may or may not extend beyond the pancreas but does not involve the major local arteries. Local lymph nodes are involved.	Locally Advanced
STAGE III	Tumor involved in 4 or more regional lymph nodes OR tumor involved in major local arteries.	Locally Advanced
STAGE IV	Primary tumor may be any size. Disease has metastasized (spread) to another part of the body, including the liver, abdominal wall, lungs and/or distant lymph nodes.	Metastatic

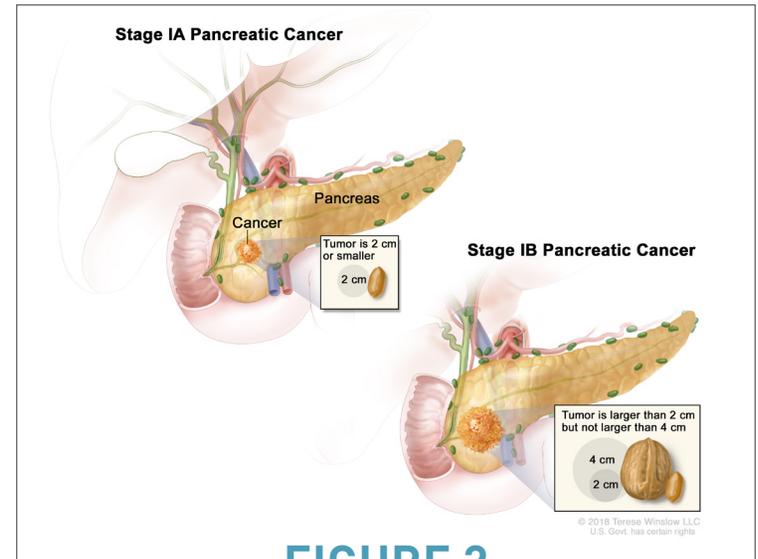


FIGURE 2

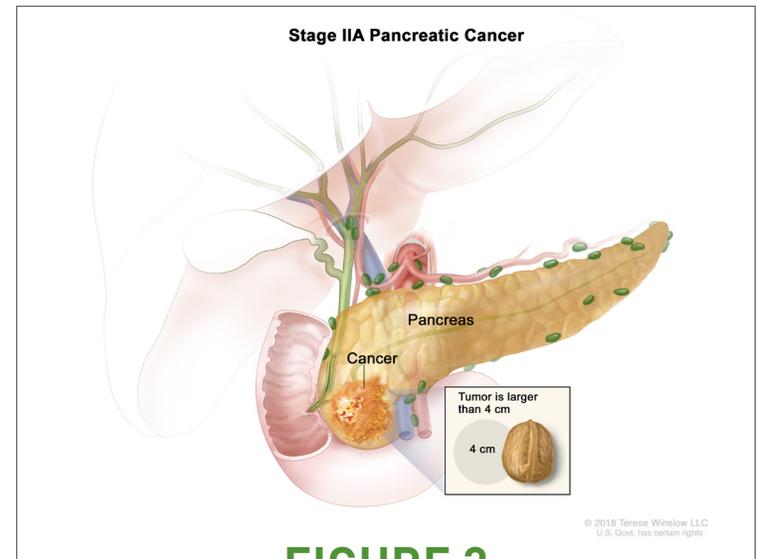


FIGURE 3

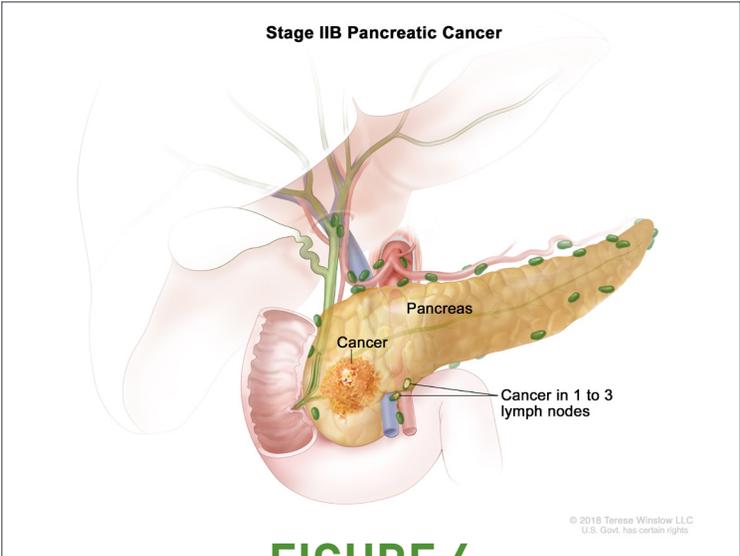


FIGURE 4

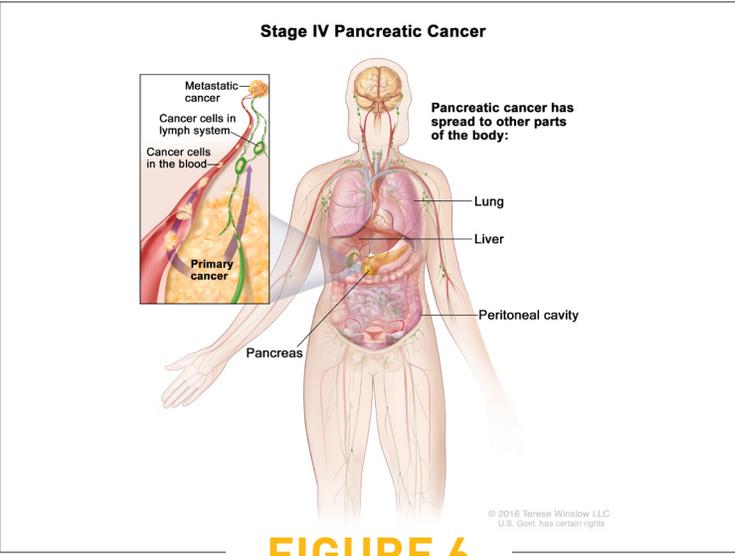


FIGURE 6

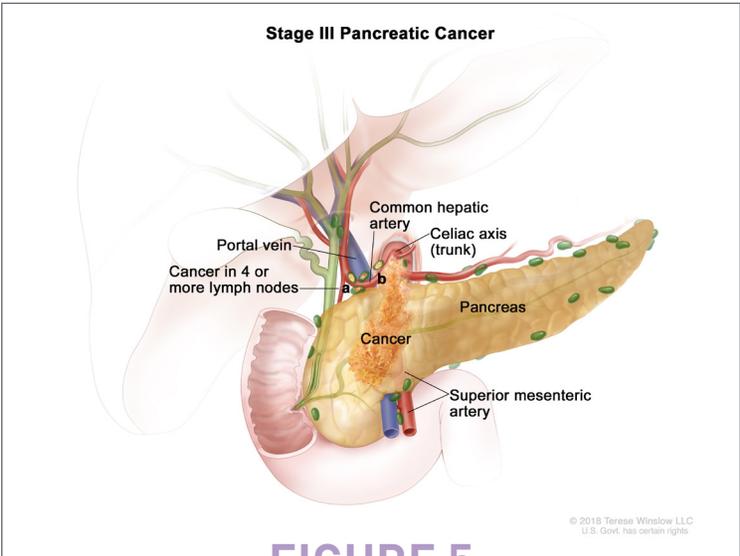


FIGURE 5

Stage IIIa: Tumor involved in 4 or more regional lymph nodes. Stage IIIb: Tumor involved in major local arteries.

SURGICAL RESECTION CATEGORY

Resectable

This category is used for tumors that can be surgically removed. The tumor is contained within the pancreas, or extends just beyond it, but does not involve any major local arteries or veins.

Borderline Resectable

This category is used for tumors that may or may not be resectable at the time of diagnosis. The tumor may or may not involve major local arteries (**celiac axis** and superior mesenteric artery) and/or veins, but has not metastasized (spread) to distant organs. Patients diagnosed with borderline resectable pancreatic cancer may be offered **neoadjuvant therapy** as a treatment option. Neoadjuvant therapy involves chemotherapy, radiation or both, prior to surgery. If blood vessels, such as veins and arteries, are affected by the tumor, neoadjuvant therapy may improve the chances for a complete surgical removal.

