

HUMAN PAPILOMAVIRUS AND HIV DISEASE

information about the special concerns
for people living with h.i.v and h.p.v.

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The human papillomavirus (HPV) is the most common sexually transmitted infection in the US. About 20 million people are infected at any one time. Nearly half of all sexually active people have had HPV at some point in their lives. Since it often doesn't cause symptoms, many never know they've had it.

Though most types of HPV do not cause serious disease, some can lead to cancerous conditions. Left untreated, these high-risk types can cause cervical and anal cancers and other cancers much less often in the vulva, penis and scrotum. HPV has become a growing concern for people living with HIV since they're at higher risk for both HPV infection and disease.

What is HPV?

HPV is a virus that lives in the flat, thin cells on the surface of your skin, called *epithelial cells*. These cells are also found on the surface of the vagina, vulva, cervix, anus, penis head, mouth and throat, which is why having sex can easily pass the virus onto others. Most people who get HPV clear the infection on their own, often within 6 months to a year.

More than 200 types of HPV exist. Some do not appear to cause health problems while others cause the common wart. (Most of these are caused by types 1, 2 and 4.) About 40 types are responsible for *genital warts*, while about a dozen high-risk types can cause *dysplasia*, which are abnormal cells that can lead to cancer. HPV types 6 and 11 cause about 90% of genital warts. Types 16 and 18 cause about 70% of cervical and anal cancers. Other high-risk types include 31, 35, 39, 45, 51, 52 and 58.

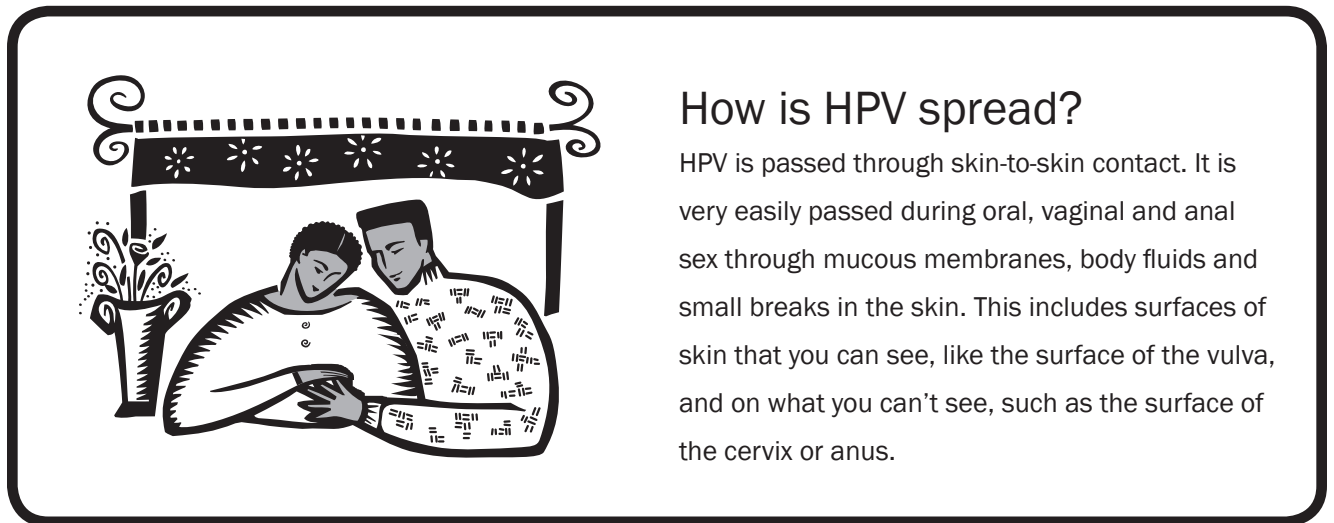
Some people fear that having genital warts can lead to cancer. The HPV types that cause genital warts are not linked to cancer. However, if you have one type of HPV you may also have others, which could be ones that cause cancer. This is especially true for people with HIV.

What are the symptoms?

Symptoms often don't appear when you have HPV, for both high- and low-risk types. This makes it difficult to know if you have HPV; but it also means that considering HPV may be an essential part of your routine health care. Some doctors may not consider it an important issue, which may leave you to bring up the topic during your visits.

