

HPV, Cervical Dysplasia and Cancer

Summary

Cervical dysplasia is an abnormal change in the cells of the cervix in the uterus. Early changes, called low-grade lesions by doctors, may persist and develop into high-grade lesions that can lead to cervical cancer. Mildly abnormal cervical cells will most of the time clear up on their own. Both cervical dysplasia and cervical cancer can be best treated effectively when they are caught early. A sexually transmitted virus called HPV (human papillomavirus) causes most cervical dysplasia and all cervical cancers. In women who are HIV positive, cervical dysplasia is common. However, among HIV positive women living in high-income countries who get regular gynecologic monitoring and care, cervical cancer is not common.

Dysplasia and cancer of the cervix

The cervix is the opening of the uterus (womb) that leads into the vagina. The cervix can be felt with the tip of a finger inside the vagina.

In cervical dysplasia, abnormal cells develop on the surface of the cervix. These abnormal cells are called lesions. Cervical dysplasia lesions can **regress** (which means they shrink and may even disappear), **persist** (the lesions remain present but don't change), or **progress** to become a high-grade lesion or cervical cancer.

Cervical cancer is an abnormal growth of the cells of the cervix. Over several years, abnormal lesions on the cervix can slowly turn into cancer.

What causes cervical dysplasia and cancer?

Cervical dysplasia and cancer have been linked to a very common virus called human papillomavirus (HPV). There are over 100 strains of HPV, about 40 of which can be transmitted sexually. Some strains cause warts, including genital warts (abnormal growths on the skin), some lead to cancer of the genitals or anus, the intestines or the lungs, throat and mouth. Some have no known effect.

The immune system helps protect against the development of cervical dysplasia and cancer. Women whose immune systems are weakened by transplant drugs or illnesses such as HIV are at greater risk for HPV infection, cervical dysplasia and cervical cancer. All women with

HIV are at higher risk, and this risk seems to increase as CD4+ counts drop.

Although HPV is necessary for cervical cancer, other factors contribute to the development of cervical dysplasia and cancer. Cigarette smoking has been linked to this condition. Cancer-causing chemicals in cigarette smoke concentrate in cervical fluids and these can affect the health of cervical cells, increasing the risk that these cells become abnormal. Having had a prior sexually transmitted infection (STI), having been pregnant many times and eating a poor diet can also increase the risk of cervical dysplasia and cancer. Because HPV is sexually transmitted, having multiple sexual partners will increase a woman's risk of being exposed to this virus. However, even women with few partners are still at risk of being infected by HPV.

Prevention

Practising safer sex by using condoms or having non-penetrative sex can help reduce the risk of becoming infected with HPV. However, condoms do not completely block HPV transmission because the virus may be present on skin not covered by the condom, but they should still be recommended as they reduce the risk of other STIs that contribute to the development of dysplasia and cancer. Stopping cigarette smoking can help reduce the risk of cervical dysplasia and cancer.

A vaccine against four common HPV genotypes, or types for short, Gardasil, is approved in Canada for use for in girls and young women age 9 to 26 years. It protects against HPV types 16 and 18, which cause approximately 70% of cervical cancers, as well as HPV types 6 and 11, which do not cause cancer but cause approximately 90% of warts on or around the genitals and anus. In clinical trials, the vaccine provided between 96 and 100% protection against HPV-related complications such as cervical and anal dysplasias as well as genital warts. Protection has lasted for at least five years after vaccination; ongoing studies in Scandinavia will help evaluate whether this

high level of protection lasts over many years. For the vaccine to work, three doses given over six months are necessary.

The vaccine does not provide protection against HPV that people are already infected with but provides excellent protection against HPV the person has not been exposed to. Also the vaccine has not been shown to be effective for the treatment of established HPV infection and is not approved in Canada for this use. Gardasil should be avoided in pregnant women but can be given in breastfeeding women.

It is important to remember that even if someone has received the vaccine, they are only protected against two cancer-causing HPV types. Regular medical checkups with pelvic examinations and cervical cancer screening with Pap smears in their 20s and viral testing starting in their 30s are still needed to help all women, regardless of their HIV status HIV-positive women and their doctors watch for signs of cervical dysplasia and cancer.

Symptoms

Usually, there are no symptoms of cervical dysplasia. Genital warts are a sign that someone has been exposed to certain strains of HPV. Treating warts deals with lesions but not the viral infection. However, note that a woman or a man can have HPV and not have genital warts.

