Virology for 2nd Year MD Students

(08) DNA viruses: *Herpesviridae* 2

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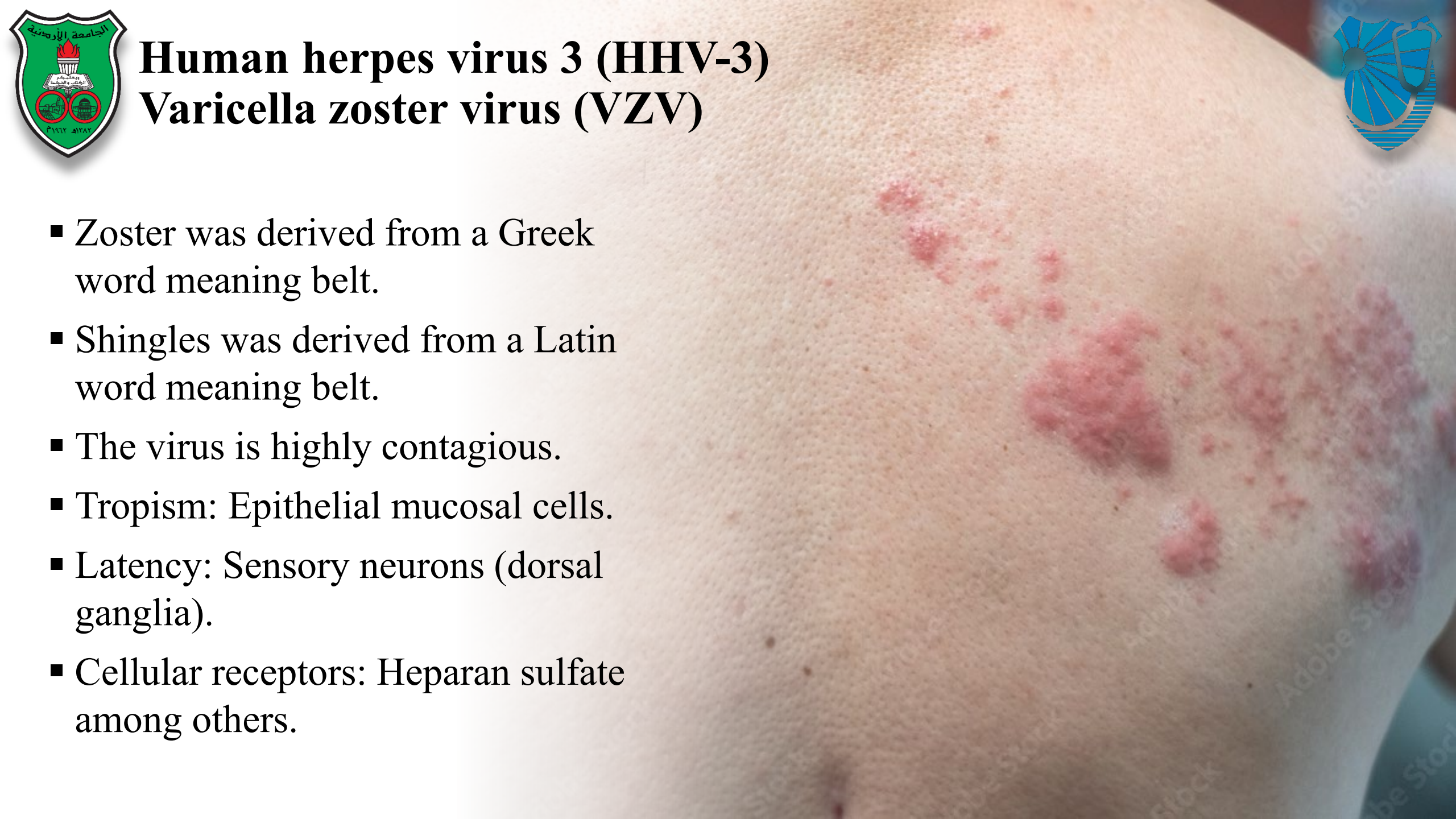
Human herpes virus 3 (HHV-3)
Varicella zoster virus (VZV)