For genital warts, symptoms include small bumps or growths on the skin. They can appear as one or several bumps, or even in groups. They can be round and flat or differ in size. Other times they're shaped like the surface of a cauliflower. Genital warts can appear on the vagina, vulva, cervix, penis, scrotum, anus and the areas around the sex organs like the groin or inner thighs. Rarely, genital warts appear in the mouth or throat. When they're present, genital warts are usually painless, though some itching or discomfort may occur.

For dysplasia, since symptoms are often not present, it's important to get regular Pap smears to diagnose dysplasia as early as possible. Pap smears can be used to check the cervix as well as the anus. Routine Pap tests in women have greatly decreased the number of cervical cancers in the US since the 1960s to about 11,000 each year.



How is HPV spread?

HPV is passed through skin-to-skin contact. It is very easily passed during oral, vaginal and anal sex through mucous membranes, body fluids and small breaks in the skin. This includes surfaces of skin that you can see, like the surface of the vulva, and on what you can't see, such as the surface of the cervix or anus.

Who is at risk for HPV?

You are more at risk for HPV infection and disease if you're sexually active, especially at an early age. The more sex partners you have and having a sex partner who has had many partners also puts you at higher risk. HPV occurs more often in people 17–33 years of age, though anyone can get HPV. Also, if you smoke, you are at an increased risk for getting HPV.

People living with HIV are more at risk for getting HPV and for having more stubborn symptoms. This includes genital warts that persist or reappear after treatment and higher rates of cervical and anal dysplasia. Sexually active gay and bisexual men have about a 17 times higher risk of anal dysplasia and cancer. All people living with HIV are also at a higher risk for anal dysplasia, whether or not they've had anal sex.

How do you prevent HPV?

The only way to prevent getting HPV is by not having sex. Since this is not an option for many people, there are other ways to reduce your risk of getting HPV. Limiting the number of partners and choosing partners who've had few or no sexual partners can reduce your risk.

Using a condom can help you prevent getting HPV, but it doesn't fully protect you. This is because HPV can live in skin areas that are not covered by a condom. However, studies show a noticeable drop in HPV cases when condoms are used. Also, stopping smoking will help reduce your risk of getting HPV.

Lastly, for women, getting an HPV vaccine can greatly reduce their risk of getting certain types of HPV. Currently, the vaccine called Gardasil protects against low-risk HPV types 6 and 11 and high-risk types 16 and 18. For those who haven't already had these types of HPV, Gardasil is nearly 100% effective. Federal guidelines recommend Gardasil for girls 11–12 years of age before they become sexually active, though girls as young as 9 and women up to age 26 are also recommended.



A second vaccine, Cervarix, is now in large study and should be available soon. It protects against high-risk HPV types 16, 18, 31 and 45. It also is nearly 100% effective in those who haven't already had those four types. Cervarix will not prevent genital warts.

Getting a vaccine does not substitute for getting regular Pap tests. Women who get vaccinated should still stay on regular Pap schedules. Since higher rates of anal dysplasia occur in people with HIV, these individuals may want to discuss with their doctors about getting anal Paps done. Neither vaccine is used in boys or men, though some studies are now looking at its safety and effectiveness.

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How is HPV diagnosed?

Genital warts are diagnosed by a visual exam by your doctor. The areas can include the outside the body in and around the genital area and inside the body such as the vagina, cervix, anus or rectum.

Dysplasia is diagnosed through a cervical or anal Pap test done by your doctor. An HPV DNA test may also be done. If it hasn't been done and the Pap results come back showing dysplasia, your doctor may do the DNA test to see what types of HPV are present. DNA tests are currently done in women only.

Other types of exams may also be done depending upon the results from or in addition to a Pap test. To further examine the cervix, your doctor may use a *colposcope*, which is a special microscope that looks at the cells of the cervix, vagina and vulva.

To examine the anus, you may have a DRE (*digital rectal examination*) done, which is when your doctor inserts a finger into the anus to check for bumps or other abnormal tissue. An HRA (*high-resolution anoscopy*) may also be done, which is when your doctor inserts a special microscope into the anus to more closely check the tissue.

A biopsy of cervical or anal tissue may also be done. This is done during a Pap test and removes a small piece of tissue to be screened for abnormal cells. The procedure can be painful.



HPV and cervical dysplasia

Standards of care for screening cervical dysplasia have been in place since the 1960s. All women should start getting routine Pap smears within three years of becoming sexually active and no later than 21 years. *Routine* most often means every three years if Pap results come back normal and more frequently if the results show dysplasia.

