Virology for 2nd Year MD Students

(07) DNA viruses: *Herpesviridae* 1

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Overview

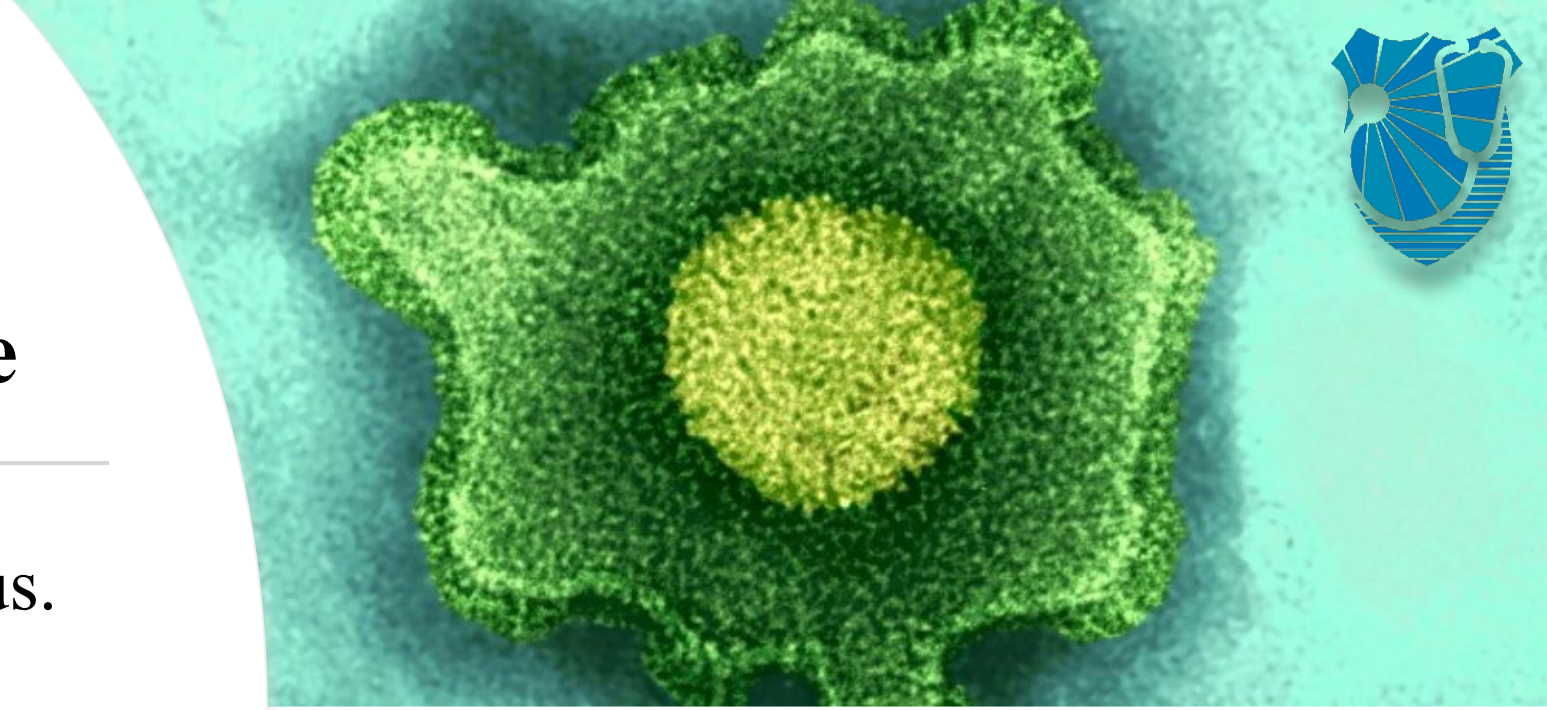
- *Herpesviridae* contains several of the most important human pathogens.
- Some have a wide host-cell range, whereas others have a narrow host-cell range.
- The outstanding property of herpesviruses is their ability to establish lifelong persistent infections in their hosts and to undergo periodic reactivation.
- Their frequent reactivation in immunosuppressed patients causes serious health complications.

