

# PENILE 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 may 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 (noncancerous) 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. 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 Penile Cancer?

### About the penis

The penis is the external male genital organ, and contains several types of tissue, including skin, nerves, smooth muscle, and blood vessels. Inside the penis is the urethra, the tube through which urine and semen exit the body. The head of the penis is called the *glans*. At birth the glans is covered by a loose piece of skin called the *foreskin* or *prepuce*.

Inside the penis are three chambers that contain a soft, spongy network of blood vessels. Two of these cylinder-shaped chambers, known as the *corpora cavernosa*, lie on either side of the upper part of the penis. The third lies below them and is known as the *corpus spongiosum*. This chamber widens at its end to form the *glans*. The *urethra*, a tube that carries urine from the bladder through the penis, runs between the *corpus spongiosum*. The opening at the end of the urethra is called the *meatus*. Semen consists of *prostatic fluid* produced by the seminal vesicles and prostate gland and transports sperm cells from the testicles. This fluid is produced and stored in the *seminal vesicles* (two small sacs near the bladder and prostate). During ejaculation, semen from the seminal vesicles passes through the *ejaculatory ducts* into the urethra, and leaves the body through the *meatus* at the tip of the penis.

When a man gets an erection, nerves signal the body to send blood into the vessels inside the corpora cavernosa and corpus spongiosum. As the blood fills the chamber, the spongy tissue expands, causing the penis to elongate and stiffen. After ejaculation, the blood flows out of the penis, causing it to become soft again.

### Cancers of the penis

Each of the tissues in the penis contains several types of cells. Different types of penile cancer (cancer of the penis) can develop in each kind of cell. The differences are important, because they determine the seriousness of the cancer and the type of treatment needed. About 95% of penile cancers develop from flat, scale-like skin cells called *squamous* cells.

Like most other forms of nonmelanoma skin cancer, these tumors tend to grow slowly. When detected in the early stages, these tumors can usually be cured. Squamous cell penile cancers can develop anywhere on the organ, but most develop on the foreskin (in men who have not been circumcised) or on the glans.

*Verrucous carcinoma* is an uncommon form of squamous cell cancer that can occur on the male or female genitals, skin, mouth, larynx, and anus. Verrucous carcinoma of the genitals is sometimes also called a *Bushke-Lowenstein tumor*. Due to its appearance, it is often difficult to distinguish from a benign genital wart (see the section "Benign and Precancerous Conditions" for more information). These low-grade cancers can spread deeply into surrounding tissue but very rarely do they metastasize.

A very rare type of penile cancer called *adenocarcinoma* can develop from sweat glands in the skin of the penis. *Paget's disease* of the penis is a condition in which adenocarcinoma cells are

found in the penile skin. The cancer cells at first spread within the skin, but may eventually invade underneath the skin and spread to lymph nodes. 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.

The earliest stage of squamous cell cancer of the penis (or any other organ) is called squamous cell *carcinoma in situ* (abbreviated as *CIS*). Penile *CIS* is contained entirely within the skin of the penis and has not yet spread to deeper tissues of the penis. Depending on the exact location of a *CIS* of the penis, doctors may give additional names to the disease. *CIS* of the glans is sometimes called *erythroplasia of Queyrat*. The same condition, when found on the shaft of the penis (or skin of other parts of the body), is called *Bowen's disease*.

About 2% of penile cancers develop from pigment-producing skin cells called *melanocytes*. Cancers of these cells are called *melanoma*. These cancers are more dangerous because they grow and spread more rapidly. Melanomas usually develop from sun-exposed areas of skin. Although sun exposure is an important risk factor for melanoma, a few of these cancers can develop on the penis, or other areas not likely to become sunburned.

*Basal cell cancers* are most common cancers of sun exposed areas of skin, such as the face, neck and arms. Basal cell cancers represent less than 2% of penile cancers. They are slowly growing tumors that very rarely spread to other parts of the body.

The remaining 1% of penile cancer consists mostly of *sarcomas*, cancers that develop from the blood vessels, smooth muscle, and other connective tissue cells of the penis.

### **Benign and precancerous conditions**

Sometimes abnormal growths develop on the penis which are benign (not cancerous). Some of these benign growths may eventually evolve into invasive cancer if they are not treated. These premalignant conditions can resemble warts or irritated patches of skin. Like penile cancer, they usually develop on the glans or on the foreskin, but they can also occur along the shaft of the penis.

*Condylomas* are wart-like growths that resemble tiny cauliflowers. Some are so small that they are apparent only when the skin is viewed under a magnifying lens. Others may reach an inch or more in diameter.

Squamous cell cancer of the penis usually forms slowly over many years, and is usually preceded by precancerous changes that may last for several years. The medical terms for this precancerous condition are *penile intraepithelial neoplasia*, or dysplasia. "Intraepithelial" means that the precancerous cells are confined to the epithelium (surface layer of the penile skin).