Different institutions and different surgeons use varying definitions of the term “borderline resectable.” Therefore, it is extremely important to seek an opinion from a specialized pancreatic surgeon with experience in advanced techniques, such as vein resection, at an institution that performs a high volume of pancreatic surgeries.

Unresectable

This category is used for tumors that cannot be surgically removed. The tumor has either metastasized (spread) to distant organs or cannot be completely removed with surgery.

TREATMENT AND CLINICAL TRIALS FOR PANCREATIC CANCER

SELECTING A DOCTOR OR HOSPITAL AND TREATMENT PLAN

Patients should seek care from hospitals and/or doctors that specialize in treating pancreatic cancer, especially when undergoing pancreatic surgery. Pancreatic cancer is relatively uncommon, and general oncologists and surgeons may not see patients with this type of cancer very often. Pancreatic cancer specialists see and treat a high number of individuals with pancreatic cancer, so they have greater knowledge of the disease and treatment options. In addition, pancreatic surgery is very complicated, so it is important to find a surgeon at a hospital that performs a large number of pancreatic surgeries.



You should feel comfortable and supported by your healthcare team. The Pancreatic Cancer Action Network strongly recommends seeking a healthcare team that suits all of your physical, mental and emotional needs.

Before a scheduled visit with the doctor, it is helpful to gather the patient's medical paperwork, including previous test results. Having this information available may help prevent the duplication of diagnostic tests. Each hospital will usually need to perform a review of the biopsy slides and imaging studies, so bringing original slides and films, or digital copies of the films, is helpful. For a list of questions to help the patient and family gather important information, please contact Patient Services to request the fact sheet called *Questions to Ask the Healthcare Team*.

It is common for individuals to get a second opinion about their pancreatic cancer diagnosis and treatment plan. This does not mean the first doctor's assessment is wrong. It simply means the individual would like to confirm the diagnosis and treatment options before continuing with a course of action. Valuable information is gained by speaking to other doctors before choosing a specialist to provide treatment. Every patient has the right to seek a second opinion and feel confident in the doctor who ultimately provides their care.

TREATMENT OPTIONS FOR PANCREATIC CANCER

Once an accurate diagnosis is made, the patient will be asked to consider treatment options. Treatment of pancreatic cancer depends on the stage of the disease and the patient's general health.

Patients may be treated with standard (approved) treatments or may participate in **clinical trials**. Clinical trials are conducted to investigate and develop new treatments for pancreatic cancer. Pancreatic cancer patients who participate in clinical research have better outcomes. Every treatment available today was approved through a clinical trial. The Pancreatic Cancer Action Network strongly recommends clinical trials at diagnosis and during every treatment decision. [see pages 49-52].

STAGE I	<ul style="list-style-type: none"> • Surgery • Chemotherapy, with or without radiation, after or before surgery • Clinical trial
STAGE II	<ul style="list-style-type: none"> • Surgery • Chemotherapy, with or without radiation, after or before surgery • Clinical trial
STAGE III	<ul style="list-style-type: none"> • Chemotherapy and/or radiation • Surgery when appropriate • Clinical trial
STAGE IV	<ul style="list-style-type: none"> • Chemotherapy • Targeted therapy • Clinical trial

The table above shows the different treatment options that may be used to treat pancreatic adenocarcinoma based on the stage of the cancer.

Treatments for pancreatic neuroendocrine tumors differ from treatments for pancreatic adenocarcinoma. For more information about treatments specific to neuroendocrine tumors, contact Patient Services.

SURGERY

The surgical removal of a tumor offers the best chance for long term control of pancreatic cancer. If a tumor has not spread beyond the pancreas to other areas of the body and is able to be removed surgically, it is considered resectable. Approximately 15-20% of patients with pancreatic adenocarcinoma have tumors that are surgically resectable. In some cases, tumors may spread to nearby veins (portal or superior mesenteric vein) or arteries (superior mesenteric, celiac or hepatic artery), which might make them difficult or impossible to remove. However, in many cases where the tumor has vein involvement and in select cases when the tumor has arterial involvement, patients may still be able to undergo successful resection by a qualified surgeon. This type of surgery would typically involve blood vessel reconstruction.

Determining a patient's eligibility for surgery is not always easy. Even sophisticated imaging tests may not provide perfect information. In some cases, despite testing prior to surgery, the surgeon may find at the time of surgery that the cancer has spread or cannot be removed and the planned operation cannot be completed. In some cases, other interventions may be performed to help alleviate blockages or manage other symptoms.

Pancreatic surgery is very complicated, especially the most common surgery, called a **pancreaticoduodenectomy** (also known as the **Whipple procedure**). It is important to find a surgeon at a hospital that does a large number, or high volume, of these procedures. Studies show that patients who undergo pancreatic surgery performed by an experienced surgeon with experienced supporting staff have fewer complications and better results. When finding a surgeon, it is important to ask how many pancreatic surgeries they perform each year. The National Comprehensive Cancer Network (NCCN) defines high volume as a surgeon who performs more than 15 pancreatic

surgeries per year. The Pancreatic Cancer Action Network strongly recommends that patients have a high volume pancreatic surgeon perform the surgery. For more information on locating surgeons who perform a high volume of pancreatic surgeries, contact Patient Services.

After pancreatic surgery, it can take a patient anywhere from a few months to a year to feel relatively "normal" again. It takes time for the digestive system to start working again, and some patients find that they must make permanent changes in their diets to alleviate symptoms of diarrhea, gas and stomach pain. As previously mentioned, the two main functions of the pancreas are to assist in digestion through the production of pancreatic enzymes and to regulate blood sugar through the production of insulin and similar substances. Both of these functions may be affected by the removal of a portion of the pancreas, and both the patient and doctor should be educated on how to recognize pancreatic enzyme insufficiency and diabetes. For more information on pancreatic enzyme insufficiency and diabetes, contact Patient Services and request a copy of the educational booklet, *Diet and Nutrition: Nutritional Concerns with Pancreatic Cancer*.

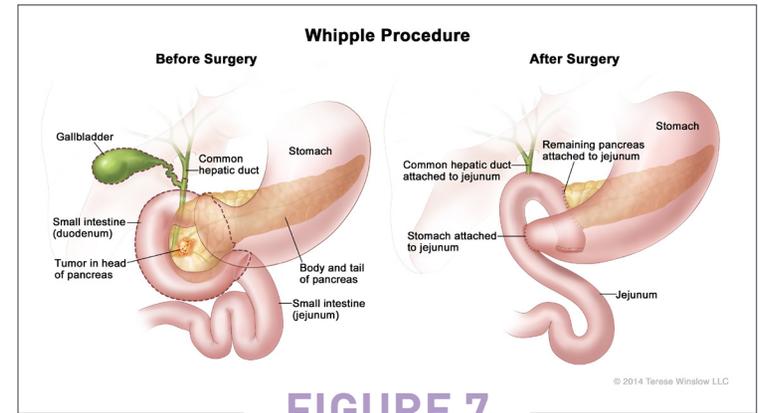
Different types of surgery are performed, depending on the exact location of the pancreatic tumor. If surgery to remove the tumor is not possible, palliative surgery may be considered (see page 41).

Whipple Procedure

The Whipple procedure (also known as a pancreaticoduodenectomy) is the most commonly performed surgery to remove tumors in the pancreas. The Whipple procedure may be attempted if a tumor is located in the head of the pancreas, which is the portion of pancreas closest to the intestine, and meets other criteria for resection. In a standard

Whipple procedure, the surgeon removes the head of the pancreas, the gallbladder, the duodenum, a small portion of the stomach called the antrum along with the stomach valve called the pylorus and surrounding lymph nodes. The surgeon then reconnects the remaining pancreas and digestive organs (see Figure 7 on page 39). In some cases, patients may undergo a modified version of this surgery which preserves the entire stomach and the pylorus. This is called a pylorus-preserving Whipple. Both types of surgery will typically take 5-7 hours.

