PANCREATIC CANCER

What is cancer?

Cancer develops when cells in a part of the body begin to grow out of control. Although there are many kinds of cancer, they all start because of out-of-control growth of abnormal cells.

Normal body cells grow, divide, and die in an orderly fashion. During the early years of a person's life, normal cells divide more rapidly until the person becomes an adult. After that, cells in most parts of the body divide only to replace worn-out or dying cells and to repair injuries.

Because cancer cells continue to grow and divide, they are different from normal cells. Instead of dying, they outlive normal cells and continue to form new abnormal cells.

Cancer cells develop because of damage to DNA. This substance is in every cell and directs all its activities. Most of the time when DNA becomes damaged the body is able to repair it. In cancer cells, the damaged DNA is not repaired. People can inherit damaged DNA, which accounts for inherited cancers. Many times though, a person’s DNA becomes damaged by exposure to something in the environment, like smoking.

Cancer usually forms as a tumor. Some cancers, like leukemia, do not form tumors. Instead, these cancer cells involve the blood and blood-forming organs and circulate through other tissues where they grow.

Often, cancer cells travel to other parts of the body, where they begin to grow and replace normal tissue. This process is called metastasis. Regardless of where a cancer may spread, however, it is always named for the place it began. For instance, breast cancer that spreads to the liver is still called breast cancer, not liver cancer.

Not all tumors are cancerous. Benign (non-cancerous) tumors do not spread (metastasize) to other parts of the body and, with very rare exceptions, are not life threatening.

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

Cancer is the second leading cause of death in the United States. Nearly half of all men and a little over one third of all women in the United States will develop cancer during their lifetimes. Today, millions of people are living with cancer or have had cancer. The risk of developing most types of cancer can be reduced by changes in a person's lifestyle, for example, by quitting smoking and eating a better diet. The sooner a cancer is found and treatment begins, the better are the chances for living for many years.

What Is Cancer of the Pancreas?

The Normal Pancreas

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

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

The *exocrine* glands make pancreatic "juice," which is released into the intestines. This juice contains enzymes that help you digest fats, proteins, and carbohydrates in the food you eat. Without these, some of the food you eat would just pass through your intestines without being absorbed. The enzymes are released into tiny tubes called *ducts*. These tiny ducts merge together to form larger ducts that carry the pancreatic juice to the small intestine. More than 95% of the cells in the pancreas are exocrine glands and ducts.

A small percentage of the cells in the pancreas are *endocrine* cells. These cells are arranged in small clusters called islets (or islets of Langerhans). The islets release 2 important hormones, insulin and glucagon, directly into the blood. Insulin reduces the amount of sugar in the blood, while glucagon increases it. Diabetes results from a defect in insulin production.

Types of Tumors of the Pancreas

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

Exocrine Tumors

These are far and away the most common type of pancreas cancer. Although benign (non-cancerous) cysts and benign tumors called cystadenomas can occur, most pancreatic exocrine tumors are malignant.

About 95% of cancers of the exocrine pancreas are *adenocarcinomas.* Adenocarcinomas usually begin in the ducts of the pancreas, but they sometimes develop from the cells that make the pancreatic enzymes (acinar cell carcinomas).

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

But the type of exocrine pancreatic cancer isn't as important as the stage (extent) of the cancer when it comes to treatment. The treatment of an exocrine pancreatic cancer is mostly based on the stage of the cancer, not its exact type. (Pancreatic cancer staging is described later in this document.)

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

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

Endocrine Tumors
Tumors of the endocrine pancreas are uncommon. As a group, they are known as neuroendocrine tumors, or more specifically, islet cell tumors. There are several subtypes of islet cell tumors that are named according to the type of hormone-making cell they start in:

- *insulinomas* arise from cells that make insulin
- *glucagonomas* come from cells that make glucagon
- *gastrinomas* come from cells that make gastrin
- *somatostatinomas* come from cells that make somatostatin
- *VIPomas* come from cells that make vasoactive intestinal peptide (VIP)

These tumors are called "functioning" if they make hormones or "non-functioning" if they do not. Most functioning islet cell tumors are benign, while non-functioning tumors are more likely to be malignant. Malignant tumors are called islet cell cancers or islet cell carcinomas. Treatment and prognosis (outlook) depends on the specific type and stage (extent) of the tumor.

It is very important to distinguish between exocrine and endocrine cancers of the pancreas. They have distinct risk factors and causes, have different signs and symptoms, are diagnosed using different tests, are treated in different ways, and have different prognoses (outlooks).

The remaining sections of this document refer only to exocrine pancreatic and ampullary cancers.

What Are the Key Statistics About Cancer of the Pancreas?

The American Cancer Society estimates that 37,680 Americans (18,770 men and 18,910 women) will be diagnosed with cancer of the pancreas during 2008. Over the past 15 to 25 years, rates of cancer of the pancreas have dropped slightly in men and women.

The lifetime risk of developing pancreatic cancer is about 1 in 79 (1.27%). This is about the same for both men and women. A person's risk may be altered by certain risk factors (listed in the next section).

An estimated 34,290 Americans (17,500 men and 16,790 women) will die of pancreatic cancer in 2008, making this type of cancer the fourth leading cause of cancer death overall.

What Are the Risk Factors for Cancer of the Pancreas?

A risk factor is anything that affects your chance of getting a disease such as cancer. Different cancers have different risk factors. For example, unprotected exposure to strong sunlight is a risk factor for skin cancer. But risk factors are not absolute. Having a risk factor, or even several risk factors, does not mean that you will get the disease. And many people who get the disease may not have had any known risk factors.

Researchers have found several factors that affect a person's chance of getting cancer of the exocrine pancreas.

Age

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

Gender

Men are slightly more likely to develop cancer of the pancreas than are women. This difference was more pronounced in the past, but the gap has closed in recent years. This may be due, at least in part, to increased tobacco use.

Race

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

Cigarette Smoking

The risk of getting cancer of the pancreas is 2 to 3 times higher among smokers. Scientists think this may be due to cancer-causing chemicals in cigarette smoke that enter the blood and

damage the pancreas. About 20% to 30% of pancreatic cancer cases are thought to be caused by cigarette smoking. Many experts think this is why the rate of pancreatic cancer has been increasing in the last 50 years and is only now starting to decline as smoking rates have dropped.

Diet

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

Obesity and Physical Inactivity

Very overweight people are more likely to develop pancreatic cancer, as are people who don't get much physical activity.

