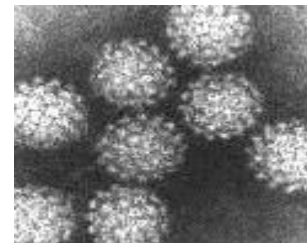


Papillomaviridae family is a very large virus family currently divided into 16 genera, of which five contain members that infect humans (*Alpha-*, *Beta-*, *Gamma-*, *Mupa-*, and *Nupapapillomavirus*). Although papillomaviruses and polyomaviruses share similarities in morphology, nucleic acid composition, and transforming capabilities, differences in genome organization and biology led to their separation into distinct virus families.

### Important Properties of Papillomaviruses:

**Virion:** Icosahedral, 55 nm in diameter, **Genome:** Double-stranded DNA, circular, **Proteins:** Two structural proteins; cellular histones condense DNA in virion, non **envelope**. Significant cause of human cancer, especially cervical cancer. Viral oncoproteins interact with cellular tumor suppressor proteins eg, the P53 gene and the reticuloblastoma(RB)gene respectively. Inactivation of P53 and RB proteins is an important step in the process by which a normal cell becomes a cancer cell. there is no in vitro infectivity assay, papillomavirus isolates are classified using molecular criteria.

Almost 200 distinct HPV types have been recovered.



**Papillomavirus**

### Papillomavirus Replication:

Papillomaviruses are highly tropic for epithelial cells of the skin and mucous membranes. Viral nucleic acid can be found in basal stem cells, but late gene expression (capsid proteins) is restricted to the uppermost layer of differentiated keratinocytes. Stages in the viral replicative cycle are dependent on specific factors that are present in sequential differentiated states of epithelial cells. This strong dependence of viral

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replication on the differentiated state of the host cell is responsible for the difficulties in propagating papillomaviruses in vitro.

### **Transmission and epidemiology:**

Papillomaviruses are transmitted primarily by:

- 1- skin to skin (Skin warts are more common in children and young adults and tend to regress in older adults.
- 2- genital contact ( genital warts are among the most common sexually transmitted disease).
- 3- and from infected mothers to their newborn baby during the birth process.

### **Pathogenesis and Immunity:**

Papillomaviruses infect squamous epithelial cells and induce within those cells a characteristic cytoplasmic vacuole. these vacuolated cells called koilocytes ,are the hallmark of infection by these viruses. Most warts are benign and do not progress to malignancy. the proteins encoded by viral genes E6 and E7 interfere with the growth –inhibitory activity of the proteins encoded by the P53 and RB tumor suppresser genes and thereby contribute to oncogenesis by these viruses. The E6 and E7 proteins of HPV type 16 bind more strongly to P53 RB proteins than the E6 and E7 proteins of HPV types not implicated in carcinomas ,a finding that explains why type 16 causes carcinoma more frequently than the other types.

Both cell-mediated immunity and antibody are induced by viral infection and are involved in the spontaneous regression of warts . Immunosuppressed patients ,eg, AIDS patients ,have more extensive warts , and women infected with HIV have a very high rate of carcinoma of the cervix.

### **Clinical finding:**

Papilloma of the various organs are the predominant finding. These papillomas are caused by specific HPV types. For example , skin and planter warts are caused primarily by HPV-1 through HPV4,whereas genital warts( condylomata acuminate ) are caused primarily by HPV-6 and HPV-11.Carcinoma of the uterine cervix ,the penis,and the anus, as well as premalignant lesions called intraepithelial neoplasia ,are associated with infection by HPV-16 and HPV-18.

## **Laboratory diagnosis:**

The traditional methods of viral diagnosis such as electron microscopy, cell culture, and certain immunological methods are not suitable for HPV detection. HPV cannot be cultured in cell cultures. The important methods to diagnose HPV infection are:

- Colposcopy and acetic acid test
- Biopsy
- DNA test (PCR, Southern Blot Hybridization, In Situ Hybridization)
- Pap smear

**Pap test.** Your doctor collects a sample of cells from your cervix or vagina to send for laboratory analysis. Pap tests can reveal abnormalities that may lead to cancer.

**DNA test.** This test can recognize the DNA of the high-risk varieties of HPV that have been linked to genital cancers. The test is conducted on a sample of cells taken from your cervix. It's recommended for women 30 and older in addition to the Pap test.

## **Treatment and prevention:**

The usual treatment for genital warts is :

-Podofilox, or Condylox ,Imiquimod, or Aldara , Alpha interferon is also effective.