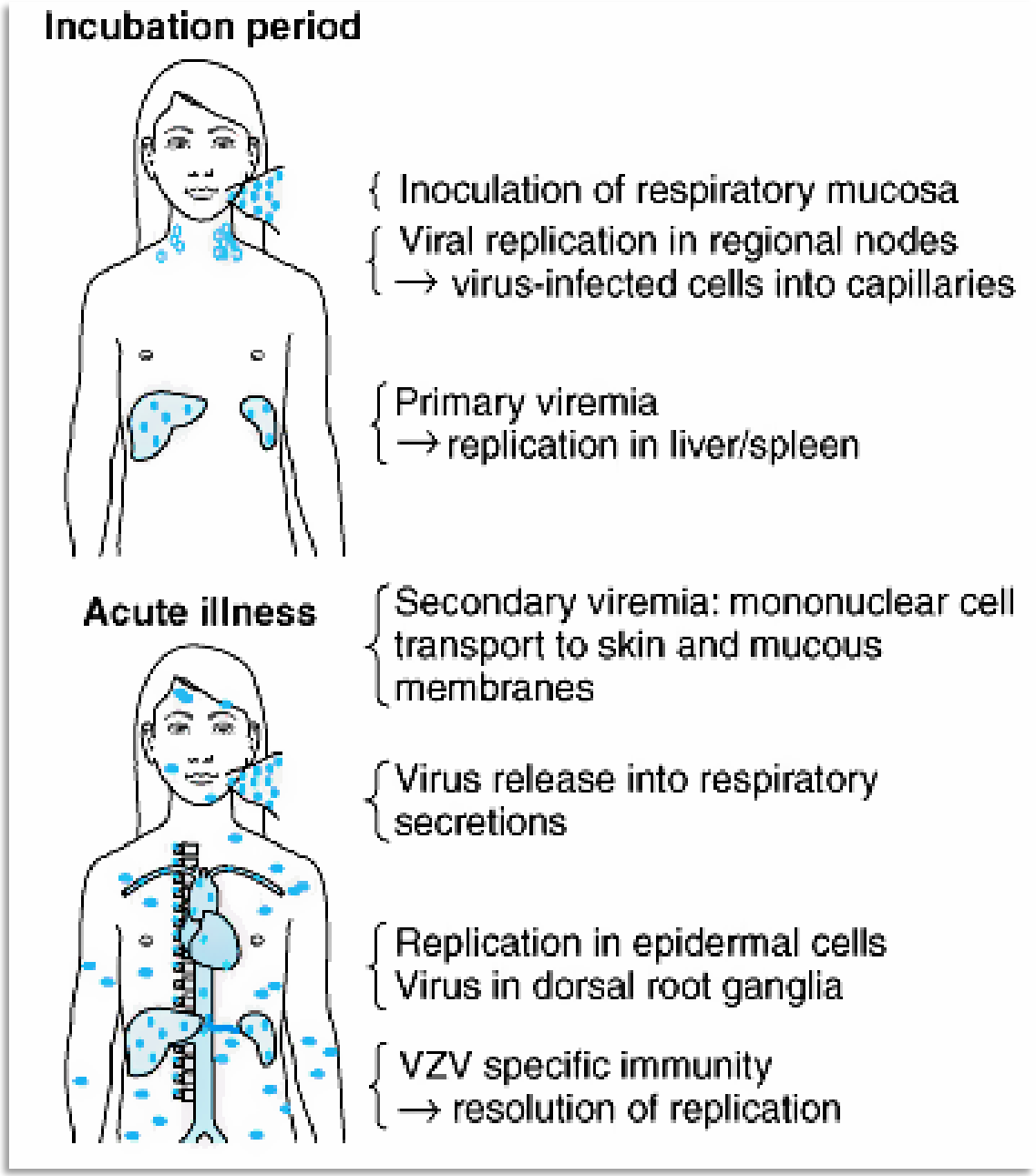


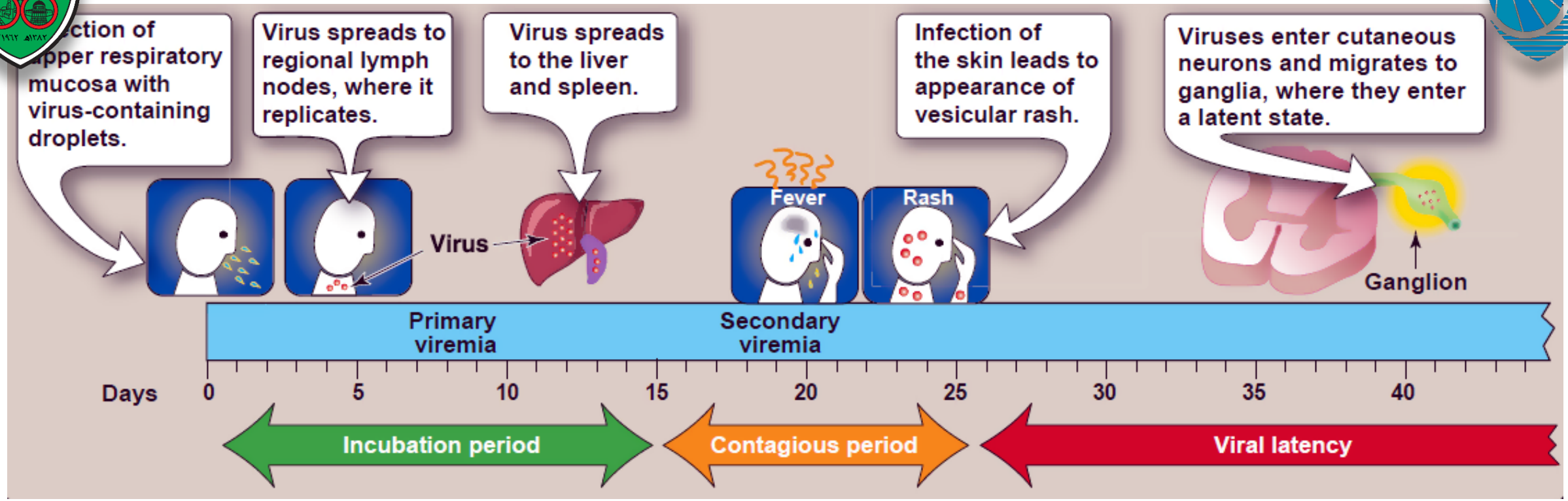
- Zoster was derived from a Greek word meaning belt.
- Shingles was derived from a Latin word meaning belt.
- The virus is highly contagious.
- Tropism: Epithelial mucosal cells.
- Latency: Sensory neurons (dorsal ganglia).
- Cellular receptors: Heparan sulfate among others.

