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Pap and HPV Testing

Key Points

- Cervical cancer screening, which includes the Pap test and HPV testing, is an essential part of a woman's routine health care because it can detect cancer or abnormalities that may lead to cancer of the cervix.
- Current guidelines recommend that women should have a Pap test every 3 years beginning at age 21. These guidelines further recommend that women ages 30 to 65 should have HPV and Pap cotesting every 5 years or a Pap test alone every 3 years. Women with certain risk factors may need to have more frequent screening or to continue screening beyond age 65.
- Women who have received the HPV vaccine still need regular cervical screening.

1. What causes cervical cancer?

Nearly all cases of cervical cancer are caused by infection with oncogenic, or high-risk, types of human papillomavirus, or HPV. There are about 12 high-risk HPV types. Infections with these sexually transmitted viruses also cause most anal cancers; many vaginal, vulvar, and penile cancers; and some oropharyngeal cancers.

Although HPV infection is very common, most infections will be suppressed by the immune system within 1 to 2 years without causing cancer. These transient infections may cause temporary changes in cervical cells. If a cervical infection with a high-risk HPV type persists, the cellular changes can eventually develop into more severe precancerous lesions. If precancerous lesions are not treated, they can progress to cancer. It can take 10 to 20 years or more for a persistent infection with a high-risk HPV type to develop into cancer.

2. What is cervical cancer screening?

Cervical cancer screening is an essential part of a woman's routine health care. It is a way to detect abnormal cervical cells, including precancerous cervical lesions, as well as early cervical cancers. Both precancerous lesions and early cervical cancers can be treated very successfully. Routine cervical screening has been shown to greatly reduce both the number of new cervical cancers diagnosed each year and deaths from the disease.

Cervical cancer screening includes two types of screening tests: cytology-based screening, known as the Pap test or Pap smear, and HPV testing. The main purpose of screening with the Pap test is to detect abnormal cells that may develop into cancer if left untreated. The Pap test can also find noncancerous conditions, such as infections and inflammation. It can also find cancer cells. In regularly screened populations, the Pap test identifies most abnormal cells before they become cancer.

HPV testing is used to look for the presence of DNA or RNA from high-risk HPV types in cervical cells. These tests can sometimes detect HPV infections before cell abnormalities are evident. The most common test detects DNA from the high-risk HPV types, but it cannot identify the specific type or types that are present. Another test is specific for DNA from HPV types 16 and 18, the two types that cause most HPV-associated cancers. A third test can detect DNA from several high-risk HPV types and can indicate whether HPV-16 or HPV-18 is present. A fourth test detects RNA from the most common high-risk HPV types.



3. How is cervical cancer screening done?

Cervical cancer screening can be done in a medical office, a clinic, or a hospital. It is often done during a pelvic examination.

While a woman lies on an exam table, a health care professional inserts an instrument called a speculum into her vagina to widen it so that the upper portion of the vagina and the cervix can be seen. This procedure also allows the health care professional to take a sample of cervical cells. The cells are taken with a wooden or plastic scraper and/or a cervical brush and are then prepared for analysis in one of two ways. In a conventional Pap test, the specimen (or smear) is placed on a glass microscope slide and a fixative is added. In an automated liquid-based Pap cytology test, cervical cells collected with a brush or other instrument are placed in a vial of liquid preservative. The slide or vial is then sent to a laboratory for analysis.

In the United States, automated liquid-based Pap cytology testing has largely replaced conventional Pap tests. One advantage of liquid-based testing is that the same cell sample can also be tested for the presence of high-risk types of HPV, a process known as “Pap and HPV cotesting.” In addition, liquid-based cytology appears to reduce the likelihood of an unsatisfactory specimen. However, conventional and liquid-based Pap tests appear to have a similar ability to detect cellular abnormalities.

