



A Review-Human Papilloma Virus

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ABSTRACT

Human Papillomavirus (HPV) infection is considered as the most common Viral sexually transmitted infection world wide. This poses on increasingly interdisciplinary medical challenge since. There is most scattered information in databases about Hip and the correlated diseases we decided to collect useful data so that the experts can get. Comprehensive view of HPV a more HPV associated diseases. prevalence prevention and new treatments are discussed. The retrieved articles reporting the latest data about the required. information for our review were selected through searching in web of science Scopus Medici Medline EMBASE Machaon Library Ovid and CINHALL with language limitations of English and Raman There are 2 groups of HPVs.1) Low-risk HPV types that can lead to genital warts, and

(2) high-risk HPV types that are indeed in HPV-associated oncogenes is. About 70% of all sexually active women are infected and most of these infections heal within many weeks or months. In the case of Hip - persistence

Keywords: Human papilloma virus, cancer, Epidemiology, Warts, Vaccines, Virology, Diagnostic

INTRODUCTION

Papilloma viruses are small, non-enveloped, epitheliotropic, double-stranded DNA viruses that infect mucosal and cutaneous epithelia in a wide variety of higher vertebrates in a species-specific manner and induce cellular proliferation. Only bovine papillomaviruses (BPVs) 1 and 2 are known to infect mesenchymal tissues and to show cross-species transmission. More than 100 types of human papillomaviruses (HPVs) have been identified and approximately half of them infect the genital tract. Many types of HPV have been found in cervical cancers, while others are found rarely or not at all in large series of cancers, which gives rise to the nomenclature of 'high-' and 'low-risk' HPVs. These other types are associated with other anogenital and oropharyngeal cancers. A number of HPVs have been found to be present in skin cancers in patients who have epidermodysplasia verruciformis (EV); these types are also found in both non-melanoma skin cancers and normal skin. The potential associations of HPVs with these and other cancers are discussed in other sections. All papillomaviruses share a common genetic structure that is distinct from that of polyomaviruses. A double-stranded circular DNA genome encodes approximately eight open-reading frames (ORFs). Similarly, all papillomaviruses have a non-enveloped icosahedral capsid. Understanding of the biology of papillomavirus infection was hindered by the lack of tissue culture systems to propagate the viruses, the lack of animal models for HPVs and difficulties in finding animal models of natural infection. The advent of molecular cloning of HPV genomes in the early 1980s provided the first opportunity to study individual viral genes. However, only in the late 1990s did propagation of viruses in organotypic cultures make the first attempts at viral genetics possible. The availability of complete and partial genomic sequences from a wide variety of HPV types has enabled the establishment of a new taxonomic structure and has provided a window to study the co-evolution of papillomaviruses with their primate hosts. Early evidence suggests that HPV types, as defined by DNA sequencing, also remain serologically distinct. HPV is a type for human papilloma infection. HPVs are in excess of 150 related infections. HPV is the most well-known sexually transmitted contamination (STI). HPV is an unexpected infection in comparison to HIV and HSV (herpes). Each HPV infection in the gathering is given a number which is called a HPV type. HPVs are called papilloma infections since a portion of the HPV short cause warts or papillomas, which are non-dangerous tumors. However, a few sorts of HPV are known for causing tumor, particularly of the cervix (the base of the womb at the highest point of the vagina). The papilloma infections are pulled in to and can live just in specific cells called squamous epithelial cells. These sort of cells are found on the surface of the skin and on moist underlying surfaces (called mucosal surfaces) like:

- The vagina, anus, cervix, vulva (around the exterior of the vagina)
- The internal skin and urethra of the penis
- Inner nose, mouth, throat
- Trachea, bronchi
- The internal eyelids.

The in excess of 150 known strains, around 3 out of 4 (75%) HPV types are called cutaneous in light of the fact that they cause warts on the skin. Locales for warts are the arms, chest, hands, and feet. These are regular warts; they are not the genital sort of war. The other 25% of the HPV composes

are viewed as mucosal sorts of HPV. "Mucosal" alludes to the body's mucous films, or the clammy surface layers that line organs and depressions of the body that open to the outside. For instance the mouth, vagina and rear-end have this sodden mucosal layer. The mucosal HPV varieties are additionally called the genital (or anogenital) type HPVs in light of the fact that they frequently influence the butt-centric and genital region. The mucosal (genital) HPVs incline toward the soggy squamous cells found around there. Mucosal HPV types largely

HISTORY OF HPV

The Times first mentioned HPV on Feb. 12, 1985. The report said that scientists, including Dr. Harald zur Hausen of the University of Heidelberg in Germany (who would later win a Nobel Prize for his work), were "finding strong evidence linking viruses in the family called papilloma with genital cancers, notably cancers of the cervix and vulva." The evidence, the article said, came "as close to proving a causal connection as is possible short of developing a vaccine against the virus and proving that it prevents the cancers." That vaccine was still 20 years in the future. In 1972, the association of the human papillomaviruses with skin cancer in epidermodysplasia verruciformis was proposed by Stefania Jabłońska in Poland. In 1978, Jabłońska and Gerard Orth at the Pasteur Institute discovered HPV-5 in skin cancer. In 1976 Harald zur Hausen published the hypothesis that human papilloma virus plays an important role in the cause of cervical cancer. In 1983 and 1984 zur Hausen and his collaborators identified HPV16 and HPV18 in cervical cancer.

