



ANAL 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 often travel to other parts of the body where they begin to grow and replace normal tissue. This process, called *metastasis*, occurs as the cancer cells get into the bloodstream or lymph vessels of our body. When cells from a cancer like breast cancer spread to another organ like the liver, the cancer is still called breast cancer, not liver cancer.

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. Scientists still do not understand what damages person's DNA becomes damaged and leads to cancer.

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.

Remember that not all tumors are cancerous. *Benign* (noncancerous) tumors do not spread to other parts of the body (metastasize) 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 aimed at their particular kind cancer.

Cancer is the second leading cause of death in the United States. Half of all men and one-third of all women in the US 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 Anal Cancer?

Anal cancer is cancer that grows in the anus. The anus is the end of the large intestine that opens to allow the passage of *feces* (stool) during a bowel movement. Other parts of the large bowel include the *colon* (the longest part of large intestine) and the *rectum* (the lower part of the large intestine that stores feces before it passes through the anus). The anus is about an inch and a half long.

The anus is a complex structure. Part of it is outside the body and part of it is inside. The anus contains several types of tissue and each of these tissues contains several types of cells. The two main types are the outer part, which is basically an extension of your skin and the inner part that connects to the rectum, which is glandular. Different cancers can develop in each part. The differences are important, because they determine the seriousness of the cancer and the type of treatment needed.

The skin on the outside of the anus is like skin elsewhere covering the body. This skin is sometimes called perianal skin ("peri-" means "near"). The *epithelium* (surface layer) of this skin contains flat cells known as *squamous cells*.

The lower part of the anus, from the outside area to just inside the body, is known as the *anal margin*. The margin includes the anal opening, called the *sphincter*. The sphincter contains two rings of muscle that help control the release of feces and gas.

Beyond the anal margin, deeper inside the body, is the *anal canal*. The canal is about 1½ inches long. Most of the anal canal is also lined by squamous epithelium. The epithelium also contains occasional melanocytes (cells that produce a brown pigment called melanin). Glands and ducts (tubes leading from the glands) are found under the epithelium. These glands produce a lubricating fluid called *mucus*.

At the upper end of the anal canal, at the boundary between the canal and the rectum, is a ring of tissue about one-third of an inch wide called the *transitional zone*. The epithelium here contains a mixture of squamous cells, cylinder-shaped cells called *columnar cells* (because under the microscope they resemble columns), and *transitional cells*. Transitional cells contain a mix of the features of squamous and columnar cells.

Many types of tumors can develop in the anus. Some of these tumors are *benign* (noncancerous). Others are cancerous, which means they can penetrate into surrounding tissues and spread to other parts of the body. There are also some growths that start off benign but can develop into cancer. These are known as precancerous conditions. This section discusses all of these types of abnormal growths.

Benign Anal Tumors

Polyps: Polyps are small, bumpy or mushroom-like growths that develop in the epithelium or just under it. There are several kinds, depending on their cause and location.

- *Inflammatory polyps* arise because of inflammation from injury or infection.
- *Lymphoid polyps* develop in lymph tissue (part of the immune system). Small nodules of lymph tissue are normally present under the anal epithelium.
- *Skin tags* are benign growths of connective tissue that are covered by a layer of squamous epithelium. Skin tags are also called *fibroepithelial polyps*.

Condylomas: Condylomas (also called warts) are growths resulting from infection by a human papillomavirus (HPV).

Adnexal tumors: Adnexal tumors are usually benign growths that start in hair follicles or sweat glands of the

skin. These tumors stay in the perianal skin area and do not grow into the anal region.

In rare cases, benign tumors can grow in the various other tissues located underneath the mucous membrane of the anus. These include:

Leiomyomas: Leiomyomas develop from smooth muscle tissue.

Granular cell tumors: Granular cell tumors are composed of cells that contain lots of granules. Under a microscope, these granules look like tiny spots that fill the cells. Scientists have not yet discovered exactly what type of tissue these tumors start growing in.

Hemangiomas: Hemangiomas develop from the lining cells of blood vessels.

Lipomas: Lipomas are tumors that start from fat cells.

Schwannomas: Schwannomas develop from cells of the protective sheath that covers nerves.

Precancerous Anal Conditions

Sometimes abnormal changes of the anal epithelium are harmless in their early stages but may later develop into a cancer. A general term for these precancerous conditions of epithelium is *dysplasia*. Some warts, for example, contain areas of dysplasia and can develop into cancer. Dysplasia occurring in the anus is also known as *anal intraepithelial neoplasia* or *AIN*. Most doctors feel that AIN will often develop into cancer

Malignant Anal Tumors

Squamous cell carcinomas: Squamous cell carcinomas are the most common type of anal cancer. They account for most anal cancers. These tumors come from squamous cells of the epithelium that lines the anal margin and most of the anal canal. In its earliest stage, squamous cell carcinoma is known as *carcinoma in situ*, (pronounced "in SY-too") meaning cancer in its original site, usually abbreviated as CIS. Another name for this condition is *Bowen's disease*. The cancerous cells of CIS are limited to the epithelium and have not spread into any other tissues. Cells of *invasive squamous cell carcinomas* have already spread beyond the epithelium and are therefore no longer considered in situ.

Cloacogenic carcinomas: This is a subclass of the squamous cell cancers. Approximately 25% to 33% of anal tumors develop in the transitional zone. Another word for this zone is the *cloaca*. Some tumors that form here are known as *cloacogenic carcinomas*.