Human herpes virus 3 (HHV-3)
Varicella zoster virus (VZV)

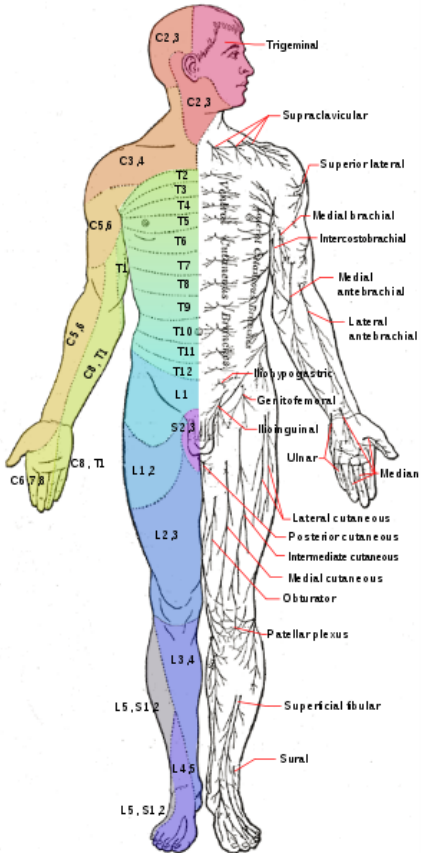
- Transmission: Respiratory, direct contact
- Varicella (chickenpox) is highly communicable and is a common epidemic disease of childhood (most cases occur in children under 10 years of age).
- Zoster occurs sporadically, chiefly in adults and without seasonal prevalence. Ten to 20 percent of adults will experience at least one zoster attack during their lifetime, usually after the age of 50.

