PANCREATIC CANCER

What Is Cancer?

Cancer is a group of many related diseases. All forms of cancer involve out-of-control growth and spread 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, normal cells of most tissues divide only to replace worn-out or dying cells and to repair injuries.

Cancer cells, however, continue to grow and divide, and can spread to other parts of the body. These cells accumulate and form *tumors* (lumps) that compress, invade, and destroy normal tissue. If cells break away from such a tumor, they can travel through the bloodstream, or the lymph system to other areas of the body. There, they may settle and form "colony" tumors. In their new location, the cancer cells continue growing. The spread of a tumor to a new site is called *metastasis.* When cancer spreads, though, it is still named after the part of the body where it started. For example, if prostate cancer spreads to the bones, it is still prostate cancer, and if breast cancer spreads to the lungs it is still called breast cancer.

Leukemia, a form of cancer, does not usually form a tumor. Instead, these cancer cells involve the blood and blood-forming organs (bone marrow, lymphatic system, and spleen), and circulate through other tissues where they can accumulate.

It is important to realize that not all tumors are cancerous. Benign tumors do not metastasize and, with very rare exceptions, are not life-threatening.

Cancer is classified by the part of the body in which it began, and by its appearance under a microscope. Different types of cancer vary in their rates of growth, patterns of spread, and responses to different types of treatment. That's why people with cancer need treatment that is aimed at their specific form of the disease.

In America, half of all men and one-third of all women will develop cancer during their lifetimes. Today, millions of people are living with cancer or have been cured of the disease. And the risk of developing most types of cancer can be reduced by changes in a person's lifestyle, for example, by quitting smoking or eating a better diet. The sooner a cancer is found, and the sooner treatment begins, the better a patient's chances are of a cure.

What Is Cancer Of The Pancreas?

The Normal Pancreas

The *pancreas* is a gland 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 six inches long but less than 2 inches wide, and extends horizontally across the abdomen. The *head* of the pancreas is located on the right side of the abdomen, behind the junction of the stomach and 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.

Think of the pancreas as two separate glands found inside the same organ: exocrine and endocrine. Exocrine glands release into ducts; endocrine glands release into the bloodstream. Over 95% of the cells in the pancreas form *exocrine glands* and *ducts.* The exocrine glands produce pancreatic juice, which contains *enzymes* that break down fats, proteins, and carbohydrates in the food you eat so the nutrients can be absorbed by the small intestine. The exocrine ducts carry this pancreatic juice to the *common bile duct* and eventually to the small intestine.

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 two hormones, *insulin* and *glucagon,* that are important in controlling the amount of sugar in the blood.

Types of Tumors of the Pancreas

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

Exocrine cells of the pancreas can form benign tumors, although these occur much less frequently than cancers. Most of these benign tumors are *cystadenomas.* About 95% of cancers of the exocrine pancreas are *adenocarcinomas.* These adenocarcinomas usually begin in the ducts of the pancreas, but sometimes may develop from the cells that actually produce the pancreatic enzymes (the acinar cells). Less common cancers of the exocrine pancreas include *adenosquamous carcinomas, squamous cell carcinomas,* and *giant cell carcinomas.* These types are distinguished from one another based on their appearance under the microscope. 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).

Tumors of the endocrine pancreas are much less common. 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 they produce. Islet cell tumors that produce insulin are known as *insulinomas,* and tumors that produce glucagon are called *glucagonomas.* Less often, islet cell tumors may produce other hormones. Most islet cell tumors are benign. Those that are malignant are called *islet cell cancers* or *islet cell carcinomas.*

It is very important to distinguish between exocrine and endocrine cancers of the pancreas. Each type of tumor has distinct risk factors and causes; produces different signs and symptoms; are

diagnosed using different tests, are treated in different ways, and have a different *prognosis* (outlook for survival). The remainder of this document refers only to exocrine cancers.

A special type of cancer that occurs where the bile duct and pancreatic duct empty into the duodenum is called *ampullary cancer* or *carcinoma of the ampulla of Vater*.

Because ampullary cancers develop so near the common bile duct, they often block the bile duct while they are still small and have not spread very far. Bile duct blockage prevents normal flow of bile from the liver to the intestines. This causes certain chemicals in bile to accumulate in the bloodstream, the skin, the eyes, and certain other tissues. This accumulation causes yellow coloration of the skin and eyes, and is known as jaundice.

This easily recognized sign alerts patients that something is wrong. This is why ampullary cancers are usually diagnosed at an earlier stage than most pancreatic cancers. And earlier diagnosis means that people with ampullary cancers usually have a better outlook for survival than people with pancreatic cancers.

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

What Are The Key Statistics About Cancer Of The Pancreas?

The American Cancer Society estimates that 29,200 Americans (14,200 men and 15,000 women) will be diagnosed with cancer of the pancreas during 2001. Over the past 20 years, the rate of pancreatic cancer has declined slightly in men. The rate among women has remained stable, but may also be beginning to decline.

An estimated 28,900 Americans (14,100 men and 14,800 women) will die of pancreatic cancer in 2001, making this type of cancer the fourth leading cause of cancer death in men and in women. Approximately 19% of patients with cancer of the exocrine pancreas survive at least one year after diagnosis. About 4% survive five years after diagnosis.

Only about 10% of cancers of the pancreas appear to be contained entirely within the pancreas at the time they are diagnosed. Attempts to remove the entire cancer by surgery may be successful in some of these patients. But, even when no spread beyond the pancreas is apparent at the time of surgery, a small number of cancer cells may already have spread to other parts of the body but have not formed tumors large enough to be detected in their new location. 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%.

The 5-year survival rate refers to the percentage of patients who live at least 5 years after their cancer is diagnosed. Many of these patients live much longer than 5 years after diagnosis, and 5-year rates are used to produce a standard way of discussing prognosis. Five-year *relative* survival rates exclude from the calculations patients dying of other diseases, and are considered to be a more accurate way to describe the prognosis for patients with a particular type and stage of cancer. Of course, 5-year survival rates are based on patients diagnosed and initially treated more

than 5 years ago. Improvements in treatment often result in a more favorable outlook for recently diagnosed patients.

What Are The Risk Factors For Cancer Of The Pancreas?

A *risk factor* is anything that increases a person's 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.

Researchers have identified several risk factors that increase a person's chance of developing cancer of the exocrine pancreas.