After a Whipple procedure the most common complication is delayed gastric emptying. This is a condition in which the stomach takes longer than normal to empty its contents. Usually, after 7-10 days the stomach begins to empty well enough that nutrition can be taken by mouth to allow healing and nutritional recovery. If delayed gastric emptying persists, supplemental feedings may be required in which nutrition is administered through a feeding tube that bypasses the stomach. Another option is to give nutrition through a vein, often called **total parenteral nutrition (TPN)**. If either are required, both forms of nutritional support typically last several weeks. The most serious potential complication of a Whipple procedure is abdominal infection due to leakage from the area where the pancreas is connected to the small intestine (see Figure 7 on page 39). This is referred to as a pancreatic leak or pancreatic fistula. This occurs in approximately 10% of patients and is usually managed by a combination of draining tubes and antibiotics. Surgery rarely needs to be repeated in these cases, and many of these patients require nutritional support. Patients who have undergone the Whipple procedure may experience other long-term effects including digestive difficulties.



Before Surgery: This figure shows a tumor on the head of the pancreas prior to surgery.

After Surgery: This figure shows the re-attachment of the common hepatic (bile) duct, remaining pancreas and stomach to the small intestine (jejunum).

For more information about dietary changes following surgery for pancreatic cancer, contact Patient Services and ask for the fact sheet on *Dietary Changes Following Pancreatic Surgery*.

Distal Pancreatectomy

A distal **pancreatectomy** is performed if a tumor is located in the body or tail portion of the pancreas (also called the distal pancreas). In this procedure, the surgeon removes the body and tail of the pancreas. The spleen, which is attached to the tail of the pancreas and shares its blood supply, is often removed as well. Except in rare instances, all other organs are left in place. The most common complication after a distal pancreatectomy is leakage of pancreatic juices (pancreatic leak or pancreatic fistula). Delayed gastric emptying or other gastrointestinal issues such as diarrhea may also be present initially, but most of these issues will resolve in several weeks.

Total Pancreatectomy

A total pancreatectomy is performed when the tumor is situated in such a way that requires the entire pancreas to be removed. It may also be performed when there are multiple tumors spread throughout the pancreas. Similar to a Whipple procedure, the gallbladder and part of the duodenum are removed along with surrounding lymph nodes. The pylorus and the spleen are sometimes removed as well, depending on the patient's situation. Because the entire pancreas is removed in a total pancreatectomy, the person will be diabetic after surgery and must use insulin to control their blood sugar levels. The patient will also need to take pancreatic enzyme supplements with meals to properly digest their food.

Laparoscopic and Robotic Surgery

Some of the surgeries mentioned above may be performed with minimally invasive techniques, meaning that some or all of the operation is performed through small incisions with the assistance of a video telescope. Laparoscopic surgery uses long instruments controlled by the surgeon while standing at the operating table, while robotic-assisted surgery uses similar but modified instruments attached to mechanical arms which are controlled by the surgeon sitting at an adjacent console. While many surgeons continue to prefer open surgery for cancer operations, especially when performing pancreaticoduodenectomies (Whipple procedures),

many different approaches to these surgical procedures are possible. The patient and surgeon should discuss the risks and benefits of each approach in advance.

Palliative Procedures

Palliative procedures are performed to alleviate (palliate) symptoms. They do not involve the complete removal of the tumor. Palliative procedures may relieve symptoms of jaundice, pain, nausea and vomiting that are caused by blockage of the bile duct and/or duodenum. The most common palliative procedures for pancreatic cancer are biliary bypass surgery, gastric bypass surgery and biliary or duodenal stent insertion.

Biliary and Gastric Bypass

Biliary bypass surgery reroutes the flow of bile around the tumor if the tumor is blocking the common bile duct. It may also relieve jaundice. Gastric bypass surgery can be performed if the tumor blocks the duodenum. A gastric bypass allows food to flow from the stomach past the blockage. If blockages in both the bile duct and the duodenum are of concern, the surgeon can do a combination procedure known as a palliative double bypass.

Stent Placement

A stent is a small plastic or metal tube that helps keep the bile duct, pancreatic duct or duodenum open. Stent insertion can relieve blockages in these areas and may be used instead of performing a bypass procedure. Plastic biliary stents are used on a short-term basis, while metal stents are intended for long-term use. The surgeon will decide upon a metal or plastic stent based on several factors. A duodenal stent may be placed, as an alternative to surgical gastric bypass, if the tumor blocks the duodenum.

It is possible, but not common, for an infection to develop around a stent if it does not provide proper drainage. Fever or a return of jaundice may indicate infection and require emergency treatment. Anyone who suspects infection due to a blocked stent should contact their doctor or the emergency room immediately.

CHEMOTHERAPY

Chemotherapy is cancer treatment that uses drugs to kill cancer cells by preventing them from growing and dividing. These drugs are systemic treatments, meaning that the drugs travel throughout the bloodstream and damage cancer cells throughout the body. Unfortunately, chemotherapy can also damage some healthy cells and cause side effects. Chemotherapy may shrink and/or prevent the growth of pancreatic tumors. It can be given alone, or in combination with surgery, **targeted therapy** and/or radiation.

Chemotherapy drugs can be given through a vein into the bloodstream (intravenously) or by mouth (orally). Usually, patients receive chemotherapy as an outpatient treatment at a hospital, clinic or doctor's office. The time needed for each treatment session depends on the type of chemotherapy.

There are also several chemotherapy drugs that are used "off label". **Off-label** treatments are **Food and Drug Administration (FDA)** approved to treat another cancer, but are not approved for pancreatic cancer. Since these treatments have shown some promise in pancreatic cancer in prior or existing clinical trials and already have FDA approval for another cancer, they can be prescribed by the doctor when appropriate.

Chemotherapy can cause side effects because it attacks and harms all rapidly dividing cells, including healthy cells. Medications and other management strategies are available to treat many of the common side effects (see pages 54-57).

IMMUNOTHERAPY

Immunotherapy is a type of treatment that stimulates the body's immune system to fight cancer. Immunotherapy works by stopping or slowing the growth or spreading of cancer cells to other areas as well as helping the immune system increase its ability to attack cancer cells.

There are no FDA approved immunotherapies for pancreatic cancer, specifically.

There are also several immunotherapies under investigation in clinical trials. In clinical trials, most immunotherapies are given with other treatments, such as chemotherapy, as this seems to work better for pancreatic cancer.

Different forms of immunotherapy may be given in different ways. The most common methods of administration are intravenous, given directly into a vein, or oral, a pill or capsule that is swallowed.

The side effects of immunotherapy are generally milder than those experienced with chemotherapy. Side effects that occur are cold or flu-like symptoms such as fever, headache, nausea and fatigue. Redness, itching and/or sores can occur around the injection site if the medication is given intravenously.

TARGETED THERAPY

Unlike chemotherapy, **targeted therapy** is cancer treatment that uses drugs to attack unique aspects of cancer cells with little harm to healthy cells. Targeted therapies often work by binding to a particular molecule in the cancer cell, which blocks the process that changes normal cells into cancer, thereby stopping the abnormal growth behavior of a tumor.

Other targeted therapies for pancreatic cancer are still under investigation in the laboratory or in clinical trials.

The chart on the next page includes information on the names of the drugs, the type of therapy and additional information about how the drug was approved. Keep in mind that not every patient will receive all of these medications. This list is meant to be a resource as you have conversations with your healthcare team about treatment options.

COMMONLY USED TREATMENTS

Type of Drug	Drug Name	Information
Chemotherapy	Gemzar® (gemcitabine)	Approved to treat pancreatic cancer and used alone or in combination with other drugs.
	5-FU, Fluorouracil	Approved to treat pancreatic cancer and used alone or in combination with other drugs.
	ABRAXANE® (nab-paclitaxel)	Approved in combination with Gemzar.
	Xeloda® (capecitabine)	Approved in combination with Gemzar.
	Platinol®-AQ (cisplatin)	Approved in combination with Gemzar for patients who have had pancreatic surgery. It can also be used off-label in those who have had surgery.
	Camptosar® (irinotecan)	Used as part of a standard of care combination called FOLFIRINOX with 5-FU, leucovorin, and oxaliplatin.
	Eloxatin® (oxaliplatin)	Used as part of a standard of care combination called FOLFIRINOX with 5-FU/leucovorin, and irinotecan.
	ONIVYDE® (Irinotecan liposome injection)	Approved in combination with 5-FU/leucovorin in patients who have previously received treatment with Gemzar.
Biomarker-based immunotherapy	KEYTRUDA (pembrolizumab)	Approved to treat any type of unresectable or metastatic solid tumor that has been identified as having a biomarker referred to as microsatellite instability-high (MSI-H), mismatch repair deficient (dMMR) and or tumor mutational burden-high (TMB-H). This accounts for 1-3% of patients..
	JEMPERLI (dostarlimab)	Approved for patients with mismatch-deficient (dMMR) recurrent or advanced solid tumors that have progressed on or following previous treatment, and who have no satisfactory alternative treatment options.