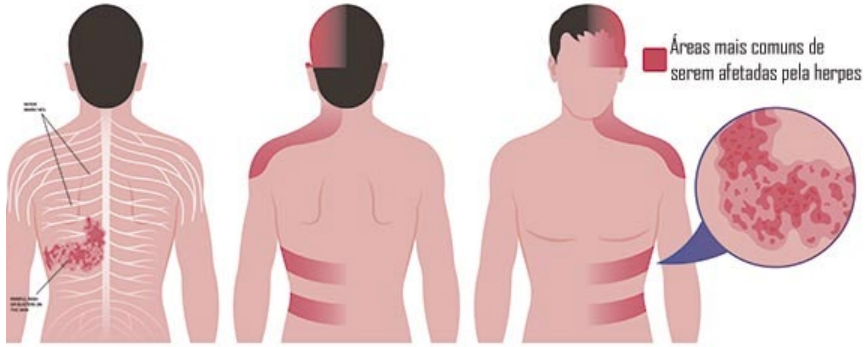
VZV Pathogenesis & Pathology





VZV Pathogenesis & Pathology

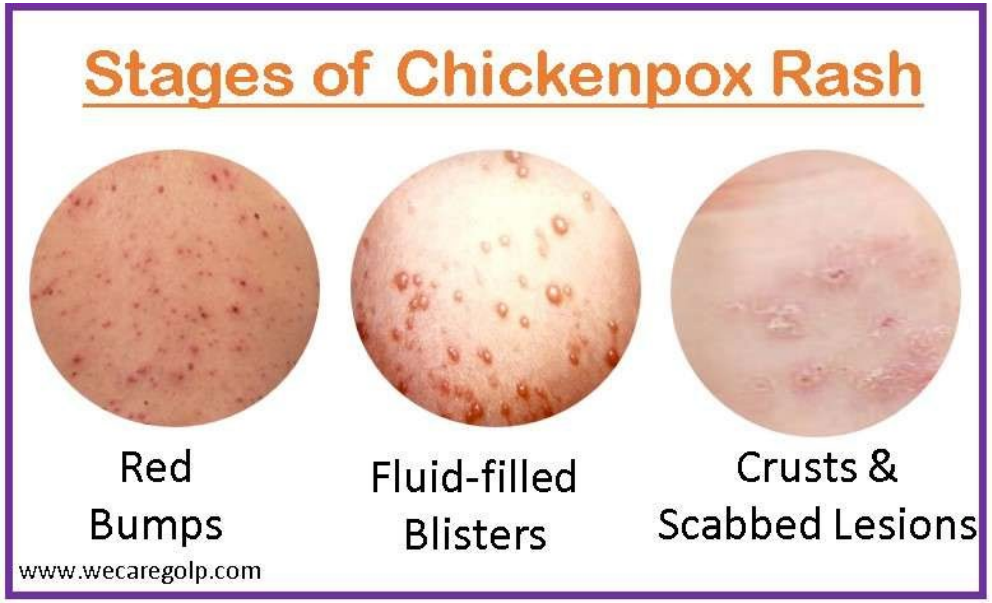




VZV Pathogenesis & Pathology

Chickenpox Clinical Features

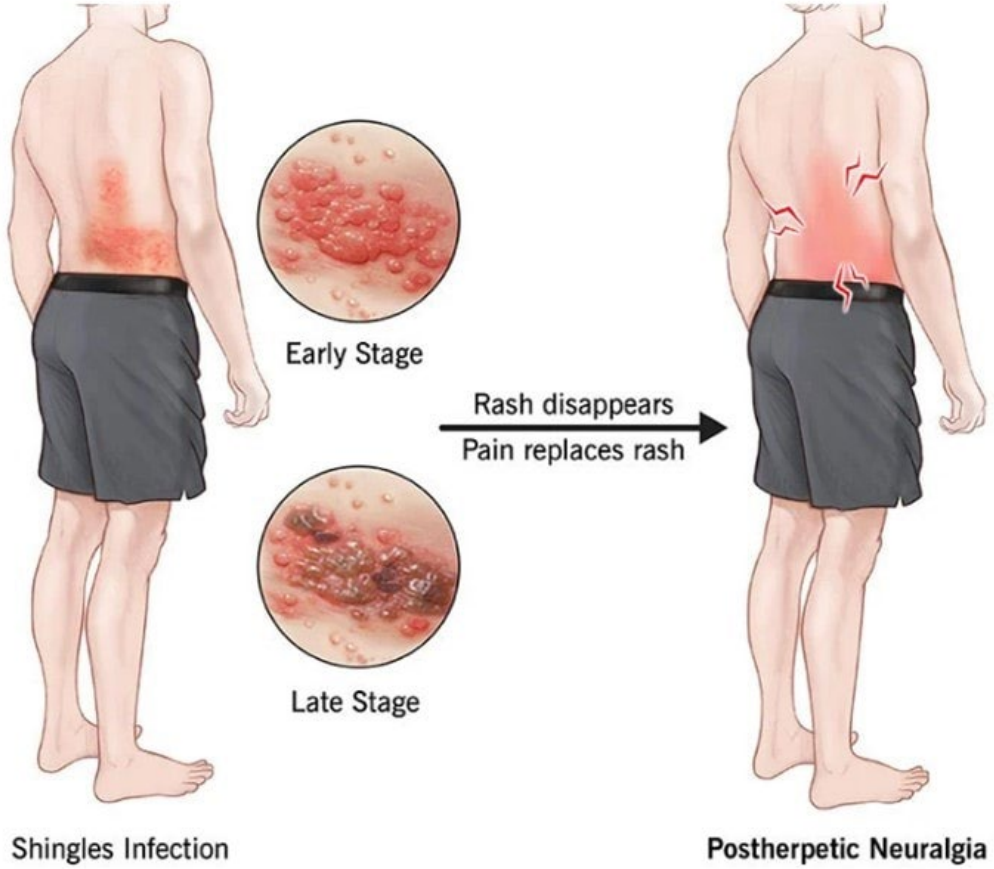
- Subclinical varicella is unusual.
- The incubation period: 10-21 days.
- Malaise and fever are prodromal, followed by rash, first on the trunk and then on the face, the limbs, and the buccal and pharyngeal mucosa.
- Successive fresh vesicles appear in crops, so all stages of macules, papules, vesicles, and crusts may be seen at one time.
- The rash lasts about 5 days.
- Complications are rare in normal children, and the mortality rate is very low.



Zoster Clinical Features

- Zoster occurs in immunocompromised persons.
- It starts with severe pain in the area of skin or mucosa supplied by the sensory nerves and ganglia.
- Within a few days, a crop of vesicles appears over the skin supplied by the affected nerves.
- The trunk, head, and neck are most commonly affected.
- The most common complication of zoster in the elderly is postherpetic neuralgia which is a protracted pain that may continue for months.