Age: The risk of developing cancer of the pancreas increases after the age of 50. Most patients are between 60 and 80 years old at the time of diagnosis.

Gender: Men are about 30% more likely to develop cancer of the pancreas than are women.

Cigarette smoking: The risk of developing pancreatic cancer is increased among smokers. About 30% of pancreatic cancer cases are thought to result directly from cigarette smoking.

Diet: A diet high in meats and fat increases pancreatic cancer risk. Fruits, vegetables, and dietary fiber appear to have a protective effect and reduce the risk of this cancer. Some older studies suggested that coffee and alcohol consumption might be a risk factor, but most recent studies have not confirmed this theory. Being obese (very overweight) is also a risk factor.

Diabetes mellitus: Pancreatic cancer is more common in people with this disease. The reason for this association is not known. Some doctors think the diabetes is a risk factor. Others feel that diabetes results if the cancer damages much of the normal pancreatic tissue.

Chronic pancreatitis: *Chronic pancreatitis* is a long-term inflammation of the pancreas. This condition is associated with an increased risk of pancreatic cancer. However, the majority of the patients with pancreatitis never develop cancer of the pancreas. Some recent studies suggest that the main reason for this association is that patients with pancreatitis are more likely to also have risk factors such as smoking. A minority of cases of chronic pancreatitis appear to be due to an inherited gene mutation. People with this familial form of chronic pancreatitis seem to have a very high lifetime risk for developing pancreatic cancer (about 40% to 75%).

Occupational Exposure: Heavy exposure to certain pesticides, certain dyes, and certain chemicals related to gasoline may increase the risk of developing cancer of the pancreas.

Family History: Cancer of the pancreas seems to run in some families. An inherited tendency to develop this cancer may be a factor in about 5% to 10% of cases. The inherited DNA changes that can increase a person's risk of developing cancer of the pancreas can also cause an increased risk for certain other cancers. Some of these DNA changes have been characterized by scientists and can be recognized by genetic testing. For more information on genetic testing, refer to the section Do We Know What Causes Cancer of the Pancreas?

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 identified several risk factors that can make a person more likely to develop this disease. And, recent research has shown that some of these risk factors affect the DNA of cells in the pancreas, resulting in abnormal growth and tumor formation.

Researchers have made great progress in understanding how certain changes in DNA can cause normal cells to become cancerous. DNA is the chemical that carries the instructions for nearly everything our cells do. We usually resemble our parents because they are the source of our DNA. However, DNA affects more than our outward appearance. Some *genes* (parts of our DNA) 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 appropriate time are called *tumor suppressor genes.* It is known that 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 breast, colon, or kidney cancer or leukemia. In some of these, there is also an increased risk of developing cancer of the pancreas. Researchers have characterized many of these DNA changes in the past few years.

For example, 5% to 10% of breast cancer cases are hereditary and result from mutations (changes) of the BRCA1 and BRCA2 genes. Normally, these genes help to prevent cancer by making proteins that keep cells from growing abnormally. However, if a person has inherited a mutated gene from either parent, this cancer-preventing protein is less effective, and chances of developing breast cancer increase. About 50%-60% of women with inherited BRCA1 or BRCA2 mutations will develop breast cancer by the age of 70. Women with these inherited mutations also have a high risk for developing cancer of the ovary. Recent studies have found that men and women with BRCA2 mutations have a risk of developing cancer of the pancreas that is 10 to 20 times higher than the risk for the general population. One recent study found that about 7% of people with cancer of the pancreas had an inherited BRCA2 gene mutation. Some people with cancer of the pancreas who have close relatives with breast cancer or ovarian cancer may have a BRCA2 mutation. These people might consider family genetic counseling, to help determine whether any of their relatives also have an increased risk of developing breast, ovarian, or pancreatic cancer. In some cases, genetic testing is an option to consider. A genetic test analyzes DNA from a blood sample to see if a person has a mutation of a certain gene, such as the BRCA2 gene. If a mutated BRCA2 gene is found, a person can take special precautions to monitor for early signs of breast cancer or ovarian cancer.

People with inherited changes in the *familial adenomatous polyposis* gene are almost certain to develop colon cancer (unless their colon is removed first). Ampullary cancer is also common in these patients, although not nearly as common as colon cancer.

Neurofibromatosis is another condition caused by genetic changes that are often inherited. People with this condition develop multiple benign nerve tumors and some have malignant nerve tumors. They are also at increased risk for developing ampullary cancer.

Mutations of another gene, known as the p16 gene, have recently been found in some people with an inherited risk for developing atypical moles and *malignant melanoma* (a type of skin cancer). People with p16 mutations may also have a slightly increased risk of developing cancer of the pancreas.

There are several other inherited gene abnormalities known to increase a person's risk of developing colorectal cancer, kidney cancer, or brain tumors, which also increase their risk for developing pancreatic cancer.

In some families, an increased pancreatic cancer risk is associated with a tendency to have chronic pancreatitis (inflammation of the pancreas). Recently, researchers have discovered that the cause of familial chronic pancreatitis is a mutation of the *cationic trypsinogen* gene.

Cationic trypsinogen is a digestive enzyme produced in the pancreas and released into pancreatic juice. Mutation of this gene results in production of an abnormal form of the enzyme that is too active. Instead of digesting food in the intestines, this abnormal enzyme becomes activated while it is still in the pancreas, where it causes damage and inflammation.

About 3% to 5% of pancreatic cancers are thought to result from inherited factors that are not yet completely understood, and are presumed to be transmitted by genes that have not yet been discovered. Because familial pancreatic cancer is often associated with other cancers, determining whether a patient's relatives are at increased risk is not simple. Consultation with a genetic counselor or an oncologist with experience in hereditary cancer syndromes is often helpful.

The American Cancer Society strongly recommends that any person considering genetic testing speak with a genetic counselor, nurse or doctor qualified to interpret and explain these test results before they proceed with testing. It is very important for people to understand and carefully weigh the benefits and risks of genetic testing before these tests are done. Testing is expensive, and is not covered by some health plans. There is concern that people with abnormal genetic test results will not be able to get insurance, or coverage may only be available at a much higher cost.

In addition, a high risk of developing pancreatic cancer seems to be passed along in some families, without increasing their risk of developing any other cancers. So far, no genetic tests are available for finding mutations of these genes.