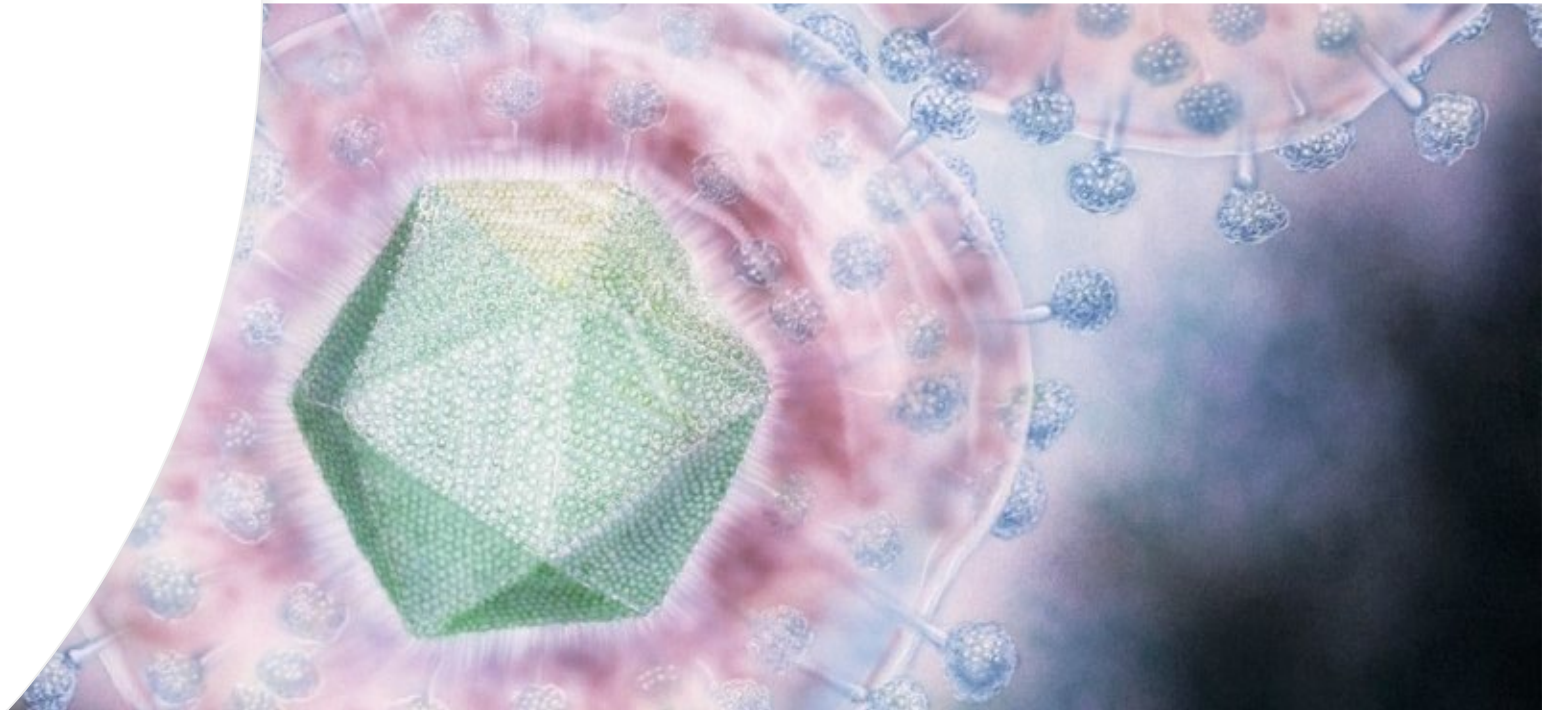
Herpesviridae has 8 members that can cause human disease:

1. Human herpes virus 1 (herpes simplex virus type 1)
2. Human herpes virus 2 (herpes simplex virus type 2)
3. Human herpes virus 3 (varicella zoster virus)
4. Human herpes virus 4 (Epstein Barr virus)
5. Human herpes virus 5 (cytomegalovirus)
6. Human herpes virus 6
7. Human herpes virus 7
8. Human herpes virus 8 (Kaposi's sarcoma-associated herpesvirus)

Herpesviridae Structure

- Double-stranded DNA virus.
- Icosahedral symmetry.
- Enveloped.
- Envelope is acquired from the nuclear membrane.