Diabetes

Pancreatic cancer is more common in people with this disease. The reason for this link is not known. Most of the risk is found in people with type 2 diabetes, which typically starts in adulthood and is often related to being overweight or obese. It is not clear if people with type 1 (juvenile) diabetes have a higher than average risk.

Chronic Pancreatitis

Chronic pancreatitis is a long-term inflammation of the pancreas. This condition is linked with an increased risk of pancreatic cancer, but most patients with pancreatitis never develop cancer of the pancreas. The main reason for this link may be that patients with pancreatitis are more likely to also have other risk factors such as smoking.

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

Occupational Exposure

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

Family History

Cancer of the pancreas seems to run in some families. As many as 10% of pancreatic cancers may be related to inherited DNA changes (mutations). These changes often increase the risk for certain other cancers as well. Some examples include:

- *BRCA2 gene mutations,* which also increase the risk of breast and ovarian cancer
- *certain p16 gene mutations,* which also increase the risk for melanoma
- *PRSS1 gene mutations,* which cause severe pancreatitis at an early age

- *hereditary non-polyposis colorectal cancer (HNPCC, also known as Lynch syndrome),* which also increases the risk of colorectal and endometrial cancers
- *Peutz-Jeghers syndrome,* which is also linked with polyps in the digestive tract and several other cancers

Some of these DNA changes have been found by scientists and can be recognized by genetic testing. For more information on genetic testing, refer to the section, "Can Cancer of the Pancreas Be Found Early?"

Stomach Problems

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

Factors With Uncertain, Controversial, or Unproven Effects on Pancreatic Cancer Risk

Coffee Drinking

Although older studies have suggested that coffee consumption might be a risk factor, most recent studies have not confirmed this.

Alcohol Consumption

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

Do We Know What Causes Cancer of the Pancreas?

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

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

Several cancer family syndromes have been found in which inherited DNA mutations cause a very high risk of developing certain cancers. In some of these, there is an increased risk of

getting cancer of the pancreas. Researchers have characterized many of these DNA changes in the past few years (see the section, "What Are the Risk Factors for Pancreatic Cancer?").

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

Often, the DNA changes seen in sporadic (non-inherited) cases of pancreatic cancer are the same as those seen in inherited cases. For example, most sporadic cases of pancreatic cancer have changes in the p16 gene. Because of this, scientists are studying inherited cases closely to learn more about what causes pancreatic cancer. Some specific DNA abnormalities recently discovered in cancer of the pancreas are discussed in the section, "What's New in Pancreatic Cancer Research and Treatment?"

Can Cancer of the Pancreas Be Prevented?

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

Cigarette smoking is the most significant and avoidable risk factor for cancer of the pancreas. It is responsible for 20% to 30% of pancreatic cancers. Tobacco use also increases the risk of developing cancers of the lung, mouth, larynx (voice box), esophagus, kidney, bladder, and some other organs. If you smoke and want help quitting, please consult your doctor or call the American Cancer Society.

Maintaining a healthy weight, eating well, and exercising are also important. The American Cancer Society recommends choosing foods and beverages in amounts that help achieve and maintain a healthy weight. Eat at least 5 servings of fruits and vegetables every day, as well as servings of whole grain foods from plant sources such as rice, breads, pasta, and cereals. Eat less processed and red meat. Following these recommendations may lower your risk of getting cancer of the pancreas, as well as several other cancers and some non-cancerous diseases.

Can Cancer of the Pancreas Be Found Early?

The main reason for the often poor outlook for people with cancer of the pancreas is that very few of these cancers are found early. Because the pancreas is located deep inside the body, early tumors cannot be seen or felt by health care providers during routine physical exams. Patients usually have no symptoms until the cancer has spread to other organs. There are currently no blood tests or easily available screening tests that can accurately detect early cancers of the pancreas.

Screening Tests

A substance called CA 19-9 is released into the blood by pancreatic cancer cells and can be detected by blood tests. But by the time blood levels are high enough to be consistently detected by available methods, the cancer is no longer in its early stages. Because of this, the

test is not recommended for routine screening of people without symptoms or a known diagnosis of cancer. The CA 19-9 test is sometimes used during treatment to see if the therapy is working or after treatment to see if the cancer has recurred (come back).

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

Genetic Testing

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

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

For people in families at high risk of pancreatic cancer, there are new tests for detecting early pancreatic cancer that may help. One of these is called endoscopic ultrasound (see the section, "How Is Pancreatic Cancer Diagnosed?"). It would not be used to screen the general public but might be used in someone with a strong family history of pancreatic cancer. Using endoscopic ultrasound, doctors have been able to find early, treatable pancreatic cancers in some members of high-risk families. In addition, interested families may wish to participate in ongoing research studies aimed at investigating the genetic factors and possible role of screening methods in those with a family history of the disease.

How Is Cancer of the Pancreas Diagnosed?

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

Signs and Symptoms of Cancer of the Pancreas

Jaundice

Jaundice is a yellowing of the eyes and skin. It occurs in at least half of all people with pancreatic cancer and in all cases when the cancer is at the ampulla of Vater.

Jaundice is caused by the buildup of bilirubin (a dark green substance made in the liver) in the body. This happens when the common bile duct becomes blocked, which prevents the bile from reaching the intestines (and eventually leaving the body in the stool).

Cancers that begin in the head of the pancreas near the common bile duct may compress the duct while they are still fairly small, which may lead to early detection. But cancers that begin in the body or tail of the pancreas do not compress the duct until they have spread through the pancreas. By this time, the cancer may have also spread beyond the pancreas.

Sometimes, the first sign of jaundice is darkening of the urine because that is where the bilirubin is excreted. Or a person may notice their stools becoming light in color because no bilirubin is getting through to the bowel from the blocked bile duct.

When bilirubin builds up in the skin, it often causes itching. As bilirubin levels in the blood increase, this substance comes out into the urine, causing a brown color.

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

Abdominal or Back Pain
Pain in the abdomen or back is a common sign of advanced cancer of the pancreas. Cancers that start in the body or tail of the pancreas may grow fairly large and start to compress on other nearby organs, causing pain. The cancer may also spread to the nerves surrounding the pancreas, which often causes back pain. It may be constant or may come and go. Of course, many non-cancerous diseases as well as several other types of cancer can also cause abdominal or back pain. These are more common causes than cancer of the pancreas.

Weight Loss and Poor Appetite
Unintended or unexpected weight loss is very common in patients with cancer of the pancreas. These people also complain of being very tired and having little or no appetite.