4. When should a woman begin cervical cancer screening, and how often should she be screened?

Women should talk with their doctor about when to start screening and how often to be screened. In March 2012, updated screening guidelines were released by the United States Preventive Services Task Force and jointly by the American Cancer Society, the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology. These guidelines recommend that women have their first Pap test at age 21. Although previous guidelines recommended that women have their first Pap test 3 years after they start having sexual intercourse, waiting until age 21 is now recommended because adolescents have a very low risk of cervical cancer and a high likelihood that cervical cell abnormalities will go away on their own. According to the updated guidelines, women ages 21 through 29 should be screened with a Pap test every 3 years. Women ages 30 through 65 can then be screened every 5 years with Pap and HPV cotesting or every 3 years with a Pap test alone.

The guidelines advise that routine Pap and HPV cotesting be limited to women age 30 and older because transient HPV infections are very common among women in their twenties. Including routine HPV testing in cervical screening of younger women would detect many infections that will be suppressed by the immune system and not lead to cancer. In older women, HPV infections are more likely to represent persistent infections—that is, infections that have the potential to progress to cervical cancer if not detected or treated. However, HPV testing can be used in women of any age to help clarify unclear Pap test findings and help doctors decide if further evaluation is needed. (See Question 9 for more information.)

The guidelines also note that women with certain risk factors may need to have more frequent screening or to continue screening beyond age 65. These risk factors include being infected with the human immunodeficiency virus (HIV), being immunosuppressed, having been exposed to diethylstilbestrol before birth, and having been treated for a precancerous cervical lesion or cervical cancer.

Women who have had a hysterectomy (surgery to remove the uterus and cervix) do not need to have cervical screening, unless the hysterectomy was done to treat a precancerous cervical lesion or cervical cancer.

5. What are the benefits of Pap and HPV cotesting?

For women age 30 and older, Pap and HPV cotesting is less likely to miss an abnormality (i.e., has a lower false-negative rate) than Pap testing alone. Therefore, a woman with a negative HPV test and normal Pap test has very little risk of a serious abnormality developing over the next several years. In fact, researchers have found that, when Pap and HPV cotesting is used, lengthening the screening interval to 5 years still allows abnormalities to be detected in time to treat them, but it reduces the detection of transient HPV infections.

Adding HPV testing to Pap testing may also improve the detection of glandular cell abnormalities, including adenocarcinoma of the cervix (cancer of the glandular cells of the cervix). Glandular cells are mucus-producing cells found in the endocervical canal (the opening in the center of the cervix) or in the lining of the uterus. Glandular cell abnormalities and adenocarcinoma of the cervix are much less common than squamous cell abnormalities and squamous cell carcinoma. There is some evidence that Pap testing is not as

good at detecting adenocarcinoma and glandular cell abnormalities as it is at detecting squamous cell abnormalities and cancers.

6. Can HPV testing be used alone for cervical cancer screening?

Not enough data are available to determine whether HPV testing can be used alone to screen for cervical cancer. Ongoing studies are investigating the possibility of using routine HPV testing as a primary screening method, with follow-up testing by a Pap test or other tests for women who test positive for a high-risk HPV type.

7. What is the best time to be screened for cervical cancer?

The best time for a woman to have cervical screening is between 10 and 20 days after the first day of her last menstrual period. A woman should not have cervical screening when she is menstruating. For about 2 days before the test, she should avoid sexual intercourse, douching, or using vaginal medicines or spermicidal foams, creams, or jellies (except as directed by a doctor) because they may wash away or hide abnormal cells. After the test, she can go back to her normal activities and return to work right away.

8. How are the results of Pap tests reported?

A doctor may simply describe Pap test results to a patient as “normal” or “abnormal.” It is important to remember that abnormalities rarely become cancerous, and even severe lesions do not always lead to cancer. Likewise, HPV test results can either be “positive,” meaning that a patient is infected with at least one high-risk HPV type, or “negative,” indicating that high-risk HPV types were not found. A woman may want to ask her doctor for specific information about her Pap and HPV test results and what these results mean.