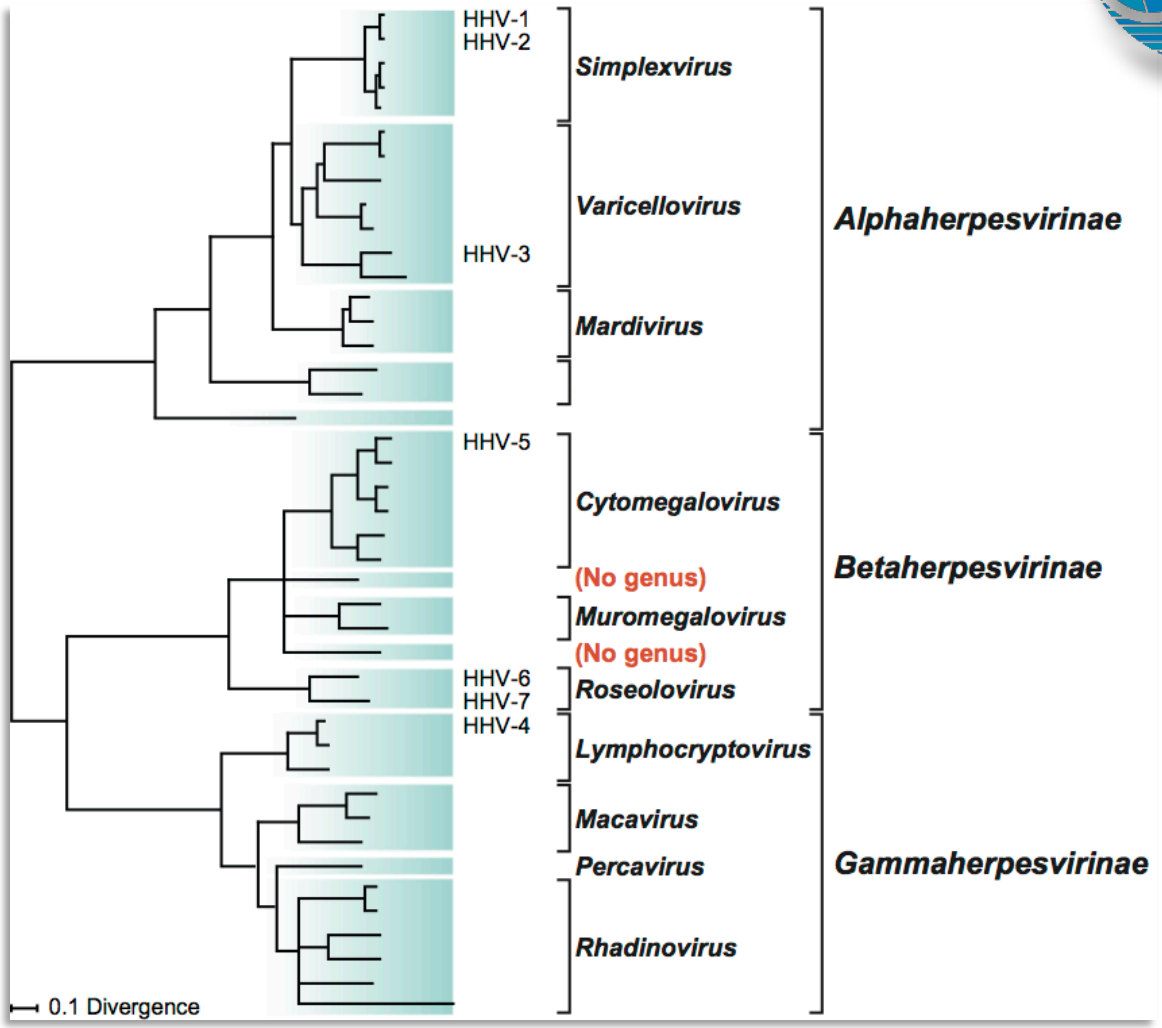


Herpesviridae Classification

HHV-1, HHV-2 and HHV-3 are *Alphaherpesvirinae* viruses

HHV-5, HHV-6 and HHV-7 are *Betaherpesvirinae* viruses

HHV-4 and HHV-8 are *Gammaherpesvirinae* viruses

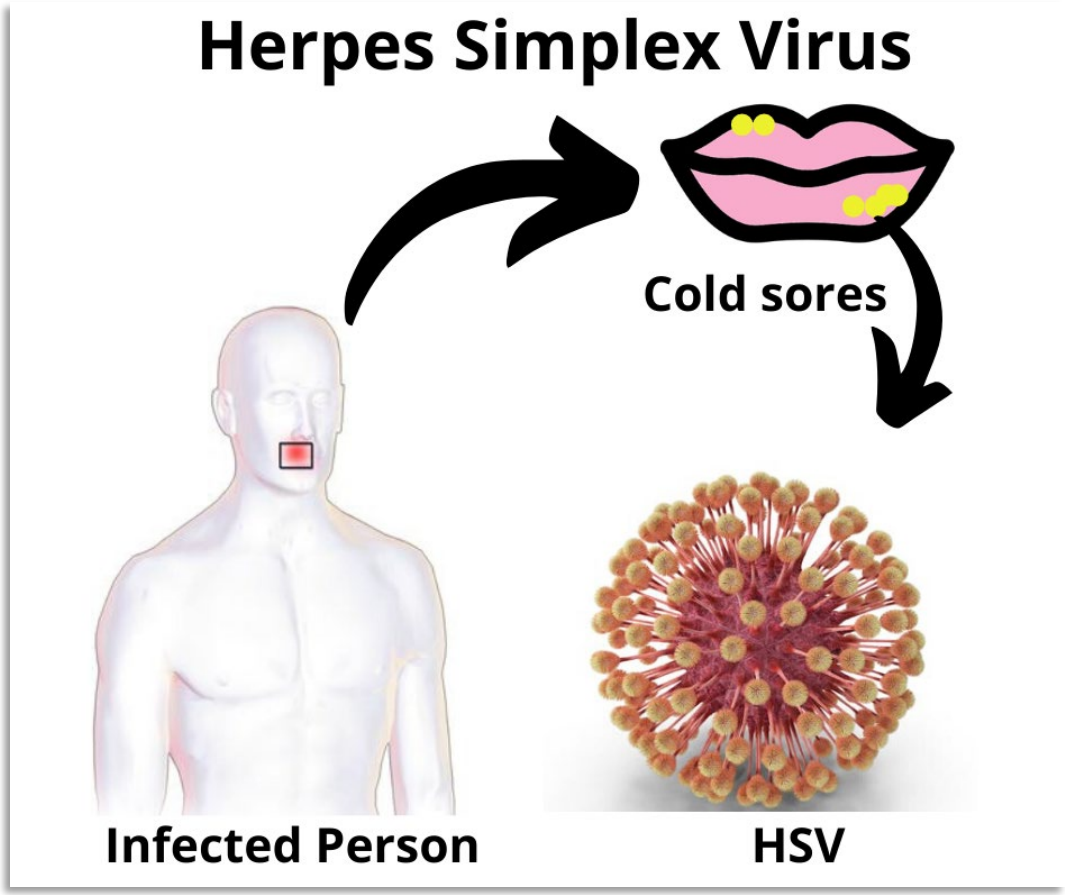


Herpes Simplex Viruses Overview

- Hippocrates used the Greek word herpes to describe lesions that seem to creep or crawl along the skin.
- ICTV designate the two species as human herpesviruses 1 and 2 (HHV-1) and (HHV-2).
- The two species were first identified as two distinct serotypes; herpes simplex viruses 1 and 2 (HSV-1) and (HSV-2).
- Natural Host: Human, mammals.
- Tropism: Epithelial mucosal cells.
- Latency: Sensory neurons (dorsal ganglia).
- Cellular receptors: Heparan sulfate among others.
- Geography: Worldwide.

