



Human papillomavirus (HPV) and the vulva

What is human papillomavirus?

Human papillomavirus (HPV) is a large family of viruses that spread between humans by touch and sexual contact. HPV is common and nearly everyone is exposed to it during their lifetime. In most cases, people never knew they had an HPV infection and never show symptoms. This is because their immune system keeps it under control. It seems that HPV can sit undetected and inactive in the human body for decades, but it maintains the ability to cause problems later. In this way, HPV is similar to herpes simplex virus (cold sores) and varicella zoster virus (chicken pox / shingles) – they all hide out in the body and can express themselves when our immune systems are less able to fight them or as we get older.

Some HPV types cause warts on the hands, feet, and other parts of the skin. This information sheet will not discuss this topic. Some HPV types cause genital warts – the 2 most common of these are types 6 and 11. Both of these are covered in the HPV vaccine that most Australians under the age of 40 received at school. Some HPV types cause pre-cancers and cancers of the vulva, vagina, penis, anus, mouth, and throat. These are called ‘high-risk’ types and 7 of these (16, 18, 31, 33, 45, 52, 58) are covered in the most recent version of the HPV vaccine (Gardasil-9).

What does HPV have to do with cervical screening or ‘Pap smears’?

Cervical screening is a very effective public health measure. In countries that do NOT have organised cervical screening programs, the rate of cervical cancer is 50 to 80 per 100,000 women. In Australia, the current yearly rate is about 7 cases per 100,000 women, with less than 2 deaths per 100,000. That means there is a good chance Australia will eliminate cervical cancer by the year 2035 through a combination of vaccination, cervical screening, and early treatment.

The current approach in Australia to cervical screening is a HPV test. The test is usually taken from the cervix during speculum examination. Screening starts at age 25. If the HPV test is negative, it is done every 5 years for most people, but every 3 years for those with immune suppression. If the HPV test is positive for a high-risk type, then the cervix cells are viewed under a microscope. This is called ‘cytology’.



The combination of results determines the next step – to repeat the CST a year later, or be referred for further investigation with colposcopy. At the time of colposcopy, the doctor or nurse looks at the cervix using a bright light, magnification, and dilute vinegar solution. They also may take a biopsy of the cervix, vagina, or vulva (see *Biopsy*). There are many reliable resources to educate people about cervical screening and colposcopy (link to *Cancer Council, HealthDirect, RANZCOG, Health.gov*)

Some people have situations that do not fit neatly into the standard Australian screening pathway. These include people with symptoms, people with vulvovaginal or anal pre-cancers, previous surgery for pre-cancers of the cervix, previous hysterectomy for unknown reasons, and people with abnormal results after age 70. Your nurse, GP, or specialist can discuss your unique circumstances with you.

What is the meaning of ‘low-grade’ versus ‘high-grade’ change due to HPV?

These terms are applied to results from cytology and biopsy of skin cells from the cervix, vulva, and vagina – also called squamous cells. ‘High-grade’ describes the appearance of skin cells when the HPV has made its way into the genetic material of the cell. HPV then has the ability to change the cells’ behaviour and cause them to multiply and spread abnormally. On the cervix and vagina, most people with high-grade cytology have a biopsy to confirm the diagnosis. On the vulva and anus, the doctor or nurse takes a biopsy of any areas of concern.

If there is a pre-cancer due to HPV, this is called high-grade squamous intraepithelial lesion (HSIL). Once HSIL is found at the cervix, vagina, or vulva, the usual recommendation is to treat. If HSIL is not treated, it can progress to cancer, it can stay the same, or it can sometimes improve on its own. There is no way to predict who will develop cancer and how long it will take. So, the safest course of action is to promptly treat everyone with HSIL of the cervix, vagina, or vulva. HSIL inside the anus is a bit different, due to the difficult location. Sometimes a colorectal surgeon or other doctor will treat it, other times they might take a ‘wait-and-see’ approach.