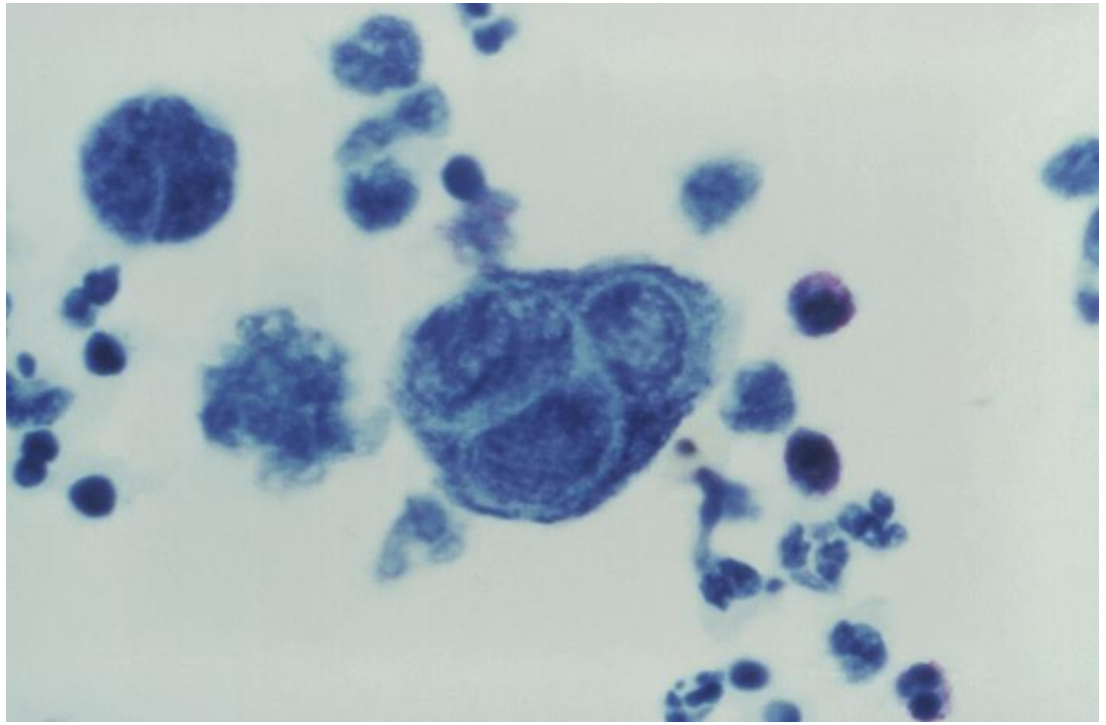
Post Herpetic Neuralgia



Neurology and Orthopaedic Clinic Singapore

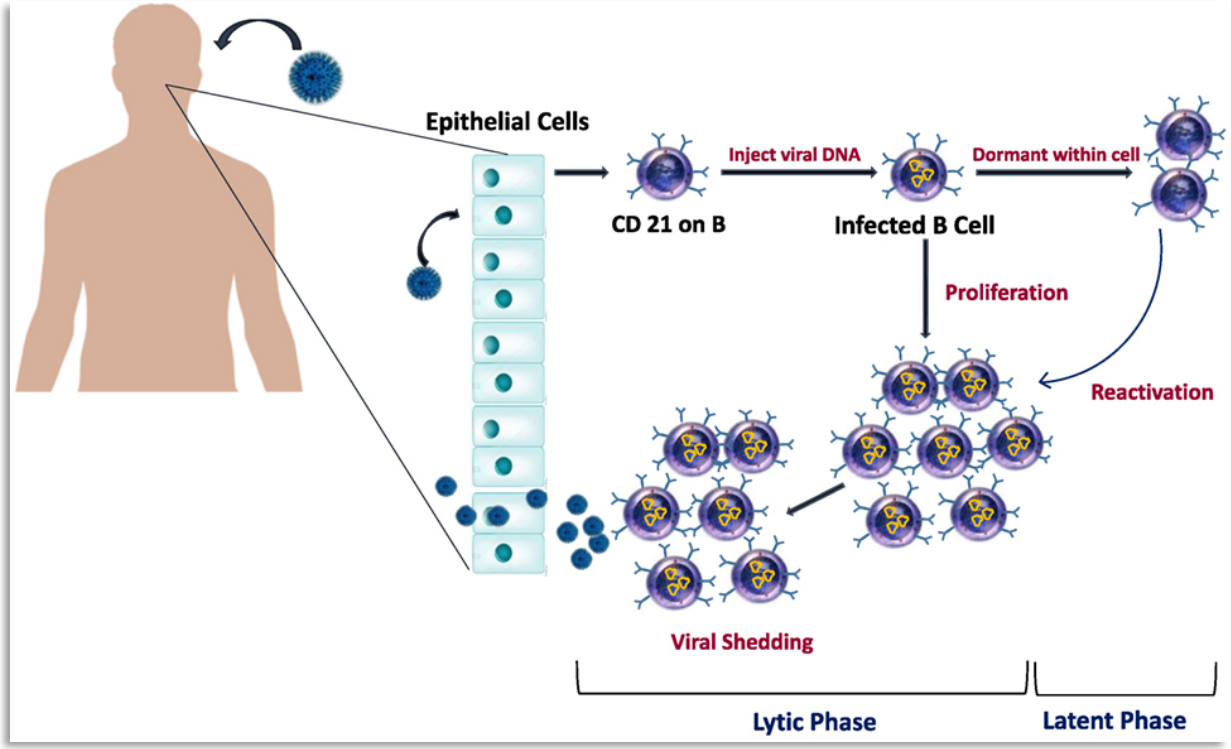
VZV – Diagnosis, Treatment, and Prevention

- Diagnosis: Clinical, Tzanck smear, Serology, PCR.
- Varicella in normal children is a mild disease and requires no treatment.
- Acyclovir can prevent the development of systemic disease in varicella-infected immunosuppressed patients and can halt the progression of zoster in adults.
- A live attenuated varicella vaccine is highly effective at inducing protection from varicella in children (80–85% effective), but less so in adults (70%).
- Varicella infections can occur in vaccinated persons, but they are usually mild illnesses.
- Zoster vaccine is indicated for prevention of shingles in adults ≥50 years.