HPV and anal dysplasia

Infection with HPV in the anus is rather common. It most often happens due to anal intercourse; however, it can occur from other areas having been infected. Only a fraction of people with anal HPV infection will develop a lasting case of *anal intraepithelial neoplasia* (AIN). Although even fewer will go on to develop anal cancer, the rate of anal cancer continues to rise especially in HIV-positive people.

How is HPV treated?

Treating HPV focuses on treating its symptoms, like genital warts and dysplasia. Since most people's immune systems are able to rid their bodies of HPV on their own within 6–12 months, treatments have not been developed to get rid of the virus.

Many treatments for HPV disease exist, and they may depend upon the level of disease you have. You can discuss the options with your health provider to find one that best suits you. Even after treatment, both genital warts

and dysplasia can return so treatment may take several months. It's wise to continue checking and report symptoms should they reappear.

Treating genital warts may be done by you or by your doctor. Treating dysplasia must be done by your doctor. Some treatments cause more discomfort than others, and some require recovery time. People living with HIV more often need more aggressive treatment to treat their HPV disease.

Treatments for genital warts and dysplasia

Procedure	Used for	What happens	Success	Side effects	Notes
Watch and wait	Internal or external warts, LSIL and HSIL.	Warts may take about 6 months to fully appear.		None.	About 2 in 5 clear warts on their own. Most LSIL resolves on its own.
Aldara (imiquimod) cream	External warts and LSIL.	Patient applies on warts 3x a week for up to 16 weeks.	30–50%	Possible burning and irritation	May take 3–4 weeks to start working. Safety in pregnancy unknown.
Condylox or Podofilox (podo-phyllotoxin)	External warts and LSIL.	Patient applies cream/gel on warts 2x a day for 3 days, then 4 days off, for up to 16 weeks.	45–80%	Possible burning, irritation, tenderness.	Warts not responsive may need other type of treatment. Safety in pregnancy unknown.
Efudex (fluorouracil) cream	External warts.	Patient applies on warts 3x a week for up to 16 weeks.	45–80%	Possible burning.	
Trichloroacetic (TCA) or bichloroacetic (BCA) acid	Internal or external warts, LSIL and HSIL.	Doctor applies directly on warts. Patient washes off later.	50–80%	Burns when applied, though usually short-term.	Usually used several times.
Cryotherapy	Internal or external warts.	Freezes warts off with liquid nitrogen or other substance.	60–90%	Possible irritation, burning, and discomfort.	For limited disease. Used several times usually. Safe during pregnancy.
Electrocautery	Internal or external warts, LSIL and HSIL.	Electric current burns off warts.	80–90%	Irritation, burning and discomfort are common.	Usually used once. Safe during pregnancy.
Infrared coagulation (IRC)	Internal or external warts, LSIL and HSIL.	Applies a lower level of heat than laser or electrocautery.		Possible discomfort, irritation and bleeding.	Briefer recovery. Usually one treatment. Safe during pregnancy.
Laser	External, possibly internal, warts, LSIL and HSIL.	Laser controls level of treatment to remove disease.	20–50%	Pain is common.	Safe during pregnancy.
LEEP (loop electro-surgical excision procedure)	Cervical LSIL and HSIL.	Thin wire electrode removes abnormal cells.		Possible pain, discomfort and bleeding.	Outpatient procedure.
Cone biopsy	Cervical LSIL and HSIL.	Removes cone-shaped amount of tissue from cervix.		Pain likely with some recovery.	Outpatient procedure.
Podophyllin solution	External warts.	Doctor normally applies to affected area. Patient washes off later.	30–80%	Possible discomfort.	Not to exceed 3–4 uses. Not safe in pregnancy. May be carcinogenic.
Outpatient surgery	Internal or external warts, LSIL and HSIL.	Occurs in doctor's office, removes disease with tool.	Up to 90%	Likely pain, irritation, ulcers and bleeding.	Longer recovery. Safe during pregnancy.

Special concerns for people living with HIV

HPV infection and disease are more common and persistent in people living with HIV. HIV-positive women are at a higher risk for cervical dysplasia. HIV-positive men and women are both at increased risk for anal dysplasia, whether or not they've engage in anal sex. A much higher rate of anal dysplasia occurs in gay and bisexual men living with HIV. Nearly all HIV-positive men who have had receptive anal intercourse

have anal HPV infection.