In contrast, low-grade intraepithelial lesion (LSIL) is a mild change that happens with when HPV is active inside the cells but not in the genetic material. This is common with the HPV types that cause warts, but can also happen with high-risk types of HPV. Warts, also called condyloma, are a type of low-grade change. Warts often come and go, and do not require treatment unless they are causing symptoms like itch or getting in the way of urine, bowel motions, or sex. Treatment for symptomatic warts includes podophyllotoxin cream twice daily, imiquimod cream 3 times a week, freezing (cryotherapy), surgical removal, and burning off with LASER or diathermy. Each of these had different side effects and success rates. LSIL of the cervix, vagina, vulva, and anus does not require treatment.

What is VIN?

VIN stands for vulvar intraepithelial neoplasia. 'Intraepithelial neoplasia' means that abnormal cells are only located in the skin, and have not invaded into the tissue underneath. So, VIN is a 'pre-cancer'. A basic definition of cancer is when abnormal cells gain the ability invade other tissues and spread throughout the body.

The suffix '-IN' is added to the various sites where pre-cancers due to HPV occur. For example, HSIL of the cervix is called 'CIN'. On the vagina, HSIL is called 'VaIN'. These terms are often modified with a number, like VaIN2 or CIN3, to describe the extent of abnormal cells across the skin. HSIL of the vulva is called 'usual VIN (uVIN)' and on the anus it is called 'AIN'. Numbers are not applied to uVIN and AIN.

There is another form of VIN that is NOT related to HPV. This is 'differentiated VIN' and usually occurs in skin affected by lichen sclerosus (see *Lichen sclerosus*). Differentiated VIN and usual VIN can look similar under the microscope, so it takes an experienced pathologist to tell the difference. Treatment options are different for usual VIN versus differentiated VIN, so it is important for your doctors to know which one you have.

What are the symptoms of VIN?

Some people with VIN have no symptoms at all. Eventually these people may feel a lump, bump, or change in the texture of the skin. Many people have itch, stinging, or discomfort with sex. Sometimes there is bleeding. The symptoms do NOT relate to



the extent or severity of the disease. Some people develop cancer without ever having pain or bleeding.

Steroid ointments and antifungal creams do not help with the symptoms of VIN. They may make them worse. If you notice a new or growing lump, bump, or texture change on your vulva, inform your doctor or nurse. They should take a look. If they do not take a look, seek out another opinion.

What does usual VIN (HSIL vulva) look like?

Usual VIN can be grey, brown, black, red, pink, white, or multi-coloured. It can look like a mole, a wart, or a skin rash. It is usually raised. It can be a single subtle spot, multiple spots across the skin, an obvious abnormal area extending across the whole vulva, and everything in between.

When the doctor or nurse looks with vinegar and magnification, the affected area might turn white and they can see a dotted or mosaic pattern. They will usually ask to take one or more biopsies. If the area of concern is in a sensitive spot like the clitoris, or there is a need to take many biopsies, they may arrange for this to be done under an anaesthetic in the operating theatre.

How does my doctor know if I have VaIN (HSIL of the vagina)?

Most people do not know if they have VaIN. Occasionally people will report a change in their discharge. In this case, the symptom is investigated with an examination, swabs, and often a test for HPV and cytology.

There are several other ways to discover VaIN. Sometimes people are having an evaluation of an abnormal cervical screening test, and during colposcopy they see the abnormal area extends on to the vagina. Another possibility is the doctor finds VIN and then examines the vagina to see if there is anything abnormal there as well. If a hysterectomy is done for a pre-cancer of the cervix, then vaginal collection of HPV and cytology is done yearly on at least two occasions afterwards. If this test is abnormal, you may be referred to a specialist to see if VaIN is present.



What are the treatment options for VIN and VaIN?

There are several treatment options for VIN and VaIN. Excision is a surgery to remove the abnormal area. If there is concern a cancer may be present, then excision should be done. Excision works especially well for smaller abnormal areas located on flexible skin, like the labia majora or buttock (*see Vulval anatomy*). If the removed area is large, the surgeon can create a skin flap to cover that space. A small excision is a day procedure, but a large excision with a flap repair requires a hospital stay and longer recovery.

