



CERVICAL 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.

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.

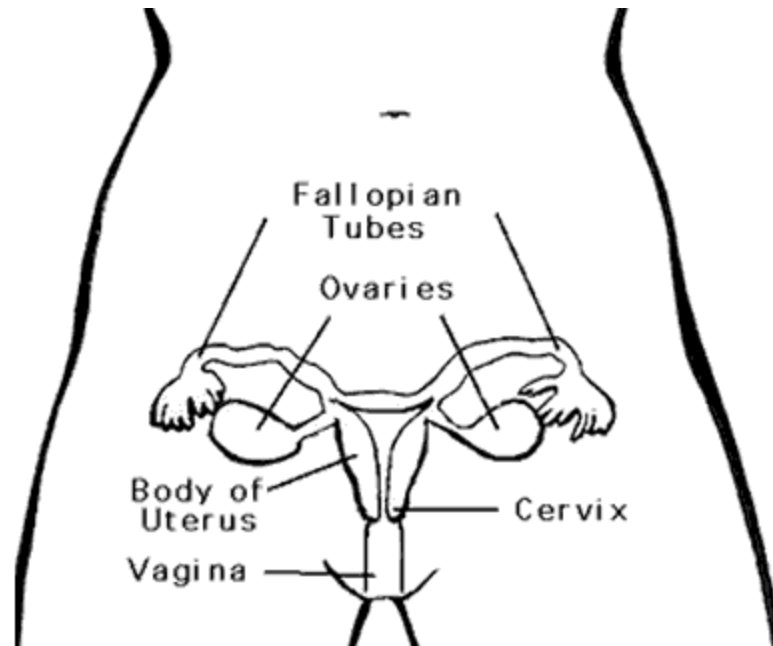
Remember that not all tumors are cancerous. Benign (noncancerous) tumors do not spread to other parts of the body (metastasize) and, with very rare exceptions, are not life threatening.

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 that is aimed at their particular kind of 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 Cervical Cancer?

The *cervix* is the lower part of the *uterus* (womb). The upper part, or *body of the uterus*, is where a fetus grows. The cervix connects the body of the uterus to the *vagina* (birth canal). The part of the cervix closest to the body of the uterus is called the *endocervix*. The part next to the vagina is the *ectocervix*. Most cervical cancers start where these two parts meet.



Cancer of the cervix (also known as *cervical cancer*) begins in the lining of the cervix. Cervical cancers do not form suddenly. Normal cervical cells gradually develop precancerous changes that turn into cancer. Doctors use several terms to describe these precancerous changes, including *cervical intraepithelial neoplasia (CIN)*, *squamous intraepithelial lesion (SIL)*, and *dysplasia*.

Some women with precancerous changes of the cervix will develop cancer. This process usually takes several years but sometimes can happen in less than a year. For most women, precancerous cells will remain unchanged and go away without any treatment. But if these precancers are treated, almost all true cancers can be prevented. Precancerous changes and specific types of treatment for precancers are discussed in the section "Can Cervical Cancer Be Prevented?"

Precancerous changes can be separated into different categories based on how the cells of the cervix look under a microscope. There are several systems for naming and describing these categories of potentially cancerous or precancerous changes. The most widely used system is discussed in the section "Can Cervical Cancer Be Prevented?"

There are 2 main types of cervical cancers: *squamous cell carcinoma* and *adenocarcinoma*. Cervical cancers and cervical precancers are classified by how they look under a microscope. About 80% to 90% of cervical cancers are squamous cell carcinomas, which are composed of cells that resemble the flat, thin cells called *squamous cells* that cover the surface of the endocervix. Squamous cell carcinomas most often begin where the ectocervix joins the endocervix.

The remaining 10% to 20% of cervical cancers are adenocarcinomas. Adenocarcinomas are becoming more common in women born in the last 20 to 30 years. Cervical adenocarcinoma develops from the mucus-producing gland cells of the endocervix. Less commonly, cervical cancers have features of both squamous cell carcinomas and adenocarcinomas. These are called *adenosquamous carcinomas* or *mixed carcinomas*.

What Are the Key Statistics About Cervical Cancer?

The American Cancer Society estimates that in 2002, about 13,000 cases of invasive cervical cancer will be diagnosed in the United States. Some researchers estimate that noninvasive cervical cancer (carcinoma in situ) is about 4 times more common than invasive cervical cancer.

About 4,100 women will die from cervical cancer in the United States during 2002. Cervical cancer was once one of the most common causes of cancer death for American women. Between 1955 and 1992, the number of cervical cancer deaths in the United States declined by 74%. The main reason for this change is the increased use of the *Pap test*, a screening procedure that permits diagnosis of preinvasive and early invasive cancer. The death rate continues to decline by about 2% a year.

The 5-year relative survival rate for the earliest stage of invasive cervical cancer is 91%. The overall (all stages combined) 5-year survival rate for cervical cancer is about 70%.

The 5-year survival rate refers to the percentage of patients who live at least 5 years after their cancer is diagnosed. Five-year rates are used to produce a standard way of discussing prognosis. Of course, many people live much longer than 5 years. Five-year *relative* survival rates exclude patients dying of other diseases. This means that anyone who died of another cause, such as heart disease, is not counted.

Keep in mind that 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 Cervical Cancer?

A *risk factor* is anything that increases your 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.

Several risk factors increase your chance of developing cervical cancer. Women *without* any of these risk factors rarely develop cervical cancer. Although these risk factors increase the odds of developing cervical cancer, many women with these risks do not develop this disease. When a woman develops cervical cancer or precancerous changes, it is not possible to say with certainty that a particular risk factor was the cause.

In considering these risk factors, it helps to focus on those that you can change or avoid (such as smoking and sexual behaviors that can lead to human papillomavirus infection), rather than those that you cannot (such as differences in age and family history). However, understanding risk factors that cannot be changed is still important because it can convince women with these factors to get a Pap test for early detection of cervical cancer. Cervical cancer risk factors include:

Age: The average age of women newly diagnosed with cervical cancer is between 50 and 55 years. This cancer rarely occurs in girls younger than 15. It begins to appear in women in their twenties. Cervical cancer is different from most cancers that tend to occur more often as people get older. Although cervical cancer does affect young women, many older women do not realize that the risk of developing cervical cancer is still present as they age, and that it is important for them to continue having regular Pap tests at least until age 70, and possibly longer. See "Can Cervical Cancer Be Prevented?" for more specific information on current ACS screening recommendations.

Human papillomavirus infection: The most important risk factor for cervical cancer is infection by the *human papillomavirus (HPV)*. HPVs are a group of more than 70 types of viruses called papillomaviruses because they can cause warts, or *papillomas*. Different HPV types cause different types of warts in different parts of your 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 female and male genital organs and the anal area. These HPV types are passed from one person to another during sexual contact.

When HPV infects the skin of the *external* (outer) genital organs and anal area, it often causes 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 seldom are associated with cervical 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, and HPV 45, as well as some others.

HPVs can also cause flat warts on the cervix or vagina 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 cervical or vaginal cancers. Most health care professionals do not determine the HPV type because these warts are usually treated.

There is currently no cure for papillomavirus infection. However, the warts and abnormal cell growth caused by these viruses can be treated effectively. These treatments can destroy flat warts on the cervix and vagina and prevent them from developing into cancers. Most women with HPV infection do not develop cervical cancer. In many cases, the infection may even disappear without any treatment, because the woman's immune system has been successful in fighting the virus.