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

Doctors still do not know why most pancreatic cancers develop in people who have no apparent risk factors. Researchers have recently developed new tests that can detect certain DNA abnormalities that predict a particularly poor prognosis. These tests might be used in the future to identify patients who are likely to respond to certain kinds of treatment. Also, researchers are just beginning to evaluate *gene therapy* as treatment for cancer of the pancreas. This approach attempts to replace abnormal DNA responsible for causing cells to behave in a malignant way. By devising replacement strategies or inserting normal DNA into cancer cells it is thought that cancer cells can be turned back into cells that grow in a normal way and are no longer able to spread abnormally. Additional 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 this is possible.

Cigarette smoking is the most significant and most avoidable risk factor for cancer of the pancreas. It is responsible for 30% of pancreatic cancers. Tobacco use also increases the risk of developing cancers of the lung, mouth, larynx, esophagus, kidney, bladder and some other organs. If you smoke, please call the American Cancer Society for information that can help you quit.

The American Cancer Society recommends eating at least five servings of fruits and vegetables every day and six servings of other foods from plant sources such as breads, cereals, grain products, rice, pasta, or beans. Eat fewer high-fat foods such as those from animal sources. Following these recommendations may lower a person's risk of developing cancer of the pancreas, as well as several other cancers and some noncancerous diseases.

Can Cancer Of The Pancreas Be Found Early?

The main reason for the poor *prognosis* (outlook for survival) of 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 examinations. There are currently no blood tests or other screening tests that can accurately detect early cancers of the pancreas.

A substance called *CA 19-9* is present in the cells of cancers of the pancreas. It is also released into the blood by these cells and can be detected by blood tests. However, by the time blood levels are high enough to be consistently detected by available methods, the cancer is no longer in its early stages. This test is sometimes used after treatment of the pancreas to see if the tumor has *recurred* (come back). But, it is not recommended for routine screening of people without symptoms or a known diagnosis of cancer.

Another important reason why most pancreatic cancers are found at an advanced stage is that patients usually have no symptoms until the cancer has reached a large size or spread to other organs.

Signs and Symptoms of Cancer of the Pancreas

Jaundice: About half of all people with pancreatic cancer develop *jaundice.* Jaundice is a yellow discoloration of the eyes and skin due to accumulation of *bilirubin* (a substance produced in the liver) in these tissues and in the blood. Bilirubin may accumulate in the blood because of a liver disease that interferes with release of this chemical into bile. Or, it may be caused by a blockage of the common bile duct that prevents the bile from reaching the intestines. Cancers that begin in the head of the pancreas near the common bile duct may compress the bile duct, causing jaundice, which may serve as an early warning signal of disease. On the other hand, cancers that begin in the body or tail of the pancreas will not compress the common bile duct until they have almost spread throughout the entire pancreas. By this time, spread beyond the pancreas has almost certainly taken place. Accumulation of bilirubin in the skin may cause itching. When bilirubin levels in the blood increase, more of this substance is excreted into the urine, causing a tan or brown color. It is important to remember that other causes of jaundice such as hepatitis or obstruction of the common bile duct by a gallstone, are much more common than cancer of the pancreas.

Abdominal pain: Abdominal pain is a common sign of advanced cancer of the pancreas. Cancer that has spread to the nerves surrounding the pancreas may cause severe pain in the middle to upper back area. Pain may also be felt in the front of the abdomen. It may be constant or may come and go. Of course, many noncancerous diseases as well as several other types of cancers can cause abdominal or back pain that can be confused with cancer of the pancreas.

Weight loss: Unintended or unexpected weight loss that has continued over a period of months is common among patients with cancer of the pancreas. This may be associated with loss of appetite and severe tiredness.

Digestive problems: If the cancer blocks the release of the pancreatic juice into the intestine, the patient may have problems with digesting fatty foods. Incomplete fat digestion 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, causing partial blockage. This will cause nausea, vomiting, and pain that tend to be worse after eating.

Gallbladder enlargement: Sometimes bile duct obstruction causes bile to accumulate in the gallbladder, which becomes enlarged. This enlargement can sometimes be felt by the examining physician and can also be detected by imaging studies.

Blood clots or fatty tissue abnormalities: Rarely, substances released by pancreatic cancer cells may cause formation of blood clots in veins, or certain abnormalities of the fatty tissue underneath the skin.

Diabetes mellitus: Rarely, exocrine cancers of the pancreas cause *diabetes mellitus* (high blood sugar). More commonly, there are subtle problems with *sugar metabolism* that do not cause symptoms of diabetes but can still be recognized by certain blood tests.

How Is Cancer Of The Pancreas Diagnosed?

If one or more of the signs and symptoms described in Can Cancer of the Pancreas Be Found Early? is present, certain examinations and tests may be done to find out if they are caused by pancreatic cancer or by some other disease.

History and Physical Examination

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

A thorough physical examination will focus mostly on the abdomen to check for any masses or fluid accumulation. The skin and the white part of the eyes will be checked for *jaundice* (yellow discoloration). Sometimes, cancer of the pancreas spreads to lymph nodes or the liver, producing an enlargement that can be felt beneath the skin surface. The cancer can also spread to lymph nodes above the collarbone and several other locations. These will be examined carefully to look for swelling that might indicate spread of a cancer.

Imaging Tests

Computed tomography (CT, CAT): CT scans are a type of x-ray procedure that produces a detailed cross-sectional image of the body. Multiple images are taken as an x-ray beam rotates around the body. A computer combines these images to produce a detailed cross-sectional image that is useful in identifying many types of pancreatic tumors. Injection of *contrast material* into a vein before CT scanning can help produce clearer images that better differentiate pancreatic tumors from one another and from normal tissue of the pancreas.

CT scanning is one of the most useful tests for finding a mass inside the pancreas. It is also useful in checking whether or not a cancer has spread to organs and tissues beyond the pancreas.

Ultrasonography (ultrasound or US): Ultrasonography uses sound waves to produce images of internal organs such as the pancreas. A *transducer* emits sound waves and detects the echoes bounced off internal organs. The pattern of echoes is processed by a computer to produce images. The echoes produced by most pancreatic tumors differ from those of normal pancreas tissue. And, different echo patterns can help distinguish some types of benign and malignant pancreatic tumors from one another.

If signs and symptoms indicate that a cancer of the pancreas is likely, a CT scan is generally more useful for an accurate diagnosis than ultrasonography. However, if it is not clear whether certain other diseases such as a *pseudocyst* (fluid accumulation in the pancreas) may account for the patient's signs or symptoms, ultrasonography may be done.