MORPHOLOGY OF HPV

The HPV is a DNA virus (non-enveloped). The DNA is having double strand which is arranged in circular manner. The DNA is having almost 8000 base pairs and packed with histone protein. The capsid is not covered with lipid membrane that is why it is termed as nonenveloped. The capsid (55–60 nm) is made up of proteins (L1 and L2). Geometrically, this capsid is regular and also symmetric-like icosahedrons. The capsomeres (unit of capsid) made up of proteins arranged in pentameric order. It also was observed that the capsid of many papillomavirus is made up of 72 capsomeres. The HPV has a circular double-stranded DNA as its genetic material. Its genome is comprised of two regions, early (E) and late (L). Early region has the coding regions which are commonly known as open reading frame (ORF) and the late region codes for 2 proteins, L1 and L2. These 2 proteins make its capsid. ORF is the region which codes for proteins or polypeptides. In spite of having two DNA strands, all the ORFs are situated on only one strand. The virus consists of six numbers of ORFs such as E1, E2, E4, E5, E6, and E7. Fig. depicts the genetic organization of a papillomavirus.

LIFE CYCLE OF HPV

The progression of the life cycle of HPV depends on many various factors like differentiation of the host cell sort of HPV or host system. HPV will solely infect para basal or basal cells undifferentiated stem cells of the cuticle most ordinarily within the transformation zone of the

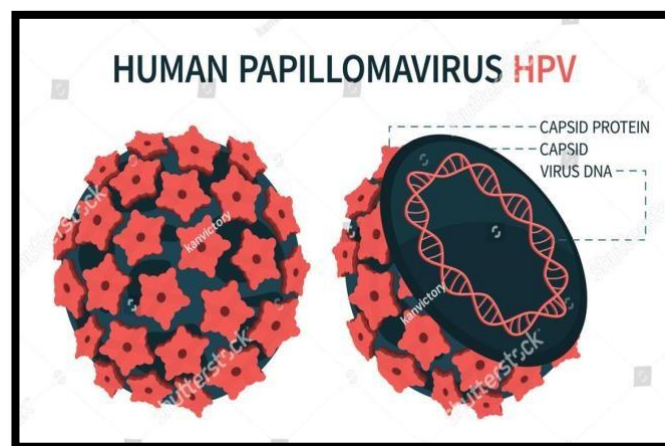


Figure 1: structure of HPV

cervix that is adjacent to the border of the tip cervix and ectocervix. This space becomes a lot of accessible throughout pubescence, pregnancy, and once using oral contraceptives. Infection could also be expedited by small abrasions on the surface this permits higher access to the basal cells that are sometimes below many layers of epithelial cells. As the host cell undergoes the conventional completely differentiation the virus undergoes different components of its life cycle. Once the virus initially enters host basal cells it cannot replicate till the cell matures into a keratinocyte. The exact mechanism the virus uses to enter the host cell continues to be unclear however it's best-known that the virus enters through endocytosis. Information has urged that this pathway could also be expedited through clathrin or caveola mediate endocytosis the virus finishes getting into the cell by membrane fusion followed by uncoating and breakdown of the capsid. The genome then enters the nucleus to use the host's deoxyribonucleic acid and ribonucleic acid polymerases. Once within the cell the deoxyribonucleic acid is kept at a low level as episomes and also the infectious agent genome will replicate because the host cell matures. Once the genes are transcribed they exit the nucleus and endure process. Within the case of the capsid proteins later within the life cycle they get in the nucleus for assembly once that they exit the cell there are information that observe HPV in cervical lesion with none apparent sickness this provides proof that HPV incorporates a latent stage. A couple of infected basal cells undergoing traditional animal tissue differentiation might justify detection with none visible cause. Once the system declines the HPV infection will resume normal activity and reproduce.