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

Gallbladder Enlargement
If the cancer blocks the bile duct, bile can build up in the gallbladder, which then becomes enlarged. Sometimes a doctor can feel this enlargement during the physical exam. It can also be detected by imaging studies.

Blood Clots or Fatty Tissue Abnormalities
Sometimes, the first clue that there is a pancreatic cancer is the development of a blood clot in a large vein. These clots can sometimes travel to the lungs and cause trouble with breathing.

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

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

History and Physical Exam

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

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

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

Imaging Tests

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

Often after the first set of pictures is taken you may be asked to drink 1 or 2 pints of a radiocontrast agent, or dye, and/or you may receive an intravenous (IV) line through which the contrast dye is injected. This dye helps better outline structures in your body. A second set of pictures is then taken. The solution you drink and the injection can cause some flushing (redness and warm feeling). Some people are allergic and get hives; rarely more serious reactions like trouble breathing and low blood pressure can occur. Please be sure to tell the doctor if you have ever had a reaction to any contrast material used for x-rays.

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

CT scans are often used to diagnose pancreatic cancer and are helpful in staging the cancer (determining the extent of its spread). CT scans show the pancreas fairly clearly and often can confirm the location of the cancer. CT scans can also show the organs near the pancreas,

as well as lymph nodes and distant organs where the cancer might have spread. The CT scan can help to determine whether surgery is a good treatment option.

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

Positron Emission Tomography (PET) Scan
PET scans involve injecting glucose (a form of sugar) that contains a radioactive atom into the blood. Because cancer cells in the body are growing rapidly, they absorb large amounts of the radioactive sugar. A special camera can then create a picture of areas of radioactivity in the body. The picture is not finely detailed like a CT or MRI scan, but it provides helpful information. This test is useful to see if the cancer has spread to lymph nodes. PET scans are also useful when your doctor thinks the cancer has spread, but doesn't know to where.

PET/CT scans combine a CT scan and a PET scan to even better pinpoint the tumor. This test may be especially useful for spotting cancer that has spread beyond the pancreas and wouldn't be treatable by surgery. It may be a useful test for staging the cancer. It may even be able to spot early cancers. Because this test is so new, it is still being studied.

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

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

If signs and symptoms indicate that a cancer of the pancreas is likely, a CT scan is often more useful than ultrasound for an accurate diagnosis. But if it's not clear whether certain other diseases may account for the patient's signs or symptoms, ultrasound may be done.

Endoscopic ultrasound is more accurate than abdominal ultrasound and is probably the best way to diagnose pancreatic cancer. This test is done with an ultrasound probe that is attached to an endoscope -- a thin, lighted, flexible, fiber optic tube that doctors use to look at the inside of the intestinal tract. Patients are first sedated (given medicine to make them sleepy). The probe is then passed through the mouth or nose into the stomach. The probe can be pointed toward the pancreas, which sits next to the small intestine. This gives a very accurate picture and is better than CT scans for spotting small tumors. It can also be used to biopsy a tumor.

Magnetic Resonance Imaging (MRI)
MRI scans use radio waves and strong magnets instead of x-rays. The energy from the radio waves is absorbed by the body and then released in a pattern formed by the type of body tissue and by certain diseases. A computer translates the pattern into a detailed image of parts of the body. Not only does this produce cross-sectional slices of the body like a CT scanner, it also produces slices that are parallel with the length of the body. A contrast material might be injected just as with CT scans, this but is used less often.

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

MRI scans are a little more uncomfortable than CT scans. They take longer -- often up to an hour. You may have to lie inside a narrow tube, which is confining and can upset people with a fear of enclosed spaces. Newer, "open" MRI machines can help with this if needed. The MRI machine makes loud noises that you may find disturbing. Some places provide headphones with music to block this out.

Endoscopic Retrograde Cholangiopancreatography (ERCP)
For this x-ray test, a thin, lighted, flexible tube is passed down the patient's throat, through the esophagus and stomach, and into the first part of the small intestine. Usually the patient is sedated first. The doctor doing this procedure can see through the end of the tube and locate the area where the common bile duct is connected to the small intestine. He or she can then guide the tube into the common bile duct. A small amount of dye (contrast material) is then injected through the tube into the common bile duct. This dye helps outline the bile duct and pancreatic duct in x-ray images that are taken. The images can show narrowing or blockage of the bile duct or pancreatic duct that might be due to a cancer of the pancreas. The doctor doing this test can also put a small brush through the tube to remove cells to view under a microscope to see whether or not they appear cancerous.

ERCP can also be used to place a stent (small tube) into the bile duct to keep it open if a nearby tumor is pressing on it. This is described in more detail in the section on palliative surgery (see the section, "How Is Cancer of the Pancreas Treated?").

Angiography
This is an x-ray procedure for looking at blood vessels. A small amount of contrast material is injected into an artery to outline the blood vessels. After this, x-rays are taken.

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

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

Blood Tests

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

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

Elevated blood levels of the tumor markers CA 19-9 and carcinoembryonic antigen (CEA) may point to a diagnosis of pancreatic cancer, although these tests aren't always accurate (see the section, "Can Pancreatic Cancer Be Found Early?").

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

Biopsy

Although the patient's history, physical exam, and imaging test results may strongly suggest cancer of the pancreas, the only way to be sure is by removing a small sample of tumor and looking at it under the microscope. A procedure to remove a tissue sample is called a biopsy.

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

Doctors can also biopsy the tumor by using the endoscopic ultrasound to place the needle directly through the wall of the duodenum into the tumor. In either case, small tissue samples can be removed through the needle. The main advantages of the test are that the patient does not require general anesthesia (is not "asleep" during the test, although some sedation may be used) and there are almost never any major side effects.

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

needle biopsy). The main drawback of this type of biopsy is that the patient must have general anesthesia and remain in the hospital for a period of time to recover.

Laparotomy is now rarely recommended. Doctors prefer to use *laparoscopy* (sometimes called keyhole surgery) as a way of looking at and perhaps taking a piece of the pancreas with a biopsy. Patients are usually sedated for this procedure. The surgeon makes several small incisions in the abdomen and inserts small telescope-like instruments into the abdominal cavity. One of these is usually connected to a video monitor. The surgeon can view the abdomen and see how big the tumor is and whether it has spread, and may take tissue samples as well.

Most doctors who treat pancreatic cancer try to avoid surgery unless imaging tests suggest that an operation might be able to remove all of the visible cancer. Even after doing imaging tests and laparoscopy, there are times when the surgeon begins an operation with the intent of removing the cancer but finds during surgery that it has spread too far to be removed completely. In these cases, a sample of the cancer is taken only to confirm the diagnosis, and the rest of the planned operation is stopped.