Magnetic resonance imaging (MRI): An MRI scan uses radiowaves and strong magnets instead of x-rays. Tissues of the body absorb energy from the radiowaves. The energy is then released in a pattern affected by the type of tissue and by certain diseases. A computer then translates the pattern of radiowaves given off by tissues into a very detailed image of parts of the body. MRI provides more detailed images than CT and US, and is utilized to determine if major blood vessels located near the pancreas are compressed or invaded by the cancer.

Endoscopic retrograde cholangiopancreatography (ERCP): In this procedure, a long flexible tube is passed down the patient's throat, through the esophagus and stomach, and into the first part of the small intestine. The doctor performing 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. The doctor can then guide the tube into the common bile duct. A small amount of harmless dye 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 as part of this procedure. 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 place a small brush through the tube into an area of narrowing and use the brush to remove cells for examination under a microscope to see whether they appear malignant or not.

Angiography: This is an x-ray procedure for examining blood vessels. *Contrast material* is injected into an artery to outline the blood vessels. Angiography can show distortion or displacement of vessels by a tumor, or growth of any abnormal vessels in the area of the tumor. This test is also useful in finding out if a pancreatic cancer has grown through the walls of certain blood vessels. Its main use is in helping doctors decide if it is possible to completely remove a cancer of the pancreas from the particular patient.

Blood Tests

Certain blood tests are useful in determining whether a patient's jaundice is due to diseases of the liver or to blockage (by a gallstone, a tumor, or other disease) of bile flow between the liver and the small intestine. Other blood tests are useful in evaluating the patient's general state of health to determine whether or not they will be able to withstand the stress of a major surgical operation. Also, blood levels of the tumor markers CA 19-9 and/or by carcinoembryonic antigen (CEA) may be elevated.

Biopsy

Although the patient's history, physical examination, and imaging test results may strongly suggest cancer of the pancreas, the only way to confirm this diagnosis is by removing a sample of tumor for examination under the microscope. A procedure to remove a tissue sample is called a *biopsy.* There are several types of biopsy procedures. The procedure used most often to diagnose cancer of the pancreas is called a *fine needle aspiration biopsy (FNA).* For this test, a doctor inserts a thin needle through the skin and into the pancreas. The doctors use CT scanning images or, less often, ultrasonography to view the position of the needle and make sure that it is in the tumor. Small fragments of tissue can be removed through the needle for examination under

the microscope. The main advantages of the test is that the patient does not require *general anesthesia* (is not "asleep" during the test) and there are almost never any significant side effects.

In the past, surgical biopsies were performed more commonly. This type of biopsy requires a *laparotomy* (an operation in which the surgeon makes an incision through the skin into the wall of the abdomen so that internal organs can be examined). Areas that look or feel abnormal to the surgeon can be sampled by removing a small portion of tissue with a scalpel or through 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. The main disadvantage 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. Most doctors specializing in treatment of pancreatic cancer try to avoid surgery unless imaging tests indicate a chance that an operation might be able to completely remove all of the cancer. Even with thorough evaluation by imaging tests, there are times when the surgeon will begin an operation with the intention of completely removing the cancer but, during surgery, will find evidence that it has spread too far beyond the pancreas to be completely removed. In these cases, a sample of the cancer is taken only to confirm the diagnosis, and the rest of the planned operation is discontinued.

How Is Cancer Of The Pancreas Staged?

In *staging* pancreatic cancer, the physician uses imaging tests to find out how widespread the cancer is. The stage of a pancreas cancer is the most important factor in deciding treatment options.

One system that is used to describe the stages of cancers of the pancreas is the *American Joint Committee on Cancer (AJCC) TNM system.* ***T*** stands for tumor (its size and how far it has spread within the pancreas and to nearby organs). ***N*** stands for spread to lymph nodes (bean-sized collections of immune system cells that help fight infections and cancers). ***M*** is for *metastasis* (spread to distant organs).

T Categories of Cancer of the Pancreas

T1: The cancer has not spread beyond the pancreas and is smaller than 2 cm (about ¾ inch).

T2: The cancer has not spread beyond the pancreas but is larger than 2 cm (about ¾ inch).

T3: The cancer has spread from the pancreas to the *duodenum* (first part of the small intestine next to the pancreas), or the bile duct, or other tissues directly around the pancreas.

T4: The cancer has extended further beyond the pancreas into the stomach, spleen, colon, or nearby large blood vessels.

N Categories of Cancer of the Pancreas

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

N1: Cancer has spread to regional lymph nodes.

M Categories of Cancer of the Pancreas

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 patient's cancer of the pancreas have been determined, this information is combined in order to assign a stage that is expressed in Roman numerals I through IV. The process of assigning a stage number based on TNM stages is called *stage grouping*.

Stage I: T1 or T2, N0, M0
Stage II: T3, N0, M0
Stage III: T1 or T2 or T3, N1, M0
Stage IVA: T4, any N, M0
Stage IVB: Any T, any N, M1

For example, cancer that has extended beyond the pancreas into the spleen and part of the colon (T4) but has not spread to lymph nodes (N0) or distant organs (N0) can be considered a stage IVA cancer. A cancer that has spread to the tissues immediately around the pancreas (T3) as well as to nearby lymph nodes (N1) but has not involved distant organs (M0) is defined as a stage III cancer.

Although some doctors use the TNM staging system, this system has some limitations. For example, it doesn't account for whether the cancer has invaded blood vessels. Many surgeons feel that if the cancer has invaded blood vessels around the pancreas, the cancer can't be completely removed. These surgeons would prefer a staging system that would be more relevant for them in making treatment decisions. This simpler system classifies cancer of the pancreas as either resectable, locally advanced, or metastatic.

Resectable: The surgeon is able to remove all the tumor nodules large enough to be seen.

Locally advanced: There is too much cancer spread to tissues around the pancreas or into blood vessels to permit complete removal, although the cancer has not yet spread to distant organs. These are considered *unresectable*.

Metastatic: Spread to distant organs has been identified.

The TNM stage is more precise, however, and is often used to determine the extent of disease that remains after surgery.

How Is Cancer Of The Pancreas Treated?

The three main types of treatment for cancer of the pancreas are surgery, radiation therapy, and chemotherapy. Depending on the stage of the cancer, two or even all of these types of treatment may be combined at the same time or after one another.