## **What Are The Key Statistics About Penile Cancer?**

The American Cancer Society estimates that in 2001 about 1,200 new cases of penile cancer will be diagnosed in the United States. An estimated 300 men will die of penile cancer during 2001 in the United States. The incidence rate of penile cancer in the United States is about 0.001%, which means it occurs in about 1 man out of 100,000.

Penile cancer is very rare in North America and Europe. It accounts for about 0.2% of cancers in men and 0.1% of cancer deaths in men in the United States. However, penile cancer is much more common in some parts of Africa and South America, where it accounts for up to 10% of cancers in men.

The overall 5-year survival rate for all stages of penile cancer together is about 50%. When penile cancer is detected early, treatment is simplest, most effective and less likely to result in significant side effects or complications.

The 5-year survival rate refers to the percent 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 Penile 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, unprotected exposure to strong sunlight is a risk factor for skin cancer, and smoking is a risk factor for lung, laryngeal, esophageal, oral, and several other cancers. Scientists have found certain risk factors that make a man more likely to develop penile cancer. Even if a man does have one or more risk factors for penile cancer, it is impossible to know for sure how much that risk factor contributed to causing the cancer. On the other hand, some men who develop penile cancer have no known risk factors.

**Circumcision:** Whether or not circumcision is a negative risk factor (if it protects against penile cancer) is a very controversial issue.

Circumcision is the removal of a part or all of the foreskin at birth or later on in life. This practice has been suggested as conferring some protection against cancer of the penis by contributing to improved hygiene. However, the penile cancer risk is low in some uncircumcised populations, and the practice of circumcision is strongly associated with socio-ethnic factors which in turn are associated with lessened risk. The consensus among studies that have taken these other factors into account is that circumcision is not of value in preventing cancer of the penis. It is important that the issue of circumcision not distract the public's attention from avoiding known penile cancer risk factors -- having unprotected sexual relations with multiple partners (increasing the likelihood of human papillomavirus infection) and cigarette smoking.

**Human papillomavirus infection:** Infection by *human papillomavirus (HPV)* is believed by many researchers to be the most important avoidable risk factor for penile cancer. HPVs are a group of more than 70 types of viruses that are called papillomaviruses because they can cause warts, or papillomas. Different HPV types cause different types of warts in different parts of the body. Some types cause common warts on the hands and feet. Other types tend to cause warts on the lips or tongue. Certain HPV types can infect the male and female genital organs and the anal area. These HPV types are passed from one person to another during sexual contact. Practicing sexual intercourse at an early age, having multiple sexual partners, having sex with a partner who has had multiple other partners, and having unprotected sex (not using a condom) at any age increase a person's risk of getting HPV infection.

When HPV infects the skin of the external (outer) genital organs and anal area (around the opening of the intestinal tract), they often cause raised bumpy warts. These may be barely visible or they may be several inches across. The medical term for genital warts is *condyloma accuminatum*. Most genital warts are caused by two HPV types, HPV 6 and HPV 11. These rarely develop into cancer and are called "low risk" viruses. However, other sexually transmitted HPVs have been linked with genital or anal cancers in both men and women. These are called "high risk" HPV types and include HPV 16, HPV 18, HPV 33, HPV 35, HPV 45, as well as some others.

HPVs can also cause flat warts on the penis that are not visible and cause no symptoms. Flat warts caused by low risk HPV types have little or no effect on cancer risk. Flat warts caused by high risk HPV types can develop into cancers. There is currently no cure for human papillomavirus infection. However, the warts and abnormal cell growth caused by these viruses can be effectively treated. These treatments can destroy warts and prevent them from developing into cancers. New tests are now available that can directly identify DNA from HPVs, and identify the exact HPV type causing the infection. At this time, it is not clear how treatment should be affected by this information. HPV testing and typing is not presently routinely recommended and most health care providers do not use this testing. However, clinical research is underway to determine the role of this test in preventing cancers of the male and female genital organs.

**Smoking:** Smoking exposes the body to many cancer-causing chemicals that affect more than the lungs. These harmful substances are absorbed into blood flowing through the lungs and carried in the blood stream throughout the body. Researchers believe that these substances damage the DNA of cells in the penis and contribute to the development of penile cancer, especially in men who also have HPV infections.

**Smegma:** Oily secretions from the skin and dead skin cells can also accumulate under the foreskin. The result is a thick, sometimes odorous substance called *smegma*. Some studies suggested that smegma may contain cancer-causing substances, but most recent studies have disagreed. Smegma is unlikely to have a significant impact, if any, on a man's risk of developing penile cancer. Nonetheless, if uncircumcised men do not retract the foreskin and thoroughly wash the entire penis, the presence of smegma may cause irritation and inflammation of the penis.