TYPES OF INFECTION CAUSED BY HPV

Cancer

to HPV infections. The HPV16, HPV18, HPV31, and HPV45 are known to highly risky for all the types of previously said cancers. Some infected patient's immune system Cancer in vagina, anus, vulva, penis, and most important in cervix is caused due to it does not respond after this infection and this will enhance the growth of cancers. Additional effects such as cigarette smoking enhance the chance of getting cancer associated with HPV. The types of cancers associated with HPV infections are as follows

Cervical cancer

HPV infection is the foremost cause of cervical cancer, which is the leading cancer in India and second utmost common cancer worldwide. Approximately, all the types of cervical cancers are caused due to the infection of HPV. In 70% of cervical cancers, the HPV18 and HPV16 infections are found to be responsible. About 41–54% cervical cancers are found to be occurring for the HPV16, the one strain which is mostly malignant. HPV16 is also responsible for anal, vaginal, head and neck, vulvar, and also penile cancers. In general, in cervical cancer, the rate of transformation of normal cells into cancerous cells is relatively slower. The persons infected with HPV more than a decade or a much longer duration are more prone to having cervical cancers.

➤ Genital cancer

Penile cancer and anal cancer also caused by HPV when transmitted sexually. The risk for getting anal cancer with the HPV is higher for the Penile cancer and anal cancer also caused by HPV when transmitted sexually. The risk for getting anal cancer with the HPV is higher for the

➤ Oropharyngeal cancer

Oral HPV infection causes oropharyngeal cancer. This is also termed as HPV+OPC (HPV16+ oropharyngeal cancer). This type of cancer is also relatively slowly showed symptoms such as cervical cancers, and risk is shown after 15 years from when that person infected by HPV. Tobacco increases the risk of retrogression of disease with HPV+OPC patient.

➤ Lung cancer

The HPV can cause malignant as well as benign tumors in the upper part of respiratory tract. Antibodies for HPV are found in many cases of lung cancers [36]. The expression of the proteins (structural) of HPV shows the presence of HPV in bronchial cancers in in vitro and immunohistochemistry studies.

➤ Cancer on head and neck

The HPV16 and HPV18 are found to be responsible for head-and-neck cancers. HPV infection spread by sexual contact is increased the risk of oral cancers, tonsil cancers, oropharyngeal cancer as well as upper throat and mouth cancer in non-smokers also. Oropharyngeal cancer caused by HPV termed as HPV+OPC (HPV16+ oropharyngeal cancer).

➤ Warts

Warts are generally found with all the types of HPV infections. Noncancerous warts are very common in people. HPV2, HPV27, and HPV57 cause warts while types 2, 1, and 63 do not cause warts. The types of warts are common warts (found in feet, hands, knees, and elbows), plantar warts (found in feet soles), flat warts (found in foreheads, faces, and arms), and periangular warts (found in fingernails around cuticles and nails

also) .

Genital warts associated with HPV are one of the very usual sexually transmitted diseases. More than 90% of cases of the all types of genital warts are caused by HPV6 and HPV11 . Infection in anus and genitals caused by HPV (40 types) is transmitted by sexual activities . This type of infection leads to warts in genital areas. It is found that most of the population gets HPV infection at least once in their life. It is not obvious that genital warts lead to cancers, some cured without any kind of medications or attentions.

Respiratory papillomatosis .

The presence of warts in respiratory tract including larynx or other parts is termed

as respiratory papillomatosis. HPV6 and HPV11 cause respiratory papillomatosis. Inhalation is one of the aspects for the spreading of respiratory papillomatosis. A surgeon infected by HPV during laser ablation on anogenital condyloma can suffer from laryngeal papillomatosis .

➤ Epidermodysplasia Verruciformis

Epidermodysplasia verruciformis is also termed as tree man disease and is an abnormality in autosomal recessive gene along with HPV infection leads to high risk skin carcinoma . The patient's immune system fails to check HPV and produce keratin in an excess level, which causes horns in the skin

1. MODE OF TRANSMISSION OF HPV

The HPV infection occurs by the HPV . Some of the HPV infection does not show any symptoms and can be cured spontaneously [16]. This infection causes warts or sometimes precancerous lesions. This kind of precancerous lesions can lead to cancers, for example, vaginal, anal, cervical, oropharyngeal, and penile cancers . HPV18 and HPV16 are found to be responsible in 70% of cases of cervical cancers, whereas HPV11 and HPV6 are responsible for respiratory papillomatosis and genital warts . There are various ways by which HPV infections can occur (Table 1). These are summarized as follows.

Risk factors	Infection	Transmission mode	Severity	Preventive measure
Multiple sexual partner, feeble immunity system, Age, Broken skin, Skin contact, Tobacco use	Cancer(cervical, genital, oropharyngeal lungs, head and neck) warts, genital warts, respiratory papillomatosis	Sexual contact, perinatal, blood, hands, surgery, sharing objects	In 2012, world-wide, 5,30,000 new cases of cervical cancer were reported. Alongside, 270,000 incident of mortality caused by cervical cancer every year	Vaccines, condoms, disinfectant

Table 1: Risk factors, infection, transmission mode, severity, and preventive measures HPV

Sexual content

Sexual contact is one of the major risk factors for HPV infections . From the known 120 species of papillomaviruses, 51 types along with However, the rate of JORRP increases if the mother has genital warts during childbirth though it is very less.