Surgery

There are two general types of surgical treatments used for cancer of the pancreas.

Potentially curative surgery is used when imaging studies indicate a high likelihood that the surgeon will be able to remove all of the cancer that is visible during the operation.

Palliative surgery may be performed if imaging studies indicate that the tumor is too widespread to be completely removed, to relieve symptoms or prevent certain complications such as blockage of the bile ducts due to compression by the cancer.

Several studies have shown that surgery does not prolong survival of patients with *unresectable* (unable to be completely removed) cancer of the pancreas. Pancreatic cancer surgery has significant side effects and may require several weeks for recovery. Because many patients with unresectable cancer of the pancreas survive less than six months after diagnosis, doctors should avoid suggesting treatments that require a significant fraction of this time for recovery unless there is clear evidence that such treatments will improve the patient's chance for survival or quality of life.

Potentially curative surgery: There are three procedures used to remove tumors of the pancreas:

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, but it is rarely used for cancers of the exocrine pancreas.

Total pancreatectomy: This operation removes the entire pancreas and the spleen. It is sometimes used to treat exocrine cancers of the pancreas.

Pancreaticoduodenectomy (*Whipple procedure)* The most commonly used operation for attempting to completely remove a cancer of the exocrine pancreas is a pancreaticoduodenectomy . This operation removes the head of pancreas and sometimes removes the body of the pancreas as well. It also removes part of the stomach, the entire *duodenum* (first part of the small intestine), a small part of the *jejunum* (second part of the small intestine), and lymph nodes near the pancreas. 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 operation is difficult for surgeons to perform successfully and requires much skill and experience. Because the pancreas releases enzymes in

its pancreatic juice that can digest tissue, leakage of pancreatic juice after surgery can cause the pancreas to begin digesting itself and nearby tissues. When this operation is performed in cancer centers by surgeons experienced in the procedure, approximately 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 10% of patients may die as a result of surgical complications. It cannot be emphasized too strongly that for patients to have the most successful outcomes, they must be treated by a surgeon who has performed many of these operations and at a hospital that has had a large experience with pancreatic surgery. There is no substitute for experience.

Palliative procedures: When imaging studies indicate that a pancreatic cancer has spread too far to be completely removed by surgery, the doctors will focus on palliative treatments (intended to relieve or prevent symptoms).

Cancers growing in the head of the pancreas can cause blockage of the common bile duct as it passes through this part of the pancreas. This obstruction may cause pain, may cause digestive problems due to lack of bile reaching the intestine, and often causes accumulation of certain bile-related chemicals in the bloodstream. There are two options for relieving bile duct blockage. One is an operation that reroutes the flow of bile from the common bile duct directly into the small intestine without the need to pass through the head of the pancreas. This operation requires an incision in the abdomen and it may take weeks to recover from it completely. One advantage is that during this procedure, the surgeon may be able to cut the nerves leading to the pancreas. This will reduce or eliminate any pain that may be caused by the cancer.

Another part of the palliative operation that can be performed is to reroute the stomach connection around the duodenum (the first part of the small intestine). Often, late in the course of pancreatic cancer, the duodenum becomes blocked by cancer. This will cause pain and vomiting that requires surgery. Bypassing the duodenum when the other palliative procedure is done can often avoid a second operation.

A second approach is placement of a *stent* (tube) through an endoscope. In this procedure a doctor views the bile duct through a long lighted tube placed down the patient's throat, through the esophagus, through the stomach, and into the small intestine. The doctor can then insert a small length of tubing (the stent) through the endoscope. This tube 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 replaced.

In general, a surgical operation to relieve bile obstruction is considered when the cancer is too widespread to be completely removed by surgery but is still localized enough that the patient has a life expectancy longer than six months. If the cancer is more widespread and the life expectancy is shorter than six months, endoscopic stent placement is recommended. Also, if the patient is in a weakened condition, stent placement is preferred.

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 precisely focusing the radiation on the cancer from a machine outside the body. This type of radiation therapy is similar to having a diagnostic x-ray, except that each treatment lasts longer, and the patient usually receives five treatments per week over a period of weeks or months. Patients may receive *preoperative* (before surgery) treatment or *postoperative* (after surgery) treatment. If surgery is planned, preoperative treatment is often preferred. Postoperative treatment is often delayed for several weeks while the patient recovers from surgery (treatment right after surgery can interfere with wound healing). This delay may give the cancer an opportunity to continue growing. Radiation therapy, often combined with chemotherapy (chemoradiation), may be used for patients whose tumors are too widespread to be removed by surgery.
Intraoperative electron beam radiation therapy is a new approach to treating patients with cancers of the pancreas that is being studied at some cancer centers. With this treatment, external beam radiation therapy using *electrons* (a type of high-energy particle) is delivered from a machine in the operating room, while the operation is in progress. The advantage to this approach is that the doctors can move nearby organs aside temporarily and deliver a large dose of radiation to the pancreas without doing much damage to other organs in the area.

Side effects of radiation therapy may include mild skin changes resembling sunburn or suntan, nausea, vomiting, diarrhea, and fatigue. Often these go away after a short while. Radiation may make the side effects of chemotherapy worse. Talk with your doctor about these side effects since there are ways to relieve them.

Chemotherapy

Systemic chemotherapy uses anticancer drugs that are 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.

Until recently, fluorouracil (5-FU) was the chemotherapy drug most often used in treating cancer of the pancreas. Recent studies have found *gemcitabine* to be more effective than 5-FU in treating metastatic cancer of the pancreas. Studies comparing the effectiveness of these two drugs in treating resectable and locally advanced cancers are currently in progress. Other studies in progress are attempting to improve the effectiveness of chemotherapy by combining gemcitabine and 5-FU with each other or with other chemotherapy drugs. Other drugs that are used include cisplatin and streptozotocin.

Chemotherapy drugs kill cancer cells but also damage some normal cells. Therefore, careful attention must be given to avoiding or minimizing side effects, which depend on the type of drugs, the amount taken, and the length of treatment. Temporary side effects might include nausea and vomiting, loss of appetite, loss of hair, and mouth sores. Because chemotherapy can damage the blood-producing cells of the bone marrow, patients may have low blood cell counts. This can increase the chance of infection (due to a shortage of white blood cells), bleeding or bruising after minor cuts or injuries (due to a shortage of blood platelets), and fatigue (due to a shortage of red blood cells).