Type of Drug	Drug Name	Information
Germline (inherited) mutation based	LYNPARZA (olaparib)	Approved as a maintenance therapy for patients with germline BRCA-mutated metastatic pancreatic adenocarcinoma. It is indicated in patients whose disease has not progressed or has remained stable for at least 16 weeks on a first-line platinum- based chemotherapy regimen.
Biomarker-based targeted therapies	VITRAKVI (larotrectinib)	Approved for the treatment of any locally advanced or metastatic solid tumors that have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion. (NTRK fusions are very rare in pancreatic cancer, with only about 0.5% of patients affected.)
	ROZLYTREK (entrectinib)	Approved for the treatment of any locally advanced or metastatic solid tumors that have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion. (NTRK fusions are very rare in pancreatic cancer, with only about 0.5% of patients affected.)
	LUMAKRAS (sotorasib)	Approved for patients with non-small cell lung cancer whose tumors have a KRAS G12C mutation. Although the approval is for patients with lung cancer, it's possible that the small subset of patients with pancreatic or other cancer types whose tumors have KRAS G12C mutations may be able to access this drug through an "off-label" use.
	TAFINLAR (dabrafenib)	Approved in combination with MEKINIST in patients who have BRAF V600E mutations. This accounts for about 2.2% of patients.
	MEKINIST (trametinib)	Approved in combination with TAFINLAR in patients who have BRAF V600E mutations. This accounts for about 2.2% of patients.
	RETEVMO (seliprecatinib)	Approved for patients who have locally advanced or metastatic solid tumors with a RET fusion. These are rare and occur in 7-8% of patients with gastrointestinal (GI) cancers, including pancreatic cancer.
Targeted therapy	erlotinib	Erlotinib was approved in combination with Gemzar. Is not commonly used because only a small group of patients benefited in clinical trials.

RADIATION THERAPY

Radiation therapy is a cancer treatment that uses high-energy radiation, in the form of waves (such as x-rays) or particles (such as protons), to kill cancer cells or prevent them from growing and dividing. During radiation therapy, the patient lays on a table, and in most cases, a large machine rotates around the table and directs the radiation through several areas around the abdomen into the pancreatic tumor. The goal of all radiation is to treat the tumor or tumor bed (area around the tumor) with a high enough dose to prevent recurrence or tumor growth, while sparing the healthy organs or tissue nearby. While radiation may shrink the size of the tumor, most often, radiation kills the cancer cells in the tumor but with minimal size difference. Since radiation therapy is directed to a specific (focused) area of cells, it is considered a localized treatment.

Radiation therapy may be used in all stages of pancreatic cancer. In patients with resectable tumors, radiation can be given as neoadjuvant treatment to decrease the risk of leaving cancer cells behind and to lessen the chance of the cancer coming back after surgery. In some cases, radiation therapy is given as **adjuvant therapy**. With adjuvant radiation, the goal is to help prevent the cancer from recurring, and to kill microscopic cancer cells that may have been left behind after surgery (positive margin or nodes). When patients have borderline resectable pancreatic cancer, radiation therapy is often given prior to surgery to prevent a local recurrence.

Patients with unresectable tumors may also receive radiation. In these cases, radiation therapy is often given to prevent the tumor from growing, which could cause pain or other symptoms. This may include radiation therapy to relieve pain caused by the tumor or to control bleeding that can occur if the tumor involves the bowel and/or stomach.

It may be given alone or in combination with chemotherapy. When chemotherapy is given with radiation, a lower dose of chemotherapy is typically used. Chemotherapy acts as a “radiosensitizer” that can enhance the effect of the radiation on the tumor. The chemotherapy drugs most commonly used with radiation therapy are fluorouracil

(5-FU), capecitabine (Xeloda®) and gemcitabine (Gemzar®). 5-FU is used most often since there is more experience using this drug in combination with radiation and there are generally fewer side effects.

Clinical trials are currently taking place to study different types of radiation therapy in combination with chemotherapy or investigational therapies such as immunotherapy. More clinical trials are needed to determine the efficacy of radiation therapy both alone and in combination with other therapies.

There are many options for the treatment of pancreatic cancer with external beam radiation therapy, either alone or in combination with other treatment modalities. Patients are encouraged to discuss the treatment options with their radiation oncologists, who are ideally part of a multidisciplinary team.

Radiation therapy is usually an outpatient treatment. Patients go either to the hospital or to an outpatient clinic for radiation therapy, but rarely need to stay overnight in the hospital. Radiation therapy treatments do not hurt during the procedure. While individuals may experience some abdominal discomfort toward the end of the treatment series, the actual treatment session is not painful. The effects of radiation therapy can build up over time, and they vary depending on the type of radiation therapy given. If patients develop pain in the stomach area after radiation, have black stools or have other side effects, it is important to consult with the radiation oncologist. Many side effects can be treated with medications or supportive care prescribed by a healthcare professional. However, ibuprofen should be avoided during and after radiation therapy, as it can increase the risk of getting an ulcer.

The chart on the next page contains information on the different types of radiation therapy starting with the most common type. It also includes additional details about the radiation type and the length of time the treatment will take. Keep in mind that not every patient will receive all of these types of radiation. This list is meant to be a resource as you have conversations with your healthcare team about treatment options.

TYPES OF RADIATION THERAPY

Radiation Type	Details	Length of Time
External beam radiation therapy	Delivers radiation by using a machine outside the body which directs a beam or multiple beams of radiation through the abdomen to the tumor or tumor bed.	5 days a week for 2-5 weeks. Each treatment lasts only a few minutes.
Stereotactic body radiation therapy (SBRT)	A type of external beam radiation therapy designed to deliver high doses of radiation precisely to small tumors, usually in five or fewer treatments. Uses multiple narrow radiation beams to target small, well-defined areas. Patients may be fitted with a customized device to keep the body perfectly still or the treatment machine may have the ability to limit, monitor and adjust for any movement during the treatment. Also, small metallic seeds may be implanted near the tumor before treatment begins to better track the location of the tumor during treatment. CyberKnife® is one type of SBRT.	Usually 1-5 sessions.
Intensity-modulated radiation therapy (IMRT)	A type of external beam radiation therapy. Delivers focused radiation to the tumor by modulating (varying) the intensity of the radiation beam under precise computer control. IMRT allows a higher dose of radiation to be administered to the tumor while minimizing the amount of radiation delivered to healthy tissue near the pancreas. This may lead to fewer side effects and allow higher doses of radiation to be delivered safely, compared to standard radiation therapy.	5 days a week for a number of weeks. Each treatment session takes 10-30 minutes.
Proton beam radiation therapy	A type of external beam radiation therapy that uses proton beams rather than x-rays. Protons are charged particles that deposit most of their energy at a very narrow area within the body. Proton beam therapy allows a higher, more conformed dose of radiation to be delivered to the tumor, while sparing surrounding healthy tissue. Therefore, it generally causes fewer side effects. Proton therapy is only available at very few centers throughout the country and is being studied in clinical trials for pancreatic cancer.	Frequency of treatment will vary and can often take a few weeks. Each treatment session can take 15-30 minutes.
Internal radiation therapy (brachytherapy)	Delivers radiation through radioactive material implanted in or near the cancer. There are different types of internal radiation therapy, including high-dose rate and low-dose rate brachytherapy. Internal radiation therapy is not commonly used in pancreatic cancer.	Frequency of treatment will vary depending on the type of brachytherapy. Treatment can range from a few days to several weeks.



CLINICAL TRIALS

Clinical trials are research studies that investigate treatments, diagnostic tools, early detection methods and ways to prevent diseases such as pancreatic cancer. Many pancreatic cancer clinical trials are conducted to investigate and develop new treatments and observe patient performance with new treatments. Before any new treatment can be tested in humans, it must show positive results in the laboratory and/or in animal studies.

