

HUMAN PAPILLOMA VIRUS (HPV)

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EPIDEMIOLOGY

- Human papillomavirus (HPV) is a member of the family Papillomaviridae. They are small DNA viruses.
- These infections are highly transmissible, primarily transmitted by sexual contact.
- Most HPV infections are transient, self-regressing and benign, persistent genital infection with certain viral genotypes can lead to the development of anogenital precancers and cancers

- More than **100** genotypes of HPV, *45 of which can infect the genital epithelium.*
- Genotypes 6 and 11 - 90% of Anogenital warts.
- Oncogenic “**High risk**” HPVs -**16, 18, 45, and 46.**
In Indian women, the most common prevalent genotypes are HPV-16 and -18.
- HPV has been implicated in anal, penile, vulvar, vaginal, and oropharyngeal cancers.

CERVICAL CANCER MORBIDITY AND MORTALITY IN INDIA

- Globally cancer of the cervix uteri is the 2nd most common cancer among women with an estimated 604,127 new cases and 341,831 deaths in 2020.
- **Second MC Cervical cancer in India**
- About 86% of the cases occur in developing countries, representing 13% of female cancers.
- It is estimated that 123,907 cases of cervical cancer cases occur in India and 77,348 die every year

HUMAN PAPILLOMAVIRUS PREVALENCE IN MEN

- A multicenter clinical trial examined the baseline prevalence of penile, scrotal, and perineal/perianal HPV infection in heterosexual men.
- The prevalence of any HPV type was 18.7% at the penis, 13.1% at the scrotum, 7.9% at the perineal/perianal region, and 21.0% at any site.

CERVICAL CANCER SYMPTOMS

- Vaginal bleeding after sex.
- Vaginal bleeding after menopause.
- Vaginal bleeding between periods or periods that are heavier or longer than normal.
- Vaginal discharge that is watery and has a strong odor or that contains blood.
- Pelvic pain or pain during sex.

SYMPTOMS OF ADVANCED CERVICAL CANCER

- May include:
- Back pain.
- Bone pain or fractures.
- Fatigue.
- Leaking of urine or feces from the vagina.
- Leg pain.
- Loss of appetite.
- Pelvic pain.
- Single swollen leg.

PREVENTION OF CERVICAL CANCER: SCREENING OR VACCINATION

- Cervical cancer is essentially a preventable cancer as it has a long preinvasive stage
- It has been shown that it is possible to screen and treat cervical cancer in early stages with high success even in rural India
- However, information on screening behaviors of Indian women related to cervical cancer is very little

HPV TESTING AND TREATMENT

- What tests can a woman have related to HPV?
- Two tests for women are available:
- **Pap test** — A Pap test is done by scraping some cells from the cervix and examining them microscopically. If +ve, it does not mean cervical cancer. In some cases, the cell changes are minor and will return to normal when tested in the future. In other cases the changes are more dramatic and need to be monitored more closely.
- **HPV test** — The HPV test determines if the virus is present in the cervix.

- **If there are no screening tests for men, how can they tell if they have HPV and if so, what is the treatment?**
- Although there is no approved test for men to know their "HPV status," most HPV infections resolve without causing any problems. The problems caused by HPV in men can include genital warts, anal and penile cancers, or cancers of the oropharynx. There are ways to check for those:
- **Genital warts** - If there is abnormalities in the area of the penis, scrotum or anus, such as warts or blisters.

- **Anal cancers** - Gay, bisexual, and HIV +ve men may consider annual screening by digital rectal exam as these men are at higher risk.
- **Penile cancers** - No screening tests are currently available, but early signs can include color changes or build-up or thickening of the tissue.
- **Cancers of the oropharynx** - Signs include issues associated with the throat including pain, constant coughing, voice changes or hoarseness, lumps or masses in the necks, and trouble swallowing or breathing.

- HPV vaccines are necessary to significantly reduce the health care burden currently required for cervical cancer prevention
- Cervical cancer screening is necessary due to the limitations of current HPV vaccines both in their lack of therapeutic effect (thus not protecting women with an ongoing neoplastic processes) and in their limited number of HPV types.

HUMAN PAPILLOMAVIRUS VACCINES

- It is estimated that HPV-16/18 vaccines will provide over 80.3% protection against ICC in South Asia
- Higher immune response is seen in preadolescents through 9–13 years as compared to adolescents and young adults.
- These vaccines are equally safe and have shown nearly complete protection against precancerous and other anogenital lesions caused by the respective vaccine related HPV-types during the 10–14 years of observation so far.

