



ABNORMAL PAPSMEAR

These materials are for your general information and are not a substitute for medical advice. You should contact a physician or other healthcare provider with any questions about your health, treatment, or care.

INTRODUCTION — The surface of the cervix comprises several layers of squamous cells. As these cells grow and develop, they move from the bottom inside layer to the top outside layer where they can be sampled easily. These cells and the glandular cells that line the endocervical canal (opening in the cervix that connects the uterus to the vagina) can be sampled for a precancerous (or cancerous) condition using cervical cytology screening tests, such as the Papanicolaou (PAP) smear or liquid-based cervical cytology (eg, ThinPrep, SurePath). Testing for the presence of DNA from human papilloma virus (HPV) is an additional screening test that may be useful in some women.

There is no reason to think the worst should you have an abnormal screening test. The vast majority of abnormal screening tests suggest a precancerous condition that will either resolve on its own or can be treated before it progresses to cancer. Furthermore, the results of these tests cannot be used to make a definitive diagnosis. The tests are used to identify women who need to go on to have detailed evaluation of their cervixes and possible therapy.

RISK FACTORS FOR CERVICAL CANCER — Cervical cancer is almost never observed in women who have never had sexual relationships and is more common in women who have had multiple sexual partners or whose partners have had multiple sexual partners. Other risk factors for cervical cancer include: HIV infection, the chronic use of immunosuppressive medications (eg, corticosteroids, azathioprine, cyclosporine), first intercourse before age 17, cigarette smoking, and history of sexually transmitted diseases (eg, herpes and chlamydia). In some studies, women who took birth control pills were more likely to develop cervical cancer.

Human papilloma virus — The critical risk factor for development of cervical cancer is HPV infection. HPV infects cells in the genital area of both men and women and can be transmitted during sexual intercourse. It is very common: most sexually active young men and women have been exposed to it.

HPV can cause genital warts, but may not be associated with any visible lesions or symptoms. Most HPV infections are temporary, resolving within two years. When the virus persists (in 10 to 20 percent of cases), there is a higher likelihood of developing cervical cell abnormalities and cancer.

It usually takes several years for HPV infection to cause cervical cancer. Furthermore, not all HPVs cause cancer. Of the more than 70 subtypes of HPV, only 10 to 15 subtypes (especially types 16 and 18) have been associated with the development of cervical cancer.

It is not completely known how HPV causes precancerous and cancerous changes in cells. It appears that the virus enters the DNA of cervical cells and thereby impedes their ability to control their growth.

We do not know whether HPV testing or cervical cytology is the better screening test for precancerous and cancerous lesions of the cervix. The advantage of the HPV test is that it identifies more women with severe cervical cellular abnormalities than a single PAP smear (90 versus 80 percent, respectively). However, since there are many more false positive results (abnormal HPV test but no or only minimal cervical abnormalities) among women who are only tested for HPV, these women end up having a lot of unnecessary follow-up testing.

At this time, HPV testing is primarily used in the following ways:

- Reflex testing, which refers to obtaining cervical cytology and then performing HPV testing if it shows an abnormality such as atypical squamous cells of uncertain significance (ASC-US).
- Combined testing, which consists of both cervical cytology and an HPV test whenever screening for cervical cancer is performed.

Further research is needed to determine what role HPV testing should play as part of a cervical cancer screening program.

CERVICAL CYTOLOGY RESULTS — The cervical cytology report has two components: adequacy of the cervical specimen and categorization of the cells.

Adequacy — In terms of the adequacy, a specimen is either:

Satisfactory — The specimen contains an adequate number of clearly visible cells, including some endocervical cells or squamous metaplastic cells from the transformation zone, the area where precancerous and cancerous changes are likely to arise.

Unsatisfactory — There is insufficient cellular material for analysis or the sample was unable to be processed for technical reasons (eg, mislabeled, broken slide).

An unsatisfactory specimen should always be repeated in six weeks. It is important not to repeat the test too soon so as to allow the cervix to heal after the minor trauma of being scraped for the previous cytology sample.

Categorization — The cells are categorized according to the Bethesda system:

Negative for intraepithelial lesion or malignancy — The cells on the smear do not have changes that could represent a precancerous or cancerous abnormality.

Smears which are negative for an intraepithelial lesion or malignancy may show other abnormalities, such as organisms suggestive of vaginal infection (Trichomonas, yeast, herpes, or bacterial vaginosis) or cellular changes in response to irritation from dryness, radiation, or an intrauterine device (IUD) string.

Epithelial cell abnormalities — There are several types of epithelial cell abnormality.

Atypical squamous cells (ASC) — This is an imprecise finding reported by the cytologist when cellular changes are not obviously precancerous, but warrant further study. ASC is subdivided into ASC-US and ASC-H, the latter category is more likely to be associated with a precancerous cervical lesion.