**Phimosis:** Sometimes the foreskin becomes constricted and difficult to retract. This condition, known as *phimosis*, can cause a buildup of smegma around the glans. Men with phimosis are less likely to clean the penis routinely and effectively, greatly increasing their risk of developing penile cancer.

**Treatment of psoriasis:** There is a higher rate of penile cancer among men who have a skin disease called psoriasis and who have been treated with a combination involving a drug called psoralen and exposure to ultraviolet light.

**Age:** Age is a risk factor. Most cases of the disease are diagnosed in men over age 50, but about 20% occur in men under 40 years of age.

## **Do We Know What Causes Penile Cancer?**

The exact cause of most penile cancers is not known. However, scientists have found that the disease is associated with a number of other conditions, which are described in the section on risk factors. A great deal of research is now under way to learn more about the way these risk factors cause cells of the penis to become cancerous.

Research has shown that substances called *tumor suppressor gene products* are produced by normal cells to prevent them from growing too rapidly and becoming cancers. Two proteins (E6 and E7) produced by high risk human papillomavirus (HPV) types can interfere with the functioning of known tumor suppressor gene products.

Smoking produces cancer-causing chemicals that spread throughout the body and may damage the DNA of cells of the penis. DNA damage that affects genes involved in regulation of cell growth can contribute to the development of cancer.

## **Can Penile Cancer Be Prevented?**

The large variations in penile cancer rates throughout the world strongly suggest that penile cancer is a preventable disease. The best way to reduce the risk of penile cancer is to avoid known risk factors whenever possible.

In the past, circumcision has been suggested as a strategy for preventing penile cancer. This suggestion is based on studies that reported much lower penile cancer rates among circumcised men than among uncircumcised men. However, most researchers now believe those studies were flawed, because they failed to consider other factors that are now known to affect penile cancer risk. For example, some recent studies suggest that circumcised men tend to have certain other lifestyle factors associated with lower penile cancer risk -- they are less likely to have multiple sexual partners, less likely to smoke, and more likely to have good personal hygiene habits. Most public health researchers believe that the penile cancer risk among uncircumcised men without known risk factors living in the United States is extremely low. The current consensus of most

experts is that circumcision should not be recommended as a strategy for penile cancer prevention.

On the other hand, it is reasonable to suspect that avoiding sexual practices likely to result in human papillomavirus (HPV) infection might lower penile cancer risk. In addition, these practices are likely to have an even more significant impact on cervical cancer risk. Until recently, it was thought that the use of condoms ("rubbers") could prevent infection with HPV. But recent research shows that condoms cannot protect against infection with HPV. This is because HPV can be passed 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. It is still important, though, to use condoms to protect against AIDS and other sexually transmitted diseases that are passed on through some body fluids. 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, so it can be difficult or impossible to know whether a person with whom you might have sex might be infected with HPV.

It is also known that the longer a person remains infected with any type of HPV that can cause cancer, the greater the risk that infection will lead to cancer. For these reasons, postponing the beginning of sexual activity in life and limiting the number of sexual partners are two ways to reduce the chances of developing penile cancer.

Smoking is another factor associated with increased penile cancer risk. And, it is even more strongly associated with several very common and frequently fatal cancers, as well as noncancerous conditions such as heart disease and stroke. Quitting smoking or never starting in the first place is an excellent recommendation for preventing a wide variety of diseases, including penile cancer.

Because poor hygiene habits are associated with increased penile cancer risk, and some studies suggest that smegma (the material that accumulates underneath the foreskin) may contain cancer-causing substances, many public health experts recommend that uncircumcised men practice good genital hygiene by retracting the foreskin and cleaning the entire penis. If the foreskin is constricted and difficult to retract, a physician may be able to place a small cut (incision) in the skin to make retraction easier.

Since some men with penile cancer have no known risk factors, it is not possible to completely prevent this disease.

## **Can Penile Cancer Be Found Early?**

Many cases of penile cancer can be found early in the course of the disease. Many early cancers have symptoms that cause patients to seek medical attention. Some penile cancers may not cause symptoms until reaching an advanced stage, and others may cause symptoms that appear to be due to a disease other than cancer.

Men should be alert in recognizing any abnormal growths or other abnormalities of their penis. Warts, blisters, sores, ulcers, white patches, or other abnormal areas should prompt a visit to a physician. Even if they are not cancerous, they may be infections or represent other serious conditions that may need to be treated.

Unfortunately, many men are reluctant to see a doctor for treatment of *lesions* (abnormalities) on the penis. Research (in some countries other than the United States) has found that about half of men with penile lesions delay seeking treatment for at least a year or more after they first notice the problem. This delay can allow cancers to grow and spread, making treatment more difficult and, sometimes, less effective even impossible. When detected and treated in the early stages, however, penile cancer is a very curable disease.