Most laboratories in the United States use a standard set of terms, called the Bethesda System, to report Pap test results. Under the Bethesda System, samples that have no cell abnormalities are reported as “negative for intraepithelial lesion or malignancy.” A negative Pap test report may also note certain benign (non-neoplastic) findings, such as common infections or inflammation. Pap test results also indicate whether the specimen was satisfactory or unsatisfactory for examination.

The Bethesda System considers abnormalities of squamous cells and glandular cells separately. Squamous cell abnormalities are divided into the following categories, ranging from the mildest to the most severe.

Atypical squamous cells (ASC) are the most common abnormal finding in Pap tests. The Bethesda System divides this category into two groups, which are described below.

- **ASC-US:** atypical squamous cells of undetermined significance. The squamous cells do not appear completely normal, but doctors are uncertain about what the cell changes mean. Sometimes the changes are related to an HPV infection, but they can also be caused by other factors. For women who have ASC-US, a sample of cells may be tested for the presence of high-risk HPV types. If high-risk HPV type is present, follow-up testing will usually be performed. On the other hand, a negative HPV test can provide reassurance that cancer or a precancerous condition is not present.
- **ASC-H:** atypical squamous cells, cannot exclude a high-grade squamous intraepithelial lesion. The cells do not appear normal, but doctors are uncertain about what the cell changes mean. ASC-H lesions may be at higher risk of being precancerous compared with ASC-US lesions.

Low-grade squamous intraepithelial lesions (LSILs) are considered mild abnormalities caused by HPV infection. Low-grade means that there are early changes in the size and shape of cells. Intraepithelial refers to the layer of cells that forms the surface of the cervix. LSILs are sometimes classified as mild dysplasia. LSILs may also be classified as cervical intraepithelial neoplasia (CIN-1).

High-grade squamous intraepithelial lesions (HSILs) are more severe abnormalities that have a higher likelihood of progressing to cancer if left untreated. High-grade means that there are more evident changes in the size and shape of the abnormal (precancerous) cells and that the cells look very different from normal cells. HSILs include lesions with moderate or severe dysplasia and carcinoma in situ (CIS). HSIL lesions are sometimes classified as CIN-2, CIN-3, or CIN-2/3. CIS is commonly included in the CIN-3 category.

Squamous cell carcinoma is cervical cancer. The abnormal squamous cells have invaded deeper into the cervix or into other tissues or organs. In a well-screened population, such as that in the United States, a finding of cancer during cervical screening is extremely rare.

Glandular cell abnormalities are divided into the following categories:

Atypical glandular cells (AGC), meaning the glandular cells do not appear normal, but doctors are uncertain about what the cell changes mean.

Endocervical adenocarcinoma in situ (AIS), meaning that precancerous cells are found only in glandular tissue of the cervix.

Adenocarcinoma includes not only cancer of the endocervical canal itself but also, in some cases, endometrial, extrauterine, and other cancers.

9. What follow-up tests are done if cervical cancer screening results are abnormal?

If a woman receiving Pap and HPV cotesting is found to have a **normal Pap test result with a positive HPV test** that detects the group of high-risk HPV types, the doctor will probably have the woman return in a year for repeat screening to see if the HPV infection persists and whether any cell changes have developed that need further follow-up. Alternatively, the woman may have another HPV test that looks specifically for HPV-16 and HPV-18, the two HPV types that cause most cervical cancers. If either of these types is present, a woman will likely have follow-up testing.

If a woman is found to have an **ASC-US Pap test result**, her doctor may have the sample tested for high-risk HPV types or may repeat the Pap test to determine whether further follow-up is needed. Many times, cell changes in the cervix go away without treatment, especially if there is no evidence of infection with high-risk HPV. Doctors may prescribe estrogen cream for women with ASC-US who are near or past menopause. Because ASC-US cell changes can be caused by low hormone levels, applying an estrogen cream to the cervix for a few weeks can usually help to clarify their cause.