Precancerous changes are diagnosed when abnormal cells are found in *specimens* (samples) taken from a Pap test or biopsy (these are discussed further in "Can Cervical Cancer Be Prevented?"). HPV infection can cause changes in cells of the cervix that can be detected by the Pap test. New tests can directly identify DNA from HPVs and identify the exact HPV type causing the infection. Many doctors are now testing for HPV if the Pap smear result is only slightly abnormal (doctors refer to these findings as *atypical squamous cells*, or ASC). If a high-risk type of HPV is present, they will perform a colposcopy and consider further treatment.

Certain types of sexual behavior increase a woman's risk of getting HPV infection:

- Intercourse at an early age
- Having many sexual partners
- Having unprotected sex at any age

HPV can be present for years with no symptoms, and HPV infection does not always produce warts or other symptoms; so you can be infected with HPV and pass it on without knowing it. Recent studies show that condoms ("rubbers") cannot completely protect against HPV infection. 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. The absence of visible warts cannot be used to decide whether caution is needed, because HPV can be passed to another person even when there are no visible warts or other symptoms.

Although studies completed so far do not provide conclusive results as to whether condoms might offer limited protection against HPV infection, some studies have found that condom users are less likely to develop cervical cancer and precancerous cervical changes. 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.

Smoking: Smoking exposes the body to many cancer-causing chemicals that affect more than the lungs. These harmful substances are absorbed by the lungs and carried in the bloodstream throughout the body. Tobacco by-products have been found in the cervical mucus of women who smoke. Researchers believe that these substances damage the DNA of cells in the cervix and may contribute to the development of cervical cancer. Women who smoke are about twice as likely as nonsmokers to get cervical cancer.

Human immunodeficiency virus (HIV) infection: HIV is the virus that causes the *acquired immunodeficiency syndrome (AIDS)*. Because this virus damages the body's immune system, it makes women more susceptible to HPV infections, which may increase the risk of cervical cancer. Scientists believe that the immune system is important in destroying cancer cells and

slowing their growth and spread. In women infected with HIV, a cervical precancer might develop into an invasive cancer faster than it normally would.

Chlamydia infection: Chlamydia is a relatively common kind of bacteria that can infect the female reproductive system. It is spread by sexual contact. Although infection may cause symptoms, many women do not know they are infected unless samples taken at the time of their Pap test are analyzed for this type of bacteria.

Some recent studies suggest that women whose blood test results indicate past or current chlamydia infection are at greater risk for cervical cancer than are women with a negative blood test. Although further studies are needed to confirm this finding, there is already good reason to avoid this infection and to have it treated with antibiotics promptly after diagnosis. Long-term chlamydia infection is well known as a cause of pelvic inflammation that can lead to infertility.

Diet: Women with poor diets may be at increased risk for cervical cancer. Diets low in fruits and vegetables are associated with an increased risk of cervical cancer and several other cancers.

Oral contraceptives: No definite evidence exists linking the use of oral contraceptives (birth control pills) with cervical cancer. There is some statistical evidence that long-term oral contraceptive (OC) use may slightly increase the risk of cancer of the cervix. Some research suggests a relationship between using OCs for 5 or more years and an increase in the risk of cervical cancer. Research is underway to resolve this issue.

In the meantime, the American Cancer Society believes that a woman and her doctor should discuss whether the benefits of using OCs outweigh this very slight potential risk. A woman with multiple sexual partners should use condoms to lower her risk of sexually transmitted diseases no matter what form of contraception she uses.

Low socioeconomic status: Low socioeconomic status is also a risk factor for cervical cancer. Many women with low incomes do not have ready access to adequate health care services, including Pap tests and treatment of precancerous cervical disease. Such women may also be undernourished, which may play a role in increasing their risk.

Diethylstilbestrol (DES): DES is a hormonal drug that was prescribed between 1940 and 1971 for some women thought to be at increased risk for miscarriages. Of every 1,000 women whose mother took DES when pregnant with them, about 1 develops clear-cell adenocarcinoma of the vagina or cervix. Stated another way, about 99.9% of "DES daughters" do not develop these cancers.

Clear cell adenocarcinomas are more common in the vagina than the cervix. The risk appears to be greatest in those whose mothers took the drug during their first 16 weeks of pregnancy. The average age at diagnosis of DES-related clear-cell adenocarcinoma is 19 years. Most DES daughters are now between 30 and 60, so the number of new cases of DES-related cervical and vaginal clear-cell adenocarcinoma has been decreasing during the past 2 decades. However, this type of cancer has recently been found in a woman in her early 40s, and doctors still do not know exactly how long women remain at risk for DES-related cancers.

Although DES daughters have an increased risk of developing clear cell carcinomas, about 40% of women with this cancer have not been exposed to DES or related medications. Some of these patients' mothers might have taken DES but did not recall the name of the drug. It is certain, however, that women don't have to be exposed to DES for clear cell carcinoma to develop since some cases of the disease were diagnosed before DES was invented. Some studies suggest that DES daughters are also at somewhat increased risk of developing squamous cell cancer of the cervix and precancerous changes of cervical squamous cells.

Family history of cervical cancer: Recent studies suggest that women whose mother or sisters have had cervical cancer are more likely to develop the disease, themselves. Some researchers suspect this familial tendency is due to an inherited condition that makes some women less able to fight off HPV infection than others.

Do We Know What Causes Cervical Cancer?

In recent years, scientists have made much progress toward understanding the steps that take place in cells of the cervix when cancer develops. In addition, they have identified several risk factors that increase the odds that a woman might develop cervical cancer.

Human papillomavirus (HPV): HPV infection is the most important risk factor. This disease is passed from one person to another by sexual contact. (Please see "What Are the Risk Factors for Cervical Cancer?" for more details about HPV.)

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

But HPV infection does not completely explain what causes cervical cancer. Most women with HPV don't get cervical cancer, and some women get cervical cancer without having HPV infection.

Smoking: Smoking produces cancer-causing chemicals that damage cervical cells' DNA and contribute to the development of cancer.

Immune system deficiency: Another possible cause is immune system deficiency. Our immune system helps keep us free of cancer. HIV (the AIDS virus) infection makes a woman's immune system less able to fight HPV and early cervical cancers.

Poor nutrition: Poor nutrition also increases risk, perhaps by depressing the immune system, so a woman is less able to fight HPV and cancers.

Can Cervical Cancer Be Prevented?

Since the most common form of cervical cancer starts with precancerous changes, there are 2 ways to stop this disease from developing. The first way is to prevent the precancers, and the second is to detect and treat precancers before they become cancerous

Avoiding Risk Factors

You can prevent most precancers of the cervix by avoiding risk factors, notably the human papillomavirus (HPV). Delaying having sexual intercourse if you are young can help you avoid HPV infection. Limiting your number of sexual partners and avoiding sex with people who have had many other sexual partners decrease your risk of exposure to HPV. HPV infection does not always produce warts or other symptoms, so a person may be infected with, and pass on, HPV without knowing it.

Be aware that condoms ("rubbers") cannot protect against infection with HPV. This is because HPV can be passed from person to person through any 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. Even if there are no visible warts or other symptoms, a person with HPV can still pass on the virus to another person. HPV can be present for years with no symptoms.

It is still important to use condoms to protect against AIDS and other sexually transmitted diseases that are passed on through some body fluids. Not smoking is another way to reduce the risk of cervical cancer and precancer.

Detecting Precancerous Changes

The second way to prevent invasive cancer is to have a Pap test to detect HPV infection and precancers. Treatment of these disorders can stop cervical cancer before it is fully developed. Most invasive cervical cancers are found in women who have not had regular Pap tests.