For treatment the skin warts used:

- 1-Cryotherapy, the freezing off of the wart with liquid nitrogen
- 2-Trichloroacetic acid, a chemical applied to the surface of the wart
- 3-Surgical removal, cutting the cells out with a scalpel
- 4-Electrocautery, burning off warts using an electric current
- 5-Laser vaporization or excision of the warts

Two HPV vaccines can prevent diseases and cancers caused by HPV. The Cervarix and Gardasil vaccines.

# Medical microbiology

## Virology

Dr.Zeytoon Alkhafaji

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Cervarix, was licensed in 2009 for use in females aged 10-25. protects against types 16 and 18, which cause 70% of cervical cancers

Gardasil(quadrivalent vaccine) use in 2006 . It targets four types of HPV: 6, 11, 16 and 18. Types 16 and 18 lead to cervical cancer. HPV 6 and HPV 11 cause about 90% of genital warts. It is recommended as a routine vaccination for males and females aged 9-26 years old. More recently, Gardasil 9 was approved by the FDA. It prevents infection by the same HPV types as Gardasil plus HPV-31, HPV-33, HPV-45, HPV-52, and HPV-58. Collectively, these types are implicated in 90% of cervical cancers. **Gardasil 9** can be used in the same age group for females and for males ages 9 through 15. It is given as a 3-dose vaccine over 6 months. It should not be administered to **pregnant** women.

HPV infection and cancer development: As in( figure 1):

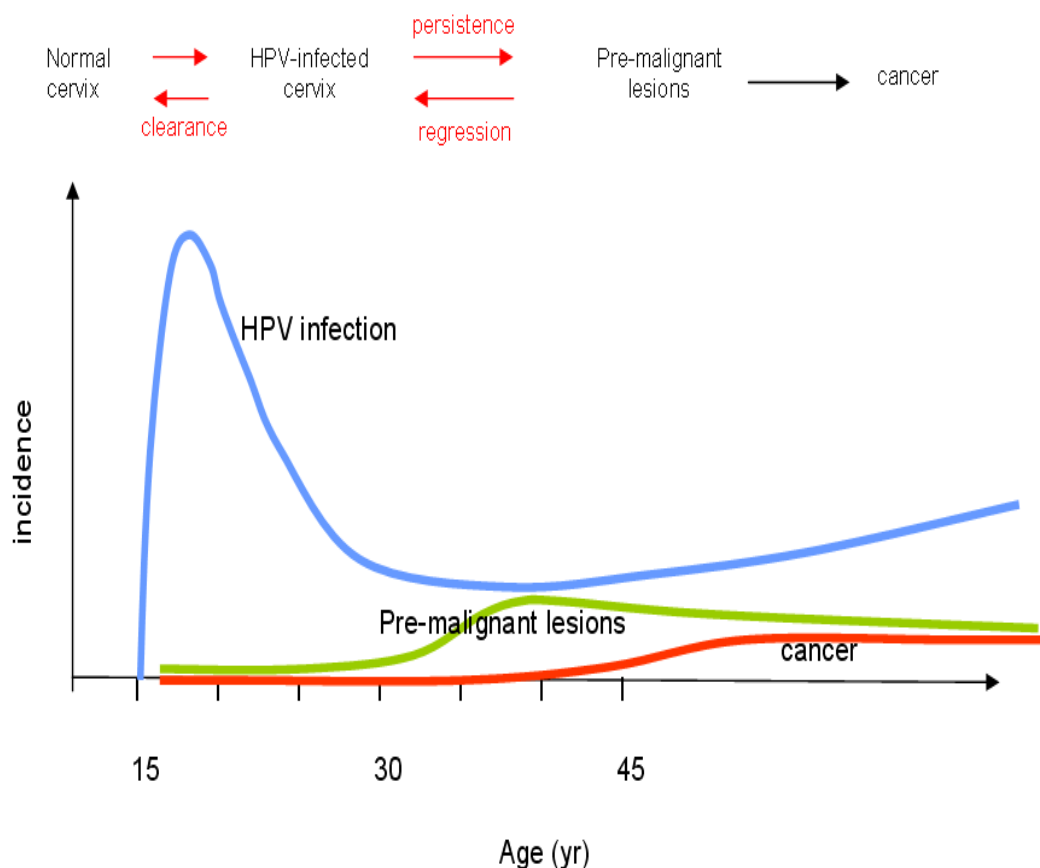


Figure 1: The evolution of cancer following infection takes many years.