### **Signs and symptoms of penile cancer**

In most cases, the first sign of penile cancer is a painless ulcer or growth on the penis, especially on the glans or foreskin but also sometimes developing on the shaft. Changes in color, skin thickening, or accumulation of tissue may be present. Most penile cancers do not cause pain, but some can cause ulceration and bleeding.

Sometimes the cancers appear as a reddish, velvety rash, small crusty bumps, or flat growths that are bluish-brown in color. They may not be visible unless the foreskin is pulled back. A persistent discharge, usually with a foul odor, may be present beneath the foreskin.

If cancer has progressed to a more advanced stage, there may be swollen lymph nodes in the groin. Lymph nodes are bean-sized collections of immune system cells that fight infection. The patient or doctor is often able to detect these swollen nodes by feeling the groin area. However, infections of the penis can also cause swelling of lymph nodes in the groin.

There are a number of benign conditions, such as genital warts, that can produce similar signs. 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.

### **How Is Penile Cancer Diagnosed?**

If any of the signs or symptoms discussed in the section "Can Penile Cancer Be Found Early?" suggest that this disease may be present, more medical procedures will be needed.

Because penile lesions affect the skin tissue on the surface of the organ, cancers and other abnormalities are usually detected during a visual examination of the penis. Swelling at the end of the penis, especially when the foreskin is constricted, is another common sign that penile cancer may be present.

To determine the exact nature of the abnormality, a biopsy is needed. In this procedure, a small piece of the skin 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 to see whether cancer cells are present.

The type of biopsy depends on the nature of the abnormality. If the doctor detects nodules (swollen lumps) or plaques (raised, flat areas) that are 1 cm (about 3/8 inch) or less in size, an *excisional biopsy* will be performed in which the entire lesion is removed. An *incisional biopsy*, in which only a portion of the affected tissue is removed, will be performed on lesions that are larger or ulcerated or that appear to grow deeply into the tissue. These biopsies use local anesthesia (numbing medication) and are done in a doctor's office, clinic, or outpatient (1 day) surgical center. The tissue is then sent to a laboratory, where a pathologist examines the tissue under a microscope. The results of this test are available within usually 3-4 days.

If cancer is found in the biopsy sample, you will probably be asked to undergo imaging tests such as ultrasound, computed tomography (CT) scanning, or magnetic resonance imaging (MRI), to see how far the cancer has spread.

*Ultrasound*, also known as *ultrasonography*, uses sound waves to penetrate deep into tissues. Sound waves are sent out from the ultrasound probe, which is placed on the skin of the penis. The sound waves that bounce off the normal tissues and the cancer are detected by the probe and analyzed by a computer to determine how deeply the tumor has invaded into the penis.

The CT scan uses a rotating x-ray beam to create a series of pictures of your body from many angles. A computer processes the information provided by the scan, producing a detailed image of a selected part of your body. To highlight details on the CT scan, a harmless dye may be injected into a vein. The CT scan may reveal the presence of enlarged lymph nodes, which could be a sign of a spreading cancer, or they could mean that your body is fighting an infection.

MRI uses magnetic fields and radio waves instead of x-rays to create images of selected areas of your body. These images can also show enlarged lymph nodes that might be cancer, or a reaction to infection.

Although imaging tests can identify large lymph nodes that might contain cancer, they cannot prove whether their large size is a response to an infection or due to the spread of cancer. When large groin nodes are surgically removed from men with penile cancer, only about half are actually found to contain cancer. The most accurate method to check for cancer in these groin lymph nodes is to remove them by an operation called an inguinal lymph node dissection (surgical removal of lymph nodes in the groin).

*Fine needle aspiration (FNA)* is a type of biopsy that can be done in a doctor's office or clinic. Local anesthesia may be injected into the skin over the mass. Anesthesia may not be needed in some cases. The doctor places a thin needle directly into the mass for about 10 seconds and withdraws cells and a few drops of fluid. These cells can then be viewed under a microscope to determine if cancer is present. If the mass is deep inside the body and cannot be felt by the doctor, imaging methods such as ultrasound or a CT scan can be used to guide the needle into the enlarged lymph node. FNA is not used in every case, but is one alternative to lymph node dissection for some patients.