The American Cancer Society recommends:

- All women begin cervical cancer screening about 3 years after they begin having vaginal intercourse, but no later than when they are 21 years old. Screening should be done every year with the regular Pap test or every two years using the newer liquid-based Pap test.
- Beginning at age 30, women who have had 3 normal test results in a row may get screened every 2 to 3 years. Women who have certain risk factors such as diethylstilbestrol (DES) exposure before birth, HIV infection, or a weakened immune system due to organ transplant, chemotherapy, or chronic steroid use should continue to be screened annually.
- Women 70 years of age or older who have had 3 or more normal Pap tests in a row and no abnormal Pap test results in the last 10 years may choose to stop having cervical cancer screening. Women with a history of cervical cancer, DES exposure before birth, HIV infection or a weakened immune system should continue to have screening as long as they are in good health.
- Women who have had a total hysterectomy (removal of the uterus and cervix) may also choose to stop having cervical cancer screening, unless the surgery was done as a

treatment for cervical cancer or precancer. Women who have had a hysterectomy without removal of the cervix should continue to follow the guidelines above.

Some women believe that they do not need examinations by a health care professional once they have stopped having children. This is not correct. They should continue to follow ACS guidelines.

Although the Pap test has been more successful than any other screening test in preventing a cancer, it is not perfect. One of its limitations is that Pap tests are examined by humans, so an accurate analysis of the hundreds of thousands of cells in each sample is not always possible. Engineers, scientists, and doctors are working together to improve this test. Because some abnormalities may be missed (even when samples are examined in the best laboratories), it is not a good idea to have this test less often than ACS guidelines recommend.

Increasing the Accuracy of Your Pap Tests

There are several things you can do to make your Pap test as accurate as possible:

- Try not to schedule an appointment for a time during your menstrual period.
- Do not douche for 48 hours before the test.
- Do not have sexual intercourse for 48 hours before the test.
- Do not use tampons, birth control foams, jellies, or other vaginal creams or vaginal medications for 48 hours before the test.

Pelvic Examination versus Pap Test

Many people confuse pelvic examinations with Pap tests. The pelvic exam is part of a woman's routine health care. During a pelvic exam, the doctor looks at and feels the reproductive organs, including the uterus and the ovaries, and may screen for sexually transmitted diseases. But the pelvic exam will not find cervical cancer at an early stage, and cannot find abnormal cells of the cervix. The Pap test is usually done just before the pelvic exam, when the doctor removes cells from the cervix by gently scraping or brushing with a special instrument. Pelvic exams may help find other types of cancers and reproductive problems, but only Pap tests will provide information on early cervical cancer or precancers.

How Cervical Cytology (a Pap Test) Is Done

Cytology is the branch of science that deals with the structure and function of cells. It also refers to tests to diagnose cancer by examination of cells under the microscope. The Pap test (or *Pap smear*) is a procedure used to obtain cells from the cervix for cervical cytology screening.

The health care professional first inserts a *speculum*, a metal or plastic instrument that keeps the vagina open so that the cervix can be seen clearly. Next, a sample of cells and mucus is lightly

scraped from the ectocervix (part next to the vagina) using a small spatula. A small brush or a cotton-tipped swab is used to take a sample from the endocervix (part closest to the body of the uterus). These are 2 main options for preparing the cell samples for testing in the laboratory, where specially trained technologists (cytotechnologists) and doctors (pathologists) examine the samples under a microscope.

The sample can be smeared directly onto a glass microscope slide, which is then sent to the laboratory. For about 50 years, all cervical cytology samples were handled this way. This method works quite well and is relatively inexpensive. However, cells smeared onto the slide are sometimes piled up on each other, so cells at the bottom of the pile cannot be clearly seen. Also, infections of the cervix or vagina may cause *inflammatory* (pus) cells, increased mucus, yeast cells, or bacteria that hide the cervical cells. Another problem with direct smears is that the cells may become distorted by drying out. Cells can be difficult to examine accurately if they are not treated with alcohol to preserve them immediately after they are spread on the slide.

A newer method called *liquid-based cytology*, or liquid-based Pap test, can remove some of the mucus, bacteria, yeast, and pus cells in a sample and can spread the cervical cells more evenly on the slide. Instead of being directly placed on a slide, the sample is placed into a special preservative solution. This new method, also known by brand names *ThinPrep* or *AutoCyte*, also prevents cells from drying out and becoming distorted. Recent studies show that liquid-based testing can slightly improve detection of cancers, greatly improve detection of precancers (SILs - described below), and reduce the number of tests that need to be repeated. This method is more expensive than a usual Pap smear.

Another approach to improving the Pap test is the use of computerized instruments that can recognize abnormal cells in Pap smears. The *AutoPap* instrument has been approved by the U.S. Food and Drug Administration (FDA) for retesting Pap test samples that were interpreted as normal by technologists. It is also approved by the FDA for initial screening of Pap smears, instead of screening by a technologist. However, a technologist would still examine all smears identified as abnormal by the AutoPap.

These computerized instruments can detect abnormal cells that are sometimes missed by technologists. Most of the abnormal cells found in this way are in rather early stages, such as atypical squamous cells (ASCs), but high-grade abnormalities missed by human screening are sometimes found by the computerized instrument. Scientists do not yet know whether the instrument can find enough high-grade abnormalities missed by human screening to have a significant impact on preventing invasive cervical cancers. Automated screening also increases the cost of the cervical cytology testing.

For now, the most important way to improve early detection of cervical cancer is to make certain that all women are tested according to ACS guidelines. Unfortunately, many of the women most at risk for cervical cancer are not being tested often enough or at all.

How Pap Test Results Are Reported

The most widely used system for describing Pap test results is *The Bethesda System (TBS)*. This system was revised twice since it was developed in 1988 -- first in 1991 and, most recently, in 2001. The information that follows is based on the 2001 version. The general categories are:

- Negative for intraepithelial lesion or malignancy
- Epithelial cell abnormalities
- Other malignant neoplasms

Negative for intraepithelial lesion or malignancy: This first category means that no signs of cancer or precancerous changes or other significant abnormalities were found. Some specimens in this category appear entirely normal. Other findings may be unrelated to cervical cancer, such as evidence of reproductive system infections (yeast, herpes, or *Trichomonas*, for example). Some cases may also show *reactive cellular changes*, which is a response of cervical cells to infection or other irritation.

Epithelial cell abnormalities: The second TBS category, *epithelial cell abnormalities*, means that the cells of the lining layer of the cervix show changes that might indicate cancer or a precancerous condition. This category is divided into several groups for squamous cells and glandular cells.

- The epithelial cell abnormalities for squamous cells are called *atypical squamous cells (ASCs)*, *low-grade squamous intraepithelial lesion (SIL)*, *high-grade SIL*, and *squamous cell carcinoma*:
 - *Atypical squamous cells:* This term is used when it is not possible to tell (from how the cells look under a microscope) whether the abnormal cells are caused by an infection or another cause of irritation or by a precancer. The Pap test is repeated in 4 months, or other tests, such as colposcopy (explained below) and biopsy, may be recommended, depending on the patient's history and the results of previous Pap tests. Some doctors recommend having an HPV test in this situation.
 - *Squamous intraepithelial lesions (SILs)* are subdivided into *low-grade SIL* and *high-grade SIL*. High-grade SILs are less likely than low-grade SILs to go away without treatment and are more likely to eventually develop into cancer if they are not treated. However, treatment can cure all SILs and prevent true cancer from developing. A Pap test cannot determine for certain whether or a woman has a high- or low-grade SIL. It merely flags the result as fitting into one of these abnormal categories. The need for treatment is based on further testing and examination (see below).
 - *Squamous cell carcinoma:* This cytology result indicates that the woman is likely to have an invasive squamous cell cancer. Further testing will be done to be sure of that diagnosis before doctors recommend treatments such as radiation therapy, chemotherapy, or radical surgery.
- The Bethesda System also describes epithelial cell abnormalities for glandular cells. Cancers of the glandular cells are reported as *adenocarcinomas*. In some cases, the pathologist examining the cells can suggest whether the adenocarcinoma started in the endocervix, in the

endometrium (the upper part of the uterus), or elsewhere in the body. When the glandular cells have features that do not permit a clear decision as to whether or not they are cancerous, the term used is *atypical glandular cells*. The patient will usually undergo further testing if her cervical cytology result shows atypical glandular cells.