Epstein-Barr Virus (EBV)

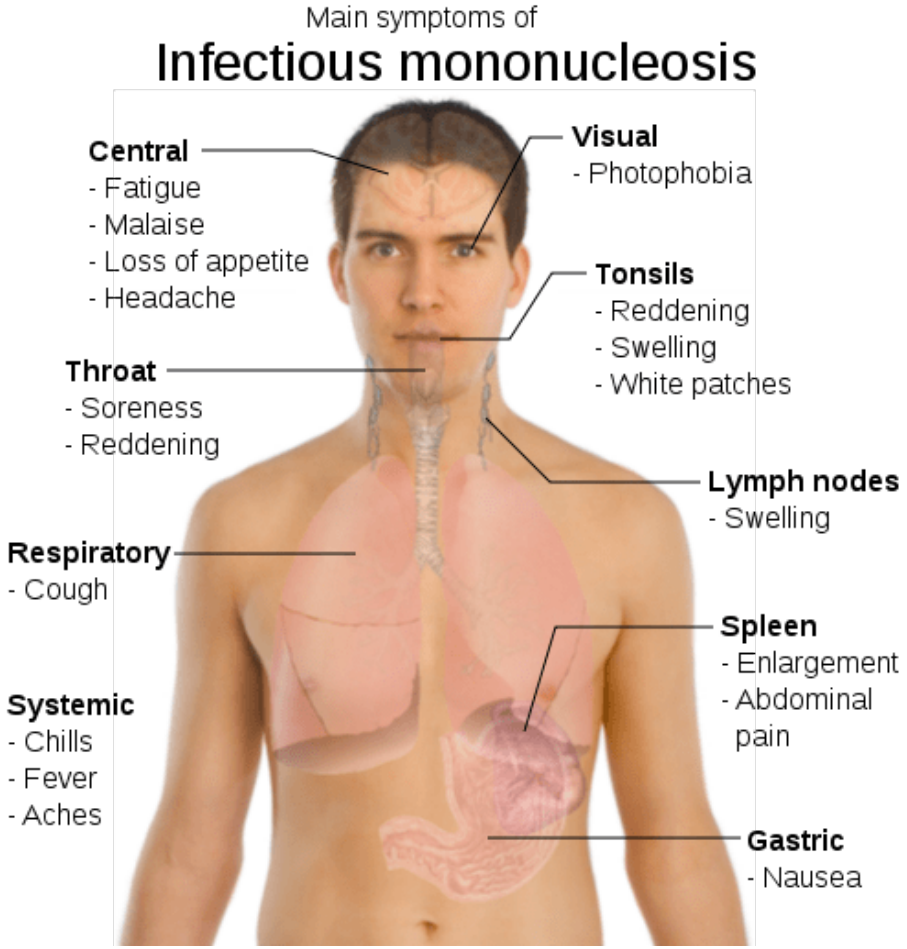
- Tropism: B cells, oral epithelial cells.
- Latency: B cells.
- Cellular receptors: CR2 (CD21).
- Transmission: Contact with oropharyngeal secretions, saliva.
- In developing countries, infections occur early in life; more than 90% of children are infected by age 6.
- These infections in early childhood usually occur without any recognizable disease.
- The inapparent infections result in permanent immunity to infectious mononucleosis.

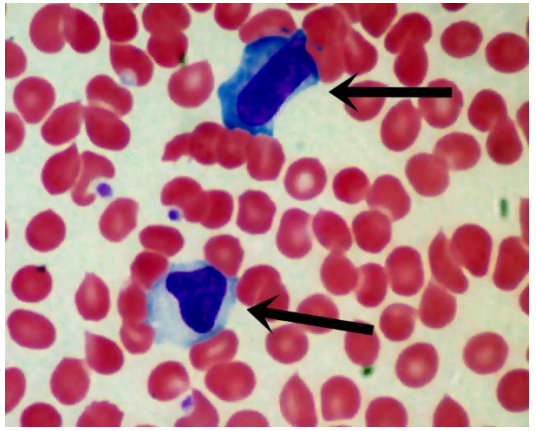


Infectious Mononucleosis (IM)

The incubation period for IM is about 4 to 6 weeks.

The peripheral blood shows leukocytosis, an increase in T cells but not B cells, and atypical lymphocytes (predominantly activated T cells having large amounts of cytoplasm).