Clinical trials may be carried out using treatments that are new, treatments that are already available for other diseases or a combination of both. Since all cancers are different, a drug that is already approved by the FDA to treat one type of cancer may not be approved to treat pancreatic cancer. In order for any pancreatic cancer therapy to be approved, it must pass through the clinical trial process involving patients who have pancreatic cancer. The FDA closely monitors clinical trials to protect the participants and the general public. Clinical trials are the safest and quickest way to confirm whether new treatments are effective and beneficial for patients.

When a new therapy enters the clinical trial process, it must pass through three **phases** of testing before becoming eligible for FDA approval. Only if the treatment proves safe and effective at each phase does it proceed to the next phase of clinical trial testing.

Phase I

Phase I is the first step in testing a new treatment or combination of treatments in humans. At this point, the experimental treatment has already shown effectiveness in the laboratory. In phase I studies, a small group of participants, typically 20 to 40 people, are tested with the new treatment. The goal of phase I studies is to determine safety, appropriate dosage, and how the treatment is processed inside the body. Participants are closely monitored for side effects and doses are adjusted as needed. Often, eligibility requirements with regard to prior treatment are less strict in phase I trials than in phase II or phase III trials, allowing patients who have had multiple treatments to participate in these studies, regardless of their prior treatment. Phase I trials may be open to participants with any type of solid tumor, such as breast, lung and prostate tumors, and not only to those with pancreatic tumors. Patients often choose to participate in phase I clinical trials when they are not eligible for later-phase trials or when they are not responding to current treatments.

Phase II

Phase II clinical trials involve a larger group of participants, typically 25 to 100 people. In these studies, participants generally have a specific type of disease, such as pancreatic cancer. The goal of a phase II clinical trial is to determine the treatment's effect against pancreatic cancer while further testing its safety. Some phase II trials may be randomized, which means that patients are randomly assigned (by chance) to different treatment groups. These trials may involve randomization between the standard of care treatment and the experimental treatment or randomization between two experimental treatments.

Phase III

Phase III studies test how the new treatment compares with the currently approved standard of care treatment. These clinical trials may involve 100 to 1000 or more people. They are designed to determine if the new treatment is statistically more effective than the standard of care in the group of people who participated in the study. Phase III trials are randomized, which means that patients are randomly assigned (by chance) to different treatment groups — the new treatment group or the control group, which likely includes the standard of care treatment. In order to prevent bias, neither the doctor nor the participant gets to choose the treatment group, and in some phase III trials, neither the participant nor the doctor knows to which treatment group the participant has been assigned. If the new treatment is found to be effective and meets safety requirements through all three phases, the sponsor of the trial may submit an application to the FDA asking for approval of the new treatment.

Phase IV

Phase IV trials take place after a therapy has been approved by the FDA. The treatment is observed in larger populations to determine long-term safety and cost effectiveness and to improve the management of side effects.

FINDING A CLINICAL TRIAL

The Pancreatic Cancer Action Network highly recommends that all patients consider clinical trials when exploring treatment options. We maintain the most comprehensive and up-to-date database of pancreatic cancer clinical trials in the U.S. PanCAN Patient Services can perform personalized clinical trials searches based on a patient's diagnosis, prior treatment, geographic location and willingness to travel.

To have a personalized clinical trials search performed, contact Patient Services.

Or you can start a clinical trial search yourself using our Clinical Trial Finder, an easy-to-use online tool.

Visit clinicaltrials.pancan.org.

For more detailed information on clinical trials, please ask Patient Services for the educational booklet, *Clinical Trials: Understanding How Pancreatic Cancer Clinical Trials Work*.

PRECISION MEDICINE

Precision medicine is an emerging field in cancer treatment. The goal of precision medicine is to identify specific treatments and drugs that may be more beneficial for a specific patient or tumor by analyzing the tumor's biological makeup, including genetic mutations (damage to genes) and proteins within the tumor. Rather than basing treatment decisions solely on the tumor type (i.e., pancreatic cancer), precision medicine may provide information about the unique biological features of a patient's tumor on which to base treatment decisions.

Drugs that may target specific genetic mutations and proteins common in tumors are being studied in clinical trials. They are known as targeted therapy drugs. In order to determine if a particular targeted therapy drug is effective in stopping the growth of a tumor by targeting a specific mutation, the tumor being

treated must have that mutation. To identify if a tumor has a specific mutation, a tissue sample from the tumor is collected through a biopsy, and an analysis of the tissue is performed. This process is known as "biomarker testing". Biomarker testing may identify genetic mutations and protein changes. Patients who receive treatment based on their biology can live longer. The Pancreatic Cancer Action Network strongly recommends all pancreatic cancer patients get genetic testing for inherited mutations as soon as possible after diagnosis and biomarker testing of their tumor tissue to help determine the best treatment options. Patients should discuss both tests with their care team. The tests can be available through their treating institution or PanCAN's Know Your Tumor® precision medicine service.

Know Your Tumor®

Know Your Tumor is a precision medicine service provided by the Pancreatic Cancer Action Network that provides eligible pancreatic cancer patients and their oncologists information about the biology of their specific tumors and relevant treatment options. Many patients who have used the Know Your Tumor service have found it to be an important part of their treatment decision-making process.

Contact PanCAN Patient Services for more information about this service.



SIDE EFFECTS OF TREATMENT

Careful attention should be given to avoid or minimize side effects of treatment. Side effects vary depending on the type of therapy, dosage and length of treatment. Normal, healthy cells that divide rapidly, including bone marrow, blood cells, cells of hair follicles and cells in the reproductive and digestive tracts, are more likely to be damaged during chemotherapy treatment. The doctor and patient must often balance possible side effects with potential benefits of treatment. Under a doctor's care, many side effects can be prevented or managed.

The next pages list common side effects related to chemotherapy, targeted therapy or radiation therapy. This list is not comprehensive. Side effects are individual and may not occur in each person receiving treatment. Please talk to your doctor before using these tips to manage your side effects.

MANAGEMENT SUGGESTIONS FOR SIDE EFFECTS OF TREATMENT

Changes in Taste (food may taste bland or metallic)

Avoid foods that cause unpleasant tastes. Changes in the dose of the chemotherapy and radiation therapy may help. Eat small, frequent meals. Eating tart foods may help overcome metallic or bitter taste. Cold food might taste better than hot food.

Constipation

Drink plenty of non-caffeinated fluids each day. Eat foods high in fiber. Avoid fatty and fried foods. Moderate exercise can help.

Diarrhea or Abdominal Cramping

Treat with over-the-counter or prescribed medications as directed by a doctor. A variety of dietary changes can also be made under the guidance of a **dietitian**.

Fatigue

Treat with medications prescribed by a doctor. Drugs may boost red blood cells and help prevent fatigue. A dietitian can provide guidance on a variety of dietary changes. It is important to maintain activity in order to treat fatigue. Taking short walks can boost energy. In addition, taking short rests throughout the day may help.

Hair Loss

Avoid frequent hair washing and use a gentle shampoo. Gently pat hair dry, use a wide-tooth comb instead of a brush and avoid the use of barrettes, rubber bands, hair products and hair dryers. Wear head coverings when outdoors.

Hand/Foot Syndrome

This is a condition that causes redness, tenderness, dryness and peeling of the palms and soles. Numbness or tingling may also develop. To avoid trauma to hands and feet, wear cotton socks or gloves and avoid tight-fitting shoes. Soak hands in cool water for 10 minutes and then apply a mild moisturizer

or petroleum jelly. Cooling the skin with ice packs may also help relieve pain and tenderness. Ask your doctor if an oral supplement of vitamin B6 is appropriate.

Loss of Appetite

Schedule 6-8 small meals and snacks per day. Medications prescribed by a doctor can help stimulate the appetite.

Low White Blood Cell Count

Medications prescribed by a doctor and/or changes in the dose of the chemotherapy can increase white blood cell counts.

Low Red Blood Cell Count

A blood transfusion or medication prescribed by a doctor may be required. Changes in the dose of the chemotherapy can also raise red blood cell counts.