Adenocarcinomas: A small number of anal cancers are known as *adenocarcinomas*. (The prefix "adeno-" means gland.) Adenocarcinomas can develop in glands located under the anal epithelium that release their secretions into the anal canal. They can also arise in *apocrine glands* (a type of sweat gland of the perianal skin). Paget's disease is a type of apocrine gland carcinoma that spreads through the surface layer of the skin. Paget's disease can affect skin anywhere in the body but most often affects skin of the perianal area, vulva, and the breasts. This condition should not be confused with Paget's disease of the bone, an entirely different disease also named after Dr. James Paget.

Basal cell carcinomas: Basal cell carcinomas are a type of skin cancer that can develop from the perianal skin. These tumors account for only a small percentage of anal cancers. They are much more common in areas of skin that are exposed to sun, such as the face and hands.

Malignant melanoma: This cancer develops from cells in the skin or anal epithelium that produce the brown

pigment called melanin. About 1% to 2% of anal cancers are melanomas. Melanomas are far more common on parts of the body that are exposed to sun. If melanomas are found at an early stage, before they have invaded deeply into the skin or spread to lymph nodes, the outlook for long-term survival is excellent. As more people learn to recognize melanomas, more of these cancers are being found at an early stage by patients who examine their own skin. Most anal melanomas are found at a late stage because they are hard to see. If you would like more information on melanoma skin cancer, see the American Cancer Society document, "Melanoma Skin Cancer."

What Are the Key Statistics about Anal Cancer?

Anal cancer is fairly rare. The American Cancer Society estimates that in 2004 about 4,010 new cases of anal cancer will be diagnosed in the United States. However, the number of new anal cancer cases diagnosed each year is increasing.

The disease affects women somewhat more often than men. Of the 4,010 new cases, 2,120 will occur in women and 1,890 in men. Women are more likely to have cancers in the inner part of the anus (the anal canal), while anal tumors in men tend to develop on the outside of the anus. In recent years, the rate of anal cancer among men, particularly homosexual men, has increased.

Anal cancer can be a serious condition. An estimated 580 people (370 women and 210 men) will die of anal cancer in 2004. But treatment for anal cancer is very effective and most patients with this cancer will be cured.

What Are the Risk Factors for Anal Cancer?

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, exposing skin to strong sunlight is a risk factor for skin cancer. Smoking is a risk factor for cancers of the lung, mouth, larynx, bladder, kidney, and several other organs. But having a risk factor, or even several, does not mean that a person will get the disease

Human papillomavirus: Most doctors feel that squamous cell anal cancer is caused by the human papillomavirus (HPV), the same virus thought to be responsible for cervical cancer. There are several types of the virus but the one most likely to cause this cancer is called HPV-16. This virus is most often transmitted by sexual contact. It is more likely to be found in people who have many sex partners.

Smoking: Smoking also increases the risk of anal cancer. Current smokers are about 8 times more likely to have cancer of the anus compared with people who do not smoke. People who used to smoke but have quit are twice as likely to develop this cancer compared with people who have never smoked. Thus, quitting smoking can help reduce the risk.

Fistulas: People with certain medical conditions are also at higher risk of anal cancer. Long-term problems in the anal area, such as *fistulas* (abnormal openings), can increase the chances of developing the disease.

Lowered immunity: Higher rates of the disease occur among people with reduced immunity, such as organ transplant patients who must take medications that suppress their immune system. Another important risk factor is infection with the human immunodeficiency virus (HIV), the virus that causes AIDS. This is especially important in men who have sex with men. HIV can be transmitted by rectal intercourse.

Age: Age is a risk factor. Most cases of the disease are diagnosed in people between the ages of 50 and 80.

The rate of anal cancer is highest in those over age 85.

Do We Know What Causes Anal Cancer?

The exact cause of most anal cancer is not known. However, scientists have found that the disease is associated with a number of other conditions, some of which are described in the section on risk factors. A great deal of research is now underway to learn more about the causes of anal cancer.

It is important to remember that some patients with anal cancers do not have any known risk factors and the causes of their cancers are not known.

There is good evidence that the human papillomavirus (HPV) causes many squamous cell anal carcinomas and transitional cell (cloacogenic) anal carcinomas. But, the role of this virus in causing anal adenocarcinomas is less certain. More than 100 types of HPV have been found by scientists. The type known as HPV-16 is often found in anal squamous cell carcinoma and is also found in some anal warts. HPV-6 and HPV-11 cause most cases of anal warts. Warts containing HPV-6 or HPV-11 are much less likely to become cancerous than those containing HPV-16.

Research has recently shown that HPV produces proteins called E6 and E7 that can inactivate two important tumor suppressor proteins in normal cells. These two proteins, p53 and Rb, help suppress cell growth. When they are inactive, cells can grow out of control.

HIV, the virus that causes AIDS, weakens the body's immune system. The immune system of patients with kidney, heart, liver, or other organ transplants is purposely weakened by medication to prevent rejection of their new organs. When the body is less able to fight off infections, viruses such as HPV may become more active and thus trigger the development of anal cancer.