Low-grade squamous intraepithelial neoplasia lesion (LSIL) — These are mild cellular changes often induced by HPV. A small number of them will progress to cancer if untreated and a large number (50 to 90 percent) will return to normal if left alone. In 15 percent of smears, the presence of LSIL is a signal that there are more serious cellular changes on the cervix that were not identified by cervical cytology.

High-grade squamous intraepithelial neoplasia lesion (HSIL) — These are moderate to severe changes in the cells and are considered precancerous (20 percent progress to invasive cancer if left untreated). HPV can induce these cellular changes.

Atypical glandular cells (AGC) — These abnormal cells usually arise from the endocervical canal, but may come from the endometrium (uterine lining), the fallopian tube, or ovary. They often indicate the presence of a precancerous or cancerous lesion.

ACCURACY OF CERVICAL CYTOLOGY REPORTS — From 5 to 25 percent of cervical cytology specimens reported as normal will have an abnormality when reviewed a second time; this is the false negative rate for a single smear. There are several important points to consider when discussing falsely negative cervical cytology results:

- The rate varies among cytology laboratories and the type of test performed (traditional PAP versus liquid-based cytology)

- A cervical abnormality is less likely to be missed by a false negative PAP smear in a woman who has annual PAP tests. A normal PAP smear is very reliable in women at low risk for cervical cancer who have had three consecutive annual normal PAP smears.

- Many false negative smears are due to sampling problems, not errors in reading the smear. Sampling problems occur if the cervix is not seen well when the specimen is obtained, the area of abnormality is very small or high up in the endocervical canal, not enough cells are obtained, the specimen dries too quickly, the patient douches prior to the procedure, or the cells are obscured by blood or other cellular debris.

- It usually takes many months or years for precancerous cervical cells to progress to cancer, and progression to cancer does not always occur.

- Liquid based cytology tests, such as the ThinPrep and SurePath, reduce, but do not eliminate, the false negative rate. These new tests are more likely to detect cellular abnormalities than the traditional PAP smear.

FOLLOW-UP OF THE ABNORMAL CERVICAL CYTOLOGY — Further evaluation and possible treatment of abnormal cervical cytology depends upon the degree and type of abnormality and whether the patient has risk factors for developing cervical cancer. There is some variation among health care providers regarding specific follow-up and treatment procedures.

A common follow-up procedure is colposcopy, a painless office procedure performed during a pelvic examination. The colposcope (similar to a large microscope) magnifies the cervix 10-fold and allows the physician to better visualize the location, extent, and degree of cellular abnormalities and any changes in the capillaries (small blood vessels) on the surface of the cervix. Capillary changes, which are not detected by cervical cytology or HPV tests, correlate with the degree of cervical cellular abnormalities. Using the colposcope, areas of the most severe cellular abnormalities and the endocervical area can be identified and biopsied (removal of a small piece of tissue for microscopic examination) to obtain a precise diagnosis.

These general guidelines for follow-up of abnormal cervical cytology are based upon those proposed by the National Cancer Institute:

ASC-US — There are three options:

- Perform HPV testing. This is the preferred approach.

Women who test positive for high risk HPV types are referred for colposcopy because they are at high risk for persistently abnormal cervical cytology as well as a more severe underlying abnormality of the cervical cells; those who have negative tests are followed with repeat cervical cytology in 12 months. The cervical cytology of HPV negative women is more likely to spontaneously revert to normal.

- Repeat the cervical cytology in four to six months. If repeat cervical cytology is normal, perform serial cervical cytology every four to six months until there have been two consecutive normal tests. If two cervical cytology specimens are both read as ASC, the patient should have colposcopy.

- Colposcopy for all women with this finding.

In postmenopausal women, a trial of vaginal estrogen cream for one month prior to repeating the cervical cytology should be considered because estrogen deficiency can cause mild cellular abnormalities that revert to normal in 90 percent of women after estrogen treatment. Colposcopy should be performed if ASC-US persists after estrogen therapy.

Women who are HIV positive and other immunosuppressed women should have colposcopy after one ASC-US cervical cytology because of their higher risk of having a precancerous lesion.

ASC requires evaluation because more serious abnormalities may be present. If no such abnormalities are present, ASC does not require treatment because it is not a precancerous or cancerous condition.

ASC-H — This finding on cervical cytology should be followed by colposcopic examination.

LSIL — Colposcopy is recommended because:

- About 15 percent of women will have a more severe abnormality that was not detected by the initial cervical cytology, but will be identified by colposcopy and biopsy.
- Determining the size and location of the lesion is helpful in deciding whether to treat the lesion or follow it with serial colposcopies. Large lesions are less likely to spontaneously resolve.
- Observing the extent and severity of the lesion is useful for establishing a baseline in women who are not treated and followed with colposcopy.

However, LSIL in postmenopausal or adolescent women may be approached differently. Serial cervical cytology or HPV testing may be considered in these groups, with referral for colposcopy if abnormalities are noted. Postmenopausal women may be treated with a course of estrogen cream, as described above under AS.