Other malignant neoplasms: This third TBS category refers to forms of cancer such as malignant melanoma, sarcomas, and lymphoma. Compared with squamous cell carcinoma and adenocarcinoma, these cancers affect the cervix very rarely.

Additional Tests for Women with Abnormal Cervical Cytology Results

Because cervical cytology is a screening test rather than a diagnostic test, if you have an abnormal result, you will need to have additional tests (colposcopy and biopsy, and sometimes an endocervical scraping) to find out whether a precancerous change or cancer is present. Nearly all doctors recommend one or more of these tests for women with a Pap result of SIL or atypical glandular cells.

Doctors are less certain about what to do when the result is atypical squamous cells. Some recommend colposcopy and biopsy, and others recommend a repeat Pap test in 6 months. In making decisions about follow-up, some doctors will consider your previous Pap test results, whether you have any cervical cancer risk factors, and whether you have remembered to have Pap tests done in the past.

Recently, some doctors have started using an intermediate step, testing for HPV. If a high-risk type of HPV is found in women with atypical squamous cells, particularly if they are middle aged or older, doctors are more inclined to perform a colposcopy. Generally, if you have SIL, a colposcopy will be done. If the biopsy shows SIL, or dysplasia, steps will be taken to prevent progression to an actual cancer.

Colposcopy: If certain symptoms suggest cancer or if the Pap test shows abnormal cells, you will need to have an additional test called a *colposcopy*. In this procedure the doctor views the cervix through a *colposcope*, an instrument with magnifying lenses very much like binoculars. With the colposcope, doctors can see the surface of the cervix closely and clearly.

The exam is not painful, has no side effects, and can be performed safely even if you are pregnant. If abnormal areas are seen on the cervix, a *biopsy* (removal of a small tissue sample) is done. The sample is sent to a pathologist to examine under a microscope. A biopsy is the only way to tell for certain whether an abnormal area is a precancer, a true cancer, or neither.

Cervical biopsies: Several types of biopsies are used to diagnose cervical precancers and cancers. For precancers and early cancers, some types of biopsies can completely remove the abnormal tissue and may be the only treatment needed. In some situations, additional treatment of precancers or cancers is needed.

- **Colposcopic biopsy:** For this type of biopsy, a doctor or other health care professional first examines the cervix with a colposcope to find the abnormal areas. Using a biopsy forceps, he

or she will remove a small (about 1/8 inch) section of the abnormal area on the surface of the cervix. The biopsy procedure may cause mild cramping or brief pain, and you may have light bleeding afterward. A local anesthetic may be used to numb the cervix.

- **Endocervical curettage (endocervical scraping):** This procedure is usually done during the same session as the colposcopic biopsy. A narrow instrument (the *curette*) is inserted into the *endocervical canal* (the passage between the outer part of the cervix and the inner part of the uterus). Some of the tissue lining the endocervical canal is removed by scraping with the curette, and this tissue sample is sent to the laboratory for examination.

Because the colposcope allows a view only of the outer part of the cervix and not into the endocervix, health care professionals use endocervical scraping to find out if this area is affected by precancer or cancer. A local anesthetic may be used to numb the cervix. Patients may have a temporary sensation, similar to a severe menstrual cramp, and they may have light bleeding after the procedure.

- **Cone biopsy:** In this procedure, also known as *conization*, the doctor removes a cone-shaped piece of tissue from the cervix. The base of the cone is formed by the ectocervix (outer part of the cervix), and the point or apex of the cone is from the endocervical canal.

The *transformation zone* (the border between the ectocervix and endocervix) is contained within the cone. This is the area of the cervix where precancers and cancers are most likely to develop. The cone biopsy is also a treatment and can be used to completely remove many precancers and very early cancers.

There are 2 methods commonly used for cone biopsies: the *loop electrosurgical excision procedure* (LEEP; also called large loop excision of the transformation zone [LLETZ]) and the *cold knife cone biopsy*.

- **LEEP (LLETZ):** The tissue is removed with a wire that is heated by electrical current. For this procedure, a local anesthetic is used, and it can be done in your doctor's office. It takes only about 10 minutes. You may have mild cramping during and after the procedure, and mild to moderate bleeding may persist for several weeks.
- **Cold knife cone biopsy:** A surgical scalpel or a laser as a scalpel is used rather than a heated wire to remove tissue. It requires general anesthesia (you are asleep during the operation) and is done in a hospital, but no overnight stay is needed. After the procedure, cramping and some bleeding may persist for a few weeks.

How biopsy results are reported: The terms for reporting biopsy results are slightly different from The Bethesda System for reporting Pap test results. Instead of The Bethesda System term squamous intraepithelial lesion (SIL), biopsy reports use 2 other terms, *cervical intraepithelial neoplasia (CIN)* and *dysplasia*, to refer to precancerous changes. The terms for reporting cancers (squamous cell carcinoma and adenocarcinoma) are the same.

How Patients with Abnormal Pap Test Results Are Treated to Prevent Cervical Cancers from Developing

If an area of SIL is seen during the colposcopy, your doctor will be able to remove the abnormal area by using such biopsy techniques as the LEEP (LLETZ procedure) or a cold knife cone biopsy or by destroying the abnormal cells with cryosurgery or laser surgery.

- During *cryosurgery*, the doctor uses a metal probe cooled with liquid nitrogen to kill the abnormal cells by freezing them.
- In *laser surgery*, the doctor uses a focused beam of high-energy light to vaporize (burn off) the abnormal tissue.

Both of these outpatient treatments can be done in a doctor's office or clinic. After treatment, you may have a watery brown discharge for a few weeks.

These treatments are almost always effective in destroying precancers and preventing them from developing into true cancers. You will need follow-up examinations to make sure that the abnormality does not come back. If it does, treatments can be repeated.

Can Cervical Cancer Be Found Early?

Cervical cancer can usually be found early by having regular cervical cytology (Pap) tests. Being alert to any signs and symptoms of cervical cancer (see "How Is Cervical Cancer Diagnosed?") can also help avoid unnecessary delays in diagnosis. Early detection greatly improves the chances of successful treatment.

The Importance of the Pap Test in Finding Cervical Cancer and Precancerous Changes

Cervical cancer deaths are higher in populations around the world where women do not have routine Pap tests. In fact, cervical cancer is the major cause of cancer deaths in women in many developing countries. These cases are usually diagnosed at an invasive late stage, rather than as precancers or early cancers.

Despite the recognized benefits of Pap test screening, not all American women take advantage of it. Between 60% and 80% of American women with newly diagnosed invasive cervical cancer have not had a Pap smear in the past 5 years, and many of these women have never had a Pap test. In particular, elderly, African-American, and low-income women are less likely to have regular Pap tests.