How Is Cancer of the Pancreas Staged?

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

The American Joint Committee on Cancer (AJCC) TNM System

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

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

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

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

T Categories

- **TX:** The main tumor cannot be assessed
- **T0:** No evidence of a primary tumor
- **Tis:** Carcinoma in situ (very few tumors are found at this stage)
- **T1:** The cancer has not spread beyond the pancreas and is smaller than 2 cm (about ¾ inch) across.
- **T2:** The cancer has not spread beyond the pancreas but is larger than 2 cm across.
- **T3:** The cancer has spread from the pancreas to surrounding tissues near the pancreas but not to blood vessels.
- **T4:** The cancer has extended further beyond the pancreas into nearby large blood vessels.

N Categories

- **NX:** Regional lymph nodes cannot be assessed
- **N0:** Regional lymph nodes (lymph nodes near the pancreas) are not involved.
- **N1:** Cancer has spread to regional lymph nodes.

M Categories

- **MX:** Spread to distant organs cannot be assessed
- **M0:** The cancer has not spread to distant lymph nodes (other than those near the pancreas) or to distant organs such as the liver, lungs, brain, etc.
- **M1:** Distant metastasis is present.

Stage Grouping for Cancer of the Pancreas

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

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

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

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

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

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

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

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

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

For patients who have surgery, the *extent of the resection* -- whether all of the tumor is removed -- is also important with regard to outlook. This is sometimes listed on a scale from R0 (where all of the visible and microscopic tumor has been removed) to R2 (where some visible tumor could not be removed).

Resectable, Locally Advanced -- Unresectable, and Metastatic Cancer

From a practical standpoint, the extent of the cancer spread (especially to the lymph nodes) often can't be determined accurately unless and until surgery is performed. Therefore, doctors often use a simpler staging system, which divides cancers into groups based on whether or not it is likely they can be removed surgically.

Resectable
The cancer is still localized to the pancreas (or has spread just beyond it) and the surgeon is able to remove the entire tumor.

Locally Advanced -- Unresectable
Too much cancer is present in nearby blood vessels to permit complete surgical removal of the cancer, although it has not yet spread to distant organs. Cancer that cannot be removed entirely by surgery is called unresectable. Surgery would only be done to relieve symptoms or problems such as obstruction of the bile duct or intestinal tract.

Metastatic
Spread to distant organs has been identified and surgery would only be done to relieve symptoms or problems such as obstruction of the bile duct or intestinal tract.

Survival by Whether Cancer Is Localized, or Has Regional or Distant Spread

The National Cancer Institute (NCI) maintains a large national database on survival statistics for different types of cancer. But the NCI uses a slightly different staging system when compiling their numbers, grouping cancers into local, regional and distant stages.

For the fewer than 10% of people with pancreatic cancer who are diagnosed with *local disease* (cancer that has not spread beyond the pancreas to other organs), which is likely to be resectable, the 5-year relative survival rate is about 20%.

For the 1 out of 4 pancreatic cancer patients with *regional disease* (with spread to nearby organs and tissues, but no evidence of distant spread) the 5-year relative survival is about 8%.

More than half of all pancreatic cancer patients are diagnosed with *distant disease*, where the 5-year relative survival is about 2%.

The 5-year survival rate refers to the percentage of patients who live *at least* 5 years after their cancer is diagnosed. Of course, some people live much longer than 5 years. Five-year rates are used as a standard way of discussing prognosis. Five-year *relative* survival rates compare the observed survival of people with pancreatic cancer to that expected for people without pancreatic cancer. Therefore, relative survival mainly talks about deaths from pancreatic cancer; it tries to exclude people with pancreatic cancer who might die from other causes.

Overall, only about 5% of all people with pancreatic cancer will still be alive 5 years after diagnosis.

How Is Cancer of the Pancreas Treated?

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

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

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

The 3 main types of treatment for cancer of the pancreas are surgery, radiation therapy, and chemotherapy. Depending on the stage of the cancer, some of these treatments may be combined.

Surgery

There are 2 general types of surgery used for cancer of the pancreas:

- *Potentially curative surgery* is used when imaging tests suggest that it is possible to remove all the cancer.

- *Palliative surgery* may be done if imaging tests show that the tumor is too widespread to be completely removed. This is done to relieve symptoms or to prevent certain complications such as blockage of the bile ducts or the intestine by the cancer.

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

Potentially Curative Surgery
Most curative surgery is designed to treat cancers at the head of the pancreas. Because these cancers are near the bile duct, some of them cause jaundice and are found early enough to be removed. Surgeries for other parts of the pancreas are mentioned below, but these are only done when complete removal of the cancer will be possible.

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

Pancreaticoduodenectomy (Whipple procedure): This is the most common operation to remove a cancer of the exocrine pancreas. It involves removing the head of pancreas and sometimes the body of the pancreas as well. Part of the stomach, small intestine, and lymph nodes near the pancreas are also removed. The gallbladder and part of the common bile duct are removed and the remaining bile duct is attached to the small intestine so that bile from the liver can continue to enter the small intestine.

This is a complex operation that requires much skill and experience. It carries a relatively high risk of complications that may even be fatal. When this operation is performed in cancer centers by surgeons experienced in the procedure, about 2% to 5% of patients die as a direct result of complications from surgery. When the operation is done in small hospitals or by doctors with less experience, up to 15% of patients may die as a result of surgical complications. Even in the best of hands, anywhere from 30% to 50% of patients will suffer complications from the surgery. These can include:

- leaking from the various connections that the surgeon has to make
- infections
- bleeding
- trouble with the stomach emptying itself after eating

For patients to have the best outcomes, they must be treated by a surgeon who has performed many of these operations and at a hospital that has had extensive experience with pancreatic surgery.

Only about 10% of cancers of the pancreas appear to be contained entirely within the pancreas at the time of diagnosis. Only about half of these turn out to be truly resectable once the surgery is started. But even when there appears to be no spread beyond the pancreas at the time of surgery, some cancer cells may already have spread to other parts of the body.

Among patients who have surgery with the intent of completely removing a cancer of the exocrine pancreas, the 5-year survival rate is about 20%.

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

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

Palliative Surgery

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

Cancers growing in the head of the pancreas can block the common bile duct as it passes through this part of the pancreas. This may cause pain and digestive problems because the bile can't get into the intestine. The bile chemicals will build up in the body. There are 2 options for relieving bile duct blockage.