Most side effects disappear once treatment is stopped. There are remedies for many of the temporary side effects of chemotherapy. For example, *antiemetic* drugs to prevent or reduce nausea and vomiting can be given.

Hormone Therapy

Both estrogens and androgens may affect the growth of pancreatic tissue. There have been some reports of occasional success in treating pancreatic cancer with tamoxifen, a hormonal therapy drug commonly used for women with breast cancer. There hasn't been any overall benefit for most people, however. Other hormones that are produced by the stomach and intestines may also affect the growth of pancreatic cancer. Treatments designed to block these hormones are currently being studied.

Complementary and Alternative Methods

If you are considering any unproven alternative or complementary method of treatment, it is best to discuss this openly with your cancer care team and request information from the American Cancer Society or the National Cancer Institute. Some unproven treatments can interfere with standard medical treatments or may cause serious side effects.

Clinical Trials

Studies of promising new or experimental treatments in patients are known as clinical trials. A clinical trial is only done when there is some reason to believe that the treatment being studied may be of value to the patient. Treatments used in clinical trials are often found to have real benefits. There are three phases of clinical trials in which a treatment is studied before the treatment is eligible for approval by the FDA (Food and Drug Administration).

The purpose of a Phase I study is to find the best way to give a new treatment and how much of it can be given safely. Physicians watch patients carefully for any harmful side effects. The research treatment has been well tested in laboratory and animal studies, but the side effects in patients are not completely predictable.

Phase II trials determine the effectiveness of a research treatment after safety has been evaluated in a Phase I trial. Patients are closely observed for an anticancer effect by careful measurement of cancer sites present at the beginning of the trial. In addition to monitoring patients for response, any side effects are carefully recorded and assessed.

Phase III trials require entry of large numbers of patients. Some trials enroll thousands of patients. One of the groups may receive standard (the most accepted) treatment, so the new treatments can be directly compared. The group that receives the standard treatment is called the "control group." For example, one group of patients (the control group) may receive the standard chemotherapy for a certain type of cancer, while another patient group may receive a different type of chemotherapy, which may or may not contain an investigational drug, to see if this

improves survival. All patients in Phase III trials are monitored closely for side effects, and treatment is discontinued if the side effects are too severe.

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

- Is the treatment likely to be helpful?
- Does this new type of treatment work?
- Does it work better than other treatments already available?
- What side effects does the treatment cause?
- Do the benefits outweigh the risks, including side effects?
- In which patients is the treatment most likely to be helpful?

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 discover. While most side effects will disappear in time, some can be permanent or even life-threatening. Keep in mind that even standard treatments have side effects. Depending on many factors, a patient may decide that a clinical trial will be beneficial.

Enrollment in any clinical trial is completely up to you. Your doctors and nurses will explain the study to you in detail and will give you a form to read and sign indicating your desire to take part. This process is known as giving your *informed consent.* Even after 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 the study does not prevent you from getting other medical care you may need.

If you want to find out more about clinical trials, ask your cancer care team. Among the questions you should ask are:

- What is the purpose of the study?
- What kinds of tests and treatments does the study involve?
- What does this treatment do?
- What is likely to happen in my case with, or without, this new research treatment?
- What are my other choices and their advantages and disadvantages?
- 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 be hospitalized? 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?

You can get a list of current clinical trials by calling the National Cancer Institute's Cancer Information Service toll free at 1-800-4-CANCER or visiting the NCI clinical trials website for patients (cancertrials.nci.nih.gov) or healthcare professionals (cancernet.nci.nih.gov/prot/protsrch.shtml).

Treatment of Pancreatic Cancer by Stage

As noted earlier, many doctors feel that the designations of resectable, locally advanced, or metastatic are more helpful than the TNM tumor stage (I, II, III, or IV) in selecting treatment options.

Treatment of resectable cancer of the pancreas: If imaging studies indicate a reasonable chance of completely removing the cancer by surgery, surgery should be used since this represents the only opportunity to cure this disease. Depending on the location of cancer, either a total pancreatectomy or a pancreaticoduodenectomy will usually be used. In most but not all cases, the patient will receive radiation therapy and chemotherapy (usually with fluorouracil) as well. The combination of chemotherapy and radiation therapy is often called *chemoradiation*. This treatment may be given before or after surgery. Treatment with electron beam radiation therapy during surgery *(intraoperative radiation therapy)* is being evaluated at certain cancer centers.

The average survival time for patients with resectable cancer of the exocrine pancreas treated by surgery and chemoradiation is about 15 to 20 months.

Treatment of locally advanced cancer of the pancreas: Locally advanced cancers of the pancreas are those which have spread too far to be completely removed by surgery. Several studies have shown that attempts to partially remove these cancers do not help the patients to live longer. The role of surgery in these cases is to relieve bile duct blockage due to compression by cancer.

The standard treatment option for locally advanced cancers are chemotherapy with gemcitabine or the combination of radiation therapy and chemotherapy with 5-FU and/or gemcitabine. At some institutions, patients with locally unresectable disease receive chemotherapy and radiation together and are then reevaluated to see if the cancer has shrunk enough to be completely removed by surgery. Some patients can undergo curative surgery after the chemotherapy and radiation. In one study of patients who were treated this way, those with locally advanced disease actually had a longer survival than patients who had resectable cancer treated first by surgery followed by chemotherapy and/or radiation.

Treatment of metastatic (widespread) cancer of the pancreas: Because these cancers have spread through the lymphatic system or bloodstream, it is not possible to remove all the cancer by surgery. These cancers have also spread too far to be successfully treated by radiation therapy. Even when metastasis to only one area of the body is noted on imaging studies, it is assumed that small groups of cancer cells (too small to be seen on imaging studies) are already present in many organs of the body. For this reason, systemic chemotherapy with gemcitabine or 5-FU is the standard treatment strategy for these patients. Participation in clinical trials of new chemotherapy combinations (with or without radiation therapy) and new biological therapies should be considered. Many other drugs have also been used. These include Adriamycin, etoposide, and streptozotocin. In general, none of these drugs have been able to increase the lifespan of patients with metastatic cancer of the pancreas. Some studies have shown, however,

that after patients with pancreatic cancer receive chemotherapy drugs, they have fewer symptoms.

For patients with metastatic cancer of the pancreas who have common bile duct blockage, placement of an endoscopic stent to relieve blockage is generally recommended. Whenever possible, doctors avoid any surgical treatment that will require a significant amount of recovery time in the hospital.