Financial Assistance for Low-Income Women

Breast cancer and cervical cancer screening is now more available to medically underserved women through the National Breast and Cervical Cancer Early Detection Program (NBCCEDP). This program provides breast and cervical cancer early detection testing to women without health insurance for free or at very little cost.

The NBCCEDP tries to reach as many women in medically underserved communities as possible, including older women, women without health insurance, and women of racial and ethnic minority groups. Although each state runs its own program, the Centers for Disease Control and Prevention (CDC) provide matching funds and support to each state program.

Offered mainly through non-profit organizations and local health clinics, this program is aimed at providing testing for breast and cervical cancer in medically underserved women. Each state's Department of Health will have information on how to contact the nearest program participant.

How Is Cervical Cancer Diagnosed?

Signs and Symptoms of Cervical Cancer

Cervical precancers and early cancers usually show no symptoms or signs. A woman usually develops symptoms when the cancer has become invasive.

- An unusual discharge from the vagina (separate from your normal monthly menstrual period) can be a sign of cervical cancer. Such discharges may include blood spots or light bleeding and may occur between your periods.
- Bleeding following intercourse is a common symptom.
- Pain during intercourse may also indicate cervical cancer.

However, all of these signs and symptoms can be caused by conditions other than cervical cancer. For example, an infection can cause pain or bleeding. If you have any of these signs or other suspicious symptoms, you should see your health care professional right away. Ignoring symptoms may allow the cancer to progress to a more advanced stage and lower your chance for effective treatment.

Even better, don't wait for symptoms to appear. Have a regular Pap test and pelvic examination.

Your routine health care professional can treat precancers. However, if your biopsy result indicates that you have cervical cancer, you may need to consult with a surgeon who specializes in treating this type of cancer. If there is a question of invasive cancer, your doctor will refer you to a *gynecologic oncologist*, a doctor who specializes in women's reproductive system cancers. Some patients will be referred to a *radiation oncologist*, a doctor who specializes in treating cancers with radiation.

Many of the diagnostic tests described below are not necessary for every patient. Decisions about using these tests are based on the results of the physical examination and initial biopsy.

Medical History and Physical Examination

Getting your complete personal and family medical history will be the first step your doctor will take in your consultation. This will include information related to risk factors and symptoms of cervical cancer. A complete physical examination will help evaluate your general state of health. In addition, special attention will be paid to your lymph nodes for evidence of *metastasis* (cancer spread).

Cystoscopy, Proctoscopy, and Examination Under Anesthesia

In *cystoscopy* a slender tube with a lens and a light is placed into the bladder through the urethra. If you have cervical cancer, this allows your doctor to check your bladder and urethra to see if your cancer is growing into these structures.

Small tissue samples can also be removed during cystoscopy for pathologic (microscopic) testing. This procedure can be done using a local anesthetic, but some patients may need general anesthesia. Your doctor will let you know what to expect before and after the procedure.

Proctoscopy is a visual inspection of the rectum through a lighted tube to check for spread of cervical cancer into your rectum. Your doctor will also do a pelvic examination while you are under anesthesia to find out whether the cancer has spread beyond the cervix.

Imaging Studies

If your doctor finds that you have cervical cancer, certain imaging studies will be done. These include *magnetic resonance imaging (MRI)* and *computed tomography (CT)* scans. These studies can show whether the cancer has spread beyond the cervix.

Chest x-ray: A plain x-ray of your chest will be done to see if your cancer has spread to your lungs. This is very unlikely unless your cancer is far advanced. This x-ray can be done in any outpatient setting. If the results are normal, you probably don't have cancer in your lungs.

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 pelvis. The machine will create multiple images of your abdomen and pelvis.

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.

You will need an IV (intravenous) line through which the contrast dye is injected. The injection can also cause a flushed feeling. 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.

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. MRI scans are very helpful in looking at the pelvis.

A contrast material might be injected, just as with CT scans, but is used less often. The machine makes a thumping noise that you may find disturbing; however, some places will provide headphones with music to block this out.

Positron emission tomography (PET): PET uses *glucose* (a form of sugar) that contains a radioactive atom. Compared with normal cells, the cancer cells absorb more of the radioactive sugar because of their high rate of metabolism. A special camera can detect the radioactivity. PET may be used to tell if your cancer has spread to lymph nodes in the pelvis. There are usually no side effects, and you are exposed to only a tiny amount of radioactivity.

Intravenous urography: Intravenous urography (also known as *intravenous pyelogram*, or *IVP*) is useful in finding abnormalities of the urinary tract, such as changes caused by spread of cervical cancer to the pelvic lymph nodes, which may compress or block a ureter. An IVP is an x-ray of the urinary system taken after injecting a special dye into a vein. This dye is removed from the bloodstream by the kidneys and passes into the ureters and bladder. You might not need an IVP if you have already had a CT or MRI.

How Is Cervical Cancer Staged?

The process of finding out how far the cancer has spread is called *staging*. Information is gathered from exams and diagnostic tests to determine the size of the tumor, how deeply the tumor has invaded tissues within and around the cervix, and the presence of *metastasis* (spread to lymph nodes or distant organs). This is an important process because the stage of the cancer is the key factor in selecting the right treatment plan.

A *staging system* is a way for members of the cancer care team to summarize the extent of a cancer's spread. Cervical cancer is staged with the *FIGO* (International Federation of Gynecology and Obstetrics) System of Staging. This system classifies the disease in stages 0 through IV. It is based on clinical staging rather than surgical staging. This means that the extent of disease is evaluated by the doctor's physical examination and a few other tests that are done in some cases, such as cystoscopy and proctoscopy.

If surgery is done, it may reveal that the cancer has spread more than the doctors initially thought. This new information may change the treatment plan, but it does not change the patient's FIGO stage.

Stage 0: The tumor is *carcinoma in situ*. If your cancer is in this stage, it is very superficial, is found only in the layer of cells lining the cervix, and has not invaded deeper tissues of the cervix.

Stage I: If your cancer is this stage, it has invaded the cervix, but it has not spread anywhere else.

Stage IA: This is the earliest form of stage I. There is a very small amount of cancer, and it is visible only under a microscope.

Stage IA1: The area of invasion is less than 3 mm (about 1/8 inch) deep and less than 7 mm (about 1/4 inch) wide.

Stage IA2: The area of invasion is between 3 mm and 5 mm (about 1/5 inch) deep and less than 7 mm (about 1/4 inch) wide.

Stage IB: In this stage, the cancer usually can be seen without a microscope. But this stage also includes cancers that have spread deeper than 5 mm (about 1/5 inch) into connective tissue of the cervix or are wider than 7 mm and can only be detected using a microscope.

Stage IB1: The cancer is no larger than 4 cm (about 1 3/5 inches).

Stage IB2: The cancer is larger than 4 cm.

Stage II: In this stage, the cancer has spread beyond the cervix to nearby areas, but it is still inside the pelvic area.

Stage IIA: The cancer has spread beyond the cervix to the upper part of the vagina. It is not in the lower third of the vagina.

Stage IIB: The cancer has spread to the tissue next to the cervix, called the *parametrial tissue*.

Stage III: The cancer has spread to the lower part of the vagina or the pelvic wall. The cancer may be blocking the *ureters* (tubes that carry urine from the kidneys to the bladder).

Stage IIIA: The cancer has spread to the lower third of the vagina but not to the pelvic wall.

Stage IIIB: The cancer extends to the pelvic wall and/or blocks urine flow to the bladder.

Stage IV: This is the most advanced stage of cervical cancer. The cancer has spread to nearby organs or other parts of the body.