Blood

Previously, it was believed that HPV infection cannot transmit by blood. However, in 2005, a study was done in 57 pediatric patients (naive in sexual contact) who were transfusion acquired or vertical HPV infected, and among 8 of them, HPV16 was detected in their blood samples . Although

in blood, the existence of the DNA of HPV cannot prove that the person is infected by HPV. To prove this, in 2009, a test was done with 180 healthy male's blood sample and 15 among the samples were found one or more than one type of HPV. The conclusion about this topic is yet not decided whether HPV is transmitted through blood or not.

- **Hand**

The HPV infection can be spread among sexual partners or the same person through their genitals and hands. A study done with 25 couples for 7 months tested on their hands and genitals. The outcome of this study demonstrated that 2 among 25 couples infected by HPV (high risk). The hands of females infected for the genital infections of the men. In

2 couples, the hands of women infected men's genitals. In one couple, the man's hand is infected by this woman's genitals. In 2 couples, each of them infects their own hand. This experiment showed that hand was not the primary source of HPV infection, but hands played a key role in this infection. However, non-sexual contact by hand had very little or generally no role in this HPV infection.

- **Sharing object**

The object which is contaminated with HPV can cause HPV infection in case of sharing. Except sexual contact, other possible routes are not common for genital HPV infection in female. However, sharing common things such as toilet seat cannot cause HPV infection.

- **Surgery**

It has been documented that HPV infection can be spread by inhalation of viral particles by any person in the surgery room during laser ablation on condyloma or electrocautery. A surgeon infected by HPV during laser ablation on anogenital condyloma can suffer from laryngeal papillomatosis.

2. SIGN AND SYMPTOMS OF HPV

Many strains of HPV have no signs or symptoms. However, some strains can cause genital warts or cancer. Genital warts are small, flesh-colored bumps that usually occur in the genital area. The bumps may be flat or bumpy and shaped like cauliflower. HPV can cause the following types of cancer in women:

- Cervical
- Vulvar
- Anal
- Throat

cervical cancer

Signs of cervical cancer include:

- Abnormal vaginal discharge

Vaginal bleeding (not during normal period)

Painful sex

- Abnormal vaginal discharge

- General pelvic pain

Vulvar cancer

Some people with vulvar cancer may have no symptoms, depending on the type. Those who do have symptoms may experience:

- Itching
- Changes to the skin
- Bumps
- Lumps
- Spotting (light vaginal bleeding between periods)
- Sores that will not go away
- Abnormal vaginal discharge

Anal cancer

Signs of anal cancer include:

- Anal bleeding
- A lump near the anus
- Pain
- Pressure
- Itching
- Anal discharge
- Changes in bathroom habits

Throat cancer

Signs of throat cancer include:

- Chronic sore throat
- Neck lump
- Ear pain
- Ringing in the ears (tinnitus)
- Difficulty swallowing

➤ Warts

Skin infection ("cutaneous" infection) with HPV is very widespread. Skin infections with HPV can cause noncancerous skin growths called warts (verrucae). Warts are caused by a rapid growth of cells on the outer layer of the skin. While cases of warts have been described since the time of ancient Greece, their viral cause was not known until 1907. Skin warts are most common in childhood and typically appear and regress

spontaneously over the course of weeks to months. Recurring skin warts are common. All HPVs are believed to be capable of establishing long-term "latent" infections in small numbers of stem cells present in the skin. Although these latent infections may never be fully eradicated, immunological control is thought to block the appearance of symptoms such as warts. Immunological control is HPV type-specific, meaning an individual may become resistant to one HPV type while remaining susceptible to other types.

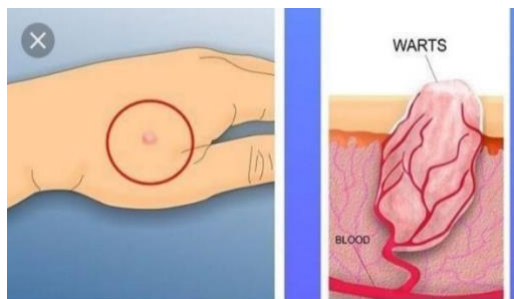


Fig. 2 Warts of Skin



Fig.3 Different types of warts found on body

Types of warts include:

- **Common warts** are usually found on the hands and feet, but can also occur in other areas, such as the elbows or knees. Common warts have a characteristic cauliflower-like surface and are typically slightly raised above the surrounding skin. Cutaneous HPV types can cause genital warts but are not associated with the development of cancer.
- **Planter warts** are found on the soles of the feet; they grow inward, generally causing pain when walking.
- **Subungual or periungual warts** form under the fingernail (subungual), around the fingernail, or on the cuticle (periungual). They are more difficult to treat than warts in other locations.
- **Flat warts** are most commonly found on the arms, face, or forehead. Like common warts, flat warts occur most frequently in children and teens. In people with normal immune function, flat warts are not associated with the development of cancer. Common, flat, and plantar warts are much less likely to spread from person to person.