LASER is offered in some centres. LASER burns off the abnormal area, down to the layer just underneath the skin. This starts a healing process that activates your immune system, so hopefully the skin that grows back does not have VIN. LASER works well for the vagina and hairless skin of the vulva. Often this skin is close to important structures like the clitoris, vestibule, perineum, and anus. LASER is also used when there have been previous excisions but HSIL keeps coming back.

Imiquimod is a cream that stimulates the local immune system. It is placed 3 times per week for 16 weeks on the area of VIN or VaIN. It is successful in about half of cases. It works best in people with otherwise healthy immune systems. It is expensive and some people find it difficult to use. It can cause dermatitis where it is applied. At the moment, it is the best option for people who wish to avoid an operation.

Rarely, you and your specialist may decide to watch and wait, rather than treat straight-away. This might be because you have a temporary immune problem, and the hope is that HSIL will go away when your immune system recovers. Sometimes you have other health problems that are more pressing. Sometimes your risk of death from an operation is much higher than your risk of death from the VIN turning into cancer. In these unusual situations, it is especially important to follow-up regularly with your specialist.



I have HSIL (of cervix, vagina, vulva, or anus) and have not been vaccinated against HPV. What should I do?

Any adult who did not receive HPV vaccination in school can talk with their doctor about getting it. At this point, Gardasil-9 requires a prescription and Medicare will not pay for adult vaccination. It is a series of 3 injections and each one costs around \$170.

Some people say that you are 'too old' for the vaccination after age 45. This is because the research on the vaccine was done in people age 45 and under. As a result, we don't have the same amount of information about the effectiveness of the vaccine when it is given to middle-age and older people. However, we do know that the HPV vaccine is safe, and we know that people do not suddenly stop responding to vaccines at age 46. Over time, there will likely be more research into the strength of the protective response in people over 45.

There are several reasons adults may wish to be vaccinated, even if they know they are positive for at least one type of HPV. The first is to prevent getting a different type of HPV if they have a new partner, or their current partner has other sex partners. The second involves people age 45 and under who are treated for HSIL of the cervix, vulva, vagina, or anus. Multiple studies have shown that taking the vaccination around the time of treatment reduces the chance of having recurrent HSIL by 60-90%. It is unknown exactly how this works, but perhaps vaccination improves people's immune response to the HPV they already have. If you are older than 45 and in one of these situations, your specialist can speak with you about your individual circumstances and they may suggest vaccination even though we don't yet know how effective it would be.

What is the follow-up after treatment for VIN or VaIN?

There are no clear, specific guidelines for specialists about how to follow-up people treated for VIN and VaIN. For this reason, different specialists take different approaches, based on their experience and local protocols. Usually the follow-up will involve a look at the vulva and vagina every 6 to 12 months. Sometimes it is necessary to do or repeat the HPV test or vaginal cytology. If there are areas of



concern at these follow-up visits, then another biopsy may be done and repeat treatment arranged. If there is no recurrence of VIN or VaIN over several years, follow-up may be spaced out.

It is important to attend these visits, because people who have been treated for VIN and VaIN have around a 40% chance of HSIL coming back in the same place or at a different place. Since many people with recurrence do not have symptoms, the only way to find the problem is to attend appointments with your specialist. It is not possible to prevent every cancer relating to HPV, but with regular review, prompt recognition, and repeat treatment of pre-cancers, it is possible to prevent most cancers.

Can't the doctors just cut off the whole area to cure the problem?

Unfortunately, surgery doesn't cure the underlying problem of the HPV. Many people who have a hysterectomy for CIN (HSIL of the cervix) hope it will fix the problem and they'll never have to see a gynaecologist again. Unfortunately, HPV may still be active and cause problems at the vagina, vulva, or anus. Likewise, removing the entire vulva does not prevent future problems with HPV on the remaining skin or inside the vagina. Removal of the vulva (vulvectomy) or vagina (vaginectomy) are both major surgeries with substantial risks and complications. What makes this especially difficult is that the vulva and vagina are closely involved with urine and bowel motions, so incontinence or a need for drainage into bags may occur. Obviously, sex may be difficult or impossible after vulvectomy or vaginectomy. Due to all these issues, these major surgeries are only recommended when there is a cancer that requires removal of all the surrounding tissue.