Stage IVA: The cancer has spread to the bladder or rectum, which are organs close to the cervix.

Stage IVB: The cancer has spread to distant organs beyond the pelvic area, such as the lungs.

How Is Cervical Cancer Treated?

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

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

Of course, your cancer care team may have reasons for suggesting a treatment plan different from these general guidelines. Don't hesitate to ask them questions about your treatment options. In addition to the information in this document, we encourage interested patients to seek out treatment information from other reliable sources.

The options for treating each patient with cervical cancer depend on the stage of disease. The stage of a cancer describes its size, depth of invasion, and how far it has spread.

After establishing the stage of your cervical cancer, your cancer care team will recommend one or more treatment options. Consider your options without feeling rushed. If there is anything you do not understand, ask for explanations. Although the choice of treatment depends largely on the stage of the disease at the time of diagnosis, other factors that may influence your options are your age, your general health, your individual circumstances, and your preferences. Be sure that you understand all the risks and side effects of the various treatments before making a decision.

It is often a good idea to seek a second opinion, especially with doctors experienced in treating cervical cancer. A second opinion can provide more information and help you feel more confident about the treatment plan that is being considered. Some insurance companies require a second opinion before they will agree to pay for certain treatments. Almost all will pay for a second opinion.

The 3 main methods of cancer treatment are surgery, radiation therapy, and chemotherapy. Sometimes the best treatment approach uses 2 or more of these methods. 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 to prevent the tumor from growing, spreading, or returning for as

long as possible. Sometimes treatment is aimed at relieving symptoms. This is called *palliative* treatment.

Surgery

Cryosurgery: A metal probe cooled with liquid nitrogen is used to kill the abnormal cells by freezing them. Cryosurgery is used for treating preinvasive cervical cancer but not for treating invasive cancer.

Laser surgery: A focused laser beam is used to *vaporize* (burn off) abnormal cells or to remove a small piece of tissue for study. Laser surgery is used as treatment for preinvasive cervical cancer. It is not used to treat invasive cancer.

Cone biopsy: A cone-shaped piece of tissue is removed from the cervix. This is done using a surgical or laser knife (cold knife cone biopsy) or using a thin wire heated by electricity (the LEEP or LEETZ procedure). See the section "Can Cervical Cancer Be Prevented?" for more information. A cone biopsy is rarely used as the sole treatment, except in women with early (stage IA) cancer who might want to have children. It may be used to establish the diagnosis of cancer before treatment with additional surgery or radiation. This procedure is also known as *conization*.

Simple hysterectomy: This is surgical removal of the *uterus* (the body of the uterus and the cervix). The structures next to the uterus (parametria and uterosacral ligaments) are not removed. The vagina remains entirely intact, and pelvic lymph nodes are not removed. The ovaries and fallopian tubes are usually left in place unless they are affected by some other disease or the patient is at least 45 to 50 years old.

The uterus is removed through a surgical incision in the front of the abdomen or through the vagina. General or *epidural* (regional) anesthesia is used. A hospital stay of 3 to 5 days is common for an abdominal hysterectomy, and complete recovery takes about 4 to 6 weeks. For a vaginal hysterectomy, the hospital stay is usually 1 to 2 days followed by a 2- to 3-week recovery period. This surgery results in *infertility* (inability to have children). Complications are unusual but could include excessive bleeding, wound infection, or damage to the urinary or intestinal systems.

A simple hysterectomy is done to treat some stage IA cervical cancers. The operation is used for some stage 0 cancers (*carcinoma in situ*), for instance, when the abnormal cells are in the surgical *margins* (edges) of the cone biopsy. The same operation is also used to treat some noncancerous conditions. The most common of these is leiomyomas, a type of benign tumor commonly known as fibroids.

Radical hysterectomy and pelvic lymph node dissection: Like a simple hysterectomy, this operation removes the entire uterus. However, the tissues next to the uterus (parametria and uterosacral ligaments), the upper part (about 1 inch) of the vagina next to the cervix, and lymph nodes (bean-shaped collections of immune system tissue) from the pelvis are also removed. The ovaries and fallopian tubes are not removed unless there is some other medical reason to do so.

Although this surgery is usually performed through an abdominal incision, it is also possible to use a vaginal approach, in combination with a laparoscopic pelvic node dissection. *Laparoscopy* is a method for viewing the inside of the abdomen and pelvis through a tube inserted into a very small surgical incision. Small instruments can be controlled through the tube, so the surgeon can remove lymph nodes through the tube without making a large cut in the abdomen. The laparoscope can also help doctors remove the uterus, ovaries, and fallopian tubes through a vaginal incision, so that an abdominal incision is not needed. This approach is called *laparoscopic-assisted vaginal hysterectomy*.

Since more tissue is removed than in a simple hysterectomy, the hospital stay after a radical hysterectomy is longer -- about 5 to 7 days. The surgery results in infertility. Complications are unusual but could include excessive bleeding, wound infection, or damage to the urinary and intestinal systems. A radical hysterectomy and pelvic lymph node dissection are the usual treatment for stages IA2, IB, and IIA cervical cancer, especially in young people.

Sexual impact of hysterectomy: Radical hysterectomy does not change a woman's ability to feel sexual pleasure. Although the vagina is shortened, the area around the clitoris and the lining of the vagina remains as sensitive as before. A woman does not need a uterus or cervix to reach orgasm.

Some women feel less feminine after a hysterectomy. They view themselves as "an empty shell." Such thoughts do not enhance sexual pleasure. However, when cancer has caused pain or bleeding with intercourse, the hysterectomy should actually improve a woman's sex life by stopping these symptoms.

Pelvic exenteration: In addition to removing all of the organs and tissues as in a radical hysterectomy and pelvic lymph node dissection, this operation may also remove the bladder, vagina, rectum, and part of the colon. This operation is used to treat recurrent cervical cancer.

If the bladder is removed, a new way to store and eliminate urine is needed. This usually means using a short segment of intestine to function as a new bladder. The new bladder may be connected to the abdominal wall so that urine is drained periodically when the patient places a catheter into a *urostomy* (a small opening). Or urine may drain continuously into a small plastic bag attached to the front of the abdomen.

If the rectum and part of the colon are removed, a new way to eliminate solid waste must be created. This is done by attaching the remaining intestine to the abdominal wall so that fecal material can pass through a *colostomy* (a small opening) into a small plastic bag worn on the front of the abdomen. It may be possible to remove the involved colon (next to the cervix) and reconnect the colon so that no bags or external appliances are needed. If the vagina is removed, a new vagina can be surgically created out of skin, intestinal tissue, or *myocutaneous* (muscle and skin) grafts.

Sexual impact of pelvic exenteration: Recovery from total pelvic exenteration takes a long time. Most women don't begin to feel like their normal selves again for 6 months after surgery. Some say it takes a year or two to adjust completely.

Nevertheless, these women can lead happy and productive lives. With practice and determination, they can also have sexual desire, pleasure, and orgasm. The outer genitals, including the clitoris, are not usually removed. Therefore, a woman can still feel pleasure and reach orgasm when touched in this area.

Radiation Therapy

Radiation therapy uses high energy x-rays to kill cancer cells. These x-rays may be given externally in a procedure that is much like having a diagnostic x-ray. This is called *external beam radiation therapy*. The second type of radiation therapy is called *brachytherapy*. It may be given as a capsule of radioactive material placed in the vagina near the tumor, or the radioactive material may be placed in thin needles that are inserted directly in the tumor.