Most people know that smoking is the main cause of lung cancer. But few realize that the cancer-causing chemicals in tobacco smoke are absorbed by the lungs and can spread through the bloodstream to the rest of the body. Several studies have noted an increased rate of anal cancer in smokers, and the effect of smoking is especially important in people with other anal cancer risk factors. Smoking also lowers immunity, which may add to the increased risk of this disease among smokers.

Can Anal Cancer Be Prevented?

As noted in the previous section, the cause of many cases of anal cancer is unknown. Since some people with anal cancer have no known risk factors, it is not possible to completely prevent this disease.

The best way to reduce your risk of anal cancer is to avoid sexual practices that carry a high risk of HPV infection (particularly in the anal area) and HIV infection. This means not having unprotected sex, especially anal sex.

Infection with HPV increases the risk of developing anal cancer. Until recently, it was thought that the use of condoms ("rubbers") could prevent infection with HPV. But recent research shows that condoms do not offer total protection. This is because you can pass HPV from person to person by skin-to-skin contact with any HPV-infected area of the body, such as skin of the genital or anal area not covered by the condom. The absence of visible warts cannot be used to decide whether caution is warranted, since HPV can be passed on to another person even when there are no visible warts or other symptoms. HPV can be present for years with no symptoms. For these reasons, it can be very difficult or impossible to know whether a person with whom you

might have sex is infected with HPV. It is still very important, though, to use condoms to protect against AIDS and other sexual diseases that are passed on through body fluids.

If you stop smoking you will also lower your risk of anal cancer, as well as many other cancers.

Sometimes there is nothing a person can do about certain diseases that affect their immune system. For many patients, a weakened immune system is an unavoidable side effect of treatment for some other disease.

Can Anal Cancer Be Found Early?

Many cases of anal cancer can be found early in the course of the disease. Anal cancers develop in a part of the digestive tract that your doctor can see and reach. Many early anal cancers have symptoms that should make you see your doctor. Unfortunately, some anal cancers may not cause symptoms until they reach an advanced stage, and others may cause symptoms that appear to be due to a disease other than cancer.

A digital rectal exam (DRE) will find some cases of anal carcinoma early. The ACS suggests this be performed annually on all men over 50 to look for prostate cancer (because the prostate gland is next to the rectum). The DRE is done routinely as part of a pelvic exam on women. In this exam, the doctor inserts a gloved, lubricated finger into the anus to feel for unusual lumps or growths. If you are at high risk for anal cancer ask your doctor if additional or more frequent examinations are needed.

The odds that anal cancer can be found early are influenced by the location and type of the cancer. Cancers that begin deeper in the anal canal are less likely to be found early. Melanomas tend to spread earlier than other cancers.

Recently doctors have tested people at high risk for sexually transmitted disease for anal intraepithelial neoplasia. The test is carried out much like a Pap smear for cervical cancer. The anal lining is swabbed and cells that come off on the swab are examined under the microscope. Some doctors have advocated doing this routinely on people at high risk for anal cancer, particularly HIV positive men who have sex with men.

How Is Anal Cancer Diagnosed?

Anal cancer is relatively easy to diagnose because it is located in a very accessible site. Although some cases of anal cancer in people at high risk for that disease are diagnosed by screening tests, such as the digital rectal exam and/or anal cytology as mentioned above, most people are diagnosed after their cancer starts to cause symptoms.

Signs and Symptoms of Anal Cancer

Some cases of anal cancer cause no symptoms at all. Bleeding occurs in more than half of patients and is usually the first sign of the disease. Often the bleeding is minor. At first, most people assume that hemorrhoids are the cause of their bleeding.

Other common symptoms of anal cancer include:

- Pain in the anal area
- Straining during a bowel movement
- Anal itching
- Change in bowel habits such as more frequent or less frequent movements
- Change in the diameter of stool
- Abnormal discharge from the anus

- Swollen lymph nodes in the anal or groin areas

There are a number of benign conditions, such as hemorrhoids or anal warts, that can produce similar symptoms. In about 65% of anal cancers, benign anal conditions are present also. Many people who have minor symptoms, such as itching, try to treat the problem themselves using over-the-counter products. These medications will not do anything to treat anal cancer. If you have any of these signs or symptoms, discuss them with your doctor without delay. Remember, the sooner you receive a correct diagnosis, the sooner you can start treatment and the more effective your treatment will be.

Procedures Used to Diagnose Anal Cancer

Sometimes your doctor will detect anal cancer during a routine physical exam or during a minor procedure, such as removing a hemorrhoid. Treatment of cancers found in this way is often very effective, because the tumors are found early in the course of the disease.

The digital rectal exam often reveals the presence of an unusual growth. However, since doctors cannot see what they feel, other steps are needed if you have symptoms or if your doctor suspects you have anal cancer.

Among the procedures used in diagnosing anal cancer are:

- Anoscopy -- use of a special device to view the anus
- Proctoscopy -- use of a lighted scope to view inside the anal canal
- Transrectal ultrasound -- use of a device that is inserted into the rectum and produces sound waves. Echoes of these sound waves are detected and analyzed by a computer to create an image of the anus and nearby tissues. Ultrasound helps your doctor see how far an anal cancer may have penetrated and whether it has spread to nearby organs or tissues.

Your doctor also may ask you to have an exam using a sigmoidoscope or a colonoscope. These instruments allow the doctor to see inside the colon and look for abnormal growths, bleeding, or other signs of disease.