Genital warts

HPV infection of the skin in the genital area is the most common sexually transmitted infection worldwide. Such infections are associated with genital or anal warts (medically known as condylomata acuminata or venereal warts), and these warts are the most easily. The strains of HPV that can cause genital warts are usually different from those that cause warts on other parts of the body, such as the hands or feet, or even the inner thighs. A wide variety of HPV types can cause genital warts, but types 6 and 11 together account for about 90% of all cases. However, in total more than 40 types of HPV are transmitted through sexual contact and can infect the skin of the anus and genitals. Such infections may cause genital warts, although they may also remain asymptomatic. The great majority of genital HPV infections never cause any overt symptoms and are cleared by the immune system in a matter of months. Moreover, people may transmit the virus to

others even if they do not display overt symptoms of infection. Most people acquire genital HPV infections at some point in their lives, and about 10% of women are currently infected. A large increase in the incidence of genital HPV infection occurs at the age when individuals begin to engage in sexual activity. As with cutaneous HPVs, immunity to genital HPV is believed to be specific to a specific strain of HPV.

Laryngeal papillomatosis

In addition to genital warts, infection by HPV types 6 and 11 can cause a rare condition known as recurrent laryngeal papillomatosis, in which

warts form on the larynx or other areas of the respiratory tract. These warts can recur frequently, may interfere with breathing, and in extremely rare cases can progress to cancer. For these reasons, repeated surgery to remove the wart may be advisable.

Cancer

Virus types About a dozen HPV types (including types 16, 18, 31, and 45) are called "high-risk" types because persistent infection has been linked to cancer of the oropharynx, larynx, vulva, vagina, cervix, penis, and anus. These cancers all involve sexually transmitted infection of HPV to the stratified epithelial tissue. Individuals infected with both HPV and HIV have an increased risk of developing cervical or anal cancer. HPV type 16 is the strain most likely to cause cancer and is present in about 47% of all cervical cancers, and in many vaginal and vulvar cancers, penile cancers, anal cancers, and cancers of the head and neck.

Squamous cell carcinoma of the skin

Studies have also shown a link between a wide range of HPV types and squamous cell carcinoma of the skin. In such cases, in vitro studies suggest that the E6 protein of the HPV virus may inhibit apoptosis induced by ultraviolet light. Some HPV types, such as HPV-5, may establish infections that persist for the lifetime of the individual without ever manifesting any clinical symptoms. HPV types 1 and 2 can cause common warts in some infected individuals. HPV types 6 and 11 can cause genital warts and laryngeal papillomatosis. Many HPV types are carcinogenic. The table below lists common symptoms of HPV infection and the associated strains of HPV.

Disease	HPV type
Common warts	2,7,22
Planter warts	1,2,4,63
Flat warts	3,10,28
An genital warts	6,11,42,44 and others
Anal dysplasia	16,18,31,53,58
Genital cancers	Highest risk 16,18,31,45,other 33,35,39,51,52,56,58,59 probability high risk 26,53,66,68,73,82
Epidermodysplasia verruciformis	More than 15type
Focal epithelial hyperplasia(mouth)	13,32
Mouth papilloma's	6,7,11,16,32
Oropharyngeal cancer	16
Verrucous cyst	60

Table no. 2: diseases and their HPV types

Skin cancer

In very rare cases, HPV may cause epidermodysplasia verruciformis (EV) in individuals with a weakened immune system. The virus, unchecked by the immune system, causes the overproduction of keratin by skin cells, resulting in lesions resembling warts or cutaneous horns which can ultimately transform into skin cancer, but the development is not well understood. The specific types of HPV that are associated with EV are HPV5, HPV8, and HPV1

Cervical Cancer

Nearly all cases of cervical cancer are associated with HPV infection, with two types, HPV16 and HPV18, present in 70% of cases. In 2012,

twelve HPV types were considered carcinogenic for cervical cancer by the International Agency for Research on Cancer: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59. HPV is necessary for cervical cancer to occur.[51] Persistent HPV infection increases the risk for developing cervical carcinoma. Individuals who have an increased incidence of these types of infection are women with HIV/AIDS, who are at a 22-fold increased risk of cervical cancer. The carcinogenic HPV types in cervical cancer belong to the alpha papillomavirus genus and can be grouped further into HPV clades. The two major carcinogenic HPV clades, alpha papillomavirus-9 (A9) and alpha papillomavirus-7 (A7), contain HPV16 and HPV18, respectively. These two HPV clades were shown to have different effects on tumour molecular characteristics and patient prognosis, with clade A7 being associated with more aggressive pathways and an inferior prognosis. In 2012, about 528,000 new cases and 266,000 deaths from cervical cancer occurred worldwide. Around 85% of these occurred in the developing world.