HUMAN PAPILLOMAVIRUS VACCINES

	<i>Gardasil 4</i>	<i>Gardasil 9</i>	<i>Cervavac -SII</i>
HPV types in vaccine	6, 11, 16, 18	6, 11, 16, 18, 31, 33, 45, 52, 58	6, 11, 16, and 18
Age recommendations	Females: 9–45 years	Females: 9–26 years Males: 9–14 years (Licensed in India for Males)	Males and females: 9–26 years 4 k per dose

EFFICACY

- Clinical trials with three doses at 0, 2, and 6 months have shown 99% efficacy at a median follow-up of 3.9 years against types 16, 18 related CIN-2/3, and AIS in per protocol analysis
- Additionally, 99–100% efficacy was seen against vaccine type related genital warts, vaginal intraepithelial neoplasia (VaIN), and vulvar intraepithelial neoplasia (VIN). Reduction in HPV-16 related lesions and HPV-18 related lesions are 98% and 100%, respectively

INDICATIONS OF HPV VACCINE

- In girls and women 9 - 26 years of age for the prevention of the following diseases caused by HPV types, included in the vaccine:
- Cervical, vulvar, vaginal, and anal cancer caused by HPV types 16 and 18
- Genital warts (condyloma acuminata) caused by HPV types 6 and 11
- CIN grade 2/3 and cervical AIS,
- CIN grade 1 caused by types 6, 11, 16, and 18
- VIN , VaIN grades 2 and 3
- Anal intraepithelial neoplasia (AIN) grades 1, 2, and 3.

Contd.....

- In boys and men 9 through 26 years of age for the prevention of the following diseases caused by HPV types included in the vaccine:
- Anal cancer caused by HPV types 16 and 18
- Genital warts (condyloma acuminata) caused by HPV types 6 and 11
 - AIN grades 1, 2, and 3 caused by 6, 11, 16, and 18.

SCHEDULE

- *9–14 years of age (boys and girls):* Two-doses (0.5 mL at 0 and 6 months). The interval between the 1st and 2nd dose should not be <5 months.
- *15–26 years of age (females and males):* 3-dose (0.5 mL at 0, 2, and 6 months) schedule. All three doses should be given within a 1-year period.

SAFETY OF HUMAN PAPILLOMAVIRUS VACCINES

- Local adverse effects with quadrivalent vaccines reported were **pain at the injection site in 83%** of vaccines (**mild and moderate** intensity) and **swelling and erythema in 25%**. Systemic AEs such as **fever in 4%** of vaccines. They are **all minor AEs** and no serious vaccine-related AEs
- Local SEs with bivalent vaccines reported were pain (mild and moderate intensity) in 90% and swelling and erythema in 40%. Systemic SEs such as fever were seen in 12%. No serious vaccine-related AEs. Both the vaccines have very good safety record.

IMPORTANT FACTS

- ***Storage:*** The vaccines should be stored at +2 to +8°C and must not be frozen.
- ***Dose:*** The dose is 0.5 mL intramuscular in deltoid.
- HPV vaccines **can be given** simultaneously **with other vaccines**
- vaccine is administered in a **sitting/lying down** position
- The vaccines **may be administered in the immunocompromised**, but immunogenicity and efficacy may be lower
- **Breastfeeding is not a contraindication** for HPV vaccination

TREATMENT

- Treatment consists of **local wart removal** (in case needed) and **supportive therapy**
- There's no cure for the virus and warts may go away on their own. Treatment focuses on removing the warts. A vaccine that prevents the HPV strains most likely to cause genital warts and cervical cancer is recommended for boys and girls.
- **Treatment for HPV in the cervix:**
- Options include freezing (cryosurgery), laser, surgical removal, loop electrosurgical excision procedure (LEEP) and cold knife conization.

FAQs

- **Is HPV serious?**
- Most HPV infections go away on their own and don't cause any health problems. However, if HPV does not go away, it can cause health problems like genital warts. It also can cause certain kinds of cancer.

- **If someone is infected with one type of HPV and their immune system clears it, are they immune to other types of HPV too?**
- Immunity to one type of HPV does not protect against other types. The current vaccine protects against 9 different types of HPV protects against the types most likely to cause disease.
- **If a person is diagnosed with genital HPV, does that mean they also have HPV orally, and is there a test for the presence of HPV orally?**
- The HPV virus does not travel to other parts of the body, so a genital infection does not automatically mean an oral infection. Unfortunately, no test is available to check for oral HPV at this time.