If a suspicious growth is found, your doctor will want to do a biopsy. In this procedure, a small piece of the tissue is cut out and sent to a laboratory. There, a *pathologist* (a doctor specializing in laboratory diagnosis of diseases) looks at the tissue under a microscope. If cancer cells are present, the pathologist sends back a report describing the cell type and extent of the cancer. Usually, a biopsy causes only slight discomfort and you will not have to stay in the hospital. However, if you have pain or muscle spasms during the exam, an anesthetic can be given.

If the tumor is very small and has not grown below the surface of the anus into other tissues, your doctor may attempt to remove the entire tumor during the biopsy.

There is a risk that anal cancers, like other forms of cancer, can spread through the lymphatic system. *Lymph nodes* are bean-sized collections of immune system cells. Swollen lymph nodes are sometimes a sign of spreading cancer but are most often a reaction to infections. To distinguish between these two causes, your doctor may use a thin needle to withdraw a small sample of fluid and tissue fragments from the lymph node. The lab will study this fluid to look for the presence of cancerous cells. This procedure is called a *fine needle aspiration biopsy*. In some cases, an operation to remove the lymph nodes may be done.

Imaging Studies

If cancer is found, you will need to have certain tests to determine the *stage* (extent) of the disease.

Ultrasound: A transrectal ultrasound can show how far the cancer has invaded nearby tissues. Ultrasound

uses sound waves and their echoes to produce a picture of internal organs or masses. A small microphone-like instrument called a *transducer* emits sound waves. These high-frequency sound waves are transmitted into the area of the body being studied and echoed back. The sound wave echoes are picked up by the transducer and converted by a computer into an image that is displayed on a computer screen.

Normally, ultrasound is a very easy procedure to have. It uses no radiation, which is why it is frequently used to look at developing fetuses. With *endorectal ultrasound*, the transducer is inserted directly into the rectum and this can be uncomfortable.

Computed tomography (CT): The CT scan is an x-ray procedure that produces detailed cross-sectional images of your body. Instead of taking one picture, as does a conventional x-ray, a CT scanner takes many pictures as it rotates around you. A computer then combines these pictures into an image of a slice of your body. The machine will take pictures of multiple slices of the part of your body that is being studied. This test can help tell if your anal cancer has spread into your liver or other organs. Often after the first set of pictures is taken you will receive an intravenous injection of a "dye" or *radiocontrast agent* that helps better outline structures in your body. A second set of pictures is then taken.

CT scans can also be used to precisely guide a biopsy needle into a suspected metastasis. For this procedure, called a *CT-guided needle biopsy*, the patient remains on the CT scanning table, while a radiologist advances a biopsy needle toward the location of the mass. CT scans are repeated until the doctors are confident that the needle is within the mass. A fine needle biopsy sample (tiny fragment of tissue) or a core needle biopsy sample (a thin cylinder of tissue about ½ inch long and less than 1/8 inch in diameter) is removed and examined under a microscope.

CT scans are more tedious than regular x-rays because they take longer and you usually need to lie still on a table for 15 to 30 minutes while they are being done. But just like other computerized devices, they are getting faster and your stay might be pleasantly short. Also, you might feel a bit confined by the equipment you lie within when the pictures are being taken.

You will need an IV (intravenous) line through which the contrast "dye" is injected. The injection can also cause some flushing. Some people are allergic and get hives or rarely more serious reactions like trouble breathing and low blood pressure. Be sure to tell the doctor if you have ever had a reaction to any contrast material used for x-rays. You may be asked to drink 1 to 2 pints of a contrast solution. This helps outline the intestine so that it is not mistaken for tumors.

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

MRI scans are very helpful in looking at the brain and spinal cord. MRI scans are a little more uncomfortable than CT scans. First, they take longer -- often up to an hour. Also, you have to be placed inside tube-like equipment, which is confining and can upset people with claustrophobia. The machine also makes a thumping noise that you may find disturbing. Some places will provide headphones with music to block this out.

Chest x-ray: This test may be done to determine whether anal cancer has spread to the lungs.

Positron emission tomography: Positron emission tomography (PET) uses *glucose* (a form of sugar) that contains a radioactive atom. A special camera can detect the radioactivity. Cancer cells of the body absorb high

amounts of the radioactive sugar, because of their high rate of metabolism. PET is useful when your doctor thinks the cancer has spread, but doesn't know where. PET scans can be used instead of several different x-rays because it scans your whole body.

How Is Anal Cancer Staged?

Staging, the process of finding out how far the cancer has spread, is very important because your treatment options and the outlook for your recovery and survival depend on the stage of your cancer. If you have anal cancer, ask your cancer care team to explain the staging in a way that you understand. Knowing all you can about staging lets you take a more active role in making informed decisions about your treatment.

Staging of anal cancer uses a system created by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC). Many of these skin tumors can be treated by surgery. In contrast, most cancers of the anal canal call for treatment with surgery, radiation, or chemotherapy, or some combination of these. The staging description that follows applies only to anal canal tumors.