The skin in the treated area may look and feel sunburned, but this gradually fades to a tanned look, returning to a normal appearance in 6 to 12 months. Many women also notice tiredness, upset stomach, or loose bowels. Pelvic radiation therapy may cause vaginal *stenosis* (narrowing of the vagina by scar tissue), which might make intercourse painful. Premature menopause and problems with urination may also occur.

If you are having side effects from radiation, discuss them with your cancer care team. There are things you can do to get relief from these symptoms or to keep them from happening, such as using vaginal dilators to manage vaginal stenosis.

Chemotherapy

Systemic chemotherapy uses anticancer drugs that are injected into a vein or given by mouth. These drugs enter the bloodstream and reach all areas of the body, making this treatment potentially useful for cancers that have metastasized (spread to distant organs).

Drugs most often used in treating cervical cancer include cisplatin, paclitaxel, ifosfamide, hydroxyurea, fluorouracil and, irinotecan. If chemotherapy is chosen, you may receive a combination of drugs. Chemotherapy drugs kill cancer cells but also damage some normal cells, which can lead to side effects.

Chemotherapy side effects depend on the type of drugs, the amount taken, and the length of time you are treated. Temporary side effects of chemotherapy might include:

- Nausea and vomiting
- Loss of appetite
- Loss of hair
- Mouth sores

Because chemotherapy can damage the blood-producing cells of the bone marrow, the blood cell counts might become low. 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)
- Shortness of breath (due to low red blood cell counts)

Fatigue is also quite common and may be caused by low red blood cell counts, by other reasons related to the chemotherapy, or by the cancer itself.

Most side effects of chemotherapy (except premature menopause and infertility) disappear once treatment is stopped. Hair will grow back after treatment ends. Premature menopause can be treated with hormones.

If you have problems with side effects, talk with your cancer care team. There are remedies for many of the temporary side effects of chemotherapy. For example, antiemetic (antinausea) drugs to prevent or reduce nausea and vomiting can be given. Other drugs can be given to boost blood cell production.

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. Doctors 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: These 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 results 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 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 Web site (www.cancer.gov/clinical_trials).

Treatment Options for Cervical Cancer by Stage

The stage of a cervical cancer is the most important factor in choosing treatment. However, other factors that affect this decision include the exact location of the cancer within the cervix, the type of cancer (squamous cell or adenocarcinoma), your age, your overall physical condition, and whether you want to have children.

Stage 0 (carcinoma in situ): Treatment options are the same as for precancerous changes (dysplasia or cervical intraepithelial neoplasia [CIN]). Options include cryosurgery, laser surgery, loop electrosurgical excision procedure (LEEP/LEETZ), and cold knife conization. A simple hysterectomy may be done if the cancer returns and you do not want to have more children. All of these cancers can be cured with appropriate treatment. However, the precancerous changes or the stage 0 cancer can *recur* (come back) in the cervix or vagina, so close follow-up is very important.

Stage IA: If you have stage IA cervical cancer, your treatment will most likely be a simple hysterectomy. However, if the amount of cancer is more than 3 mm or the cancer has invaded the blood vessels or lymph vessels, you will need a radical hysterectomy.

If your tumor invasion is very superficial and you want to have additional children, treatment by cold knife conization is another option. This approach requires careful medical follow-up so that additional treatment can be given if the cancer *recurs* (comes back). You might want to consult with a gynecologic oncologist to see if you qualify for this treatment. The 5-year survival rate for treatment at this stage is more than 95%.

If you have a hysterectomy, tissue removed by this procedure will be examined in the laboratory to see if the cancer has spread further than expected. If the cancer has spread to the parametrium (tissue next to the uterus) or to lymph nodes or if it has not been completely removed by surgery, radiation therapy is usually recommended.

Stage IB: Either of 2 treatments may be used if you have stage IB cervical cancer. The first option is a radical hysterectomy with selective para-aortic (high up in the back of the abdomen) and radical bilateral (both sides) pelvic lymph node dissection. If cancer cells are found in the edges of the organs removed or if cancer cells are detected in lymph nodes in this operation, you may be given radiation therapy, possibly with chemotherapy, after surgery. Rarely, women with stage IB cancers with certain patterns of growth and invasion are given radiation therapy before a hysterectomy.

The second treatment option is high-dose internal and external radiation therapy. Cure rates (about 85% to 90%) are about the same for high-dose radiation therapy or radical hysterectomy with pelvic lymph node dissection. So, how a woman feels about the side effects of the 2

treatments and the presence of any other medical conditions that might make surgery dangerous should be the basis for deciding between the 2 options.

Recent clinical trial results indicate that the combination of radiation therapy and chemotherapy with cisplatin is more effective than radiation alone for women with stage IB2 cervical cancer. This prompted the National Cancer Institute to recommend that chemotherapy be considered in all patients receiving radiation therapy for cervical cancer larger than 4 cm (about 1 3/5 inches).

Stage IIA: Just as in stage IB, either of 2 treatments may be used. The first is high-dose internal and external radiation therapy. The second option is radical hysterectomy with selective para-aortic (high up in the back of the abdomen) and radical bilateral (both sides) pelvic lymph node dissection.

Cure rates (about 75% to 80%) are about the same for radiation therapy or radical hysterectomy with lymph node dissection. Your treatment choice will depend on the size and other characteristics of the tumor, your feelings about the side effects of the 2 treatments, and the presence of any other medical conditions that might make surgery or radiation therapy dangerous.

If you have a hysterectomy, tissue removed by this procedure will be examined in the laboratory to see if the cancer has spread further than expected. If the cancer has spread to the parametrium (tissue next to the uterus) or to lymph nodes or if it has not been completely removed by surgery, radiation therapy is usually recommended. Recent clinical trial results indicate that the combination of radiation therapy and chemotherapy with cisplatin, possibly combined with other drugs, is more effective than radiation alone.

Stage IIB: Combined internal and external radiation therapy is the usual treatment. The 5-year survival rate is about 65%. Recent clinical trial results indicate that the combination of radiation therapy and chemotherapy with cisplatin, possibly combined with other drugs, is more effective than radiation alone.

Stage III and IVA: Most doctors combine these 2 groups in terms of treatment and predicting *prognosis* (outlook for chances of survival). Combined internal and external radiation therapy was once the recommended treatment, and the 5-year survival rates were as low as 20% to 40%.

New studies show that the combination of radiation therapy and chemotherapy with cisplatin, possibly along with other drugs, is more effective than radiation alone. This is now recommended as standard treatment for women with advanced stage cervical cancer. The 5-year survival rate in the clinical trials of radiotherapy and chemotherapy was about 50%. These studies of radiation and chemotherapy excluded women whose cancer had spread to para-aortic lymph nodes (high up in the back of the abdomen). They have a worse outlook.

Stage IVB: Cancer at this stage is not usually considered curable. Treatment options include radiation therapy to relieve the symptoms of local (near the cervix) spread or of distant metastases. Chemotherapy is often recommended. Clinical trials are in progress to test new

combinations of one or more chemotherapy drugs, as well as some other experimental treatments.

Recurrent cervical cancer: This means that the disease has come back after treatment. Recurrence can be local (in the pelvic organs near the cervix) or distant (spread through the lymphatic system and/or the bloodstream to organs such as the lungs or bone).

If the cancer has recurred in the pelvis only, treatment by *pelvic exenteration* (extensive surgery) is an option for some patients. This operation may successfully treat 40% to 50% of patients. (See the discussion under Surgery in the section "How Is Cervical Cancer Treated?") Or *palliative treatment* (treatment to relieve symptoms) using radiation or chemotherapy may be chosen.

