Viral Genital Infection

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Learning outcomes

By the end of this lecture the students will be able to:

1. Provide an overview of the HSV-2 structure, mode of transmission, pathogenesis, clinical manifestations, latency, reactivation, diagnosis, and management.

2. Describe the human papillomavirus's morphology, clinical importance, mode of transmission, laboratory diagnosis, and vaccines.

3. Link their understanding to real-world clinical issues.

Lecture Content

- **Herpes simplex viruses.**
- **Human papillomavirus.**

Case Scenario

- A 37-year-old man came to the outpatient clinic for dermatology and venereology, stating that a soft pink growth had appeared on the shaft of his penis. He reported to have had multiple extramarital encounters.

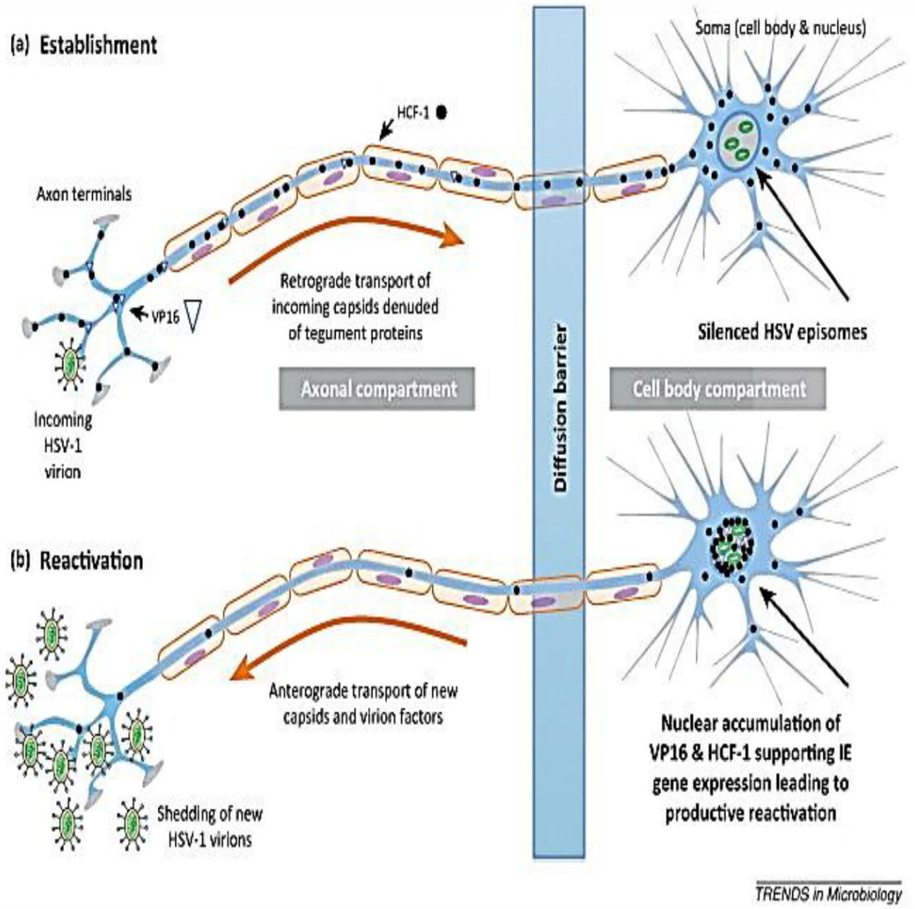
1- What is the causative organism in this case?
2- Describe its morphology.
3- Mention its mode of transmission.
4- Mention its relation to malignancy.
5- How to treat this case?