3. PREVENTIVE MEASURES

• Vaccines

Three types of vaccines are made to prevent HPV infections. They are Gardasil 9, Cervarix, and Gardasil. They are able to protect from HPV16 and HPV18, while Gardasil (a recombinant vaccine) is able to protect from HPV6 and HPV11 also. Cervarix (bivalent type) is produced by VLP (virus like particles which look like virus but do not contain viral genome) from the protein found in capsid (L1). The Gardasil 9 is able to protect from HPV16, HPV18, HPV31, HPV45, HPV52, HPV58, HPV6, and HPV11; hence, above 90% of genital cancers (cervical, anal, vaginal, and vulvar cancers) can be protected with the help of these vaccines. These vaccines show very little effects on the women who have already exposed to HPV16 and HPV18. Hence, women who are sexually naive are recommended for vaccination.

• Condoms

The CDCP suggests that the use of condoms is beneficial to decrease the risk associated to the HPV infection. Female condoms are found to be much more acceptable in terms of the reduction of HPV contact. However, condom cannot give too much protection as HPV can transmit through any area which is not covered by condoms like any mucosal surface or infected area of skin.

• Disinfectant

This virus can be killed by some disinfectant though it is very difficult to kill it. Exposed it to 90% ethanol (for 1 min), 30% savlon, 2% glutaraldehyde, and 1% sodium hypochlorite can be beneficial. This virus can be demolished at 100°C though it is resistance in temperature and drying. It can also be killed by ultraviolet radiations. To reduce the risk of contracting HPV, a person can: Get the HPV vaccine. Use barrier protection every time they have sex.

- Limit their number of sexual partners.
- Not have sex while genital warts are present.
- To help prevent the warts from spreading:
 - Avoid touching the wart unnecessarily.
 - Wash the hands after touching a wart.
 - Avoid shaving over a wart.
 - Use footwear in public areas, such as pools and locker rooms, if warts are present on the feet.
 - Treat and cover a wart until it disappears.
 - Avoid sharing towels and other personal items.

4. TREATMENT OF HPV

➤ Drugs for the treatment of HPV

Some of the most effective medications for the treatment of HPV include:

1. Gardasil is one amongst the highest medicine for the HPV virus. It's a non-infectious quadrivalent recombinant immunogen with extremely refined virus-like particles together with an aluminum-containing vaccine adjuvant.
2. Imiquimod (Aldara) may be a prescription medication that acts as an immunologic response modifier. Imiquimod may be a patient-applied cream used to treat benign diseases of the skin likewise as HPV.
3. Podofilox (Condylox) may be a drug to treat the HPV virus. It's a non-alkaloid cytotoxic lignan extracted from the roots and rhizomes of the genus Podophyllum species. It's a topical gel used for the treatment of external sex organ and opening exophytic warts (condylomata acuminata) caused by the human papillomavirus.

(HPV).

4. acetic acid is an analogue of acetic acid during which 3 hydrogen atoms of the alkyl have all been replaced by atomic number 17 atoms. Solutions containing trichloroacetic acid as an ingredient are used for the treatment of sex organ warts, caused by some sort of HPV.

5. a replacement study has found that the human papillomavirus (HPV) immunogen protects against the sexually transmitted virus that causes cervical cancer. It additionally helps prevent genital warts and inferiorcervical growths.

There are currently 3 vaccines presently out there

- Cervarix
 - Gardasil
 - Gardasil-
- 9 Genital

warts

Do not use over-the-counter products on genital warts. A doctor may recommend Trusted Source:

- Cryotherapy: This involves using liquid nitrogen to freeze off warts.
- Electrocautery: This involves using an electrical current to burn away the warts.
- Laser or light therapy: This involves using a high-powered, targeted beam to remove the unwanted tissue.
- Surgical removal: A surgeon can cut away warts in an outpatient procedure that involves a local anesthetic. The best option will depend upon the type and location of the wart. Treatments can remove warts, but the virus will remain in the body and remain transmissible.
- HPV Treatments for sex organ Warts HPV types six and eleven those related to genital warts tend to grow for concerning six months so stabilize. typically visible sex organ warts depart while not treatment.

once treatment is

- Treatment throughout physiological condition Treatment for pregnant ladies includes acetic acid (TCA) and bichloroacetic acid (BCA), that are found to be each effective and safe. Podophyllin rosin, interferon, and antimetabolite shouldn't be used throughout physiological condition, as a result of they will damage the fetus.