Surgery can be done to reroute the flow of bile from the common bile duct directly into the small intestine, bypassing the pancreas. This requires a large incision in the abdomen, and it may take weeks to completely recover. One advantage is that during this procedure, the surgeon may be able to cut the nerves leading to the pancreas or inject them with alcohol. This may reduce or get rid of any pain that may be caused by the cancer. Sometimes, the stomach connection to the duodenum (the first part of the small intestine) is rerouted at this time as well. Often, late in the course of pancreatic cancer, the duodenum becomes blocked by cancer, which can cause pain and vomiting that requires surgery. Bypassing the duodenum before this happens can help avoid a second operation.

A second approach to relieving a blocked bile duct does not involve surgery. Instead, a stent (small tube) is placed in the duct to keep it open. This is usually done through an endoscope (a long, flexible tube) while the patient is sedated. The doctor passes the endoscope down the patient's throat and all the way into the small intestine. The doctor can then insert the stent into the bile duct through the endoscope. The stent, which is usually made of metal, helps

keep the bile duct open and resists compression from the surrounding cancer. After several months, the stent may become clogged and may need to be cleared. Larger stents are also available to keep the small intestine open if it is in danger of being blocked.

In general, of the use of endoscopically-placed stents has replaced palliative by-pass surgery to relieve bile duct obstruction

Radiation Therapy

Radiation therapy is the use of high-energy x-rays (or particles) to kill cancer cells.

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

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

Radiation therapy combined with chemotherapy (called *chemoradiation*) may be used in patients whose tumors are too widespread to be removed by surgery.

Side effects of radiation therapy may include mild skin changes resembling sunburn or suntan, nausea, vomiting, diarrhea, and fatigue. Patients usually lose their appetite and have trouble keeping up their weight. Usually these effects go away a few weeks after the treatment is complete. Radiation therapy may make the side effects of chemotherapy worse. Please be sure to talk with your doctor about these side effects and ways to prevent or relieve them.

Chemotherapy

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

Gemcitabine is the chemotherapy drug most often used to treat cancer of the pancreas. Another commonly used drug is 5-fluorouracil (5-FU). Recent studies have found gemcitabine to be more effective than 5-FU in treating metastatic cancer of the pancreas. Studies testing these two drugs in treating resectable and locally advanced cancers are now in progress.

Other studies are trying to improve the effectiveness of chemotherapy by combining gemcitabine and 5-FU with each other or with other chemotherapy drugs, such as cisplatin, irinotecan, paclitaxel, capecitabine, or oxaliplatin.

Chemotherapy may be used at any stage of pancreatic cancer. It is commonly used in people with advanced cancer, and is often used after surgery in people with more localized disease. In people who are expected to have surgery, some cancer centers have used preoperative chemo and radiotherapy to shrink the tumor beforehand.

Chemotherapy drugs kill cancer cells but also damage some normal cells. This can lead to side effects, which depend on the type of drugs, the amount taken, and the length of treatment. Short-term side effects might include nausea and vomiting, loss of appetite, hair loss, and mouth sores. Because chemotherapy can damage the bone marrow, where new blood cells are made, blood cell counts might become low. This can result in:

- increased chance of infection (due to a shortage of white blood cells)
- bleeding or bruising after minor cuts or injuries (due to a shortage of platelets)
- fatigue and shortness of breath (due to low red blood cell counts)

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

Targeted Therapy

Newer drugs that target specific parts of cancer cells are now being studied. These drugs work differently from standard chemotherapy drugs, and they often have fewer side effects (See "What's New in Pancreatic Cancer Research and Treatment?" for more information.)

A drug called erlotinib (Tarceva) has helped some patients with advanced pancreatic cancer. This drug is taken as a pill. Erlotinib targets a protein on the surface of cancer cells called EGFR, which normally prompts cancer cells to grow. When combined with gemcitabine it has been shown to be slightly better than gemcitabine alone. Some people may get more benefit from this combination regimen than others. Common side effects of this drug can include an acne-like rash, diarrhea, loss of appetite, and feeling tired.

Clinical Trials

You have had to make a lot of decisions since you've been told you have cancer. One of the most important decisions you will make is deciding which treatment is best for you. You may have heard about clinical trials being done for your type of cancer. Or maybe someone on your health care team has mentioned a clinical trial to you. Clinical trials are one way to get state-of-the art cancer care. Still, they are not right for everyone.

Here we will give you a brief review of clinical trials. Talking to your health care team, your family, and your friends can help you make the best treatment choice for you.

What Are Clinical Trials?

Clinical trials are carefully controlled research studies that are done with patients. These studies test whether a new treatment is safe and how well it works in patients, or they may

test new ways to diagnose or prevent a disease. Clinical trials have led to many advances in cancer prevention, diagnosis, and treatment.

The Purpose of Clinical Trials
Clinical trials are done to get a closer look at promising new treatments or procedures in patients. A clinical trial is only done when there is good reason to believe that the treatment, test, or procedure being studied may be better than the one used now. Treatments used in clinical trials are often found to have real benefits and may go on to become tomorrow's standard treatment.

Clinical trials can focus on many things, such as:

- new uses of drugs that are already approved by the US Food and Drug Administration (FDA)
- new drugs that have not yet been approved by the FDA
- non-drug treatments (such as radiation therapy)
- medical procedures (such as types of surgery)
- herbs and vitamins
- tools to improve the ways medicines or diagnostic tests are used
- medicines or procedures to relieve symptoms or improve comfort
- combinations of treatments and procedures

Researchers conduct studies of new treatments to try to answer the following questions:

- Is the treatment helpful?
- What's the best way to give it?
- Does it work better than other treatments already available?
- What side effects does the treatment cause?
- Are there more or fewer side effects than the standard treatment used now?
- Do the benefits outweigh the side effects?
- In which patients is the treatment most likely to be helpful?

Phases of Clinical Trials
There are 4 phases of clinical trials, which are numbered I, II, III, and IV. We will use the example of testing a new cancer treatment drug to look at what each phase is like.

Phase I clinical trials: The purpose of a phase I study is to find the best way to give a new treatment safely to patients. The cancer care team closely watches patients for any harmful side effects.

For phase I studies, the drug has already been tested in lab and animal studies, but the side effects in patients are not fully known. Doctors start by giving very low doses of the drug to the first patients and increase the doses for later groups of patients until side effects appear or the desired effect is seen. Doctors are hoping to help patients, but the main purpose of a phase I trial is to test the safety of the drug.

Phase I clinical trials are often done in small groups of people with different cancers that have not responded to standard treatment, or that keep coming back (recurring) after treatment. If a drug is found to be reasonably safe in phase I studies, it can be tested in a phase II clinical trial.