The TNM System

The TNM system for staging contains three key pieces of information:

- T describes the size of the primary tumor, measured in centimeters (cm), and whether the cancer has spread to organs next to the tumor
- N describes the extent of metastasis (spread) to regional (nearby) lymph nodes
- M indicates whether the cancer has metastasized (spread) to other organs of the body

Additional letters or numbers 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 "i and s" mean "carcinoma in situ," which means the tumor is contained within the layer of anal tissue in which it first developed (the epithelium) and has not yet penetrated to a deeper layer of tissue

The possible values for T are:

- TX: Primary tumor cannot be assessed
- T0: No evidence of primary tumor
- Tis: Carcinoma in situ
- T1: The tumor is 2.0 cm (about 4/5 inch) or smaller
- T2: Tumor is larger than 2.0 but smaller than 5.0 cm (2 inches)
- T3: Tumor is larger than 5 cm
- T4: Tumor of any size that invades nearby organ(s), such as the vagina, urethra (the tube that carries urine out of the bladder), or bladder.

The possible values for N are:

- NX: Regional lymph nodes cannot be assessed
- N0: No regional lymph node metastasis
- N1: Metastasis to lymph nodes near the rectum
- N2: Metastasis to lymph nodes on one side of the groin and/or pelvis
- N3: Metastasis to lymph nodes near the rectum and in the pelvis or groin, or on both sides of the groin or pelvis

The M values are:

- MX: Presence of distant metastasis cannot be assessed

- M0: No distant metastasis
- M1: Distant metastasis is present, in the liver, other internal organs, or lymph nodes of the abdomen

Using the TNM system, a doctor will use each letter (T, N, and M) and a corresponding number. For example, an anal cancer could be T2, N0, M0.

To make this information somewhat clearer, several of these TNM descriptions can be grouped together into a simpler set of stages, labeled stage 0 through stage IV.

Stage 0 (carcinoma in situ): Tis, N0, M0: Stage 0 is very early cancer that exists only in the top layer of anal tissue (epithelium).

Stage I: T1, N0, M0: The cancer has spread beyond the top layer of anal tissue but is less than 2 cm (about 4/5 inch) in size.

Stage II: T2 or 3, N0, M0: The cancer is larger than 2 cm, but it has not spread to nearby organs or lymph nodes.

Stage IIIA: T1, 2, or 3, N1, M0 or T4, N0, M0: The cancer can be any size and has spread to the lymph nodes around the rectum or it has grown into nearby organs such as the vagina or the bladder but not spread to lymph nodes.

Stage IIIB: T4, N1, M0, Any T, N2 or 3, M0: The cancer has grown into nearby organs such as the vagina or the bladder and has spread to lymph nodes around the rectum or it can be of any size but has spread to lymph nodes in one groin or lymph nodes in both groins or lymph nodes in one groin and around the rectum.

Stage IV: Any T, Any N, M1: Cancer can be any size and may or may not have spread to lymph nodes but has spread to organs in other parts of the body.

Recurrent: Recurrent anal cancer means that the cancer has come back (recurred) after treatment in either the anus or in another part of the body.

Five-year survival by stage

Because this is an uncommon cancer, statistics on survival can only be approximate. They depend on reporting from institutions that only see a small number of patients.

For Stage I cancers, the 5-year survival is estimated at 90% to 95%. For stage II, it is 70% to 80%. For Stage III it is about 40% to 50% and about 10% for stage IV.

The 5-year survival rate refers to the percentage of patients who live *at least* 5 years after their cancer is diagnosed. Although many of these patients live much longer than 5 years after diagnosis, 5-year rates are used to produce a standard way of discussing prognosis. Of course, 5-year survival rates are based on patients diagnosed and initially treated more than 5 years ago. Recent improvements in treatment often result in a more favorable outlook for recently diagnosed patients.

How Is Anal Cancer Treated?

No matter what cell type or stage of anal cancer you have, treatment is available. The choice of treatment you receive depends on many factors. The location, type, and the stage (extent of spread) of the tumor are very important. In creating your treatment plan, you and your cancer care team will also take your age, general state

of health, personal preferences, and social circumstances into account.

The 3 main methods of treatment for anal cancer are surgery, radiation therapy, and chemotherapy. Often the best approach uses 2 or more of these strategies. Your recovery is the goal of your cancer care team. If a cure is not possible, the goal may be to remove or destroy as much of the cancer as possible and to prevent the tumor from growing, spreading, or returning for as long as possible. Sometimes treatment is aimed at relieving symptoms, such as pain or bleeding, even if a cure will not result. Another important goal is to treat the anal cancer without affecting your ability to control the passage of feces.

Surgery

Studies show that when surgery is the appropriate option, half of patients with anal cancer enjoy long-term survival. The kind of surgery used depends on the type and location of the tumor.

Local resection: One surgical procedure for anal cancer is called a *local resection*. This operation removes only the tumor, plus a small margin of noncancerous tissue around the tumor. Local resection is used if the cancer has not spread to nearby tissues or lymph nodes. In most cases, local resection preserves the sphincter (the muscular ring that opens and closes the anus). If the sphincter is saved, then after the operation you will be able to move your bowels the same way you did before. Most tumors that develop in the anal margin (the lower part of the anus) can be treated with local resection.

Abdominoperineal resection: The other surgical method is a more extensive operation known as an *abdominoperineal resection* (APR). The term means that the surgeon opens the body through the abdomen and through the perineum (the space between the anus and the sex organs) and removes the anus and part of the rectum. The surgeon may also take out some of the lymph nodes during this operation, although this step (called a lymph node dissection) can also be done later. Although this surgery was commonly done in the past for cancers of the anal canal, it can often be avoided by treating the patient with combined radiation and chemotherapy, instead.