Herpes viruses

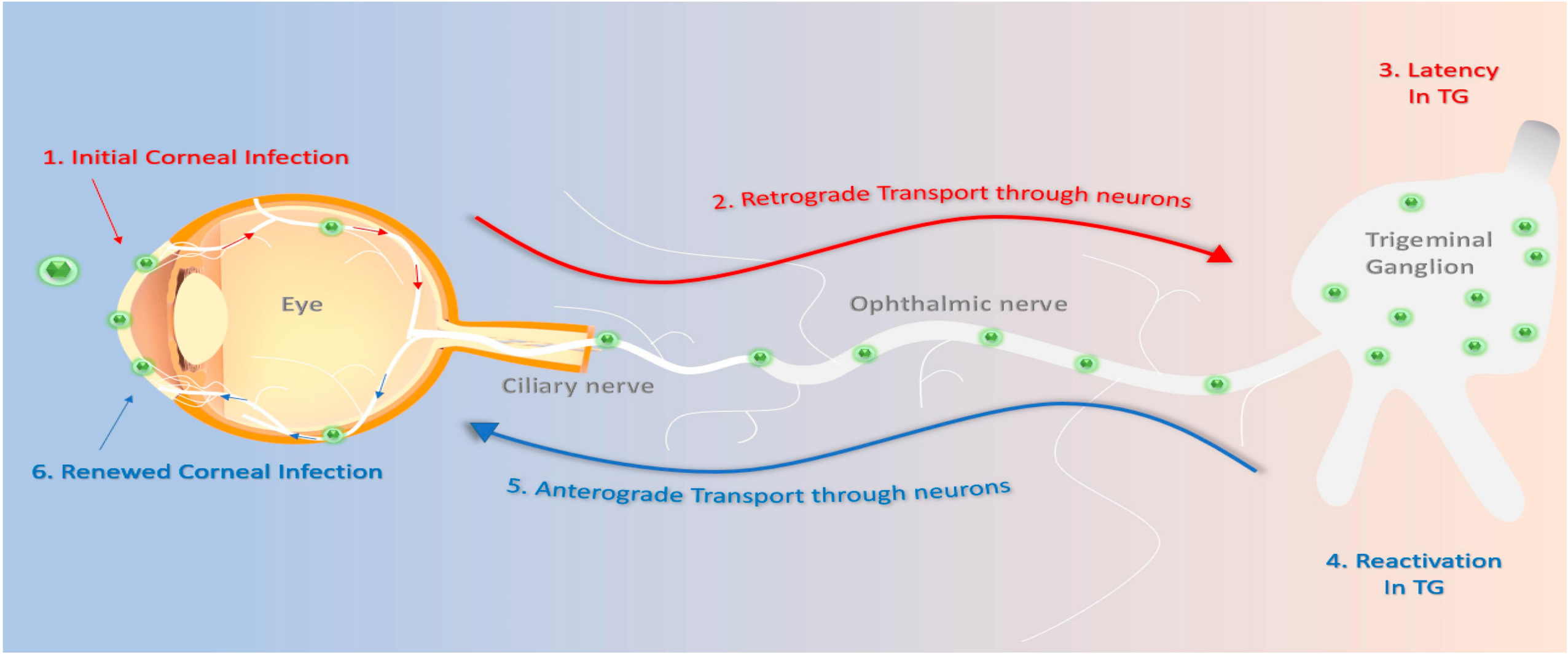
- Structure
- Classification of Herpesviruses
- Herpes simplex viruses
- Transmission and Pathogenesis
- Clinical syndromes
- Laboratory Diagnosis
- Treatment

Herpes viruses

- **Eight** human herpesvirus species are known.
- All have the ability to enter a **latent** state following primary infection and to be **reactivated** at a later time.