Similarly, there are often no physical symptoms of cervical cancer, especially in the early stages. In advanced stages of cervical cancer, there may be pain in the abdomen or lower back, pain or bleeding while having intercourse, unusual vaginal discharge, or bleeding between menstrual periods.

Diagnosis—Pap smears and colposcopy

Regular pelvic examinations including Pap smears and HPV testing can help diagnose or monitor HPV, cervical dysplasia or cancer. To do a Pap smear, the doctor inserts a tiny brush and a small wooden spatula into the vagina and rubs them over the cervix, to loosen

and collect cells. The cells are smeared on a glass slide that is sent to the lab for study. The Pap smear helps identify abnormal cells. In women with HIV, usually Pap smears are done twice during the first year after HIV diagnosis, followed by once a year if the first two smears showed normal results. However, many physicians with HIV-positive women in their care recommend doing a Pap smear every six months.

Although Pap smears are useful, they can produce “false negative” results. In other words, the lab may report a test result as “normal” when there actually are changes in the cells of the cervix. This is the reason why HPV testing is being used more and more in addition to Pap smears. For HPV testing, doctors can collect a small amount of fluid from the cervix and have it tested for the presence of HPV.

Many doctors recommend that newly diagnosed HIV-positive women have a colposcopy. A colposcope is a microscope that looks into the vagina, which has been opened by a speculum, and allows the doctor to visually examine the cervix. The cervix is lightly washed with a weak vinegar solution before the colposcope is put in place. The vinegar solution makes abnormal cells stand out more clearly against the surrounding tissue.

When a colposcopy is performed, a biopsy (removal of a tiny piece of tissue from the cervix) and sometimes an endocervical curettage (the scraping of tissue from the cervix) will be done by the doctor. This procedure can be somewhat painful or cause cramps. The biopsy sample allows lab technicians to study the tissue and confirm the status of cervical tissue.

Pap smears are done by family physicians and gynecologists as part of regular medical care. However, colposcopies and biopsies are done mostly, but not exclusively, by gynecologists.

An HIV-positive woman with signs of abnormalities on the cervix, vagina or vulva should also have an anoscopy, or visual inspection of

the anus and anal canal using a microscope similar to a colposcope. This is because the cell changes caused by HPV can also occur in anus and lead to anal dysplasia.

Test results

The results of tests for cervical dysplasia can be described by a variety of medical terms.

Pap Smear Results

Here are some of the most common test results

- **Normal:** There is no evidence of abnormal changes in the cells sampled.
- **ASCUS (Atypical Squamous Cells of Undetermined Significance):** The cells are abnormal, but no definite diagnosis can be made. This test result can be caused by a yeast infection, using oral contraceptives, or problems with taking the sample. Usually doctors repeat the Pap smear in a few weeks or test for the presence of high risk types of HPV.
- **LSIL (Low-grade Squamous Intraepithelial Lesion):** This result means an acute infection. If it persists for at least two to three visits, it can be assumed that it could lead to cancer.
- **HSIL (High-grade Squamous Intraepithelial Lesion):** This result means more advanced lesions.
- **AGC (Atypical Glandular Cells):** these abnormal cells are the precursors of about 20% of cervical cancers. These cells are very difficult to detect.

Biopsy Results

- **Normal:** There is no evidence of abnormal changes in the sampled cells.
- **CIN-1 (Cervical Intraepithelial Neoplasia, grade 1):** This result means mild or low-grade dysplasia. If it persists for at least two to three visits, it can be assumed that it could lead to cancer. For this reason, CIN-1 is usually treated.

- **CIN- 2 or CIN-3:** This result means severe or high-grade dysplasia. All or almost all of the cells in the sample may be pre-cancerous and calls for a definite therapy in most cases.
- **CIS:** CIS stands for carcinoma in situ and means a small area of cancer has been found. Further tests will be done to find out if the cancer is confined to a small area or if it has spread (called invasive carcinoma).