*Sentinel lymph node biopsy* is an alternative to total lymph node dissection that, for several years, has been used successfully for some patients with breast cancer or malignant melanoma. Some doctors recommend its use for some men with penile cancer. In this procedure, a radioactive tracer and/or a blue dye is injected into the region of the tumor. The dye or radioactive material is carried by the lymphatic vessels to a "sentinel node," the first lymph node receiving lymph from the tumor and the one most likely to contain a metastasis if the cancer has spread. The sentinel node is detected by the surgeon in the operating room by either visualization (blue dye), or with a Geiger counter (radioactive tracer). This node is removed. If the sentinel node contains cancer, more lymph nodes are removed. If the sentinel node is free of cancer, additional lymph node surgery may be avoided. Using this approach, fewer patients will need to have many lymph nodes removed. Removing lymph nodes, carries a risk of side effects such as *lymphedema* (fluid accumulation in tissues) and problems with wound healing. If your doctor is considering this procedure, it might be useful to determine how many sentinel node biopsies he/she has done, and whether this approach will be part of a research study. It is also important to note that sentinel lymph node biopsy is not accepted by all physicians as an alternative to a more traditional total lymph node removal. Discuss it with your physician.

## How Is Penile Cancer Staged?

*Staging*, the process of finding out how large the cancer is and how far the cancer may have spread, is very important because your treatment options as well as and the outlook for your recovery and survival depend on the stage of your cancer. If you have penile 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 penile cancer uses a system created by the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC). This AJCC/UICC staging system is also known as the TNM system.

The TNM system for staging contains three key pieces of information. **T** refers to the size of the primary tumor, measured in centimeters (cm), its extent of spread within the penis, and its extent of spread to tissues next to the penis. **N** describes the extent of metastasis (spread) to nearby (regional) lymph nodes. **M** indicates whether the cancer has metastasized 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 "is" mean "carcinoma in situ," which means the tumor is contained in one place 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

Ta: Verrucous (wart-like) carcinoma that does not invade deeply or to other tissue

T1: Tumor invades subepithelial connective tissue (tissue below the top layers of skin)

T2: Tumor invades corpus spongiosum or corpora cavernosum (internal chambers of the penis)

T3: Tumor invades the urethra or prostate gland

T4: Tumor invades other adjacent structures

The possible values for **N** are:

NX: Regional lymph nodes cannot be assessed

N0: No regional lymph node metastasis

N1: Metastasis to a single superficial inguinal lymph node (lymph node in the groin just under the skin surface)

N2: Metastasis to two or more superficial inguinal lymph nodes on the same side or on both sides of the body

N3: Metastasis to lymph nodes deep within the groin or pelvis, on either one or both sides of the body

The **M** values are:

MX: Presence of distant metastasis cannot be assessed

M0: No distant metastasis

M1: Distant metastasis has occurred

Using the TNM system, a doctor might describe one case of penile cancer as T2, N0, M0 and another one as T4, N1, M0.

To summarize this information, several TNM combinations can be grouped together into a simpler set of stages, labeled stage 0 through stage IV.

**Stage 0 (carcinoma in situ):**

Tis, N0, M0

Ta, N0, M0

**Stage I:**

T1, N0, M0

**Stage II:**

T1, N1, M0

T2, N0, M0

T2, N1, M0

**Stage III:**

T1, N2, M0  
T2, N2, M0  
T3, N0, M0  
T3, N1, M0  
T3, N2, M0

**Stage IV:**

T4, any N, M0  
any T, N3, M0  
any T, any N, M1

**Recurrent:**

Recurrent disease means that the cancer has come back after treatment has taken place. Recurrent penile cancer may return in the penis or in any other part of the body.

**How Is Penile Cancer Treated?**

In recent years, much progress has been made in treating penile cancer. New medications or ways to use medications have been developed. Surgical methods involving microscopic techniques and lasers have been refined (which are less disfiguring than surgical removal of the penis), and more is known about the best way to use radiation.

After the cancer is found and staged, your cancer care team will discuss *treatment options* (choices) with you. It is important to take time and think about all of the choices. In choosing a treatment plan, factors to consider include the type and stages of the cancer, your overall physical health, and your personal preferences about treatments and their side effects.

It is often a good idea to seek a second opinion. A second opinion can provide more information and help you feel more confident about the treatment plan that is chosen. Some insurance companies require a second opinion before they will agree to pay for certain treatments.

The three main methods of treatment for penile cancer are surgery, radiation therapy, and chemotherapy.

The best approach for some patients may involve two 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.

## Surgery

Surgery is the most common treatment for all stages of penile cancer. Depending on the type, size, and extent of the tumor, surgery might involve one of several techniques.

Fortunately, most early stage penile cancers can be completely cured by fairly minor surgery. There are several different kinds of surgery for these cancers.

**Simple excision:** The tumor is cut out with a surgical knife, along with some surrounding normal skin, and the remaining skin is carefully stitched back together. This is the same as an *excisional biopsy*.

**Electrodessication and curettage:** This treatment removes the cancer by scraping with a *curette* (a long, thin instrument with a scraping edge, similar in appearance to a vegetable peeler), then treating the area where the tumor was located with an electric current delivered through a needle to destroy any remaining cancer cells. This process may be repeated one to three times. Electrodessication and curettage is a good treatment for small basal cell and squamous cell (skin) cancers on the penis.