Phase II clinical trials: These studies are designed to see if the drug works. Patients are given the best dose as determined from phase I studies. They are closely watched for an effect on the cancer. The cancer care team also looks for side effects.

Phase II trials are often done in larger groups of patients with a specific cancer type that has not responded to standard treatment. If a drug is found to be effective in phase II studies, it can be tested in a phase III clinical trial.

Phase III clinical trials: Phase III studies involve large numbers of patients -- most often those who have just been diagnosed with a specific type of cancer. Phase III clinical trials may enroll thousands of patients.

Often, these studies are randomized. This means that patients are randomly put in one of two (or more) groups. One group (called the control group) gets the standard, most accepted treatment. Another group (or more than one group) will get the new treatment being studied. All patients in phase III studies are closely watched. The study will be stopped early if the side effects of the new treatment are too severe or if one group has much better results than the others.

Phase III clinical trials are usually needed before the FDA will approve a treatment for use by the general public.

Phase IV clinical trials: Once a drug has been approved by the FDA and is available for all patients, it is still studied in other clinical trials (sometimes referred to as phase IV studies). This way more can be learned about short-term and long-term side effects and safety as the drug is used in larger numbers of patients with many types of diseases. Doctors can also learn more about how well the drug works, and if it might be helpful when used in other ways (such as in combination with other treatments).

What It Will Be Like to Be in a Clinical Trial

If you are in a clinical trial, you will have a team of experts taking care of you and watching your progress very carefully. Depending on the phase of the clinical trial, you may receive more attention (such as having more doctor visits and lab tests) than you would if you were treated outside of a clinical trial. Clinical trials are specially designed to pay close attention to you.

However, there are some risks. No one involved in the study knows in advance whether the treatment will work or exactly what side effects will occur. That is what the study is designed to find out. While most side effects go away in time, some may be long-lasting or even life

threatening. Keep in mind, though, that even standard treatments have side effects. Depending on many factors, you may decide to enter (enroll in) a clinical trial.

Deciding to Enter a Clinical Trial

If you would like to take part in a clinical trial, you should begin by asking your doctor if your clinic or hospital conducts clinical trials. There are requirements you must meet to take part in any clinical trial. But whether or not you enter (enroll in) a clinical trial is completely up to you.

Your doctors and nurses will explain the study to you in detail. They will go over the possible risks and benefits and give you a form to read and sign. The form says that you understand the clinical trial and want to take part in it. This process is known as giving your informed consent. Even after reading and signing the form and after the clinical trial begins, you are free to leave the study at any time, for any reason. Taking part in a clinical trial does not keep you from getting any other medical care you may need.

To find out more about clinical trials, talk to your cancer care team. Here are some questions you might ask:

- Is there a clinical trial that I could take part in?
- What is the purpose of the study?
- What kinds of tests and treatments does the study involve?
- What does this treatment do? Has it been used before?
- Will I know which treatment I receive?
- What is likely to happen in my case with, or without, this new treatment?
- What are my other choices and their pros and cons?
- How could the study affect my daily life?
- What side effects can I expect from the study? Can the side effects be controlled?
- Will I have to stay in the hospital? If so, how often and for how long?
- Will the study cost me anything? Will any of the treatment be free?
- If I am harmed as a result of the research, what treatment would I be entitled to?
- What type of long-term follow-up care is part of the study?
- Has the treatment been used to treat other types of cancers?

How Can I Find Out More About Clinical Trials That Might Be Right for Me?

The American Cancer Society offers a clinical trials matching service for patients, their family, and friends. You can reach this service at 1-800-303-5691 or on our Web site at http://clinicaltrials.cancer.org.

Based on the information you give about your cancer type, stage, and previous treatments, this service can put together a list of clinical trials that match your medical needs. The service will also ask where you live and whether you are willing to travel so that it can look for a treatment center that you can get to.

You can also get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll free at 1-800-4-CANCER (1-800-422-6237) or by visiting the NCI clinical trials Web site at www.cancer.gov/clinicaltrials.

For even more information on clinical trials, the American Cancer Society has a document called *Clinical Trials: What You Need to Know.* You can read this on the Web site, www.cancer.org, or have it sent to you by calling 1-800-ACS-2345.

Complementary and Alternative Therapies

When you have cancer you are likely to hear about ways to treat your cancer or relieve symptoms that are different from mainstream (standard) medical treatment. These methods can include vitamins, herbs, and special diets, or methods such as acupuncture or massage—among many others. You may have a lot of questions about these treatments. Here are some you may have thought of already:

- How do I know if a non-standard treatment is safe?
- How do I know if it works?
- Should I try one or more of these treatments?
- What does my doctor know/think about these methods? Should I tell the doctor that I'm thinking about trying them?
- Will these treatments cause a problem with my standard medical treatment?
- What is the difference between "complementary" and "alternative" methods?
- Where can I find out more about these treatments?

The Terms Can Be Confusing

Not everyone uses these terms the same way, so it can be confusing. The American Cancer Society uses *complementary* to refer to medicines or methods that are used *along with* your regular medical care. *Alternative* medicine is a treatment used *instead of* standard medical treatment.

Complementary Methods: Complementary treatment methods, for the most part, are not presented as cures for cancer. Most often they are used to help you feel better. Some methods that can be used in a complementary way are meditation to reduce stress, acupuncture to relieve pain or peppermint tea to relieve nausea. There are many others. Some of these methods are known to help, while others have not been tested. Some have been proven not be helpful. A few have even been found harmful. However, some of these methods may add to your comfort and well-being.

There are many complementary methods that you can safely use right along with your medical treatment to help relieve symptoms or side effects, to ease pain, and to help you enjoy life more. For example, some people find methods such as aromatherapy, massage therapy, meditation, or yoga to be useful.

Alternative Treatments: Alternative treatments are those that are used instead of standard medical care. These treatments have not been proven safe and effective in clinical trials.

Some of these methods may even be dangerous and some have life-threatening side effects. The biggest danger in most cases is that you may lose the chance to benefit from standard treatment. Delays or interruptions in your standard medical treatment may give the cancer more time to grow.

Deciding What to Do
It is easy to see why people with cancer may consider alternative methods. You want to do all you can to fight the cancer. Sometimes mainstream treatments such as chemotherapy can be hard to take, or they may no longer be working.

Sometimes people suggest that their method can cure your cancer without having serious side effects, and it's normal to want to believe them. But the truth is that most non-standard methods of treatment have not been tested and proven to be effective for treating cancer.