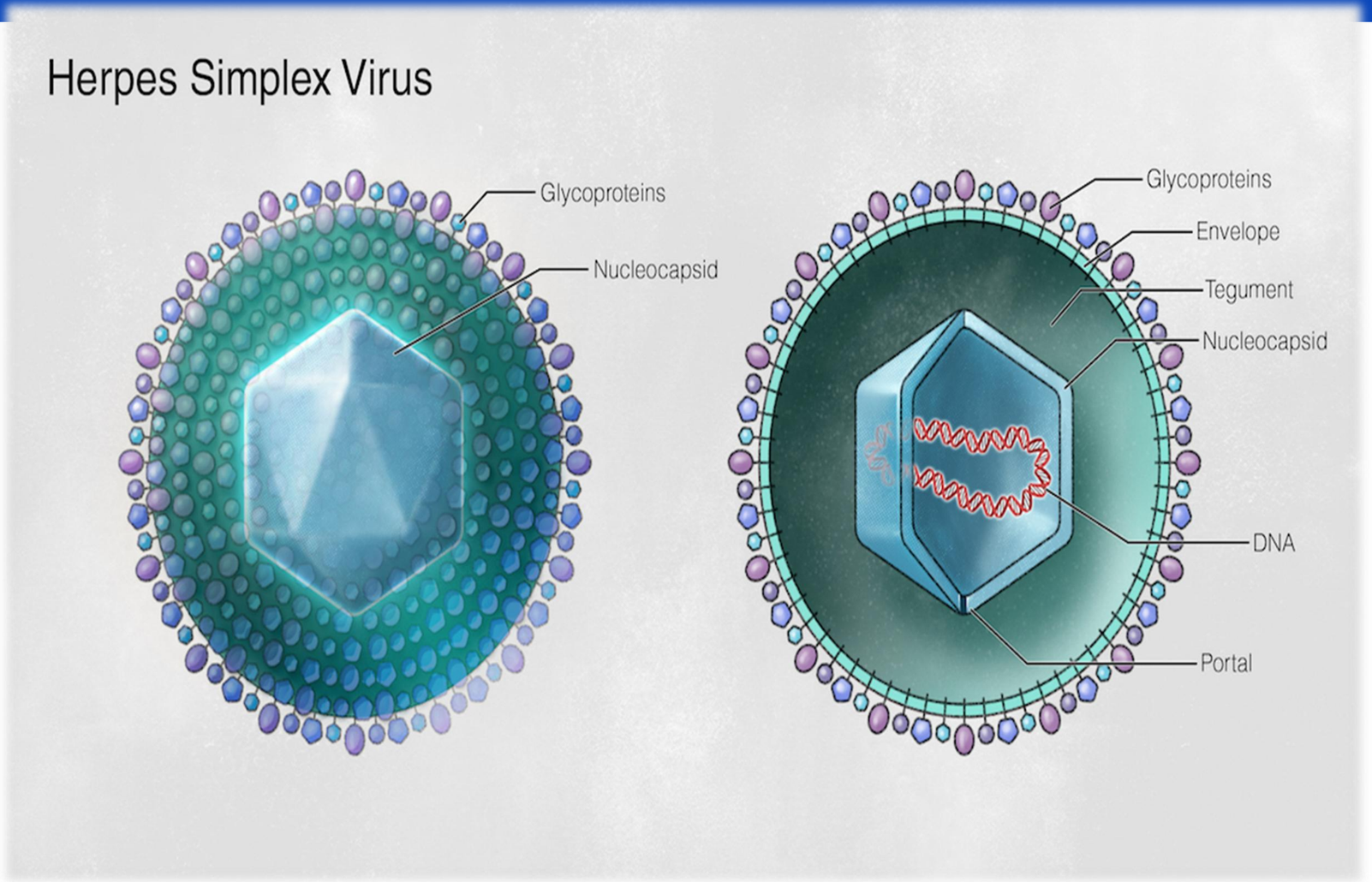


Herpes viruses



Structure

- Virion: icosahedral.
- Genome: Double-stranded DNA, linear.
- Envelope: Contains glycoprotein spikes.



Classification of Herpesviruses

- They have been divided into three subfamilies:

Alpha herpesvirinae	Beta herpesvirinae	Gamma herpesvirinae
Herpes simplex virus type 1 (HSV-1 or HHV-1).	Cytomegalovirus (HHV-5).	Epstein-Barr virus (HHV-4).
Herpes simplex virus type 2 (HSV-2 or HHV-2).	Human herpes virus type 6 (HHV-6).	Kaposi's sarcoma-associated herpes virus (KSHV) or (HHV-8).
Varicella – Zoster virus (VZV or HHV-3).	Human herpes virus type 7 (HHV-7).	

Herpes simplex viruses

- There are **2** distinct herpes simplex viruses, type 1 and type 2.
- The two viruses cross-react serologically but some unique proteins exist for each type.

Transmission and Pathogenesis

	HSV-1	HSV-2
Mode of transmission	Primarily in saliva (kissing)	By sexual contact
Multiplies locally in the mucous membrane or abraded skin causing vesicular lesions.		
Site of lesion	Mainly orofacial lesions	Genital lesions
However, both types of HSV can infect oral or genital mucosa depending on regions of contact.		

Clinical syndromes

	HSV-1	HSV-2
Primary infection	• **Acute gingivostomatitis**. • **Herpes libialis** (cold sores). • **Herpetic whitlow**: is a pustular lesion of the skin of finger or hand of medical personnel. • **Keratoconjunctivitis, encephalitis**. • **Disseminated infections**, such as esophagitis and pneumonia in immune-compromised.	• **Genital herpes**: vesiculo-ulcerative lesions on external genitalia as well as the cervix. • **Neonatal infection**: ▪ Originates chiefly from contact with vesicular lesions within the birth canal. ▪ **Neonatal herpes** varies from a severe generalized disease often involving the CNS to an asymptomatic infection. • **Aseptic meningitis**.