The average survival time following diagnosis of patients with metastatic cancer of the pancreas is in the range of 3 to 7 months.

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 is often successful with a 5- year survival rate of 30 to 50 percent. More advanced ampullary cancers are treated like pancreatic cancer. In many patients, ampullary cancer cannot be distinguished from pancreatic cancer until resection has been done.

Treatment of recurrent cancer of the pancreas: Treatment of recurrent cancer of the pancreas is essentially the same as treatment of metastatic cancer.

Palliative and Supportive Care

Treatment of bile duct blockage has already been discussed in this section. The other common problem for these patients is *anorexia* (loss of appetite), weight loss, and weakness. These symptoms are due in part to side effects of treatments and the effects of the cancer on metabolism. Dietary recommendations that include high-energy supplements may be helpful. In some cases, temporary placement of a feeding tube into the stomach can improve the patient's nutrition and energy levels.

Pain is a significant concern for patients with cancer of the pancreas. Growth of the cancer around certain nerves may cause severe pain. However, there are proven ways to relieve pain associated with cancer of the pancreas using a combination of medications and, in some cases, surgical procedures. Cutting some of the nerves that carry pain sensation or injecting concentrated alcohol into these nerves can provide relief. Often, if the cancer is being removed surgically, these nerves will be cut during the same operation.

It is important that patients not hesitate to take advantage of these treatments. For this reason, patients must tell their doctors if they have pain. Otherwise the doctor can't help. For most patients, treatment with morphine or other so-called *opioids* (medications related to opium) will reduce the pain considerably. For the treatment to be effective, the pain medicines must be given regularly on a schedule, not just when the pain becomes severe. Several long-acting forms of morphine and other long-acting opioid drugs have been developed that need only be given once or twice a day.

What Should You Ask Your Doctor About Cancer Of The Pancreas?

As noted earlier, it is important to have frank, open discussions with your cancer care team. They want to answer all of your questions, no matter how trivial 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 and what does that mean in my case?
- What treatment choices do I have?
- What do you recommend and why?
- What risks or side effects are there to the treatments you suggest?
- What are the chances of recurrence of my cancer with these treatment plans?
- What should I do to be ready for treatment?
- If the doctor recommends surgery, how many surgical procedures has he/she done for pancreatic cancer?
- How experienced is the hospital in treating people with this cancer?
- Should I be referred to a cancer center for treatment?
- Based on what you've learned about my cancer, how long do you think I'll survive?

In addition to these sample questions, be sure to write down some of your own. For instance, you might want more information about recovery times so you can plan your work schedule. Or, you may want to ask about second opinions or about clinical trials for which you may qualify.

What Happens After Treatment For Cancer Of The Pancreas?

During and after treatment for pancreatic cancer you may be able to improve your quality of life by taking an active role. Learn about the benefits and disadvantages of each of your treatment options, and ask questions of your cancer care team if there is anything you do not understand. Learn about and look out for side effects of treatment, and report these promptly to your cancer care team so that they can take steps to minimize them and shorten their duration.

Remember that your body is as unique as your personality and your fingerprints. Although understanding your cancer's stage and your treatment options can help predict what health problems you may face, no one can say precisely how you will respond to cancer or its treatment.

You may have special strengths such as a history of excellent nutrition and physical activity, a strong family support system, or a deep faith, and these strengths may make a difference in how you respond to cancer. In fact, behavioral scientists have recently found that some people who took advantage of a social support system, such as a cancer support group, survived with a better quality of life. There are also professionals with experience in mental health services, social work services, and pastoral services who may help you cope with your illness.

If you are in treatment for cancer, be aware of the battle that is going on in your body. Radiation therapy and chemotherapy add to the fatigue caused by the disease itself. Give your body all the rest it needs so that you will feel better as time goes on. When your health care team says it's ok, resume your usual activities. Ask if your cancer or its treatments might limit your participation in an exercise program or in other physical activities.

A cancer diagnosis and its treatment are major life challenges, with an impact on you and everyone who cares for you. Before you get to the point where you feel overwhelmed, consider attending a meeting of a local support group. If you need individual assistance in other ways, contact your hospital's social service department or the American Cancer Society for information about counselors or other services.

Follow-up Care: After the initial course of treatments is completed, it is very important to continue with all scheduled follow-up appointments. During these appointments, your doctors will ask questions about any symptoms, do physical examinations, and order blood tests or imaging studies to check for cancer recurrence, further spread of cancer, or side effects of certain treatments.

Usually, the earlier that recurrences and certain side effects of treatment are detected, the more effectively they can be treated. Patients should never hesitate to tell their doctors or other members of their health care team about any symptoms or side effects that concern them. There are effective treatments for pain associated with cancer and for many of the side effects of cancer treatment.

What's New In Pancreatic Cancer Research And Treatment?

Research into the causes, diagnosis, and treatment of cancer of the exocrine pancreas is currently underway 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 *familial adenomatous polyposis* and *hereditary nonpolyposis colon cancer* can increase a person's risk of developing pancreatic cancer, and have an even greater impact on risk of developing cancers of other organs such as the breast, ovaries, or colon.

Familial pancreatic cancer, on the other hand, primarily affects the pancreas. In families with this condition, about half of the children of an affected patient will inherit the abnormal gene. Among people with the abnormal gene, the risk of developing pancreatic cancer is very high, probably about 50%. The gene (or genes) responsible for this condition have not yet been found so it is not yet possible to predict which members of an affected family are most at risk for pancreatic cancer.

Recent research suggests that two imaging tests, *endoscopic ultrasound* (EUS) and *endoscopic retrograde cholangiopancreatography* (ERCP), used together, can help can find precancerous changes called *dysplasia* among members of high-risk families. Endoscopic ultrasound uses sound waves to produce images of the pancreatic ducts. For ERCP, a contrast dye is injected into the pancreatic ducts before x-rays are taken. Both tests also use *endoscopy* (a lighted tube is passed down the throat to reach the part of the intestine next to the pancreas).

If results of these tests are suspicious, *prophylactic pancreatectomy* (preventive removal of the pancreas) may be considered as an option. This operation has serious side effects, including diabetes, problems with digestion, and the risk of surgical complications. However, pancreatic cancer is so rarely curable that among people with precancerous changes likely to develop into cancer, the benefit of this operation often outweighs the risks.