Herpes Simplex Viruses Transmission

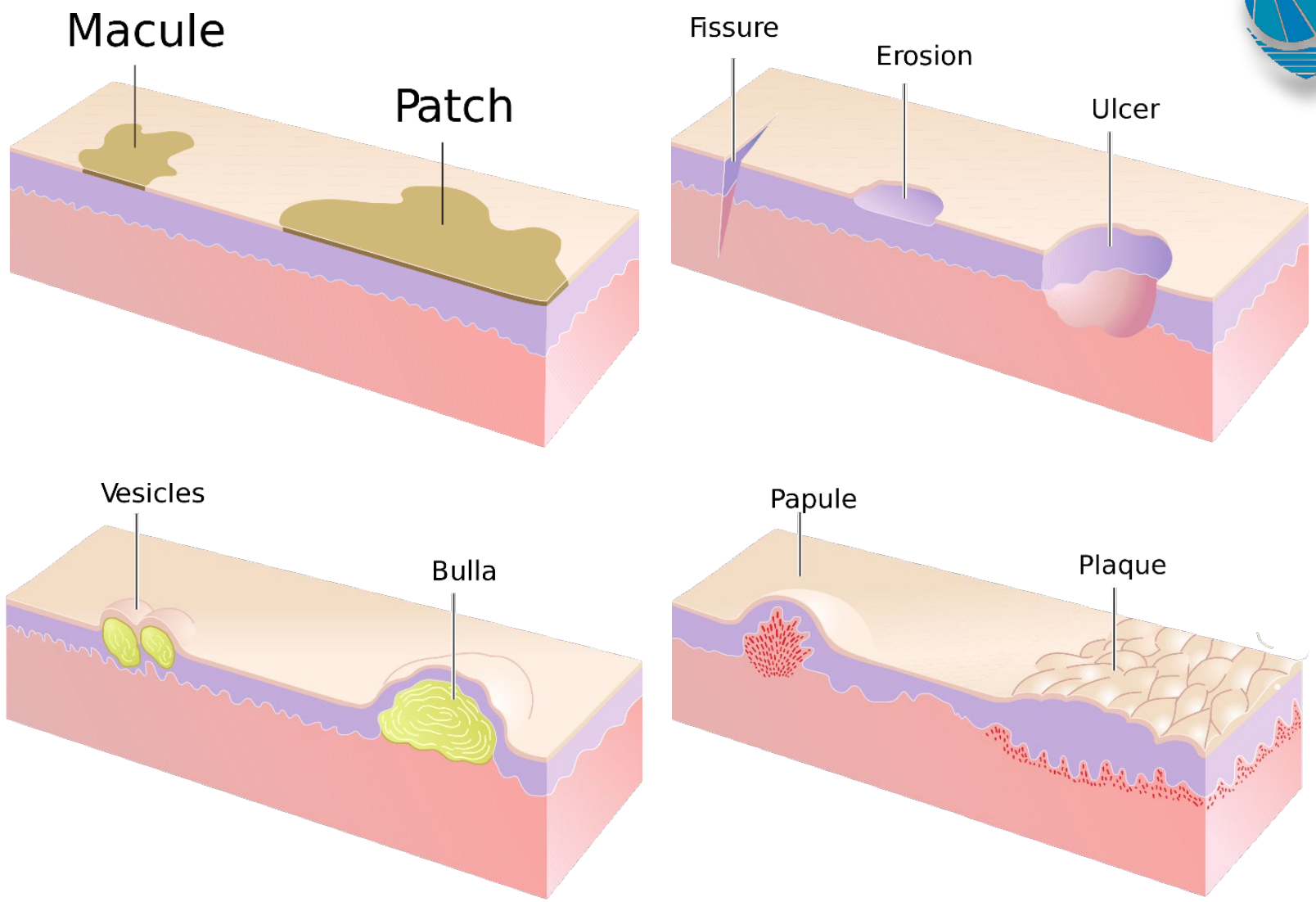
- Transmission (HHV-1): Direct contact, saliva.
- Transmission (HHV-2): Sexual contact, vertical.
- HSV is transmitted by contact with an individual excreting virus.
- The virus must encounter mucosal surfaces or broken skin in order for an infection to be initiated (unbroken skin is resistant).



Herpes Simplex Viruses
Pathogenesis

- HSVs cause cytolytic infections.
- Pathologic changes are due to:
  - Necrosis of infected cells.
  - The inflammatory response.
- Lesions in the skin and mucous membranes are similar for HHV-1 and HHV-2.
- Pathologic changes are similar for primary and recurrent infections but vary in degree, reflecting the extent of viral cytopathology.