Clinical syndromes

Latency	**Trigeminal ganglia.**	**Sacral ganglia.**
Reactivation	In response to stimuli as common colds, hormonal changes and sunlight.	
	• Cold sores. • Keratitis.	• Occur more frequently. • Often asymptomatic but still results in viral shedding.

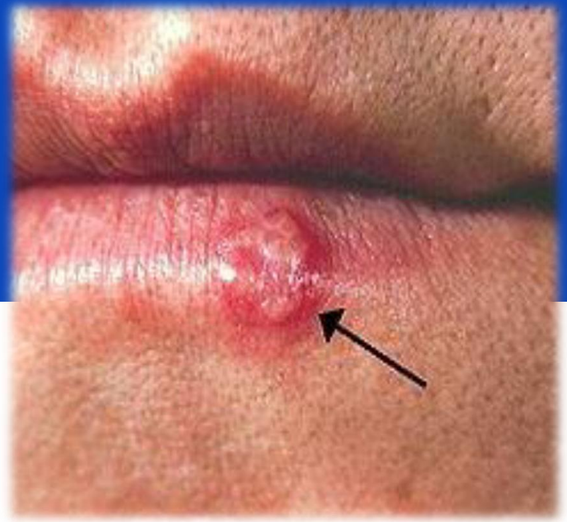
Medscape® www.medscape.com

Type of Lesion	Description
Macule	Circumscribed, flat change in color of skin; <1.0 cm diameter
Patch	Circumscribed, flat lesion (large macule); >1.0 cm diameter
Papule	Raised solid lesion; <0.5 cm diameter. Papules may become confluent and form plaque
Plaque	Circumscribed, raised superficial lesion with flat surface; >0.5 cm diameter
Nodule	Circumscribed, raised, firm lesion; >0.5 cm; may have started as a papule
Wheal	Firm, raised, pink/red swelling of the skin; size and shape varies; usually itchy; lasts <24 hours
Tumor	Large papule or nodule; usually >1 cm diameter
Pustule	Circumscribed, raised lesion containing purulent exudate that may be cloudy, white, yellow, or hemorrhagic; size varies
Vesicle	Circumscribed, raised lesion; filled with liquid or semi-solid material; may become infected
Bulla	Vesicle > 0.5 cm
Cyst	Firm, raised encapsulated lesion; filled with liquid or semi-solid material; may become infected.

Source: Dermatol Nurs © 2002 Jannetti Publications, Inc.

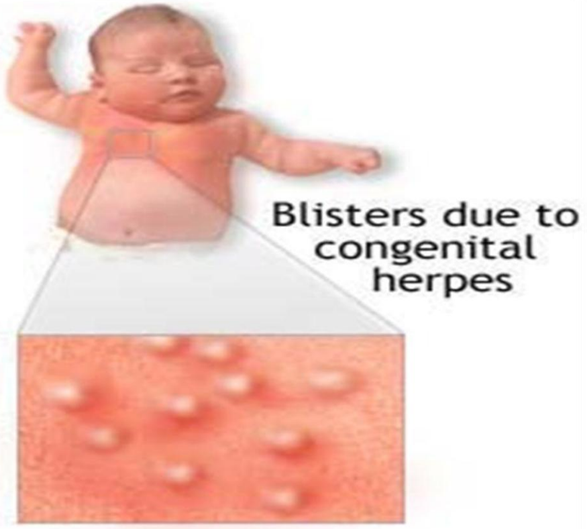
Herpes Stomatitis

Cold sore



Vesicular lesion

Mother with active herpes infection (although active infection may not be apparent)



ADAM

Laboratory diagnosis

- **Sample**: vesicular fluid.
- Detection of viral particles by electron microscope.
- Detection of viral antigens by immunofluorescence in vesicular fluid.
- Detection of HSV DNA by PCR.
- Virus isolation from herpetic lesions.
- Serologic diagnosis (Detection of IgM or 4-folds rising titer of IgG).
- Histological staining (Giemsa stain) of scrapings or swabs from the base of skin lesions.

Treatment

- Acyclovir, Famciclovir, and Valacyclovir are the treatment of choices.
- It shortens the duration of the lesion and decreases shedding of the virus.
- No drug treatment prevents recurrences.
- No effect on the latent state.