The APR procedure does not preserve the anal sphincter. As a result, you will need to have a permanent opening made in your abdomen so that feces can exit the body. This opening is called a *colostomy*. Feces passes through the opening into a collection bag attached to the body. If you would like more information on colostomies, ask for the American Cancer Society publication, *Colostomy: A Guide*.

Radiation Therapy

Radiation therapy uses a beam of high-energy rays (or particles) to destroy cancer cells or slow their rate of growth. Sometimes doctors give radiation to shrink a tumor so that it can be removed more easily during surgery. This type of therapy can be given in several ways.

External beam radiation: The most common way, delivers a carefully focused beam of radiation from a machine outside the body. This is known as *external beam radiation*. Radiation treatment given this way can harm nearby healthy tissue along with the cancerous cells. Some people experience skin changes like a sunburn on the area that receives the radiation. You will also have temporary anal irritation and discomfort when having bowel movements. Side effects of radiation therapy vary depending on the area of the body that receives the treatment. Other possible side effects include fatigue, nausea, or diarrhea when the anal area is irradiated.

To reduce the risk of side effects, doctors carefully figure out the exact dose you need and aim the beam as accurately as they can. External beam radiation therapy usually means having treatments 5 days a week for a

period of 6 weeks or so.

Internal radiation, brachytherapy, or interstitial radiation: Another method of delivering radiation is to place tiny pellets that contain radioactive materials in or near the tumor. This method is also called *internal radiation*, *brachytherapy*, or *interstitial radiation*. The radioactive pellets, or "seeds," release their dose slowly over a period of time. Although the pellets stop being radioactive after a while, they remain in place for the rest of your life. This method can be more convenient, since you will not need to make as many trips to the doctor. However, implanting the seeds requires surgery. Sometimes, both internal and external beam radiation therapy are used together.

Damage to anal tissue by radiation may cause scar tissue to form. This scar tissue can keep the anal sphincter from functioning as it should.

Chemotherapy

Chemotherapy is the use of drugs for treating cancer. The drugs can be swallowed in pill form or they can be injected from a needle into a vein or muscle. Chemotherapy is systemic therapy. This means that the drug enters the bloodstream and circulates throughout the body (through the whole system) to reach and destroy the cancer cells.

Some types of chemotherapy drugs kill cancer cells directly. Others act by making the cells more vulnerable to radiation. Chemotherapy often uses two or more drugs because one drug can boost the power of the other. Like radiation, chemotherapy can cause the tumor to shrink. In anal cancer, chemotherapy combined with radiation therapy can cure the cancer without the need for surgery. The main chemotherapy drug combinations used to treat anal cancer are 5-fluorouracil (5-FU) and mitomycin or 5-FU and cisplatin.

Chemotherapy drugs can reach just about any place inside the body. They are an effective way to destroy cancer cells that break off from the main tumor and travel in the bloodstream. Often doctors prescribe chemotherapy after surgery as a precaution, to make sure they destroy any remaining cancerous cells.

Chemotherapy drugs kill cancer cells but also damage some normal cells. Careful attention must be given to avoid or minimize side effects, which depend on the specific drugs, the amount taken, and the length of treatment. Temporary side effects might include nausea and vomiting, loss of appetite, loss of hair, diarrhea, and mouth sores. Because chemotherapy can damage the blood-producing cells of the bone marrow, patients may have low blood cell counts. This can result in:

- An 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 bloodplatelets) Fatigue or shortness of breath (due to low red blood cell counts).

It is important to tell your doctor and/or nurse about any side effects you experience. If you have side effects, your cancer care team can suggest steps to manage them. For example, anti-nausea drugs can help control nausea and vomiting. Sometimes changing the dosage or how you take your medications can reduce side effects. Fortunately, most side effects will stop when your course of treatment ends.

Clinical Trials

The purpose of 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 valuable to the patient. Treatments used in clinical trials are often found to have real benefits. Researchers conduct studies of new treatments to answer the following questions:

- Is the treatment helpful?
- How does this new type of treatment work?
- Does it work better than other treatments already available?
- What side effects does the treatment cause?
- Are the side effects greater or less than the standard treatment?
- Do the benefits outweigh the side effects?
- In which patients is the treatment most likely to be helpful?

Types of clinical trials: There are 3 phases of clinical trials in which a treatment is studied before it is eligible for approval by the FDA (Food and Drug Administration).

Phase I clinical trials: 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 treatment has been well tested in laboratory and animal studies, but the side effects in patients are not completely known. Doctors conducting the clinical trial will start by giving very low doses of the drug to the first patients and increasing the dose for later groups of patients until side effects appear. Although doctors are hoping to help patients, the main purpose of a phase I study is to test the safety of the drug.

Phase II clinical trials: These are designed to see if the drug works. Patients are given the highest dose that doesn't cause severe side effects (determined from the phase I study) and closely observed for an effect on the cancer. The doctors will also look for side effects.

Phase III clinical trials: Phase III studies involve large numbers of patients. Some clinical trials may enroll thousands of patients. One group (the control group) will receive the standard (most accepted) treatment. The other groups will receive the new treatment. Usually doctors study only 1 new treatment to see if it works better than the standard treatment, but sometimes they will test 2 or 3. All patients in Phase III studies are closely watched. The study will be stopped if the side effects of the new treatment are too severe or if one group has had much better result than the others.