Low Blood Platelet Count

A blood transfusion or medication prescribed by a doctor may be required. Changes in the chemotherapy dose can also raise blood platelet counts.

Mouth Sores

Eat soft, moist, bland foods. Avoid spicy and acidic foods. Caffeine and alcohol may irritate the mouth. Drinking through a straw may be helpful. High protein foods will help mouth sores recover more quickly. Rinse mouth with cool water or a mild solution of baking soda and water. Use a soft-bristle toothbrush.

Nail Changes

Avoid biting nails, pushing back cuticles and using fake nails or wraps. Consult a doctor before having a manicure/pedicure. Wear gloves during household chores and moisturize hands and feet frequently. If the nail area becomes inflamed, it may be treated with antibacterial soap or antibacterial/antifungal ointments to prevent infection.

Nausea and Vomiting

Treat with medications prescribed by a doctor. A dietitian can provide guidance on a variety of dietary changes. Limit the consumption of fried, spicy or rich foods. Drink cool or room-temperature liquids between meals to stay hydrated and avoid feeling overly full. Using a motion sickness wristband may help control nausea. Try wearing loose clothing and getting fresh air.

Neuropathy

This is a condition that causes tingling or numbness in the hands and feet. Sometimes it also occurs in other areas of the body. To protect hands and feet, wear cotton socks or gloves and avoid tight-fitting shoes. Also, avoid hot or cold temperatures. Ask your doctor if pain medications, antidepressants, anti-seizure or other treatments are appropriate.

Skin Rash, Redness or Irritation

Erlotinib is often associated with an acne-like skin rash on the body and/or face. However, the rash is not acne and will not respond to acne treatments. Other medications can also cause skin changes. Changes in the dose of treatments and in personal care methods may help soothe the skin. Examples include washing the affected area with warm water and mild soap; using lotions without alcohol, perfumes or other irritants; avoiding direct sunlight and using sunscreen with an SPF of 15 or higher with broad spectrum protection. Contact a doctor before using over-the-counter treatments.

It is important to keep the doctor informed of any side effects or pain. **The doctor can only make changes in treatment or treat side effects if informed by the patient.**

For more information about side effects of treatment, contact Patient Services and request a copy of the Pancreatic Cancer Action Network's educational booklet, *Supportive Care: Quality of Life and Practical Care in Pancreatic Cancer* and the fact sheet *Side Effects of Treatment*.

RISK FACTORS FOR PANCREATIC CANCER

The exact causes of pancreatic cancer are not yet well understood. Research studies have identified certain **risk factors** that may increase the likelihood that a person will develop pancreatic cancer. Having one or more of the risk factors or disorders listed below does not mean a person will develop pancreatic cancer. Some people who develop pancreatic cancer do not have any of these risk factors. Anyone who thinks they may be at risk for pancreatic cancer should discuss this with their doctor and/or genetic counselor.

Family History

If you are a first-degree relative of someone diagnosed with pancreatic cancer, you may have an increased risk of developing pancreatic cancer. Your family member with pancreatic cancer is strongly recommended to undergo genetic testing for inherited mutations. Negative results often mean you do not need to get genetic testing. If the results are positive, unknown or if you have several close family members with cancer, the Pancreatic Cancer Action Network recommends you consult with a genetic counselor to determine if you should get genetic testing for inherited cancer risk and if you should discuss options for monitoring. Risk also increases if individuals have a first-degree relative who developed pancreatic cancer before the age of 50 or an inherited genetic syndrome associated with pancreatic cancer (see page 60). The risk increases if a greater number of family members are affected. Also, the risk of pancreatic cancer increases if there is a history of **familial** breast, ovarian or colon cancer, familial melanoma or hereditary pancreatitis. Approximately 10% of pancreatic cancer cases are related to a family history of the disease.

Diabetes

Pancreatic cancer is more likely to occur in people who have long-standing (over 5 years) diabetes. Research studies suggest that sudden-onset type 2 diabetes may be an early symptom of pancreatic cancer especially in those who are over the age of 50, have a low body mass index (BMI), are losing weight or do not have a family history of diabetes. A sudden change in blood sugar levels in diabetics who previously had well-controlled diabetes may also be a sign of pancreatic cancer.

Chronic Pancreatitis and Hereditary Pancreatitis

People with **chronic** pancreatitis have an increased risk of developing pancreatic cancer. Chronic pancreatitis is common in individuals who consume large amounts of alcohol for many years. Hereditary pancreatitis causes recurrent episodes of inflammation of the pancreas that generally start by the time a person is 20 years old. The risk of developing pancreatic cancer is even higher in individuals who have hereditary pancreatitis.

Smoking

Smoking is a significant risk factor and may cause about 20-30% of all exocrine pancreatic cancer cases. People who smoke cigarettes are 2 times more likely to develop pancreatic cancer than people who have never smoked.

Race (Ethnicity)

Black Americans have a higher incidence of pancreatic cancer compared to individuals of Asian, Hispanic or Caucasian descent. There is also a higher incidence of pancreatic cancer among individuals of Ashkenazi Jewish descent. This may be due to a mutation in a cancer gene (BRCA2) that is found in about 1% of individuals of this background.

Age

The chance of developing pancreatic cancer increases with age. Most people diagnosed with pancreatic cancer are over the age of 60. The average age at the time of diagnosis is 71.

Diet

The association between diet and the development of pancreatic cancer is unclear. A diet high in red and processed meats is thought to increase the risk of developing pancreatic cancer. A diet high in fruits and vegetables may decrease the risk.

Obesity

People who are **obese** have a 20% increased risk of developing the disease compared to people who are of normal weight. The risk is even higher in people who are obese during early adulthood. People with excessive abdominal fat may have an increased risk independent of general obesity.

Alcohol

Some research suggests a link between heavy alcohol consumption and pancreatic cancer. The risk of developing pancreatic cancer is higher in people who consume more than three alcoholic drinks daily, compared those who do not.

Chemical and Heavy Metal Exposure

Research suggests that exposure to certain environmental chemicals and heavy metals such as beta-naphthylamine, benzidine, pesticides, asbestos, benzene and chlorinated hydrocarbons may increase the risk of developing pancreatic cancer.

Periodontal Disease

Periodontal (gum) disease and tooth loss appear to be linked to pancreatic cancer, even when controlling for other risk factors, though the mechanisms for this risk are unknown.

GENETIC MUTATIONS

All cancer begins with a mutation in the DNA of one cell causing the cell to grow and divide uncontrollably. Mutations that occur during a person's lifetime, rather than inherited mutations, seem to cause most pancreatic cancers. But in some families,

hereditary factors play an important role. While only about 10% of pancreatic cancers are considered familial or hereditary, pancreatic cancer researchers are interested in specific inherited genes. The following provides the names of the disorders and genes that are being studied for connections to pancreatic cancer.

Ataxia Telangiectasia (AT)

Ataxia Telangiectasia is a rare inherited condition caused by mutations in the ATM gene. Patients with AT present with a 38% lifetime risk of developing cancer. Approximately 2-3% of patients with familial pancreatic cancer have a mutation in the ATM gene.

BRCA Mutation

BRCA 1 and 2 mutations are often related to inherited breast and ovarian cancer. However, the BRCA1 mutation may also cause a small increased risk of developing pancreatic cancer.

Mutations in the BRCA2 gene are associated with a 3- to 10-fold increased risk of developing pancreatic cancer. A mutation in this gene can be found in approximately 1% of individuals of Ashkenazi Jewish descent. This is higher than in other populations. People with BRCA2 mutations have a 10% lifetime risk of developing pancreatic cancer.

Cystic Fibrosis

Cystic fibrosis affects the pancreas by causing pancreatic insufficiency and chronic pancreatitis. The risk of developing pancreatic cancer is 5 to 6 times greater in people who have cystic fibrosis compared to average risk.

Familial Adenomatous Polyposis (FAP)

FAP is a rare, hereditary form of colon cancer in which a person develops hundreds to thousands of noncancerous polyps in the colon that eventually become malignant. It is associated with higher rates of thyroid, small bowel, stomach and pancreatic cancers.