- **How long does an HPV infection last?**
- HPV infections can last up to 24 months before the immune system eliminates the infection. During this time, most people do not know they are infected. This is why it is difficult to stop transmission of the virus.
- **Am I really at risk of getting HPV?**
- HPV is spread through genital contact, most often, but not always, during sex. It can also spread through oral sex. Most people don't know they have HPV, so they often don't realize they are spreading the virus. Since HPV is so common, if you are intimate with anyone, the best way to reduce your chance of getting infected is to be vaccinated with the HPV vaccine.

- **How do I know if my partner or I have been exposed to HPV?**
- Because most people do not develop symptoms of infection, they do not know they are infected. To avoid or decrease the chance of exposure, you can abstain from sexual activity, limit the number of sexual partners you have and use condoms. Unfortunately, other than abstinence, none of these methods offers complete protection.

- **Is HPV deadly?**
- Yes, in some people the virus causes changes in cells that lead to the development of potentially fatal cancers.
- **Once a person has HPV, can he or she get rid of it?**
- Yes, in fact, most people (9 of every 10) do clear the infection within two years, often never having symptoms. Those who don't clear the infection (the remaining 1 of every 10 people) may suffer from genital warts, cervical cancer or other cancers.
- **Can someone be infected with more than one type of HPV?**
- Yes, one can be infected with more than one type of HPV at a time.

- **Do I need to worry about HPV if my boyfriend and I always use a condom?**
- If your boyfriend has an HPV infection (with or without symptoms), you can still be infected with HPV even when using a condom for two reasons. First, because condoms aren't foolproof at containing the virus, you could still be infected and, second, while HPV is most often transmitted during sexual intercourse, it can also be transmitted during oral sex or during genital-to-genital contact.

- **At what age can someone be infected with HPV?**
- Anyone can be infected with HPV regardless of their age. For example, if a pregnant woman has HPV, her baby can be born with an HPV infection.

SYMPTOM-RELATED QUESTIONS

- **How long does it take for symptoms of HPV to appear?**
- People can be infected with HPV for years, or even decades, before they experience any symptoms of infection. This is why women should get regular Pap screenings. Because Pap screenings show early signs of changes in cells of the cervix (precancerous changes), treatment is often more successful than after physical symptoms, such as bleeding and pain, appear.

- **If someone has genital warts, does that mean HPV virus is still present?**
- Yes. If a person has outward signs of infection, such as genital warts, he or she can transmit the virus. However, it is important to realize that people can also transmit HPV when they do not have any symptoms.

- **Even though I got the HPV vaccine, I got genital warts. Will I always have them?**
- Even if you had the HPV vaccine, you could still develop genital warts if you were infected with a strain of HPV not contained in the vaccine. You may want to consider visiting your healthcare provider to confirm the diagnosis of genital warts. If you do have genital warts, your doctor can go over treatment options with you depending on your particular situation.

- **How soon will genital warts appear if I get infected with HPV? Am I really at risk of getting HPV?**

- Genital warts typically develop four weeks to eight months after contracting one of the types of HPV that cause genital warts. However, HPV can also replicate without causing symptoms for several years before genital warts appear.

- **How soon after an HPV infection does cervical cancer develop?**
- Progression from an initial HPV infection to cancer requires prolonged infection with one of the types of HPV that causes cancer. For this reason, cervical cancer typically develops 20 to 25 years after the initial HPV infection. Regular Pap tests and HPV tests will help your doctor monitor for precancerous changes to the cells of the cervix.

- **Is it possible for a person who says they are a virgin to spread HPV?**
- It is possible to spread the virus through intimate contact that does not include intercourse, such as genital-to-genital contact or oral-to-genital contact. So, it is possible that someone who has not had intercourse could be infected with HPV and spread it to others.

- **If I am infected with HPV orally, can I pass the virus to my children if I kiss them?**
- While the studies looking at HPV transmission orally are minimal, it is generally agreed upon by the scientific community that HPV is spread orally through more intimate forms of engagement, such as oral sex or "open-mouth" (French) kissing, so kissing your children would not be likely to spread the virus to them if you have an oral HPV infection.

- I have heard HPV can be transmitted by skin-to-skin contact. So, if a woman has HPV, can I or my children get it by being around her?
- No. HPV is not transmitted by simply being near or touching someone who has it. The reference to skin-to-skin contact refers to intimate interactions, such as genital-to-genital or oral-to-genital contact.

- I have never been diagnosed with HPV or genital warts, so how could my child have recurrent respiratory papillomatosis?
- Recurrent respiratory papillomatosis, or RRP, is chronic infection of the vocal cords and lungs caused by passage through a birth canal infected with HPV. RRP is primarily caused by two types of HPV that also commonly cause genital warts, types 6 and 11. Because many people are infected with HPV and never have symptoms, they do not know they have an HPV infection. Therefore, unfortunately, it is possible that you could have had an undiagnosed HPV infection during delivery that led to your child's infection.