**Cryosurgery:** This treatment uses liquid nitrogen to freeze and kill abnormal cells. After the dead tissue thaws, blistering and crusting may occur. The wound may take several weeks to heal and may leave a scar. The treated area may have less color after treatment. Cryosurgery can be used for precancerous conditions and for small basal cell and squamous cell carcinomas (types of skin cancer).

**Mohs surgery (microscopically controlled surgery):** Using the *Mohs* technique, the surgeon removes a layer of the skin which the tumor may have invaded and then carefully marks its location with colored dyes. The surgeon checks the sample under a microscope immediately. If it is still malignant, more pieces of the tumor will be removed in a similar fashion and examined until the skin samples are found to be free of cancerous cells. This process is slow, but it means that normal tissue next to the tumor can be saved. This creates a better appearance and function after surgery. This is a highly specialized technique that should be used only by doctors who have been trained in this specific type of surgery.

**Laser surgery:** This relatively new approach uses a beam of laser light to vaporize cancer cells. It is useful for squamous cell carcinoma in situ (involving only the outer layer of the skin or epidermis) and for very superficial basal cell carcinomas (types of skin cancer).

**Wide local excision:** This operation removes the cancerous tissue plus some of the normal tissue on either side (known as a wide margin). Some healthy tissue must be removed to be certain that all of the cancer has been removed.

**Circumcision:** This operation may be performed to remove the foreskin and some neighboring skin. This method is used if cancer is limited to the foreskin.

**Amputation:** This operation, also called *penectomy*, removes part or all of the penis. It is the most common and most effective surgical procedure for treatment of a penile cancer that has penetrated deeply inside the penis. Lymph nodes in the groin are usually not removed at the same time. Since the enlargement may represent inflammation or infection and not spread of cancer.

Your cancer care team will discuss with you the treatment option that gives you the best chance of curing your cancer while preserving as much of the penis as possible.

### **Sexual Impact of Penectomy**

Although the surgical removal of all or part of the penis, or *penectomy* is rare it can have a devastating effect on a man's self-image and his sex life. If cancer of the penis is diagnosed early, local radiation, chemotherapy creams, or a simple surgical procedure can sometimes be used to treat it. These treatments often have little effect on sexual pleasure and function.

Partial penectomy removes only the end of the penis. The surgeon leaves enough of the shaft to allow the man to direct his stream of urine away from his body.

Men are usually surprised to learn that a satisfying sex life is possible after partial penectomy. The remaining shaft of the penis still becomes erect with excitement. It usually gains enough length to achieve penetration. Although the most sensitive area of the penis (the glans or "head") is gone, a man can still reach orgasm and have normal ejaculation. His partner also can still enjoy intercourse and often reach orgasm.

If the shaft cannot be saved, the man must have a total penectomy. This operation removes the entire penis, including the roots that extend into the pelvis. The surgeon creates a new opening for the urethra (tube from the bladder) between the man's scrotum (sac for the testicles) and his anus. The man can still control his urination, because the "on-off" valve in the urethra is above the level of the penis.

Some men give up on sex after total penectomy. Since cancer of the penis is most common in elderly men, many have already stopped sexual activity because of other health problems. If a man is willing to put some effort into his sex life, however, pleasure is possible after total penectomy. He can learn to reach orgasm when sensitive areas such as the scrotum, skin behind the scrotum, and the area surrounding the surgical scars are caressed. Having a sexual fantasy or looking at erotic pictures or stories can also increase excitement.

Men can help their partner reach orgasm by genital caressing with their fingers, by oral sex, or by stimulation with a vibrator. The activity some couples enjoy after total penectomy can give hope to those coping with lesser changes in their sex lives.

### **Radiation Therapy**

Radiation therapy uses a beam of high-energy rays or particles to destroy cancer cells.

There are several ways to apply radiation therapy. The most common way is to deliver a carefully focused beam of radiation from a machine outside the body. This is known as *external beam radiation*. External beam radiation therapy usually involves having treatments five days a week for a period of six weeks or so.

Another method of delivering radiation is to place tiny pellets or needles which contain radioactive materials in or near the tumor. This method is called *brachytherapy*, internal radiation, or interstitial radiation. The 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 or needles requires surgery. Sometimes, both internal and external beam radiation therapy are used together.

The main drawback of radiation therapy is that it can destroy nearby healthy tissue along with the cancerous cells. Many people experience temporary skin changes like a sunburn on the treated skin area. Less common but more serious side effects include destroying some of the skin at the end of the penis, narrowing of the urethra due to scar tissue (causing difficulty with urination), and abnormal healing resulting in a fistula (abnormal connection) between the urethra and skin. Possible side effects of pelvic area and groin lymph node radiation include tiredness, nausea, or diarrhea.