Researchers are also studying tests for detecting *acquired* (not inherited) genetic changes in pancreatic cancer and pancreatic ductal dysplasia (precancerous changes in pancreatic duct cells). 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, EUS, ERCP, and tests for K-ras changes are an option for people with a very strong family history of pancreatic cancer, but are not recommended for widespread testing of people at average risk who do not have any symptoms.

Gene therapy: Because abnormal genes that encourage tumor growth have been found in many pancreatic cancers, scientists are working to find ways to replace these genes with normal ones. The most widely studied gene in cancer is p53. This gene, when normal, acts to suppress tumor

growth. In many cancers, including pancreatic cancers, the p53 gene has been transformed into an inactive state. Some gene therapies aim to restore the p53 gene of pancreatic cancer cells. Most p53 gene therapy experiments use viruses carrying the normal version of the p53 gene to infect the cancer cells. Clinical trials have begun for many different cancers, including pancreatic cancer.

Immunology: Experimental treatments that boost the patient's immune reaction to fight pancreatic cancer more effectively are being tested in clinical trials.

Some treatments use drugs that boost the immune system in general, for example, interferons and interleukins.

In active immunotherapy, the patient is given a vaccine that should cause the immune system to recognize some of the abnormal chemicals in pancreatic cancer cells and kill these cells. For example, the K-*ras* gene product is altered in over 80% of pancreatic cancers and researchers are testing ways to help the patient's immune system attack cells that have an altered ras protein.

Passive immunotherapy injects antibodies made in the laboratory into patients to seek out pancreatic cancer cells that contain abnormal ras protein or other abnormal proteins like *carcinoembryonic antigen* (CEA). Toxins or radioactive atoms can be attached to these antibodies, so that the cell-killing chemicals or radiation are targeted specifically to the cancer cells and do not attack the healthy cells of the body.

Chemotherapy: Many clinical trials are in progress to test new combinations of chemotherapy drugs. Some studies are testing whether the effectiveness of drugs known to be active against pancreatic cancer, such as gemcitabine and fluorouracil can be improved by combining them with each other or with other chemotherapy drugs, such as cisplatin, mitomycin, leucovorin, dipyridamole, and doxorubicin. Other studies are testing the best ways to combine chemotherapy with radiation therapy or immunotherapy.

Gut hormone therapy: Intestinal cells release hormones that stimulate the growth of pancreatic cells. Drugs that block these hormones are being tested in clinical trials. One such drug is called octreotide. This drug blocks the action of a hormone called somatostatin. Other potential hormones that may affect pancreatic cancer growth include CCK, secretin and bombesin.

Anti-angiogenesis factors: All cancers depend on the growth or development of new vessels to nourish their growth. Blood vessel growth factors called angiogenesis factors have been discovered and purified. To block the growth of these vessels and thereby starve the tumor, scientists have developed *anti-angiogenesis* drugs. These are in clinical trials and may be used in patients with pancreatic cancer.

Additional Resources

National Organizations and Web Sites

The following organizations can also provide additional information and resources: *

National Cancer Institute
Telephone 1-800-4-CANCER or 800-422-6237
Internet Addresses: www.nci.nih.gov and cancernet.nci.nih.gov

National Coalition for Cancer Survivorship
Telephone: 1-888-650-9127
Internet Address: www.cansearch.org

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

Additional American Cancer Society Information

Murphy, Gerald P., Lois B. Morris, and Dianne Lange. *Informed Decisions: The Complete Book of Cancer Diagnosis, Treatment, and Recovery.* Viking, 1997. (Book; Code #9449)

Caregiving: A Step-By-Step Resource for Caring for the Person with Cancer at Home (Book; Code#9422)

Caring for the Patient with Cancer at Home: A Guide for Patients and Families (Booklet; Code#4656)

Other Publications*

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

Capossela, Cappy, Warnock, Sheila. *Share the Care: How to Organize a Group for Someone Who Is Seriously Ill.* New York: Simon and Schuster. 1995.

Dollinger, Malin, Ernest H. Rosenbaum, and Greg Cable. *Everyone's Guide to Cancer Therapy.* Somerville House Books, 1994.

Morra, Marion and Eve Potts. *Choices.* Avon Books, 1994.

A Cancer Survivor's Almanac: Charting Your Journey. Edited by Barbara Hoffman, JD. National Coalition for Cancer Survivorship. Chronimed Publishing, 1996.

References

American Cancer Society. *Cancer Facts and Figures 2001.* Atlanta, Ga: American Cancer Society; 2001.

Evans DB, Abbruzzese JL, Rich TA. Cancer of the pancreas. In: DeVita VT, Hellman S, Rosenberg SA, eds. *Cancer: Principles and Practice of Oncology*. Philadelphia, Pa: Lippincott-Raven; 1997: 1054-1087.

Evans DB, Wolff RA. Neoplasms of the ampulla of vater. In: Bast RC, Kufe DW, Pollock RE, Weischselbaum RR, Holland JF, Frei E, eds. *Cancer Medicine.* Hamilton, Ontario: BC Decker Inc.: 2000: 1431-1435.

Finch MD, Howes N, Ellis I, Mountford R, Sutton R, Raraty M, et al. Hereditary pancreatitis and familial pancreatic cancer. *Digestion.* 1997; 58: 564-569.

Kern, SE. Advances from genetic clues in pancreatic cancer. *Current Opinion in Oncology.* 1998; 10: 74-80.

Lillemoe KD, Yeo CJ, Cameron JL. Pancreatic cancer: State-of-the-art care. CA Cancer J Clin 2000; 50:241-268.

PDQ database. Pancreatic Cancer. Bethesda, Md: National Cancer Institute; 2000. Available at cancernet.nci.nih.gov/Cancer_Types/Pancreatic_Cancer.shtml

Tempero, M. NCCN Practice guidelines for pancreatic cancer. *Oncology.* 1997; 11: 41-55.

Williams, SR. Pancreatic cancer. In: Djulbegovic B, Sullivan DM, eds. *Decision Making in Oncology.* New York, NY: Churchill Livingstone; 1997: 187-191.

Wolff RA, Abbruzzese JL, Evans DB. Neoplasms of the exocrine pancreas. In: Bast RC, Kufe DW, Pollock RE, Weischselbaum RR, Holland JF, Frei E, eds. *Cancer Medicine.* Hamilton, Ontario: BC Decker Inc.: 2000: 1436-1464.

Revised: 10/16/2000