If your cancer has recurred in a distant area, palliation of specific symptoms using chemotherapy or radiation therapy is an option. If chemotherapy is used, you should understand the goals and limitations of this therapy. Sometimes chemotherapy can improve your quality of life, and other times it can diminish it. You need to discuss this with your doctors. From 15% to 25% of patients may respond at least temporarily to chemotherapy.

New treatments that may benefit patients with distant recurrence of cervical cancer are being evaluated in clinical trials. You may want to think about participating in a clinical trial.

Cervical Cancer in Pregnancy

A small number of cervical cancers are found in pregnant women. If your cancer is a very early cancer, such as stage IA, then most doctors believe that it is safe to continue the pregnancy to term. Several weeks after delivery, a hysterectomy or a cone biopsy is recommended (the cone biopsy is suggested only for substage IA1).

If the cancer is stage IB, then you and your doctor must decide whether to continue the pregnancy. If not, treatment would be radical hysterectomy and/or radiation. If you decide to continue the pregnancy, the baby should be delivered by cesarean section as soon as it is able to survive outside the womb. For more advanced cancers, immediate treatment is the safest option.

Financial Assistance for Low-Income Women

Breast cancer and cervical cancer screening is now more available to medically underserved women through the National Breast and Cervical Cancer Early Detection Program (NBCCEDP). This program provides breast and cervical cancer early detection testing to women without health insurance for free or at very little cost.

In 2000, the Breast and Cervical Cancer Treatment Act was signed into law. This act enhances the NBCCEDP by providing funds to pay for treatment associated with breast and cervical cancer in medically underserved populations. This new option will help women focus their energies on fighting their disease, instead of worrying about how to pay for treatment. As in the Early Detection Program, individual states must adopt the program in order to receive the matching federal funds.

For more information on this program, please contact the CDC at 1-888-842-6355 or on the Internet at www.cdc.gov/cancer.

What Should You Ask Your Doctor About Cervical Cancer?

It is important for you to have frank, open discussions with your cancer care team. They want to answer all of your questions, no matter how trivial you might think they are. Here are some questions to consider:

- What type of cervical cancer do I have?
- Has my cancer spread beyond the cervix?
- Can the stage of my cancer be determined and what does that mean?
- What treatments choices do I have?
- What treatment do you recommend and why?
- What risks or side effects are there to the treatment you suggest?
- Will I be able to have children after my treatment?
- What should I do to be ready for treatment?
- What are the chances my cancer will recur (come back) with the treatment programs we have discussed?
- Should I follow a special diet?
- Based on what you've learned about my cancer, what is my prognosis (outlook for chances of survival)?
- Where can I get a wig if I will receive chemotherapy drugs likely to cause temporary hair loss?
- What do I tell my children, husband, parents, and other family members?

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

What Happens After Treatment for Cervical Cancer?

Follow-Up Care

An important part of your treatment plan is a specific schedule of follow-up visits after surgery, chemotherapy, or radiation therapy to be sure what, if any, additional treatment is necessary.

Follow-up may include procedures such as x-rays, computed tomography (CT) scans, ultrasound studies, or magnetic resonance imaging (MRI) scans. Biopsies (to get tissue samples for microscopic evaluation), blood tests, and other examinations may also be needed.

Which tests should be done and how often will depend on the stage of your cancer. You should report any new symptoms to your doctor right away, so that cancer recurrence or side effects of therapy can be treated as effectively as possible.

Other Things to Consider

During and after treatment 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, had a better quality of life. There are also experienced professionals in mental health services, social work services, and pastoral services who may help you cope with your illness.

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. Rest as much as you need to 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.

A cancer diagnosis and its treatment are major life challenges, affecting you and everyone who cares for you. Before you reach the point of feeling overwhelmed, consider attending a meeting of a local support group. Many groups are available that provide emotional support, friendship, and understanding. Your health care team can suggest other organizations that might help you during recovery from treatment. If you need individual assistance in other ways, contact your hospital's social service department or call us (1-800-ACS-2345) for help in contacting counselors or other services.

What's New in Cervical Cancer Research and Treatment?

Research is underway to find new ways to prevent and treat cancer of the cervix. Some of the promising new developments include the following:

HPV tests: Researchers are developing new laboratory tests to detect the types of human papillomaviruses (HPVs) that cause cancer. Other studies are focusing on whether the information from these tests actually helps doctors prevent cervical cancer.

Recent studies suggest that a new test called the Hybrid Capture HPV Test may be useful and cost-effective in determining which women with cytology results of atypical squamous cells should have a colposcopy. Other trials are underway to see if self-collection of samples for the HPV test is as good as a Pap test. This may be particularly useful in developing countries where there are not enough health care professionals to collect or analyze the usual type of Pap smear specimens.

HPV vaccines: Vaccines for preventing and treating cervical cancer are being developed and tested. Some of these vaccines are intended to produce immunity to HPV, so that women who are exposed to these viruses will not develop infections that persist for a long time. Instead, a woman's immune system will destroy the virus before an infection becomes fully established.

Other vaccines are intended for women with established HPV infections, to help their immune systems destroy the virus and cure the infection before a cancer develops. Still other vaccines are meant to help women who already have advanced cervical cancer that has recurred or metastasized. These vaccines attempt to produce an immune reaction to the parts of the virus (E6 and E7 proteins) that specifically contribute to the abnormal growth of cervical cancer cells. It is hoped that this immunity will kill the cancer cells or stop them from growing.

Preliminary studies of one vaccine found that it was successful in preventing HPV-16 from causing precancerous changes. Studies are currently in progress to determine whether it actually lowers their risk of developing cervical cancer. The researchers are also working on similar vaccines that would protect women against several high risk HPV types (HPV-16, HPV-18, and several others).

Surgery: Doctors are now attempting to cure some early stage cervical cancers while removing as little normal tissue as possible. A newer procedure, known as a radical trachelectomy, may allow certain young women with early stage cancer (Stage IA) to maintain their ability to have children. This procedure involves the removal of the cervix and the upper part of the vagina, and placing a "purse-string" stitch to act as an artificial cervix. The nearby lymph nodes are also removed using laparoscopy.

Although more long-term studies are needed, early clinical trials thus far have found few cancer recurrences after the procedure. And while the risk of miscarriage appears to be higher than normal, some women are able to carry pregnancy to term and deliver healthy babies via cesarean section.

While some cancer centers US are performing radical trachelectomies on selected patients, most still consider the procedure to be experimental at this time.

Other clinical trials: Many clinical trials are underway to test new chemotherapy drugs, new ways of giving radiation therapy, and new combinations of surgery and radiation therapy or chemotherapy.

Additional Resources

National Organizations and Web Sites

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

Gynecologic Cancer Foundation

Telephone: 1-800-444-4441 or 1-312-644-6610

Internet Addresses: www.sgo.org and www.wcn.org/gcf/

National Cancer Institute

Telephone: 1-800-4-CANCER

Internet Address: www.nci.nih.gov

National Cervical Cancer Coalition

Internet Address: www.nccc-online.org

National Coalition for Cancer Survivorship

Telephone: 1-888-650-9127

Internet Address: www.cansearch.org

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

American Cancer Society Publications

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)

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

Sexuality and Cancer: For the Woman Who Has Cancer and Her Partner (Booklet; Code# 4657)

Other Publications*

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

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Dollinger, Malin, Ernest H. Rosenbaum, and Greg Cable. *Everyone's Guide to Cancer Therapy.* Kansas City, Mo: Somerville House Books, 1997.

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

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