The management of women with biopsy proven mild dysplasia (CIN I) should be individualized based upon age, immune competence (presence or absence of HIV, chronic steroid use, or other immunosuppressive drugs), and ability to comply with frequent appointments. Since spontaneous regression is observed in approximately 60 percent of CIN I, expectant management with serial cytologic smears at three to four month intervals is reasonable. Alternatively, ablation or excision of the lesion may be performed. HPV testing has been proposed as a triaging tool between expectant management and therapeutic intervention in women with CIN I; however, the usefulness of this strategy remains to be proven, since more than 80 percent of CIN I is positive for high risk HPV types.

HSIL — All women with this finding on cervical cytology should be referred for colposcopy and biopsy to confirm the diagnosis. Confirmed HSIL should be treated because approximately 20 percent of untreated patients will develop invasive cancer. If colposcopy does not confirm HSIL, then close follow-up and further testing is warranted to determine whether colposcopy has missed the lesion.

AGC — All women with this diagnosis require colposcopy, biopsy of the endocervical canal, and possibly endometrial biopsy. A literature review consisting of 1381 patients with AGC who underwent biopsy reported histologic abnormalities in one-third of cases: squamous intraepithelial lesions (28 percent), adenocarcinoma in situ (4 percent), adenocarcinoma of the cervix (2 percent), and adenocarcinoma of the endometrium (2 percent). HSIL accounted for many of the squamous intraepithelial abnormalities.

TREATMENT — The following general guidelines for treatment are based upon the findings obtained after a complete evaluation, as described above.

Infection — Women who have signs and symptoms of a vaginal infection should have the organism causing the infection confirmed by appropriate testing and then they can be treated with antibiotics.

Vaginal atrophy — Estrogen applied locally or taken orally relieves symptoms of vaginal atrophy (soreness, burning, bleeding, painful sexual relations).

LSIL — When LSIL is confirmed, there are three options:

- Close follow-up with HPV testing at 12 months or repeat cervical cytology at 6 and 12 months. Colposcopy is performed if abnormalities persist or progress. HPV testing is preferred because it is as effective as cervical cytology but requires fewer visits and less need for colposcopy.

- Treatment to eradicate the abnormal cells.

- Colposcopy and repeat cytology at 12 months.

Since many of these lesions will revert to normal spontaneously, some women prefer to avoid treatment and continue close monitoring. Treatment is the best option if LSIL persists, in patients who will have difficulty with follow-up every six months, if the lesion is large (large lesions usually persist), if the lesion extends into the endocervical canal (where it is difficult to monitor), or if the patient prefers treatment.

HSIL — HSIL is always treated to prevent progression to invasive cancer.

AGC — Treatment depends upon the underlying abnormality and may involve excision of a large portion of the endocervical canal or hysterectomy.

Treatment modalities — LSIL and HSIL on the surface of the cervix can be eradicated by a variety of techniques:

- Cryosurgery (destroys tissue by freezing using liquid nitrogen or carbon dioxide)

- Laser (high intensity energy from a light beam used to destroy tissue)

- Electrocautery (destroys tissue by burning with electric current)

- Excision. Lesions that extend into the endocervical canal should be excised to make sure they have been eradicated.

SUBSEQUENT FOLLOW-UP — Treatment will result in normal cervical cytology in over 90 percent of patients. However, there is a 12 percent risk of recurrent abnormalities (LSIL, HSIL) in low-risk women and up to a 50 percent risk of recurrence in women with certain types of HPV infection (especially subtypes 16 and 18). For this reason, continued surveillance is important.

Cervical cytology or a combination of cytology and colposcopy every four to six months is recommended after treatment of biopsy confirmed CIN II/III. Repeat colposcopy is indicated if ASC or greater occurs. Annual screening is acceptable after three normal results have been obtained.

Alternatively, HPV DNA testing for high risk types at least six months after treatment has been proposed for monitoring. However, while promising, data on high-risk HPV DNA testing for follow-up are still limited. If this approach is taken, a positive test should prompt referral to colposcopy while patients with negative results could be followed with annual cytology screening.

PREVENTION — Adopting a lifestyle that reduces the risk factors for cervical cancer may help to prevent the disease. This includes avoiding: exposure to multiple sexual partners, intercourse before age 17, cigarettes, and sexually transmitted diseases (STDs). Although condoms help prevent the transmission of most STDs, they do not effectively protect against HPV infection. A few studies have suggested dietary deficiencies of folate and beta-carotene are more common in women who develop cervical cancer. For this reason, some physicians recommend these vitamin supplements for women with abnormal PAP smears. A vaccine to protect against HPV infection has been developed, but has not yet been approved by the Food and Drug Administration.

WHERE TO GET MORE INFORMATION — A gynecologist is the best resource for finding out important information related to your particular case. Not all patients with an abnormal PAP smear are alike, and it is important that your situation is evaluated by someone who knows you as a whole person.