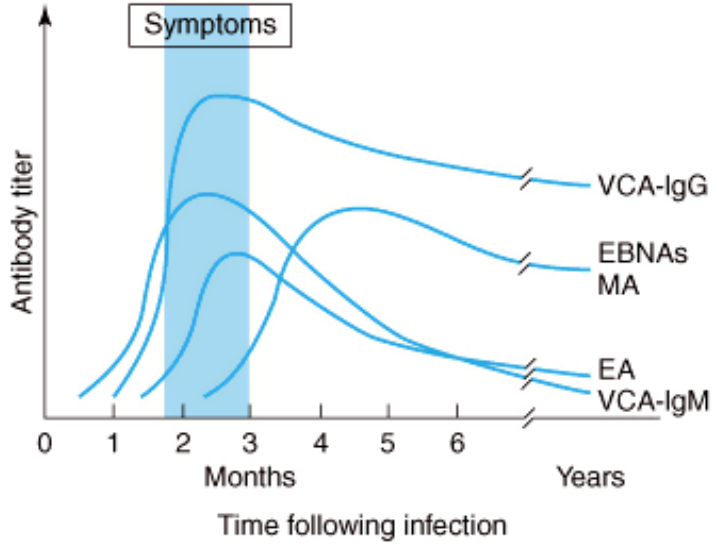


Cancers Associated with EBV Latent Gene Expression

Disease	EBERs	EBNA-1	EBNA-2	LMP-1	LMP-2
Burkitt lymphoma	+	+	-	-	-
Nasopharyngeal carcinoma	+	+	-	+	+
Hodgkin disease	+	+	-	+	+
Peripheral T-cell lymphoma	+	+	-	+	+
Lymphoproliferative disease	+	+	+	+	+

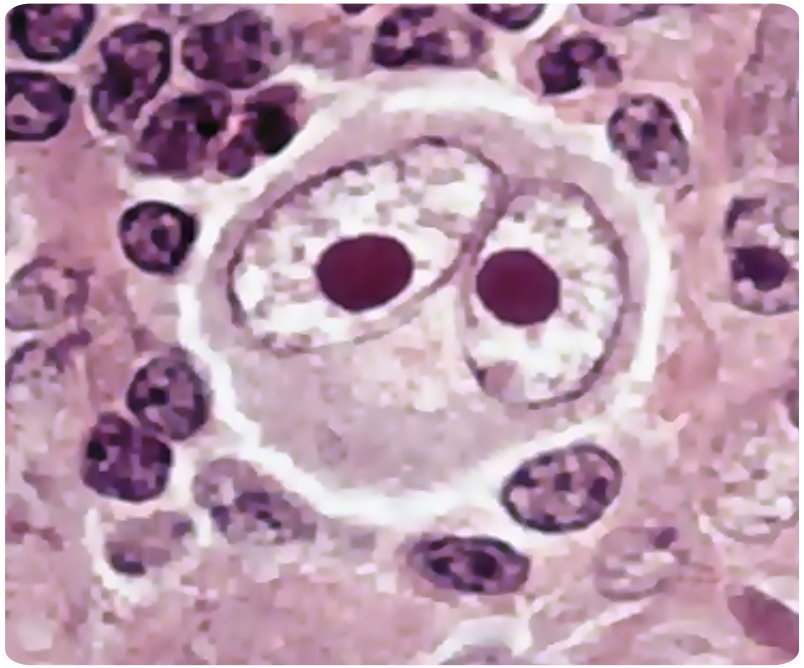
IM Laboratory Diagnosis and Rx

- The diagnosis of IM in patients with typical symptoms is made by a positive heterophile antibody.
- Titers of EBV-specific antibodies (VCA, EA, MA and EBNA) are measured.
- Detection of EBV DNA in the blood can be useful for diagnosis of IM if serologic results are equivocal.
- Treatment of IM is supportive. Contact sports should be avoided during the acute phase of the disease due to the risk of splenic rupture.



Cytomegalovirus (CMV)

- Tropism: Epithelial cells, endothelial cells, fibroblasts, smooth muscle cells, parenchymal cells and connective tissue, cells of virtually any organ and various hematopoietic cell types.
- Latency: Myeloid cells.
- Transmission: Contact with urine, saliva, congenital, sexual.
- CMV is the most common congenital viral infection in the developed world, with an overall birth prevalence of approximately 0.6%.
- CMV causes IM-like syndrome in primary infection.



CMV in Immunocompromized Host
Congenital CMV

- Pneumonia is a frequent complication.
- CMV often causes disseminated disease in untreated AIDS patients.
- Gastroenteritis and retinitis are common problems, the latter often leading to progressive blindness.
- Approximately 10% of congenitally infected infants have signs and symptoms of disease at birth.
- Symptomatic infants have a high risk for subsequent neurologic sequelae, including hearing loss, mental retardation, microcephaly, development delay, seizure disorders, and cerebral palsy.
- The cornerstone of antiviral therapy is ganciclovir.

CMV Laboratory Diagnosis

- PCR assays have replaced virus isolation for routine detection of cytomegalovirus infections. Cell culture methods of viral isolation are too slow to guide Rx.
- CMV produces a characteristic CPE (Massively enlarged "cytomegalic" cells are typical, besides Owl's eye appearance of inclusion bodies “intranuclear basophilic inclusions”).
- Blood and urine are most commonly tested.
- Serology: Detection of viral IgM antibodies suggests a current infection.