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

- Talk to your doctor or nurse about any method you are thinking about using.
- Check the list of "red flags" below.
- Contact the American Cancer Society at 1-800-ACS-2345 to learn more about complementary and alternative methods in general and to learn more about the specific methods you are thinking about.

Red Flags
You can use the questions below to spot treatments or methods to avoid. A "yes" answer to any one of these questions should raise a "red flag."

- Does the treatment promise a cure for all or most cancers?
- Are you told not to use standard medical treatment?
- Is the treatment or drug a "secret" that only certain people can give?
- Does the treatment require you to travel to another country?
- Do the promoters attack the medical or scientific community?

The Decision Is Yours
Decisions about how to treat or manage your cancer are always yours to make. If you are thinking about using a complementary or alternative method, be sure to learn about the method and talk to your doctor about it. With reliable information and the support of your health care team, you may be able to safely use the methods that can help you while avoiding those that could be harmful.

Treatment of Pancreatic Cancer by Stage

It is hard to stage pancreatic cancer accurately by imaging tests. Doctors must do their best to decide before surgery whether there is a good chance the cancer can be completely removed. Surgeons usually consider a pancreatic cancer *resectable* (completely removable by surgery) if it is staged as T1, T2, or T3. That means it doesn't extend far beyond the pancreas,

especially into nearby large blood vessels (T4). There is no accurate way to assess the lymph node spread of the tumor before or at the time of surgery.

Treatment of Resectable Cancer of the Pancreas

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

In most but not all cases, either chemotherapy alone or chemotherapy plus radiation therapy (chemoradiation) is used as well. This treatment may be given before or after surgery. Some centers favor giving it before surgery because the recovery after surgery is often long, which can delay or even prevent its use. But it is not yet clear whether this approach is better than giving it after surgery, or even not giving it at all. Many surgeons are concerned about preoperative therapy. They feel that patients may become weakened and are therefore less able to withstand the surgery.

Studies have shown that giving chemotherapy after surgery, especially gemcitabine, can delay the average time before cancer returns for at least several months. But it is not yet clear whether adding radiation to this treatment would result in more of a benefit.

Treatment of Locally Advanced Cancer of the Pancreas

Locally advanced cancers of the pancreas are those that have grown too far to be completely removed by surgery, but have not yet reached distant parts of the body. Several studies have shown that attempts to partially remove these cancers do not help patients to live longer. Therefore, surgery has a limited role in these cancers. It is used mainly to relieve bile duct blockage or to bypass a blocked intestine caused by the cancer pressing on other organs.

The standard treatment options for locally advanced cancers are chemotherapy with gemcitabine or the combination of radiation therapy and chemotherapy with gemcitabine. At some cancer centers, patients with locally unresectable disease receive chemotherapy and radiation together and are then re-evaluated to see if the cancer has shrunk enough to be completely removed by surgery. Sometimes, patients are able to have surgery at this point.

Treatment of Metastatic (Widespread) Cancer of the Pancreas

Because these cancers have spread through the lymphatic system or bloodstream, they cannot be removed by surgery. These cancers have also spread too far to be treated by radiation therapy alone. Even when imaging tests show that the spread is only to one area of the body, it has to be assumed that small groups of cancer cells (too small to be seen on imaging tests) are already present in other organs of the body.

Chemotherapy with gemcitabine is the standard treatment in this situation. Adding drugs such as capecitabine (Xeloda), oxaliplatin (Eloxatin), or erlotinib (Tarceva) to gemcitabine may improve the chance the tumors will shrink and may help people live slightly longer, although this is not yet clear. Adding other drugs such as irinotecan and 5-FU is also being

studied. So far, none of these drugs has been shown to significantly increase the lifespan of people with metastatic cancer of the pancreas. Some studies have shown, however, that people who get chemotherapy seem to have fewer symptoms related to their cancer.

Because the treatments now available are largely unsatisfactory, people may want to think about taking part in a clinical trial involving chemotherapy combinations (with or without radiation therapy) and new targeted therapies.

Treatment of Recurrent Cancer of the Pancreas
Treatment of cancer that returns after treatment is essentially the same as treatment of metastatic cancer, and is likely to include chemotherapy if the patient can tolerate it.

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

Palliative and Supportive Care

Helping people stay comfortable and maintaining a good quality of life for as long as possible are important goals in treating cancer of the pancreas. This is done through palliative care.

Nutrition
Along with possible bile duct blockage, people with cancer of the pancreas may lose their appetite and suffer weight loss and weakness. These symptoms may be caused by treatment or by the cancer itself. When possible, people are often advised to try to eat high-energy foods as well as supplements and enzymes to help in fat absorption and maintenance of weight. A nutritionist may be able to help with this. In some cases the doctors may put a feeding tube into the stomach to improve nutrition and energy levels. This is usually temporary.

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

There are proven ways to relieve pain from cancer of the pancreas. This can be done with a combination of medicines or in some cases, endoscopy or surgery. For example, cutting some

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

For more detailed information on pain and what can be done about it, see the American Cancer Society document, *Pain Control: A Guide for People With Cancer and Their Families.*

More Treatment Information

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

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

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

What Should You Ask Your Doctor About Cancer of the Pancreas?

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

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

- What should I do to be ready for treatment?

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

Other Things to Think About

How About Your Emotional Health?

During cancer treatment, you may find yourself overwhelmed by emotions. This happens to a lot of people. You may find that you think about the potential of your own death, or the effect of your cancer on your family, friends, and career. You may also begin to re-evaluate your relationship with your spouse or partner.

This is an ideal time to seek out emotional and social support. You need people you can turn to for strength and comfort. Support can come in many forms: family, friends, cancer support groups, church or spiritual groups, online support communities, or individual counselors.

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

The cancer journey can feel very lonely. It is not necessary or realistic to go it all by yourself. And your friends and family may feel shut out if you decide not include them. Let them in -- and let in anyone else who you feel may help. If you aren’t sure who can help, call your American Cancer Society at 1-800-ACS-2345 and we can put you in touch with an appropriate group or resource.

You can’t change the fact that you have cancer. What you can change is how you live the rest of your life -- making healthy choices and feeling as well as possible, physically and emotionally.

What Happens if Treatment Is No Longer Working?

If cancer continues to grow after one kind of treatment it is often possible to try another treatment plan that might still treat the cancer, or at least shrink the tumors enough to help you live longer and feel better. On the other hand, when a person has received several different medical treatments and the cancer has not been cured, over time the cancer tends to become resistant to all treatment. At this time it’s important to weigh the possible limited benefit of a new treatment against the possible downsides, including continued doctor visits and treatment side effects.