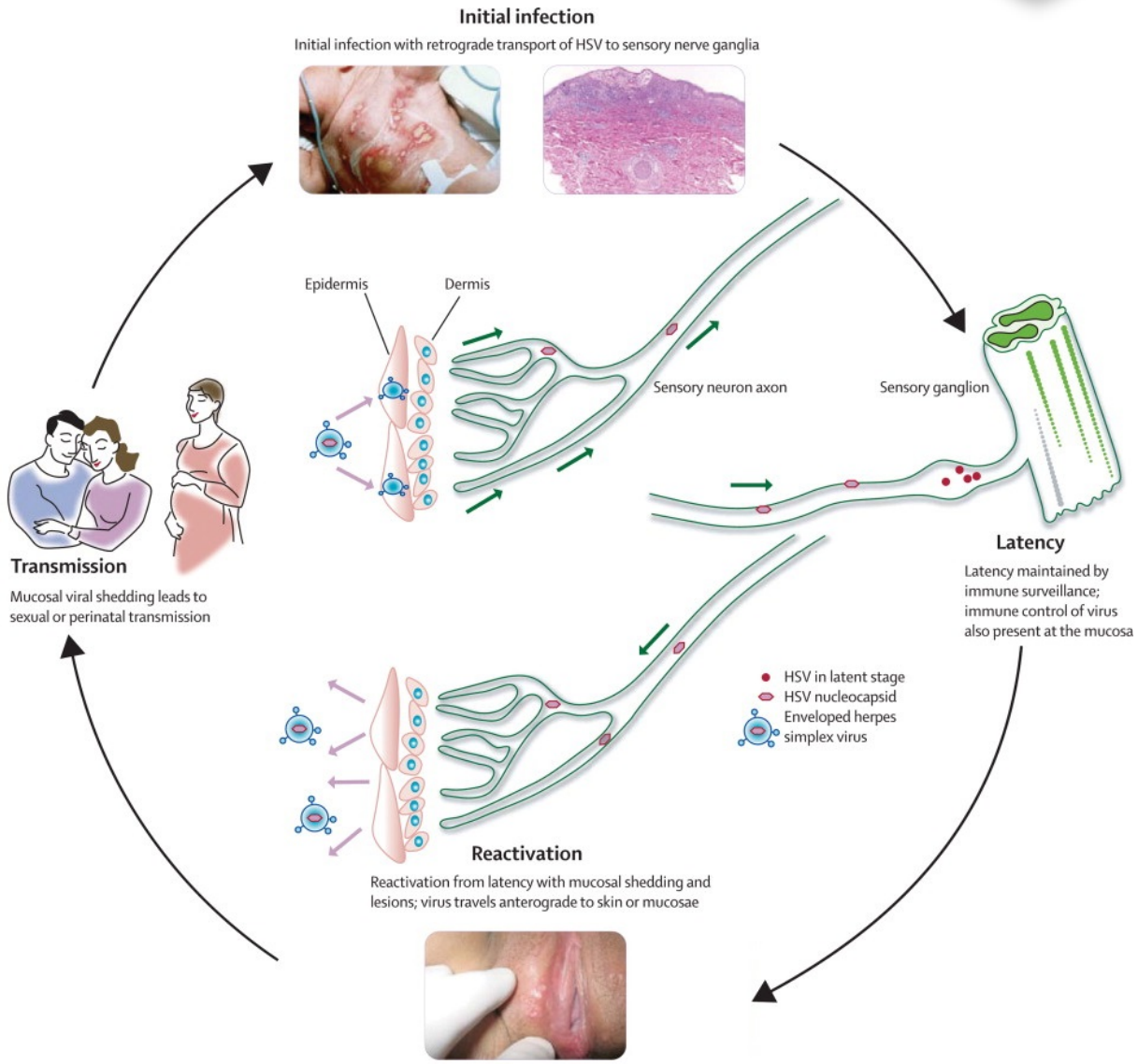
Herpes Simplex Viruses Characteristic Lesions



Herpes Simplex Viruses Pathogenesis

Primary infection

- Viral replication occurs first at the site of infection.
- HSV then invades local nerve endings and is transported by retrograde axonal flow to dorsal root ganglia.
- After further replication, latency is established.
- Oropharyngeal infections result in latent infections in the trigeminal ganglia.
- Genital infections lead to latently infected sacral ganglia.



Herpes Simplex Viruses
Pathogenesis

Latent infection

- Virus resides in latently infected ganglia with very few viral genes being expressed.
- Provocative stimuli can reactivate virus from the latent state, including: Axonal injury. Fever. Physical or emotional stress. Exposure to ultraviolet light.
- The virus follows axons back to the peripheral site, and replication proceeds at the skin or mucous membranes.
- HSV-specific immunity limits local viral replication, so that recurrent infections are less extensive and less severe.
- Many recurrences are asymptomatic, reflected only by viral shedding in secretions.
- Common sites of latency are the trigeminal nerve ganglia for HSV-1 and the sacral ganglia for HSV-2.

Herpes Simplex Viruses Clinical Features

Gingivostomatitis.

Pharyngitis, tonsillitis.

Conjunctivitis

Keratitis

Cold sores (fever blisters, herpes labialis)

Cutaneous herpes.

Herpetic whitlow (in the fingers).

Eczema herpeticum (in patients with allergic dermatitis).

Genital herpes.