Follow-up testing for **ASC-US with a positive HPV test**, for **LSIL**, or for **HSIL**, may involve a colposcopy, in which an instrument much like a microscope (called a colposcope) is used to examine the vagina and the cervix. During a colposcopy, the doctor inserts a speculum to widen the vagina and may apply a dilute vinegar solution to the cervix, which causes abnormal areas to turn white. The doctor then uses the colposcope (which remains outside the body) to observe the cervix.

If abnormal tissue is found during a colposcopy, the doctor may perform endocervical curettage or a biopsy. A biopsy is the removal of cells or tissues from the abnormal area for examination under a microscope. Endocervical curettage is a type of biopsy that involves scraping cells from inside the endocervical canal with a small spoon-shaped tool called a curette.

If follow-up testing shows cells with more severe abnormalities, further treatment is needed. Without treatment, these cells may turn into cancer. Treatment options include the following:

- LEEP (loop electrosurgical excision procedure) uses an electrical current that is passed through a thin wire loop to act as a knife to remove tissue.
- Cryotherapy destroys abnormal tissue by freezing it.
- Laser therapy uses a narrow beam of intense light to destroy or remove abnormal cells.
- Conization removes a cone-shaped piece of tissue using a knife, a laser, or the LEEP technique.

10. Do women who have been vaccinated against HPVs still need to be screened for cervical cancer?

Yes. Because current HPV vaccines do not protect against all HPV types that cause cervical cancer, it is important for vaccinated women to continue to undergo routine cervical cancer screening.

11. What are the limitations of cervical cancer screening?

Like any screening test, cervical cancer screening is not completely accurate. Sometimes a patient can be told that she has abnormal cells when the cells are actually normal (a false-positive result), or she can be told that her cells are normal when in fact there is an abnormality that was not detected (a false-negative result).

Cervical cancer screening has another limitation, caused by the nature of HPV infections. Because most HPV infections are transient and produce only temporary changes in cervical cells, overly frequent cervical screening could detect cervical cell changes that would never cause cancer. Treating abnormalities that would have gone away on their own can cause needless psychological stress. In addition, follow-up tests and treatments can be uncomfortable, and some treatments that remove cervical tissue, such as LEEP and conization, have the potential to weaken the cervix and may affect fertility or slightly increase the rate of premature delivery, depending on how much tissue is removed.

The screening intervals in the 2012 guidelines are intended to minimize the harms caused by treating abnormalities that would never progress to cancer while also limiting false-negative results that would delay the diagnosis and treatment of a precancerous condition or cancer. With these intervals, if an HPV infection or abnormal cells are missed at one screen, chances are good that abnormal cells will be detected at the next screening exam, when they can still be treated successfully.

Selected References

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3. Saslow D, Solomon D, Lawson HW, et al. American Cancer Society, American Society for Colposcopy and Cervical Pathology, and American Society for Clinical Pathology screening guidelines for the prevention and early detection of cervical cancer. *CA: A Cancer Journal for Clinicians* 2012. [[PubMed Abstract](#)]
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6. Wheeler CM. Natural history of human papillomavirus infections, cytologic and histologic abnormalities, and cancer. *Obstetrics and Gynecology Clinics of North America* 2008;35(4):519–536; vii. [[PubMed Abstract](#)]

Related Resources

- *Diethylstilbestrol (DES) and Cancer*
(<http://www.cancer.gov/cancertopics/factsheet/Risk/DES>)
- *HPV and Cancer*
(<http://www.cancer.gov/cancertopics/factsheet/Risk/HPV>)
- *Human Papillomavirus (HPV) Vaccines*
(<http://www.cancer.gov/cancertopics/factsheet/Prevention/HPV-vaccine>)
- *Understanding Cervical Changes: A Health Guide for Women*
(<http://www.cancer.gov/cancertopics/understandingcervicalchanges>)

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