Radiation therapy may be used as an alternative to surgery for treatment of the primary (main or original) penile cancer. This strategy can help some men avoid partial or complete amputation of the penis. Radiation therapy of groin and pelvic lymph nodes may be used as an alternative to their surgical removal. Or, groin and pelvic radiation therapy after lymph node removal may reduce the risk of penile cancer coming back.

## **Chemotherapy**

Chemotherapy uses drugs that kill cancer cells. Two types of chemotherapy may be used in treating penile cancer -- topical chemotherapy and systemic chemotherapy.

**Topical chemotherapy:** *Topical chemotherapy* means that an anticancer medication is placed directly onto the skin rather than being given by mouth or injected into a vein. The drug most often used in topical treatment of penile cancer is 5-fluorouracil (5-FU). When applied directly onto the skin in the form of a topical cream, 5-fluorouracil reaches cancer cells near the skin surface but does not reach cancer cells which have invaded deeply into the skin or spread to other organs. For this reason, treatment with 5-fluorouracil generally is used only for premalignant conditions or carcinoma in situ (Tis, stage 0). One of its main advantages is that the drug does not spread throughout the body. Therefore, the side effects to other organs that can occur with systemic chemotherapy (treatment that affects the whole body) do not occur with topical chemotherapy. After treatment, a biopsy is done. If cancer remains, surgery is recommended.

Treatment with 5-fluorouracil cream causes the treated skin to be red and sensitive for a few weeks. Use of other topical medications can help relieve these side effects.

**Systemic Chemotherapy:** Systemic chemotherapy uses anticancer drugs that are injected into a vein or given by mouth. These drugs travel through the bloodstream to all parts of the body. In contrast to topical chemotherapy, systemic chemotherapy can attack cancer cells that have spread beyond the penis to lymph nodes and other organs.

One or more chemotherapy drugs may be used to treat penile cancer that has *metastasized* (spread) to other organs. Some chemotherapy drugs such as cisplatin, vincristine, methotrexate, and bleomycin can temporarily delay the spread of advanced penile cancers and relieve some symptoms. These drugs are also being studied as an *adjuvant* (additional) therapy to prevent or delay cancer recurrence after surgery.

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 specific 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. It is important to communicate these side effects to the cancer care team because these side effects can be managed.

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 blood platelets), and fatigue or shortness of breath (due to low red blood cell counts).

Most side effects disappear once treatment is stopped. There are remedies for many of the temporary side effects of chemotherapy, so you should not hesitate to discuss them with your cancer care team. For example, antiemetic (antinausea) drugs to prevent or reduce nausea and vomiting can be given.

## **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, that 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.

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](http://cancertrials.nci.nih.gov)) or healthcare professionals ([cancernet.nci.nih.gov/prot/protsrch.shtml](http://cancernet.nci.nih.gov/prot/protsrch.shtml)).

### **Treatment Options by Stage**

The type of treatment your cancer care team will recommend depends on how far the cancer has spread. This section summarizes the choices available according to the stage of your cancer.

**Stage 0 and Stage I:** Cases of stage 0 and stage I penile cancer in which disease is limited to the foreskin can usually be treated with circumcision and removal of a margin of benign (noncancerous) skin. If the tumor developed in the glans and does not affect other tissues, it may be possible to treat it with topical chemotherapy (such as 5-fluorouracil cream) or Mohs (microscopically directed) surgery. Electrodesiccation and curettage, or superficial radiation therapy, may be tried. Options for tumors that penetrate deeper than the glans are partial amputation of the penis, external radiation therapy, and Mohs surgery. The use of laser surgery for superficial penile cancer is currently being studied.

**Stage II:** Stage II penile cancer usually requires a partial or total penectomy, with or without radiation therapy. Another approach is to use radiation therapy as the first treatment with surgery remaining as an option if the cancer is not completely destroyed by the radiation.

**Stage III:** Stage III penile cancer is treated with amputation of the penis and lymph node removal or amputation followed by radiation therapy. If the tumor involves the scrotum, or parts of the abdominal wall, it may be necessary to also remove the testicles and or the scrotum. A new opening can be made in the abdomen or the perineum to allow urination. In extreme cases removal of the bladder and prostate may also be needed. The use of chemotherapy or chemotherapy plus radiation are under study.

**Stage IV:** Stage IV penile cancer is not considered curable by current methods. Treatment is designed to prevent or relieve symptoms to the best extent possible. Among the possible choices are wide local excision, amputation of the penis, or radiation therapy. Studies are under way to determine the value of chemotherapy combined with surgery or radiation therapy.

**Recurrent:** Recurrent penile cancer is treated with amputation (if penectomy was not done before) or radiation therapy. Currently researchers are investigating the role of chemotherapy in treating of recurrent penile cancer.