Familial Atypical Multiple Mole Melanoma (FAMMM)

FAMMM is characterized by younger age of melanoma diagnosis, many skin moles and multiple primary melanomas. People with FAMMM have a 20-to-47 fold increased risk of developing pancreatic cancer.

Hereditary Nonpolyposis Colorectal Cancer (HNPCC) or Lynch Syndrome

This is an inherited condition that is associated with 5% of colon cancer cases. Patients with HNPCC have an approximately 9-fold increased risk of developing pancreatic cancer.

Hereditary Pancreatitis

Hereditary pancreatitis is a rare, inherited condition that usually starts before age 20. It is characterized by recurrent episodes of severe inflammation of the pancreas that can lead to chronic pancreatitis and approximately a 40-55% lifetime risk of developing pancreatic cancer. Individuals with hereditary pancreatitis who also smoke may develop earlier onset pancreatic cancer.

PALB2 Mutation

About 1-3% of patients with familial pancreatic cancer have inherited mutations in the PALB2 gene. Mutations in the PALB2 gene have also been associated with an increased risk of breast cancer.

Peutz-Jeghers Syndrome

Peutz-Jeghers Syndrome is characterized by polyps in the small intestine and pigmented spots on the lips and nose. Patients with this syndrome have an 11-36% risk of developing pancreatic cancer in their lifetime.

GLOSSARY

Abdomen: The part of the body between the ribs and the hips. It contains the following organs: stomach, liver, gallbladder, spleen, intestines, pancreas, kidneys and bladder.

Adenocarcinoma: The most common type of pancreatic cancer, involving the cells lining the pancreatic duct that produce enzymes for digestion.

Adjuvant therapy: A treatment that is administered after surgical removal of the primary tumor. Adjuvant therapy may include chemotherapy, radiation therapy, hormone therapy, targeted therapy and/or immunotherapy.

Ambulatory surgery center: A facility that provides minimally invasive surgeries on an outpatient basis. Most ambulatory surgeries require patients to stay at the center for 2-4 hours.

Ampulla of Vater: The junction of the ducts from the liver and pancreas at the point where they enter the small intestine.

Anesthesia: The loss of feeling or awareness caused by drugs. Local anesthesia causes loss of feeling in one part of the body. General anesthesia puts the person to sleep.

Antigen: A substance that causes the immune system to make a specific immune response.

Ascites: Abnormal buildup of fluid in the abdominal cavity, generally related to cancer.

Benign: A term used to describe a growth that is not cancerous. Benign tumors do not spread to, or invade, nearby tissues or other parts of the body.

Bile: A fluid made by the liver and stored in the gallbladder. Bile is excreted into the small intestine, where it helps digest fat.

Bilirubin: A substance produced in the liver when the body breaks down hemoglobin, the molecule in red blood cells that carries oxygen. Bilirubin is yellowish-green in color and is eliminated in the bile.

Biopsy: A procedure performed to remove tissue from the body for examination in order to determine whether cancer is present.

Blood clot: A clump of blood that forms in a vein either just under the skin surface or in a deep vein. A blood clot that forms in a deep vein is called deep vein thrombosis, or DVT. See deep vein thrombosis.

Body mass index (BMI): A number that measures a person's body fat based on their height and weight. For adults, BMI is interpreted by using standard weight status categories: underweight, normal weight, overweight and obese.

Cancer: A mutated group of cells in the body that grows and divides in an uncontrolled manner and is able to invade and damage nearby tissues and organs. Cancer cells sometimes metastasize from the original cancer site and form new tumors in other parts of the body.

Cancer cachexia (pronounced kə-kĕk'sē-ə): A cancer-related condition marked by weight loss due to the body's improper use of calories and proteins. Cancer cachexia creates fatigue and weakness and may impair the body's response to treatment.

Catheter: A tubular instrument that allows passage of fluid into or out of a body cavity or blood vessel.

Celiac axis: A short, thick artery arising from the largest artery in the body, the aorta. The celiac axis starts just below the diaphragm and divides almost immediately into the gastric, hepatic and splenic arteries.

Celiac plexus block: A procedure in which a substance such as alcohol is injected into the celiac plexus of the abdomen to destroy the nerves. These nerve-destroying substances prevent pain signals from traveling to the brain so the patient no longer feels pain.

Chronic: A chronic disease is a condition that lasts for a long period of time and recurs frequently. Chronic conditions are usually manageable but not curable.

Clinical trial: A research study that investigates new treatments or new combinations of treatments. Pancreatic cancer clinical trials are the only way for researchers to determine whether treatments developed in the laboratory are beneficial to people living with pancreatic cancer. They also provide patients the opportunity to receive a promising new drug or treatment.

Common bile duct: The duct that carries bile from the gallbladder and liver into the upper part of the small intestine.

Constipation: A condition characterized by hard, dry bowel movements. It is associated with discomfort in passing stools and/or infrequent passing of stools.

Cyst: An enclosed, fluid-filled sac in the body.

Deep vein thrombosis (DVT): The formation of a blood clot in a deep vein, generally in the lower extremities. DVT can cause serious problems if it breaks loose and travels through the bloodstream to the lungs. Symptoms of DVT include swelling, pain when walking or flexing the foot and sometimes redness in one leg.

Deoxyribonucleic acid (DNA): The molecules inside cells that carry genetic information and pass it from one generation to the next.

Diabetes: A chronic disease that affects the body's ability to produce or properly use the hormone insulin. In type 1 diabetes, the pancreas does not produce insulin. In type 2 diabetes, the pancreas does not produce enough insulin, or the body does not use it properly.

Diarrhea: A condition marked by frequent and loose bowel movements.

Dietitian: A healthcare professional trained in food, nutrition, biochemistry and physiology. A dietitian can provide guidance regarding an appropriate diet for each patient with pancreatic cancer.

Diuretic: A substance that promotes increased urine excretion.

Duodenum: The first portion of the small intestine, located just below the stomach.

Endocrine gland: An organ that secretes hormones into the body through the bloodstream. The endocrine function of the pancreas is to produce insulin and glucagon, which work together to control the levels of sugar in the blood.

Enzyme: A protein that induces a chemical reaction in the body. Pancreatic enzymes aid in food digestion.

Erlotinib: A targeted therapy drug approved in 2005 by the FDA to treat advanced pancreatic adenocarcinoma. It inhibits the growth of cancerous cells by blocking the human Epidermal Growth Factor Receptor (EGFR) 1 on the surface of some cancer cells.

Exocrine gland: An organ that secretes chemicals through ducts into the body. The exocrine functions of the pancreas are to produce three types of enzymes that aid in the digestion of food. Lipase helps break down fats, amylase helps metabolize carbohydrates and protease helps metabolize proteins.

Familial: A trait that is commonly seen within a family who is genetically related. This trait may be caused by genetic or environmental factors, or both.

FOLFIRINOX: A combination of three chemotherapy drugs (5-FU/leucovorin, irinotecan and oxaliplatin) which is commonly used as a standard option in the treatment of metastatic pancreatic adenocarcinoma. Patients treated with FOLFIRINOX may experience more severe side effects than those treated with Gemzar® (gemcitabine) alone, so this combination is usually given to patients who are healthy enough to tolerate the potential side effects.

Food and Drug Administration (FDA): A United States government agency that promotes and protects public health by ensuring the safety and effectiveness of medical treatments and devices.

Gallbladder: A small organ located below the liver. It stores bile made by the liver.

Gastrin: The major hormone that regulates acid secretion in the stomach.

Gastrointestinal: A term indicating any body part relating to the digestive tract. It consists of the organs and structures that process and prepare food to be used for energy.

Genetic: A term that refers to a trait that is transferred from one generation to the next through genes.

Genetic counselor: A health professional with a graduate degree in medical genetics and counseling. Genetic counselors work with families who may be at risk for a variety of inherited conditions. They help families identify and understand inherited diseases and help them interpret how that information applies to their individual situation.

Gland: An organ that produces and releases one or more substances. The pancreas is both an endocrine gland and an exocrine gland.

Glucagon: A hormone made by the islet cells of the pancreas. Glucagon increases the level of glucose (sugar) in the blood.

Hereditary: A trait that is inherited through genes passed from one generation to the next.

Hormone: A chemical made by a gland that circulates in the bloodstream and influences the actions of cells or organs in a different part of the body.