* Which of the following describes the structure of herpes viruses?

a) **Double-stranded DNA, icosahedral, enveloped**

b) Double-stranded DNA, icosahedral, non-enveloped

c) Single-stranded DNA, icosahedral, enveloped

d) Single-stranded DNA, icosahedral, non-enveloped

e) Single-stranded RNA, icosahedra, enveloped

Human papilloma virus (HPV)

- Morphology
- Mode of Transmission
- Clinical significance
- HPV and cancer
- Laboratory Diagnosis
- HPV vaccine
- Treatment

Morphology

- HPV is a small, Icosahedral non-enveloped virus with a circular double-stranded DNA genome.
- There are more than 100 different types of HPV.
- The most common sexually transmitted virus.

Mode of Transmission

- It requires direct contact with infected individuals e.g. sexual contact or contaminated surfaces e.g. common bathroom floors.

Clinical significance

HPV type	Clinical lesion	Benign/ Malignant
Type-1	Planter wart.	Benign
Type- 2, 4	Skin warts.	Benign
Type-16, 18	Carcinoma (cervix, penis) (70%).	Malignant
Type-6, 11	Anogenital condylomas (90%) and laryngeal papilloma.	Low oncogenic potential

Clinical significance

- Condylomata (genital wart) are irregular,

  soft, pink growths

  that are found on external genitalia

  or the anus.

HPV and cancer

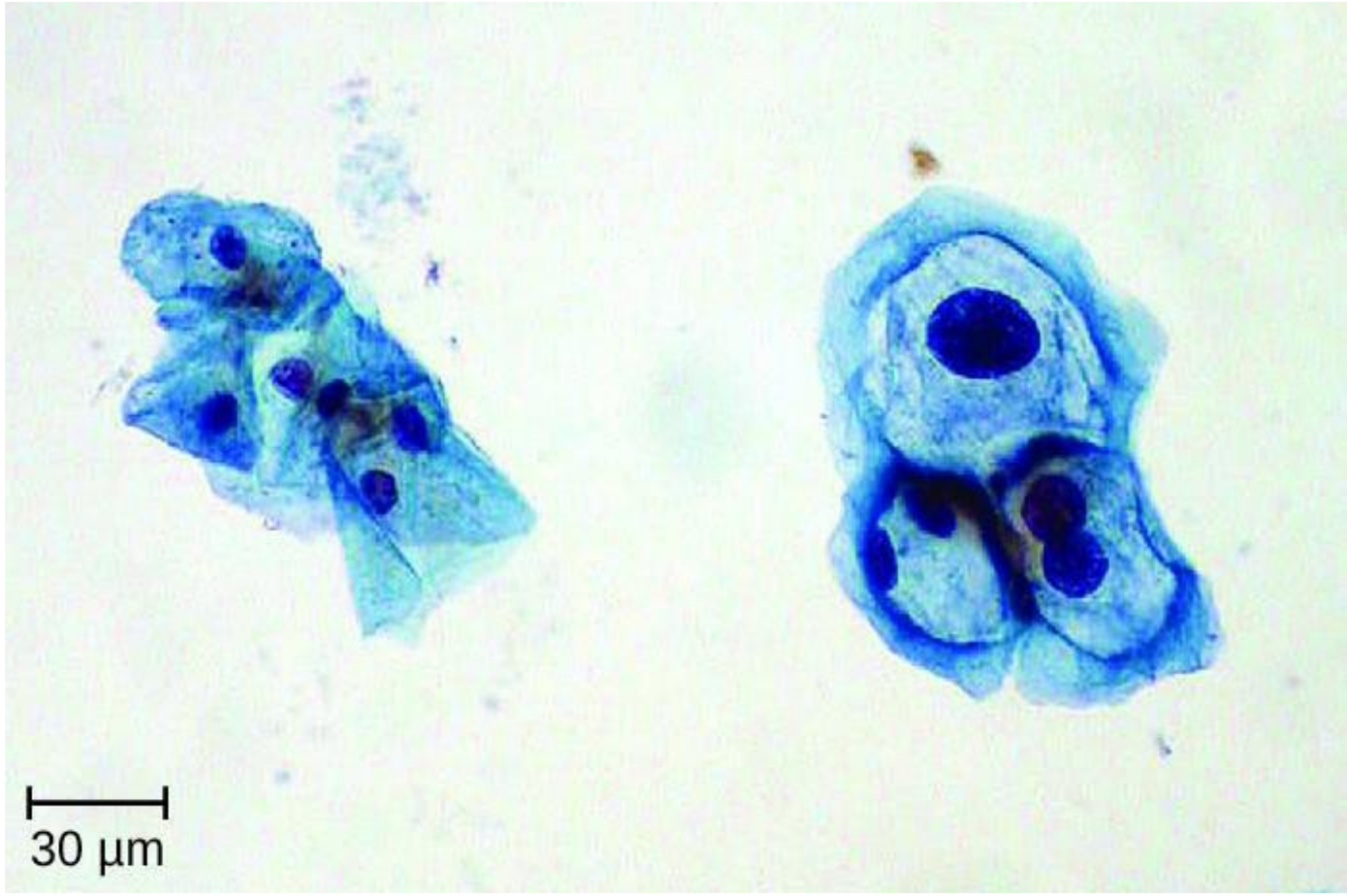
- HPV virulence factors include proteins (E6 and E7) that are capable of inactivating tumor suppressor proteins (P53) → uncontrolled cell division and the development of cancer.