Treatment

Treatment for cervical dysplasia and cancer varies from one woman to another, depending on the location and size of the lesion or cancer, and whether the lesion is low grade or high grade or whether the cancer has spread to other parts of the body. Whether or not a woman wishes to become pregnant also affects treatment decisions. Women with cervical cancer may be referred to a gynecologist-oncologist or an oncologist—a doctor who specializes in the treatment of cancer. Here are several ways that cervical dysplasia may be treated:

- **Cryotherapy** destroys the lesion by freezing. This procedure can be done in the doctor’s office. There can be some discomfort or pain. After the treatment, spotting and watery discharge are common.
- **Laser treatment** destroys the lesion with an intense beam of light. This procedure is often done in a day-surgery clinic. It can be uncomfortable and can cause spotting and discharge afterward.
- **LEEP** stands for loop electrosurgical excision procedure. The lesion is surgically removed by an electrical current that passes through a very fine wire loop and cauterizes the cervix at the same time so that it does not bleed afterward.
- **Cone biopsy** removes a cone-shaped piece of tissue from the opening of the cervix and can remove a lesion or very small cancer. It is usually done in a hospital with a laser or a

scalpel and patients are given an anesthetic. Some bleeding and pain or discomfort are common after this treatment.

Here are some treatment options if cancer is confirmed:

- **Surgery** may be used to remove cancerous tissue. If the cancer has spread, surgery to remove the cervix and uterus, called a hysterectomy, may be necessary. Sometimes the fallopian tubes, ovaries, and lymph nodes from the pelvis are removed at the same time.
- **Radiation therapy** is often prescribed for cervical cancer that has spread beyond the cervix. In radiation therapy, high-energy rays are used to kill cancer cells.
- **Chemotherapy** may be used by itself or in addition to radiation therapy if the cancer has spread. Anticancer drugs are used in the blood to kill cancer cells.

After treatment

Although cervical dysplasia and cancer can be treated successfully, HIV-positive women are at high risk for having this cancer reappear. It is important to follow up treatment with regular Pap smears and a colposcopy every three to six months.

Cervical dysplasia, HIV and HAART

Because HIV and HPV are sexually transmitted, HIV positive women are often co-infected with both of these viruses. HIV weakens the immune system and in HIV positive women, cervical dysplasia is common.

Taking HAART (highly active antiretroviral therapy) can reduce the production of HIV, improve CD4+ cell counts, and greatly lower the risk of developing many AIDS-related illnesses. HAART cannot prevent cervical cancer. However, with regular gynecologic exams and Pap smears, studies have found that cervical cancer is not common in these women in high-income countries.

The bottom line

Cervical dysplasia is **not** cancer, but it must be treated to prevent the possibility of it developing into cancer. Cervical cancer is a serious condition, especially for HIV-positive women. The earlier it is found, the better the chances are for successful treatment.

The risk of acquiring HPV, developing cervical dysplasia and cervical cancer may be reduced by:

- getting the HPV vaccine
 - practising safer sex to reduce the risk of HPV infection
 - quitting cigarette smoking
 - getting regular Pap smears and, if appropriate, colposcopies and anoscopies
 - taking an effective HAART combination
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References

- Alam S, Conway MJ, Chen HS, et al. The cigarette smoke carcinogen benzo[a]pyrene enhances human papillomavirus synthesis. *Journal of Virology* 2008 Jan;82(2):1053-1058.
- Massad LS, Seaberg EC, Wright RL, et al. Squamous cervical lesions in women with human immunodeficiency virus. *Obstetrics and Gynecology*. 2008 Jun;111(6):1388-1393.
- Barr E and Tamms G. Quadrivalent human papillomavirus vaccine. *Clinical Infectious Diseases* 2007 Sep 1;45(5):609-607.
- Chan JK, Berek JS. Impact of the human papilloma vaccine on cervical cancer. *Journal of Clinical Oncology* 2007;25(20):2975-2982.
- Strickler HD, Burk RD, Fazzari M, et al. Natural history and possible reactivation of human papillomavirus in human immunodeficiency virus-positive women. *Journal of the National Cancer Institute*. 2005 Apr 20;97(8):577-586.
- Massad LS, Seaberg EC, Watts DH, et al. Low incidence of invasive cervical cancer among HIV-infected US women in a prevention program. *AIDS*. 2004 Jan 2;18(1):109-113.
- Maiman M, Watts DH, Andersen JL, et al. Vaginal 5-fluorouracil for high-grade cervical dysplasia in human immunodeficiency virus infection: a randomized trial. *Obstetrics and Gynecology* 1999;94:954-961.
- Heard I, Schmitz V, Costagliola D, et al. Early regression of cervical lesions in HIV-seropositive women receiving highly active antiretroviral therapy. *AIDS* 1998; 12:1459-1464.

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