Roseola viruses
HHV-6 and HHV-7

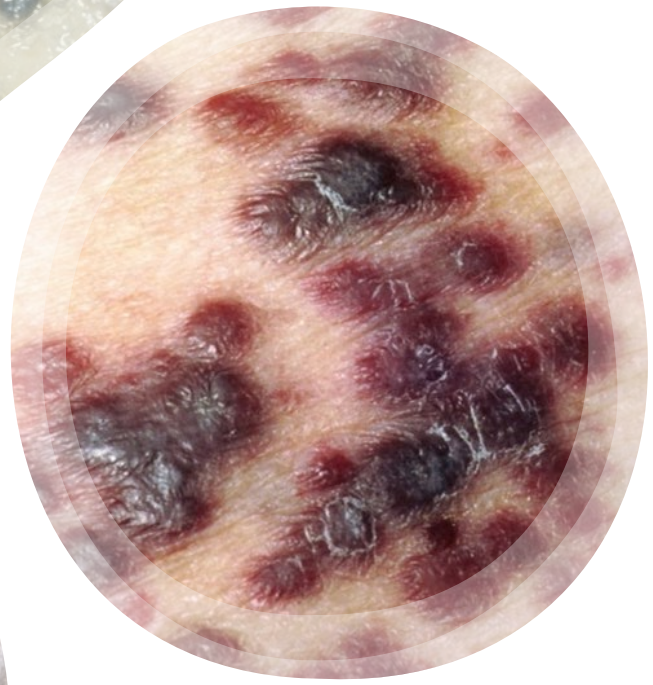
- Both HHV-6 and HHV-7 are causative agents of roseola infantum (exanthem subitum), although infection with HHV-7 is more frequently asymptomatic.
- HHV-6 exists in two variants, HHV-6A and HHV-6B.
- Transmission: Respiratory, direct contact.
- Tropism: HHV-6: T cells, B cells, natural killer (NK) cells, Monocytes-macrophages, epithelial cells and nerve cells. HHV-7: CD4+ T lymphocytes and epithelial cells of salivary glands
- Latency: Peripheral blood mononuclear cells (PBMCs).
- Cellular receptors: HHV-6: CD46. HHV-7: CD4.

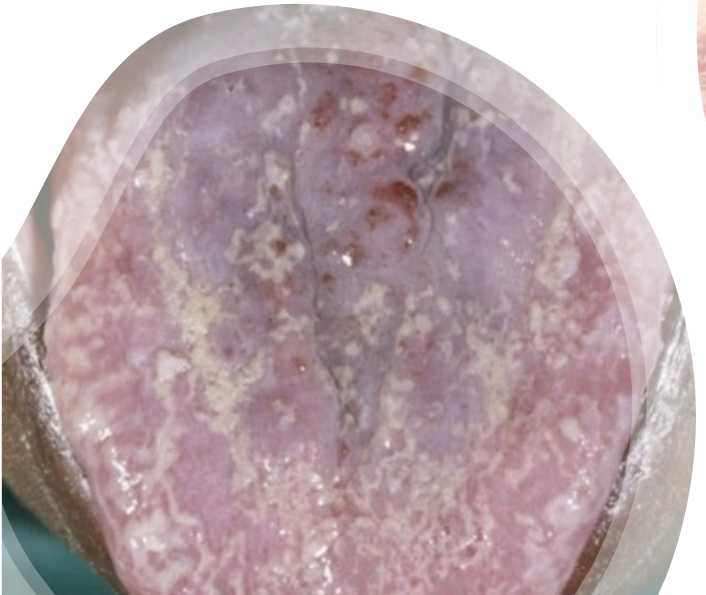
Exanthem Subitum (Roseola Infantum, Sixth Disease)

- In the classic presentation, an infant develops sudden fever, which lasts for a few days, followed immediately by a rash that appears on the trunk and face and spreads to lower extremities as the fever subsides.
- Due to the high fever, ES might be associated with febrile seizures.
- The disease is nearly always harmless, characterized by sudden onset with high fever and manifests as a typical exanthem in small children.
- Reports of HHV-6-caused illness in adults are rare and the clinical pictures described resemble mononucleosis (EBV-negative mononucleosis).

Kaposi's Sarcoma-Associated Herpesvirus

- Tropism: B lymphocytes.
- Latency: B lymphocytes.
- Transmission: Sexual contact, saliva
- Some infections are acquired early in life by nonsexual routes, possibly through contact with oral secretions.
- It appears to be sexually transmitted among gay men, who have a higher seroprevalence compared to the general population.
- Kaposi's sarcoma (KS) seems to originate from the viral modified pluripotent mesenchymal cells of the connective tissue transformed in spindle-shaped KS cells.





Kaposi Sarcoma

- Nodular lesions of variable colors affecting the skin, mouth, GI tract or respiratory tract.
- Four classes of KS including:

✓Classic KS.

✓Endemic or African KS.

✓Iatrogenic KS associated with immunosuppressive therapies in transplant patients.

✓Epidemic or AIDS-related KS.

HHV-8

- **Primary effusion lymphoma (PEL),** which is an expansion of B cells predominantly in serosal cavities such as the pericardium, pleura, and peritoneum.
- **Multicentric Castleman's disease (MCD).** MCD is a rare, polyclonal, lymphoproliferative disease that can develop in both HIV-negative and HIV-positive individuals.
- KS incidence is 1 in 100,000 in the general population, whereas in HIV-infected individuals, the incidence is around 1 in 20.
- Diagnostic confirmation of KS is done through **histopathology**.
- Confirmation is done by immunohistochemistry in tissues using monoclonal antibodies to the KSHV.
- Rx: HAART can induce AIDS-KS regression. Isolated lesions are treated with radiotherapy. Systemic chemotherapy is useful for the treatment of disseminated disease.

Thank You…
Wishing you all the best!