Laboratory Diagnosis

- Virus has not been isolated in cell line.
- Serologic tests rarely done (large number of serotypes).
- PCR to detect virus DNA is available.
- Screening by Pap smear for all women above 30 in USA (koilocytes).

Laboratory Diagnosis

- In this image, the cervical cells on the left are normal and those on the right show **enlarged** nuclei and **hyperchromasia** (darkly stained nuclei) typical of HPV-infected **koilocytes**.

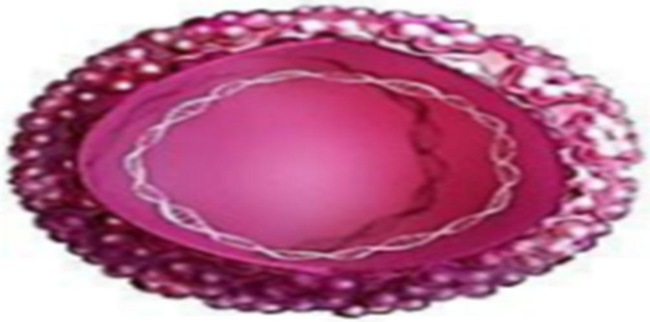


HPV vaccine

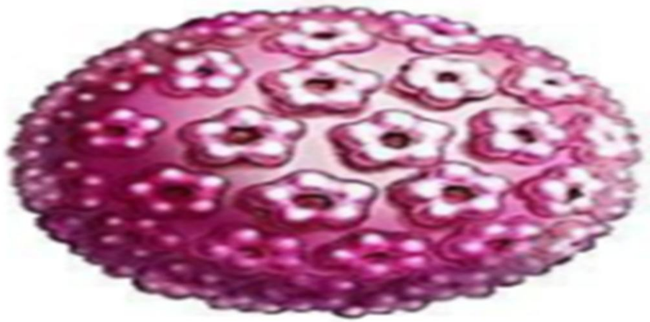
- **Virus-like particle** (VLP) vaccine. (L1 and/ Or L2 protein).
- There are 3 versions of the L1-only HPV vaccine.
    - **Gardasil**: HPV16, 18, 6 and 11.
    - **Cervarix**: HPV 16, 18.
    - **Gardasil** 9: HPV16, 18, 6, 11, 31, 33, 45, 52, and 58.
- Given to females 10 - 25 years of age.

HPV vaccine

Virus-like particles (VLPs) as HPV vaccine antigens mimic the virus structure



HPV-containing double stranded DNA



'Empty' non-infectious virus-like particle (VLP) mimics the virus

Stanley M, et al. Vaccine 2006; 24(suppl 3):S3/106–113.

Treatment

- Most HPV infections resolve **spontaneously**.

- **Topical** medications:

    - **imiquimod** (which stimulates the production of interferon).

- **Cryotherapy or surgery**, but these approaches are less effective for genital warts than for other types of warts.

- **Electrocauterization and carbon dioxide laser therapy**.

* Which of the following describes the structure of human papilloma virus?

a) Double-stranded DNA, icosahedral, enveloped, linear

b) Double-stranded DNA, icosahedral, non-enveloped, circular

c) Single-stranded DNA, icosahedral, enveloped, circular

d) Single-stranded DNA, icosahedral, non-enveloped, linear

e) Single-stranded RNA, icosahedra, enveloped, linear

References

- Topley and Wilson’s Microbiology and Microbial Infections: 10th edition.

- Brooks, G. F., Jawetz, E., Melnick, J. L., & Adelberg, E. A. (2013). Jawetz, Melnick, & Adelberg's medical microbiology. New York: McGraw Hill Medical.

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THANK YOU