If you are in a clinical trial, you will receive excellent care. You will have a team of experts looking at you and monitoring your progress very carefully. The study is especially 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 discover. While most side effects will disappear in time, some can be permanent or even life threatening. Keep in mind, though, that even standard treatments have side effects. Depending on many factors, you may decide to enroll in a clinical trial.

Deciding to enter a clinical trial: 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 will not prevent you from getting other medical care you may need.

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?

The ACS has developed an information center on clinical trials that will help you find a trial that is right for you. Simply access our web site (www.cancer.org) or call us at 1-800-ACS-2345. You also can get a list of current National Cancer Institute sponsored clinical trials by calling the NCI Cancer Information Service toll free at 1-800-4-CANCER or visiting the NCI clinical trials Web site (www.cancer.gov/clinical_trials/).

Complementary and Alternative Therapies

You may feel that it is worthwhile to explore alternative treatments offered by therapists who are not medical doctors. Before changing your treatment or adding any alternative therapy to your regimen, talk it over with members of your cancer care team. They may have additional information to give you. The American Cancer Society also has information on many of these treatments.

Treatment Options by Stage

The type of treatment your cancer care team will recommend depends on the type of cancer and how far it has spread. This section summarizes the choices available for anal cancer according to the stage. Treatment of anal melanoma is separately discussed in the American Cancer Society document, "Melanoma Skin Cancer." According to AJCC/UICC guidelines, anal tumors affecting the anal margin or the perianal skin are considered to be skin cancers and are not treated in the same way as anal canal cancers.

Stage 0: Because stage 0 tumors do not penetrate beneath the epithelium of the anal canal, they usually can be completely removed through surgery (local resection). This surgery is an option if the tumor does not involve the sphincter.

Stages I and II: Local resection can remove small tumors (usually less than 1 centimeter or ½ inch) that do not involve the sphincter.

If your cancer cannot be removed by a local resection without severely damaging the anal sphincter, you will be treated with a combination of radiation and chemotherapy. In the past, the standard treatment was a radical surgery called abdominoperineal (AP) resection that would leave you with a colostomy. Now, however, doctors have found that chemotherapy and external beam radiation given together work just as well and you don't need a colostomy.

The combination of radiation and chemotherapy has been shown to be better than radiation alone. The radiation and the chemotherapy are given at the same time. The chemotherapy usually consists of 5-FU with either mitomycin C or cisplatin. The mitomycin or cisplatin are given as a short intravenous injection, usually at the beginning of radiation treatment and then near the end, at around 4 to 6 weeks. The 5-FU is given by a long intravenous infusion over 4-5 days and repeated in 4-6 weeks. In some cases, your doctor may suggest interstitial radiation in addition to the external beam radiation.

If your cancer hasn't completely disappeared, surgery may be needed to remove the remaining cancer.

Stage IIIA: In most cases, the first choice of treatment is radiation therapy combined with chemotherapy as in stages I and II.

Sometimes part of the tumor remains despite the use of chemotherapy or radiation or both. In that case, additional treatment may be given. In certain cases, surgery, either a local resection or a more extensive operation, can be done.

Stage IIIB: Recovery is possible for stage IIIB tumors, but it is more difficult to achieve. The most common approach is radiation plus chemotherapy to shrink the tumor, followed by surgery (local resection or APR) to remove any remaining tumor. A lymph node dissection (removal of the lymph nodes) may be done during this operation or it may be done later as a separate procedure.

Many people with stage IIIB anal cancers might benefit from taking part in a clinical trial, as described earlier.

Stage IV: In this advanced stage, treatment is aimed at controlling the disease and relieving symptoms as much as possible. Toward this end, depending on your needs, doctors may recommend surgery, radiation, or chemotherapy, or some combination of these methods. People with this stage of anal cancer might consider taking part in clinical trials.

Recurrent anal cancer: If your cancer returns after treatment, the choices available to you depend on what treatment you had the first time around. For example, if you had surgery, you may receive radiation and chemotherapy. If you first had radiation, then you may need surgery. Again, clinical trials may prove to be valuable in controlling recurrent anal cancer.

HIV-positive patients: Most of the time treatment can be given the same as for people with HIV infection. Problems may arise with HIV patients with advanced stages of their disease. This usually requires decreasing the intensity of the treatment.

What Should You Ask Your Doctor about Anal Cancer?

As you deal with your cancer and the process of treatment, you need to have honest, open discussions with your cancer care team. You should feel free to ask any question that's on your mind, no matter how trivial it might seem. Among the questions you might want to ask are:

- What kind of anal cancer do I have?
- Has my cancer spread beyond the primary site?
- What is the stage of my cancer? What does the staging mean in my case?
- What treatment choices do I have?
- What treatment would you recommend for me?
- Based on what you've learned about my cancer, what is my prognosis?
- What side effects can I expect from my treatment?
- What are the other risks of treatment?
- How long will it take me to recover from treatment?
- When can I go back to work after treatment?
- How soon after treatment can I return to my normal activities, such as work, school, exercise, or sex?
- Will I have to have a colostomy?
- What are the chances that my cancer will recur?
- Does one type of treatment reduce the risk of recurrence more than another?
- What should I do to be ready for treatment?
- Should I get a second opinion?

You will no doubt have other questions about your own personal situation. Be sure and write your questions

down so you will remember to ask them during each visit with your cancer care team. Keep in mind, too, that doctors are not the only ones who can provide you with information. Other health care professionals, such as nurses and social workers, may have the answers you seek.