Herpes encephalitis (infection of the brain tissue)

Herpes meningitis (infection affecting the meninges)

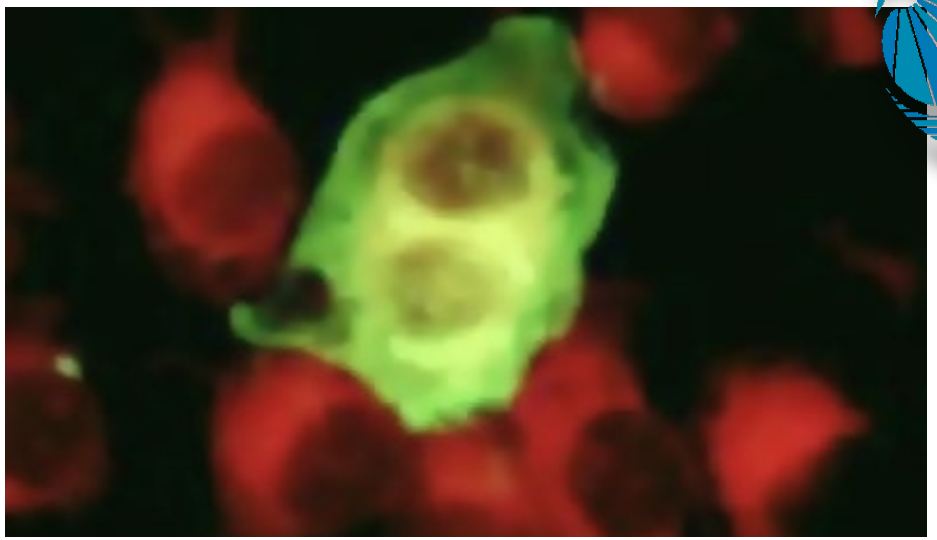
Neonatal herpes: Severe form with mortality of about 60%.

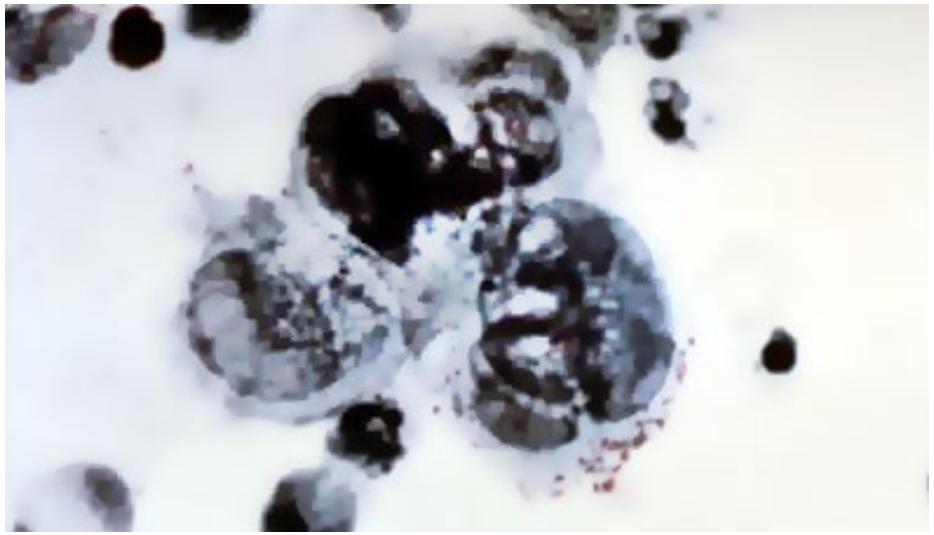
Disseminated severe disease in immunosuppressed patients (e.g., in AIDS patients).

Herpes Simplex Viruses Clinical Features

Herpes Simplex Viruses Diagnosis

- Clinical diagnosis.
- Virus isolation is a definitive diagnostic method (samples include: skin scrapings, throat swab, CSF).
- PCR detection of viral DNA.
- Cytopathology with Giemsa stain of scrapings (Tzanck smear).
- Serology.