Everyone has his or her own way of looking at this. Some people may want to focus on remaining comfortable during their limited time left.

This is likely to be the most difficult time in your battle with cancer -- when you have tried everything medically within reason and it’s just not working anymore. Although your doctor may offer you new treatment, you need to consider that at some point, continuing treatment is not likely to improve your health or change your prognosis or survival.

If you want to continue treatment to fight your cancer as long as you can, you still need to consider the odds of more treatment having any benefit. In many cases, your doctor can estimate the response rate for the treatment you are considering. Some people are tempted to try more chemotherapy or radiation, for example, even when their doctors say that the odds of benefit are less than 1%. In this situation, you need to think about and understand your reasons for choosing this plan.

No matter what you decide to do, it is important that you be as comfortable as possible. Make sure you are asking for and getting treatment for any symptoms you might have, such as pain. This type of treatment is called "palliative" treatment.

Palliative treatment helps relieve these symptoms, but is not expected to cure the disease; its main purpose is to improve your quality of life. Sometimes, the treatments you get to control your symptoms are similar to the treatments used to treat cancer. For example, radiation therapy might be given to help relieve bone pain from bone metastasis. Or chemotherapy might be given to help shrink a tumor and keep it from causing a bowel obstruction. But this is not the same as receiving treatment to try to cure the cancer.

At some point, you may benefit from hospice care. Most of the time, this can be given at home. Your cancer may be causing symptoms or problems that need attention, and hospice focuses on your comfort. You should know that receiving hospice care doesn’t mean you can’t have treatment for the problems caused by your cancer or other health conditions. It just means that the focus of your care is on living life as fully as possible and feeling as well as you can at this difficult stage of your cancer.

Remember also that maintaining hope is important. Your hope for a cure may not be as bright, but there is still hope for good times with family and friends -- times that are filled with happiness and meaning. In a way, pausing at this time in your cancer treatment is an opportunity to refocus on the most important things in your life. This is the time to do some things you’ve always wanted to do and to stop doing the things you no longer want to do.

What's New in Pancreatic Cancer Research and Treatment?

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

Genetics and Early Detection

Scientists are learning more about some of the changes in DNA that cause cells in the pancreas to become cancerous. Inherited changes in genes such as BRCA2, p16, and the genes responsible for hereditary non-polyposis colorectal cancer (HNPCC) can increase a

person's risk of developing pancreatic cancer. Researchers are now looking at how these genes may be altered in cases of pancreatic cancer that do not seem to be inherited.

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

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

Treatment

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

Chemotherapy

Many clinical trials are in progress to test new combinations of chemotherapy drugs. Some studies are testing whether drugs known to be active against pancreatic cancer, such as gemcitabine and 5-FU, can be made better by combining them with each other or with other chemotherapy drugs, such as cisplatin, oxaliplatin, docetaxel, irinotecan, or pemetrexed. Other studies are testing the best ways to combine chemotherapy with radiation therapy or newer targeted therapies.

Targeted Therapies

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

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

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

with pancreatic cancer. Some early studies have found that the anti-angiogenesis drug bevacizumab (Avastin), which is already used in several other types of cancer, may have some benefit against pancreatic cancer when combined with gemcitabine. Larger studies are now under way to figure out how active this drug is. Several other anti-angiogenesis drugs are also being studied.

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

Immune Therapy
Immune therapies attempt to boost a person's immune system or give them ready-made components of an immune system to attack cancer cells. These treatments are not yet available for pancreatic cancer, although many are being studied.

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

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

Additional Resources

More Information From Your American Cancer Society

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

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

Pain Control: A Guide for People With Cancer and Their Families (also available in Spanish)

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

American Cancer Society's Guide to Pain Control
Cancer in the Family: Helping Children Cope With a Parent's Illness
Caregiving: A Step-By-Step Resource for Caring for the Person With Cancer at Home

National Organizations and Web Sites*

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

National Cancer Institute
Telephone: 1-800-4-CANCER (1-800-422-6237)
Internet Address: www.cancer.gov

Pancreatic Cancer Action Network
Telephone: 1-877-272-6226
Internet Address: www.pancan.org

Confronting Pancreatic Cancer
Pancreatica
Internet Addresses: www.pancreatica.org

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

Please call 1-800-ACS-2345 any time, any day you have questions or need help. The American Cancer Society has information, resources, and support available on any cancer-related topic.

References

American Cancer Society. *Cancer Facts & Figures 2008*. Atlanta, Ga: American Cancer Society; 2008.

American Joint Committee on Cancer. Exocrine Pancreas. *AJCC Cancer Staging Manual*. 6th ed. New York, NY: Springer; 2002:157-164.

Debrin JA. Carcinoma of the Pancreas In: Abeloff MD, Armitage JO, Lichter AS, Niederhuber JE. Kastan MB, McKenna WG, eds. *Clinical Oncology*. 3rd ed. Philadelphia, Pa: Elsevier; 2004: 2015-2034.

Freelove R, Walling AD. Pancreatic cancer: diagnosis and management. *Am Fam Physician.* 2006;73:485-92. Available at: www.aafp.org/afp/20060201/485.html.

National Cancer Institute. Physician Data Query (PDQ). Pancreatic Cancer: Treatment. 2006. Available at: www.cancer.gov/cancertopics/pdq/treatment/pancreatic/healthprofessional. Accessed January 16, 2007.

National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Pancreatic Adenocarcinoma. V.2.2006. Available at: www.nccn.org/professionals/physician_gls/PDF/pancreatic.pdf. Accessed January 16, 2007.

Wolff RA, Crane CH, Abbruzzese JL, Li D, Evans DB. Neoplasms of the exocrine pancreas. In: Kufe DW, Bast RC, Hait WN, Hong WK, Pollock RE, Weichselbaum RR, Holland JF, Frei E. *Cancer Medicine 7*. Hamilton, Ontario: BC Decker; 2006:1331-1358.

Yang GY, Wagner TD, Fuss M, et al. Multimodality approaches for pancreatic cancer. *CA Cancer J Clin*. 2005;55:352-367.

Yeo CJ, Yeo TP, Hruban RH, et al. Cancer of the pancreas. In: DeVita VT, Hellman S, Rosenberg SA, eds. *Cancer: Principles and Practice of Oncology*. 7th ed. Philadelphia, Pa: Lippincott Williams & Wilkins; 2005:945-986.

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