- **I have been in a monogamous relationship for more than 20 years; however, I was recently diagnosed with genital warts. My wife has never had them. How could I have gotten them?**
- Almost everyone who is sexually active will be infected with HPV at some point. For many, they may never know when or how they were infected for a few reasons. First, symptoms can appear years after the initial infection. Second, the disease can be transmitted without having intercourse. Skin-to-skin contact or oral sex can also transmit the virus. Finally, even people who do not know they are infected and those who do not have any symptoms may still transmit the virus.

- **If a woman is exposed to HPV through oral sex with a man who has had genital warts, can she get HPV and if so, will her infection occur in the oral or genital region?**
- Yes. A woman can be exposed to HPV if she has oral sex with a man who has an HPV infection (with or without current symptoms). If this happens, the infection will occur in the mucosal areas of her mouth, such as in cells in her throat. In most cases, the woman's immune system will clear the infection without any symptoms. In very rare cases, the virus will persist and cause a condition known as recurrent respiratory papillomatosis (RRP). People with RRP develop warts in their throat which can become large enough that they cause hoarseness or trouble breathing.

- **Can you get HPV from someone who does not have any symptoms of HPV?**
- Yes, in fact, most people do not know when they are infected with HPV. So, even if your partner does not have any symptoms of an HPV infection, he or she can still pass the virus to you.
- **I have heard that you do not need to have intercourse to get HPV. Is that true?**
- Yes. Although most infections occur following intercourse, HPV may also be passed on during oral sex and genital-to-genital contact. Even more rarely, a mom can transmit the virus to her baby during birth.

- **Can a woman pass HPV to a male partner through intercourse?**

- Yes, a woman can pass the infection to a partner as well as to her baby during birth, although the latter is fairly uncommon. While the infection is most commonly transmitted through intercourse, the virus can also be passed to one's partner during genital-to-genital contact or oral sex.

HPV AND PREGNANCY

- **Does having HPV put my unborn baby at risk?**
- In rare instances, mothers with genital HPV can pass the virus to their baby during vaginal delivery. A small number of these babies go on to develop recurrent respiratory papillomatosis (RRP), a condition in which tumors grow in the throat or lungs, sometimes causing hoarseness, difficulty breathing, talking, and swallowing. While the tumors can be surgically removed, they tend to grow back. Some people with RRP require regular surgical intervention. RRP can also cause a disease of the lungs that resembles cystic fibrosis.

- **Can I get the HPV vaccine if I am pregnant?**
- Although the HPV vaccine has not been found to cause harm to a woman or her fetus, it is recommended to wait until after delivery to start or continue with the series.
- **I started getting the HPV vaccine and now I am pregnant. Can I still get the other doses of vaccine?**
- You should wait until after you deliver to get the remaining doses of vaccine. There is no indication that the vaccine causes harm to you or your unborn baby, but it is recommended to wait till delivery. Then, you can get the remaining doses.⁴³

- **Is there a treatment for HPV?**
- No antiviral drugs are available to treat HPV. Most HPV infections, however, clear on their own in a few years without causing any health problems. While there are no treatments for the infection, there are supportive treatments for the health problems caused by HPV, such as genital warts and cancers.

- **If a person was treated for HPV, are they protected against a future HPV infection?**
- No. While the symptoms of HPV can be treated, currently, there is not a way to treat the infection. For example, genital warts can be removed, but they may return. If a woman has changes to the cells of her cervix, she may have a procedure to remove or kill the abnormal cells. However, some cells may still contain HPV. There is not a way to know for certain, which is why regular follow-ups are important.
- Likewise, a person who has been treated for HPV can still be infected with other types of HPV.

- **Does a negative Pap test mean that I am not infected with HPV?**

- No. A Pap test is one in which cells isolated from the cervix are examined under a microscope for precancerous changes caused by a persistent, or long-term, HPV infection. So, a negative Pap test is good news in that it means the cervical cells appear normal, but it does not give any information about a person's HPV status.

- **My boyfriend recently had warts on his penis. When I went to the clinic and had a Pap test, the results were normal. Does this mean that I did not get infected, or is there still a chance I could get genital warts?**
- The types of HPV that cause genital warts typically differ from those that cause cervical cancer. Since a Pap test is meant to identify cellular changes that could potentially lead to cervical cancer, it does not provide information about HPV infections with types that cause genital warts. For this reason, your Pap test results do not mean that you did not get infected with HPV when your boyfriend had it. The good news is that for many people, the infection will clear without any symptoms, so you may never experience genital warts like your boyfriend did.