Treating HPV disease is an emerging issue for people with HIV. Standards of care are not in place to screen and treat anal dysplasia. Expanding research over the past two years has helped bring this concern closer to the forefront for both people with HIV and their doctors. However, this still may lead to gaps in medical attention, especially for people living with HIV. Those with

CD4 cell counts below 100 are more likely to have more persistent HPV disease and may not respond to HPV treatments as well as others do.

Therefore, it's wise to engage with your health provider in more routine screening for cervical and especially anal dysplasia. Though an anal Pap smear is similar to a cervical Pap, some doctors may not know how to do one or are comfortable with doing one.

Special concerns for pregnant women, children and people over 50

The risk of passing HPV onto a baby during pregnancy or birth is very low. However, treating HPV can affect a pregnancy. Make sure to tell your doctor if you're pregnant or considering pregnancy when discussing your treatment options. Some treatments, like Condylox, should not be used because of possible birth defects.

Since the HPV that causes genital warts and dysplasia is sexually transmitted, few concerns apply to children. The HPV vaccine Gardasil is recommended for girls starting at age 9, before sexual activity starts. There is currently no vaccine to protect boys from HPV.

Since cases of HPV more often occur in people aged 17–33, people over 50 are generally less at risk for getting the infection. However, it's still possible for an adult to get HPV at any age. If your immune system is weakened or if you smoke, then you are more at risk for HPV disease. HPV infection and disease is not well studied in people over 50.



What can help to ask about at a doctor's visit?

- Do you have enough information about me and my risks for HPV?
- What is my risk for getting HPV and developing HPV disease?
- What tests should I get done to screen for possible HPV?
- How often do you recommend I get a cervical and/or anal Pap smear done?

internet resource



The UCSF Anal Neoplasia Research & Treatment Unit has a website with information about anal dysplasia at www.analcancerinfo.ucsf.edu.

HPV terms

You may hear your doctor use some of the terms below when talking to you about HPV. Many of them are used interchangeably.

- **Intraepithelial:** This refers to inside the top layers of skin. (*Intra* = inside, *epithelial* = top layer.) This skin tissue is tightly packed. It covers the body and lines its inside surfaces.
- **Squamous:** This refers to the flat cells found on the surface of skin. As young cells from the bottom layer of skin rise, they mature and flatten out to become squamous cells. HPV likes to live in these cells.
- **Dysplasia:** This refers to the growth of abnormal cells. (*Dys* = abnormal, *plasia* = growth.) If skin cells don't mature properly due to HPV infection, they can look different in shape and size, which results in dysplasia.
- **AIN (anal intraepithelial neoplasia):** This refers to the growth of new cells found on the surface of the anus. There are three grades: AIN 1, which is low-grade with few cells as dysplasia; AIN 2, which is moderate with many more cells as dysplasia; and AIN 3, which is high-grade with all or nearly all the surface as dysplasia (also called CIS, see below).
- **CIN (cervical intraepithelial neoplasia):** This refers to the growth of new cells found on the surface of the cervix. Similar to AIN, there are three grades: CIN 1, CIN 2, and CIN 3.
- **CIS (carcinoma-in-situ):** Simply put, this means "cancer in place", which means cancerous cells are found in the top layers of skin and not any further into the soft tissue below.
- **SIL (squamous intraepithelial lesion):** This refers to the presence of abnormal tissue found in the top layers of skin.
- **LSIL (low-grade squamous intraepithelial lesion):** This refers to surface skin tissue that contains a few abnormal cells. Most often, LSIL will clear on its own, though routine screening should continue.
- **HSIL (high-grade squamous intraepithelial lesion):** This refers to surface skin tissue that has a moderate or severe number of abnormal cells. It is not known which types of HSIL become cancer.
- **ASCUS (atypical squamous cells of undertermined significance):** This refers to surface skin tissue that has some abnormal cells but not so much as to be called dysplasia.
- **ASCH (atypical squamous cells, cannot exclude HSIL):** This refers to surface skin tissue that has abnormal cells similar to HSIL but cannot be called HSIL.
- **Cancer:** This refers to a high level of abnormal cells found in the skin's surface tissue that continue to grow on their own. Also called CIS.
- **Invasive cancer:** This refers to a diagnosis of cancer that has moved into the soft tissue below the skin and perhaps into other parts of the body.



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