Immunotherapy: A type of treatment that stimulates the body's immune system to fight cancer. Immunotherapies may fight the cancer or control side effects from other cancer treatments.

Insulin: A hormone made by the islet cells of the pancreas. Insulin decreases the level of glucose (sugar) in the blood.

Intravenous (IV): Injection of a liquid directly into a vein.

Islet cell: A pancreatic cell that produces hormones and secretes them into the bloodstream.

Jaundice: A yellowing of the skin, whites of the eyes and mucous membranes caused by abnormally high levels of bilirubin in the blood. In the case of pancreatic cancer, most jaundice is caused by obstruction of the bile duct.

Liver: A large, glandular organ located in the upper abdomen. It cleanses the blood and helps digest food by secreting bile.

Lymph nodes: Small organs that filter harmful substances in the body. They contain immune cells that fight infections and other diseases. Lymph nodes are part of the lymph system, which is formed by the tissues and organs that produce, store and carry white blood cells that fight infections and diseases. This system includes the bone marrow, spleen, thymus, lymph nodes and lymphatic vessels.

Maintenance therapy: Therapy indicated for patients whose cancer is not progressing, or remains stable. It may pertain

to patients who have undergone successful surgery to remove pancreatic cancer, or patients with advanced pancreatic cancer that has remained stable for a certain amount of time.

Malignant: A term used to describe a tumor that is cancerous.

Melanoma: The most serious form of skin cancer. It involves the cells that produce the skin pigment called melanin.

Metabolism (Metabolic): All the chemical reactions occurring in the body that are necessary to maintain life. The human body metabolizes (breaks down and rebuilds) nutrients from food for use within the cells.

Metastasis (Metastasize): The spread of cancer from one part of the body to a different organ.

Mutation: A change in the DNA of a cell. Certain mutations can lead to cancer. Mutations can be inherited or can occur over the course of a lifetime.

Neoadjuvant therapy: A treatment that is given before surgery. Neoadjuvant therapy may include chemotherapy, radiation therapy, hormone therapy, targeted therapy and/or immunotherapy.

Neoplasm: A new, abnormal mass of cells. A group of these cells is called a tumor and can be benign or malignant.

Obese: The state of having too much body fat. Adults with a Body Mass Index of 30 or over are considered obese.

Off-label: Treatments that are FDA approved to treat another cancer, but are not approved for pancreatic cancer. Since these treatments have shown some promise in pancreatic cancer in prior or existing clinical trials and already have FDA approval for another cancer, they can be prescribed by the doctor when appropriate.

Pancreas: A long, irregularly shaped gland located behind the stomach. It produces enzymes that help with digestion and secretes hormones that control the levels of sugar in the blood.

Pancreatectomy: The surgical removal of part, or all, of the pancreas.

Pancreatic duct: The main exocrine duct of the pancreas. Pancreatic enzymes from smaller ducts empty into the pancreatic duct, join the common bile duct and enter the upper part of the small intestine.

Pancreatic enzymes: The proteins made by the pancreas that aid in food digestion. The three types are amylase, lipase and protease. Together these enzymes are commonly referred to as pancreatic juice.

Pancreatic neuroendocrine tumors (pancreatic NETs or PNETs): Rare pancreatic tumors that account for about 6% of all pancreatic tumors. These tumors develop from the abnormal growth of endocrine (hormone-producing) cells in the pancreas called islet cells.

Pancreaticoduodenectomy: See Whipple procedure.

Pancreatitis: The inflammation of the pancreas. Pain is the primary symptom.

Paracentesis: A surgical procedure to remove fluid from the abdomen.

Parathyroid glands: A group of small endocrine glands located in the neck, behind the thyroid gland. These glands help regulate calcium levels in the blood.

Pathologist: A doctor who identifies diseases by studying cells and tissues under a microscope. The pathologist plays an important role in providing an accurate diagnosis of the disease.

Peritoneum: A thin membrane lining the cavity of the abdomen.

Phase: A step in the course of the clinical trials process. There are four phases of clinical trials.

Portal vein: A large vein that carries blood from the spleen, stomach, pancreas and intestines to the liver.

Primary tumor: The original tumor. In pancreatic cancer, the primary tumor is in the pancreas.

Radiologist: A doctor who diagnoses and treats diseases using medical imaging procedures.

Resectable: Able to be removed by surgery.

Risk factor: A characteristic or behavior associated with an increased chance of developing a disease. It is not necessarily a cause of the disease but increases the likelihood of developing the disease.

Secondary tumor: A cancerous tumor that has spread from its original site of formation (the primary tumor) to another location in the body. Secondary tumors, though found in a different location, are still considered pancreatic cancer and treated as such.

Small intestine: The tube-shaped portion of the digestive (gastrointestinal) system, located between the stomach and the large intestine. Most nutrients are absorbed into the bloodstream through the small intestine.

Spleen: An organ in the upper left side of the abdomen that filters the blood. It is located near the tail of the pancreas.

Stage: A measure of how far the cancer has grown using size of the tumor, lymph node involvement and locations to which it has spread. Stages range from 1 to 4, with 1 describing the earliest form of cancer.

Stent: A small metal or plastic tube inserted into the center of a vein, artery or duct in order to open a blocked passageway.

Superior mesenteric artery: A major artery arising from the largest artery in the body, the aorta. The superior mesenteric artery is located behind the neck of the pancreas and supplies blood to the small intestines, colon and part of the pancreas.

Superior mesenteric vein: A major vein located behind the neck of the pancreas.

Symptom: An indication that a person has a condition or disease. Some examples of symptoms for pancreatic cancer include jaundice, weight loss, fatigue, nausea, vomiting and pain.

Targeted therapy: A type of treatment that attacks unique aspects of cancer cells with little harm to healthy cells.

Total parenteral nutrition (TPN): A method of giving a specialized form of food through a vein.

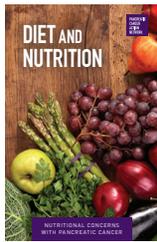
Whipple procedure: The surgical removal of the head of the pancreas, the lymph nodes near the head of the pancreas, the gallbladder, the duodenum (first part of the small intestine) and possibly a small portion of the stomach, called the pylorus.

The Pancreatic Cancer Action Network thanks the Patient Services Committee members of our

SCIENTIFIC AND MEDICAL ADVISORY BOARD

for providing their medical expertise in reviewing this booklet. These members are experts from such institutions as MD Anderson Cancer Center, Memorial Sloan-Kettering Cancer Center, Virginia Mason Medical Center, etc.

To see all of our Scientific and Medical Advisory Board members, visit pancan.org/SMAB.



Want to know more about any of the services we offer? Hablamos Español. Contact PanCAN Patient Services, Monday through Friday, 7 a.m. to 5 p.m. Pacific Time.

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PanCAN was the first organization dedicated to fighting pancreatic cancer in a comprehensive way, and for more than two decades, we've grown a nationwide movement tackling the disease from all angles.



RESEARCH

We fund transformative research—everything from early detection to innovative new treatment approaches.



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We provide information about treatment options, diet and nutrition, support resources and more, and we can answer all your questions along the way.



ADVOCACY

We work with thousands of grassroots advocates to urge Congress to increase federal research funding for pancreatic cancer, and we get results.



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Be part of our movement! You can volunteer locally, participate in a PurpleStride community event or host your own fundraiser.

ACTION FOR PATIENTS BEGINS HERE

The mission of the Pancreatic Cancer Action Network (PanCAN) is to take bold action to improve the lives of everyone impacted by pancreatic cancer by advancing scientific research, building community, sharing knowledge and advocating for patients.

Our vision is to create a world in which all patients with pancreatic cancer will thrive.

Through our Patient Services program, we provide extensive individualized support and hope. PanCAN Patient Services connects patients, their caregivers and family members to reliable information and resources. Our highly educated and expertly trained staff's passion is equaled only by their depth of knowledge about pancreatic cancer.

To learn more about our free, personalized resources and services, visit pancan.org or call 877-2-PANCAN. Hablamos Español.

**PANCREATIC
CANCER
ACTION
NETWORK**

®

1500 Rosecrans Avenue, Suite 200
Manhattan Beach, CA 90266
877-2-PANCAN
pancan.org