Herpes Simplex Viruses – Treatment

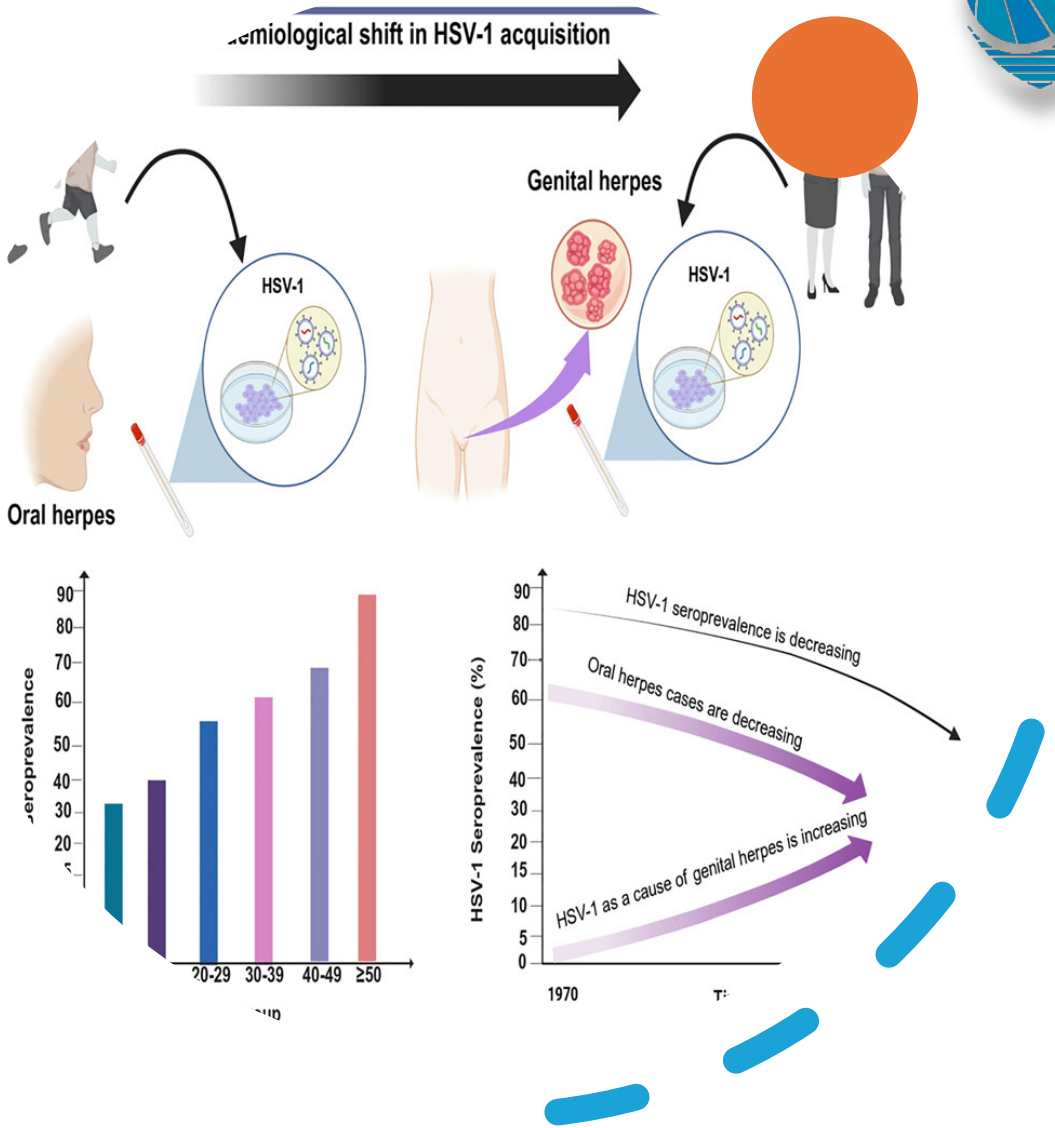
- Nucleoside analogues: acyclovir, valacyclovir, penciclovir and famciclovir.
- Mechanism of action: Inhibition of viral genome replication through inhibiting the viral polymerase.
- Treatment is important in herpes encephalitis, neonatal herpes, and disseminated infections in immunocompromised patients.
- Despite treatment, HSV remains latent in sensory ganglia.
- Drug-resistant virus strains may emerge.

Herpes Simplex Viruses Prevention and Epidemiology

- Prevention: Vaccines have not been approved for prevention so far.
- Epidemiology:

✓ In young adults, more than 90% have already been infected by HSV-1.

✓ Much lower prevalence of HSV-2 has been reported due to its sexual spread.



Source: Epidemiology of herpes simplex virus type 1 in the United States: Systematic review, meta-analyses, and meta-regressions Ageeb, Rwedah A. et al. iScience, Volume 27, Issue 9, 110652

Thank You…
Wishing you all the best!