- **What happens if my Pap test is abnormal?**
- If you have an abnormal Pap test, an HPV test may be suggested to determine if human papillomavirus DNA is present in the cells of the cervix. If the results of the HPV test are positive, your doctor will determine how frequently you should be tested. In addition to HPV and Pap tests, a colposcopy or biopsy may be suggested. A colposcopy visualizes the cells of the cervix and a biopsy takes a sample of cervical cells.

- **Can HPV tests replace Pap tests?**
- No, HPV tests should not replace routine Pap tests for two reasons:
- The tests are not measuring the same thing. Pap tests detect changes in the cells of the cervix that could lead to cancer, whereas HPV tests detect human papillomavirus DNA in the cells of the cervix. A positive HPV test could be the result of a recent infection or a chronic infection.
- The tests are recommended for slightly different age groups; routine Pap tests are recommended for all women 21 years and older, whereas HPV tests are recommended for women 30 years and older and only those women between 21 and 29 who have had an irregular Pap test.

- **If I have had an abnormal Pap test in the past, can I still get the HPV vaccine?**
- Yes. You should still get the HPV vaccine even if you have had an abnormal Pap test because even if you have been infected with HPV, it is not likely that you have been infected with all of the types that the vaccine protects against. So, you can still benefit from protection afforded by the HPV vaccine.

HPV VACCINE

- **How long after receiving the HPV vaccine does it take for the vaccine to work?**
- The immune system takes one to two weeks to generate immunity to vaccines or infections. In the case of HPV vaccine, the first dose (and the second one if the person is on the three-dose series) generates a primary immune response, so people will have some immunity, but protection can vary from one person to another. The last dose (given at least six months after the first dose) is important because it enhances the memory immune response. A person will have the greatest protection beginning about one to two weeks after receiving their last dose of the vaccine.

- **My daughter is not sexually active. Why should I even consider getting her vaccinated against HPV now?**
- The HPV vaccine is recommended before the start of sexual activity for two reasons:
- Young people tend to get infected more frequently; in fact, about half of all new infections are diagnosed in girls and young women between 15 and 24 years of age.
- It takes at least six months to complete the series, so even though your daughter may not be active now, or even in six months, it is better to have the series completed sooner rather than later.

- **Why does my son need an HPV vaccine since I heard it prevents cervical cancer?**
- Although HPV is a known cause of cervical cancer, the virus can also cause other cancers of the reproductive tract, anal cancer, penile cancer, genital warts, and on occasion, cancers of the head and neck. In fact, about 4 of every 10 cases of HPV-related cancers occur in boys or men. Because vaccinating boys will also decrease the spread of the virus, they will not only protect themselves, but also their sexual partners.

- **Does the HPV vaccine cause infertility?**
- No. HPV infections do not cause infertility, except indirectly in cases when they progress to cervical cancer, so it is not biologically plausible that the HPV vaccine would lead to infertility. To the contrary, since the HPV vaccine decreases the number of cases of cervical cancer, it may indirectly decrease the number of women unable to have a baby.

- **I heard stories of girls developing different illnesses after getting the HPV vaccine. Are these stories true?**
- The known side effects of the HPV vaccine include pain, redness or swelling at the injection site. In addition, because teens tend to faint more easily, fainting has been associated with vaccines given to this age group. Because of this, vaccine recipients should remain seated or lying down at the doctor's office for about 15 minutes after getting the vaccine.

- **How long does immunity last if you receive all doses of the HPV vaccine?**

- First, the vaccine has been studied for more than 15 years at this point, and immunity doesn't appear to wane. Second, the immune responses generated by the vaccine are stronger than those invoked after natural infection. Finally, the hepatitis B vaccine, which is made using a technology similar to the HPV vaccine, induces a memory response that lasts at least 30 years.

- **If I got all necessary doses of the HPV vaccine, can I still develop genital warts?**

- Yes, it is possible. Although the HPV vaccine protects against the two strains of HPV that most commonly cause genital warts, it will still only prevent about 9 of every 10 cases of genital warts. Therefore, someone could still get genital warts if they are infected with a type of HPV that causes genital warts but was not in the vaccine.

- **Does the HPV vaccine protect me against any other sexually transmitted diseases (STDs)?**
- No. The vaccine does not protect against any other STD. In fact, since there are more than 100 types of HPV, it does not even protect against all types of HPV.

Thank You