What Happens After Treatment for Anal Cancer?

During and after treatment for your anal cancer you may be able to hasten your recovery and 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 learning about the effectiveness of 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 experienced professionals in mental health services, social work services and pastoral services who may assist you in coping with your illness.

You can also help in your own recovery from cancer by making healthy lifestyle choices. If you use tobacco, stop now. Quitting will improve your overall health and the full return of the sense of smell may help you enjoy a healthy diet during recovery. If you use alcohol, limit how much you drink. Have no more than one or two drinks per day. Good nutrition can help you get better after treatment. Eat a nutritious and balanced diet, with plenty of fruits, vegetables, and whole grain foods. Ask your cancer care team if you could benefit from a special diet---they may have specific recommendations for people who have had radiation therapy or a colostomy.

If you are being treated 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. Exercise once you feel rested enough. Ask your cancer care team whether your cancer or its treatments might limit your exercise program or other activities.

Surgery and radiation therapy may sometimes affect the way you feel about your body, and may lead to specific physical problems that affect sexuality. Your cancer care team can help with these concerns, so don't hesitate to discuss them.

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 help in contacting counselors or other services.

Follow-up Care: For years after treatment ends, regular follow-up exams will be very important for you. Your health care team will explain what tests you need and how often they should be done. The most important tests will involve biopsies of your anal area to make sure the tumor has disappeared. This may occur over several months so don't be discouraged if early biopsies still show cancer. You may need blood tests as well as x-rays, CT scans, and other imaging studies to detect recurrence, metastasis, or a new tumor. Make a special effort to keep all appointments with your cancer care team and follow their instructions carefully. Report any new or recurring symptoms to your doctor right away.

For patients with colostomies: Few permanent colostomies are needed now in the treatment of anal cancer. If you have a colostomy, follow-up is an important concern. You may feel worried or isolated from normal activities. An enterostomal

therapist (a health care professional trained to help people with their colostomies) can teach you about the care of your colostomy. Ask the American Cancer Society about programs offering information and support in your area. For more information about your colostomy care, please contact the United Ostomy Association, Inc.

What's New in Anal Cancer Research and Treatment?

Important research into anal cancer is currently underway in many university hospitals, medical centers, and other institutions around the country. Each year, scientists find out more about what causes the disease, how to prevent it, and how to improve treatment.

Causes and prevention: Recent research has identified human papillomavirus (HPV) as a major factor in causing some types of anal cancer. It is beginning to show how HPV affects molecules inside anal cells to cause them to become cancerous.

Current research in this area includes development of vaccines to prevent HPV infection, thereby eliminating a cause of many anal cancers. Recently a vaccine has been proven successful in preventing HPV 16 infection in women. The vaccine also prevents the development of precancerous changes in the cervix.

Improved understanding of the molecular changes inside anal cancer cells is expected to help scientists develop new drugs to fight this disease.

Early detection: Ongoing research is studying the value of screening tests for anal cancer, especially in people with major risk factors. Some doctors feel that anal cancer is similar in some ways to cervical cancer. Anal cytology, a procedure similar to the Pap test for cervical cancer, may be useful in early diagnosis of anal cancer and even in finding precancerous changes called anal intraepithelial neoplasia (AIN). In this test, cells are gently scraped from the lining layer of the anus and checked under a microscope.

Treatment: In the past few years, for example, evidence has grown showing the benefits of combining radiation with chemotherapy. This approach has reduced the number of surgeries needed for anal cancer, including the need for permanent colostomies.

New combinations may be developed. For example, cisplatin may be more effective than mitomycin. This is being studied in clinical trials that compare 5-FU plus mitomycin with 5-FU and cisplatin.

New radiosensitizing agents are being developed for use as combined -- modality therapy in chemotherapy and radiation clinical trials. These trials offer new hope for patients to benefit from these therapies and to have acceptable toxicities.

Doctors are learning more about how to deliver external radiation more accurately and effectively and decrease the effect on normal healthy tissues. Other research is being done to learn about the possible benefits of using both external radiation and interstitial (implanted) radiation therapy.

Additional Resources

National Organizations and Web Sites

The following organizations can provide additional information and resources.*

National Cancer Institute

Telephone: 1-800-4-CANCER
Internet Address: www.nci.nih.gov

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

United Ostomy Association, Inc. (UOA)
Telephone: 1-800-826-0826
Internet Address: www.uoa.org

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

Additional American Cancer Society Information

Books

American Cancer Society's Guide to Pain Control (Book; Code #9438)

Cancer in the Family: Helping Children Cope with a Parent's Illness (Book; Code #9435)

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

Coming to Terms with Cancer: A Glossary of Cancer-Related Terms (Book: Code #9505)

Consumers Guide to Cancer Drugs (Book; Code #9436)

Informed Decisions, Second Edition: The Complete Book of Cancer Diagnosis, Treatment, and Recovery (Book; Code #9449.02)

Brochures

After Diagnosis: A Guide for Patients and Families (Booklet; Code #9440)

Caring for the Patient with Cancer at Home (Booklet; Code #4656)

Colostomy - A Guide (Booklet; Code#4703)

Questions and Answers About Pain Control (Booklet; Code #4518)

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For additional assistance please contact your American Cancer Society
1 · 800 · ACS·2345 or www.cancer.org