- Test for HPV

If warts or lesions are visible, a doctor can usually diagnose HPV with a visual examination. Also, tests can confirm the presence of the virus.

for HPV or related cervical cellular changes include:

- a Pap smear
- a DNA test
- a biopsy

A Pap smear, also called a cervical smear, involves collecting and testing cells from the surface of the cervix or vagina. It can reveal any cellular abnormalities that may lead to cancer. A DNA test can evaluate for high-risk types of HPV, and a doctor may use it alongside a Pap smear. A biopsy, which involves taking a sample of affected skin, may be necessary if a test reveals unusual cell changes. There is currently no routine screening for HPV in males, and the range of testing options is limited. Some experts have called for more testing, especially for men who have sex with men. Vaccination

The Centers for Disease Control and Prevention (CDC) Trusted Source recommend vaccination at the age of 11–12 years to reduce the risk of cervical and other forms of cancer.

This type of vaccine comes in two stages, 6–12 months apart. Currently, three HPV vaccines Trusted Source are available:

- Gardasil
- Cervarix
- Gardasil 9
- People aged up to 26 years Trusted Source who have not received the vaccine should ask their doctors about it.
- People aged 27–45 years Trusted Source who have not had the vaccine are eligible for vaccination with Gardasil 9.
- Speak with a doctor to see whether vaccination is appropriate. Anyone who is pregnant should wait until after delivery to have the vaccination.

9. PRESENT SCENARIO HPV VACCINATION

Globally, three types of HPV vaccines are currently available – bivalent vaccine (Cervarix™; GSK Biologicals, Belgium) targeting HPV types 16 and 18; quadrivalent vaccine (Gardasil™, Merck, USA) targeting HPV 16, 18, 6 and 11; and 9-valent vaccine (Gardasil 9™; Merck, USA) targeting HPV 31,

33, 45, 52 and 58 in addition to HPV 16, 18, 6 and 11. The first two are available in India. The L1 surface proteins of the targeted HPV types are used as the antigen. The L1 protein undergoes conformational changes to self-assemble into ‘virus-like’ particles (VLPs) in artificial production systems. The VLPs are non-infective and non-pathogenic as these are devoid of the viral DNA essential to initiate the carcinogenic process.

Adjuvants used to ensure robust and long-lasting immunogenicity include aluminium phosphate and monophosphoryl lipid A combination (AS04) in the bivalent vaccine and aluminium hydroxyl-phosphate sulphate in the quadrivalent and the 9-valent vaccine. Two intramuscular doses at six months interval are recommended for girls below 15 yr of age. For those 15 yr and above and for immune-compromised girls/women, three doses over a 6-month period are recommended. The HPV vaccines are highly immunogenic leading to seroconversion in more than 99 per cent of the vaccinated girls and women. Following vaccination, L1 proteins are recognized by the immune system in the regional lymph nodes to generate strong antibody response (IgG), and its concentration is 1-4 logs higher than the antibody levels induced by the natural HPV infections. The IgG is exuded at the possible sites of infection (mucosa of genital tract, oral cavity, etc.), neutralizes the virus and prevents its entry into the cells. The vaccine-induced immune memory in the form of circulating plasma cells and memory B-cells allows generation and exudation of protecting IgG each time the body is challenged by exposure to HPV infection. Impact of HPV vaccines on population health Models predict that vaccination programmes for young adolescent females will substantially reduce the incidence of cervical cancers associated with vaccine-related HPV types if coverage is high (>70%) and vaccine-induced protection lasts for ≥10 years. Considerable reductions in incidence may also be expected for cancers of the vagina, vulva, anus, and head and neck associated with HPV-16/18. Vaccination with the quadrivalent vaccine will substantially reduce the incidence of anogenital warts, low- grade cervical abnormalities caused by HPV-6/11 and, possibly, recurrent respiratory papillomatosis. Since the vaccines protect females who are naive for the vaccine-related HPV types at the time of immunisation, high coverage of young adolescent girls before first intercourse is expected to have a much larger impact than vaccinating older females.

WHO recommendations

WHO recommends that routine HPV vaccination should be included in national immunization programmes, provided that prevention of cervical cancer or other HPV-related diseases, or both, constitutes a public health priority; vaccine introduction is programmatically feasible; financially sustainable; and is cost effectiveness in the country. Programs should initially prioritize high coverage in the primary target population which should be selected based on data on the age of initiation of sexual activity and feasibility of reaching young adolescent girls through schools, or healthcare and community-based settings. Vaccination of secondary target populations of older adolescent females or young women is recommended only if this is feasible, affordable, cost-effective, does not divert resources from vaccinating the primary target population or effective cervical cancer screening programmes, and if a significant proportion of this target population is likely to be naive to vaccine-related HPV types. The benefits of vaccination should be available to all irrespective of their HIV status. HPV vaccination of males is not recommended. The choice between the two

vaccines should be based on the scale of the prevailing HPV problem, the target population, delivery strategies, safety concerns and the price, supply, and cold-chain requirements of the products. Cost-effectiveness and economic feasibility of HPV vaccination