## **What Should You Ask Your Doctor About Penile 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 penile 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 is the goal of treatment?
- If you were to have treatment, what kind would you choose?
- 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 have intercourse?
- 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 remember to ask them during each visit with your cancer care team. Keep in mind that doctors are not the only ones who can provide you with information. Other health care professionals, such as nurses and social workers, may have the answers you seek.

## **What Happens After Treatment For Penile Cancer?**

For any man, dealing with cancer of the penis is a frightening prospect. Partial or complete removal of the penis is usually the most effective way to cure penile cancer, but, not surprisingly, for many men this cure seems worse than the disease. It is natural for a man facing treatment for penile cancer to suffer mental distress, depression, and feelings of despair. The better you can anticipate and prepare for these feelings in advance, the better your quality of life will be following treatment.

In certain cases, a partial penectomy leaves enough of the organ behind to allow relatively normal urination. Many men who have undergone a complete penectomy must sit to urinate.

Men treated with conservative techniques (such as topical chemotherapy, Mohs surgery, electrodesiccation and curettage, laser surgery, and cryosurgery) and some men treated with a partial penectomy retain enough of the penis to achieve an erection sufficient for penetration during sexual intercourse. It is important for a man and his sexual partner to consider undergoing counseling to help them understand the impact of treatment for penile cancer and to explore other approaches to obtaining sexual satisfaction.

Each type of treatment for penile cancer has adverse effects that may last for a few months. Of course, amputation is permanent, but in some cases surgical procedures are possible to reconstruct the penis. Soon after radiation treatment, many patients may notice patches of skin that are oozing and tender. Urinating may cause burning sensations. These side effects usually disappear shortly after the end of treatment. Some adverse reactions to radiation that appear later include changes in skin color, the development of *telangiectasia* (web-like blood vessels in the skin), and atrophy (damage) to the mucous membranes. In many cases, the function and appearance of the penis gradually returns to normal in the months and years after radiation therapy. In cases where the tumor has not penetrated beyond the glans, radiation is directed only at the tip of the organ, so the ability to achieve erections should not be affected. However, there is a risk that radiation can cause permanent damage to the urethra (such as *stricture* or narrowing), making it impossible to urinate normally and requiring surgery to create a new urinary opening.

Research shows that overall, about 67% of men are likely to live 5 years or longer following the diagnosis and treatment of penile cancer. The earlier the cancer is detected and the lower its stage, the better the chances are for a complete cure and long-term survival. About 80% of men with stage I or stage II cancers that have not spread to lymph nodes can expect to live at least 5

years, but the five-year survival rate is 50% in men with stage III disease and 20% in men with stage IV penile cancer.

Remember that your body is unique, and so are your emotional needs and personal circumstances. In some ways, your cancer is like no one else's. No one can predict precisely how you will respond to cancer or its treatment. Statistics can paint an overall picture, but you may have special strengths such as a healthy immune system, a history of good nutrition, a strong family support system, or a deep spiritual faith. All of these have an impact on how you cope with cancer.

Follow-up care is important after treatment. Your health care team will explain what tests you need and how often they should be done. 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.

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.

Cancer treatment can make you feel tired. You need to give yourself time to recover. Don't feel you have to rush back to work or resume all of your normal activities right away. Give your body the rest it needs and you will feel better in the long run.

Do as much as you can to help yourself stay healthy and active. If you smoke, try to quit. Ask your health care team for suggestions about how to quit smoking. Eat a balanced diet of healthy foods, including plenty of fruits, vegetables, and whole grains. Once you get your strength back, try to exercise a few hours each week. Your care providers can suggest the types of exercise that are right for you.

Your health care team can suggest other organizations that might help you during your recovery from treatment. There are many support groups available that provide emotional support, friendship, and understanding.

## **What's New In Penile Cancer Research And Treatment?**

Important research into penile cancer is currently under way 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.

In some cases, the use of laser therapy can cure or control the disease in its early stage, and preserve the appearance and function of the penis. Research is being conducted to identify the best type of laser to use in these early tumors.

Scientists are also working to discover the best ways to use radiation. This may involve the combination of radiation with chemotherapy to avoid surgical amputation, whenever possible.

Scientists are learning much more about how certain genes called *oncogenes* and *tumor suppressor genes* control cell growth and how changes in these genes cause normal cells to become cancerous. The ultimate goal of this research is gene therapy - being able to replace the damaged genes in cancer cells with normal genes in order to stop the abnormal behavior of these cells.

## **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](http://www.nci.nih.gov)

National Coalition for Cancer Survivorship  
Telephone: 1-888-650-9127  
Internet Address: [www.cansearch.org](http://www.cansearch.org)

### **Additional American Cancer Society Information**

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

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 (Booklet; Code#4656)

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

Sexuality & Cancer: For the Man Who Has Cancer and His Partner (Booklet; Code#4658)

### **Other Publications\***

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

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

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

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