In general, models show that a substantial reduction in costs associated with cervical cancer screening and follow-up of abnormal screening tests, diagnosis, and treatment of precancerous states and cancer is expected with nationwide programs that achieve high coverage in young adolescent girls, at least in countries where gross domestic product is high. HPV vaccination may be cost-effective in low-income and middle-income countries (where quality screening is not widespread) if the cost per vaccinated girl (including three doses of vaccine and programmatic costs) is < US\$ 10–25, which is substantially lower than current costs in high-income countries. Quadrivalent HPV vaccination is expected to further reduce the costs associated with the diagnosis and treatment of genital warts in high-income settings. The respective cost of a single 0.5-ml dose of Gardasil® and Cervarix™ is approximately \$120 and \$100 in the USA versus Rs 2,800 and

Rs 3,300 in India. The cost in India for the entire three dose schedule turns out to be Rs 8,400 and Rs 9,900, respectively. The vaccine cost may drop substantially if the Government purchases vaccine in bulk by policy, or if Indian manufacturers are encouraged or enabled to manufacture vaccine. The long-term cost-effectiveness of mass HPV vaccination needs to be specifically evaluated for India, comparing the expected economic burden incurred by cost of vaccines and infrastructure for the programme against the financial benefit of reduced

health costs for diagnosis and treatment of CINs, cervical cancers and anogenital warts. **Social factors**

The median age of initiation of sexual debut in Indian adolescents has been reported to range from 15 to 16 years to 17.37 ± 1.72 years with earliest debut seen as early as 13 years of age. Thus, even in Indian females, the vaccine will be most effective if given at a younger age (prior to expected sexual debut). However, the concept of premarital sexual exposure is taboo in the Indian society and socio-cultural barriers exist to effective communication between physicians and parents regarding the sexual activities of their adolescent girls and boys. Explaining to the parents about importance of prophylactic vaccination of their children and their consent for the same is expected to be a difficult task and would require formulation of guidelines for effective counseling. It needs to be stressed upon that the risk of HPV infection and consequent cancer risk is not necessarily predicted by one's own sexual promiscuity alone as a woman is also at risk because of her partner's past or present sexual activities.

Clinical trials in India

Only two HPV vaccination projects were initiated in India. One was a post-licensure observational study for operational feasibility of school-based and community-based vaccination in Khammam district (Andhra Pradesh, Gardasil®) and Vadodara (Gujarat, Cervarix™), conducted by the State Governments in collaboration with Indian Council of Medical Research and PATH (a US based non-profit non-governmental organization). The other was a multicentric clinical trial to investigate immunogenic efficacy of two doses (6 months apart) compared with conventional three doses (at 0-2-6 months) of Gardasil®, which if found successful would have resulted in 33% cost reduction. Following media allegations of "vaccine-induced" deaths of four girls in Khammam, both studies have been suspended by the Union Government. The deaths have since been investigated and confirmed as unrelated to the vaccine. However, the studies have not been resumed (till the time of writing this article). The scepticism for the need and safety of HPV vaccines in the Indian context continues. To achieve effective prevention of HPV infection related morbidity and mortality by vaccination in India, the health authorities and Government should resort to more effective and sympathetic dialog with people to address their reasonable concerns and dispel their fears based on misinformation.

Future trends

The quadrivalent and bivalent vaccines provide only limited cross-protection to development of persistent infection and CIN 2-3/AIS caused by non-vaccine HPV types. Thus, a multivalent vaccine against a multitude of HPVs will be a major breakthrough in providing near-complete prevention of HPV-related diseases, and indeed, efforts to develop a nine-type L1 VLP combination vaccine are ongoing. Preclinical and human volunteer studies have also suggested that immunization against the minor capsid protein 2 with the candidate prophylactic/therapeutic vaccine HPV-16 L2E6E7 might work as a pan-HPV vaccine against different genotypes of HPVs. Development of low-cost vaccines using plant species such as tobacco, potatoes, and tomatoes for the production of VLPs is also underway. Therapeutic vaccines incorporating the E6E7 proteins such as the HPV-16 E6E7 ISCOMATRIX vaccine are being investigated for treatment of HPV-related anal intraepithelial neoplasia in HIV-infected men.

9. CONCLUSION

HPV vaccines are safe and efficacious against type-specific HPV-induced anogenital warts, precancerous lesions, and cervical cancer. The vaccines are most effective when given before the onset of sexual activity and provide long-term protection. While new clinical trials and follow-up of older trials will yield more information on issues such as efficacy, safety, duration of protection, need for booster dose, current evidence supports the introduction of HPV vaccination as part of a coordinated strategy to prevent cervical cancer, and other HPV-related diseases. India-specific guidelines need to be based on cost-effectiveness and feasibility of implementing HPV vaccination as a part of national immunisation schedule. Vaccination alone will not be successful unless it is coupled with education about healthy sexual behavior and information about the diagnosis and treatment of HPV-related anal intraepithelial neoplasia in HIV-infected men.

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