# Human Herpesviruses

# Human herpesviruses

- Three subfamilies (genome structure, tissue tropism, cytopathologic effect, site of latent infection)
- ***Alphaherpesvirinae:***

***Human herpesvirus 1 Herpes simplex type 1 HSV-1***

***Human herpesvirus 2 Herpes simplex type 2 HSV-2***

***Human herpesvirus 3 Varicella-zoster virus VZV***

- ***Gammaherpesvirinae***

***Human herpesvirus 4 Epstein-Barr virus EBV***

***Human herpesvirus 8 Kaposi's sarcoma related virus HHV-8***

- ***Betaherpesvirinae***

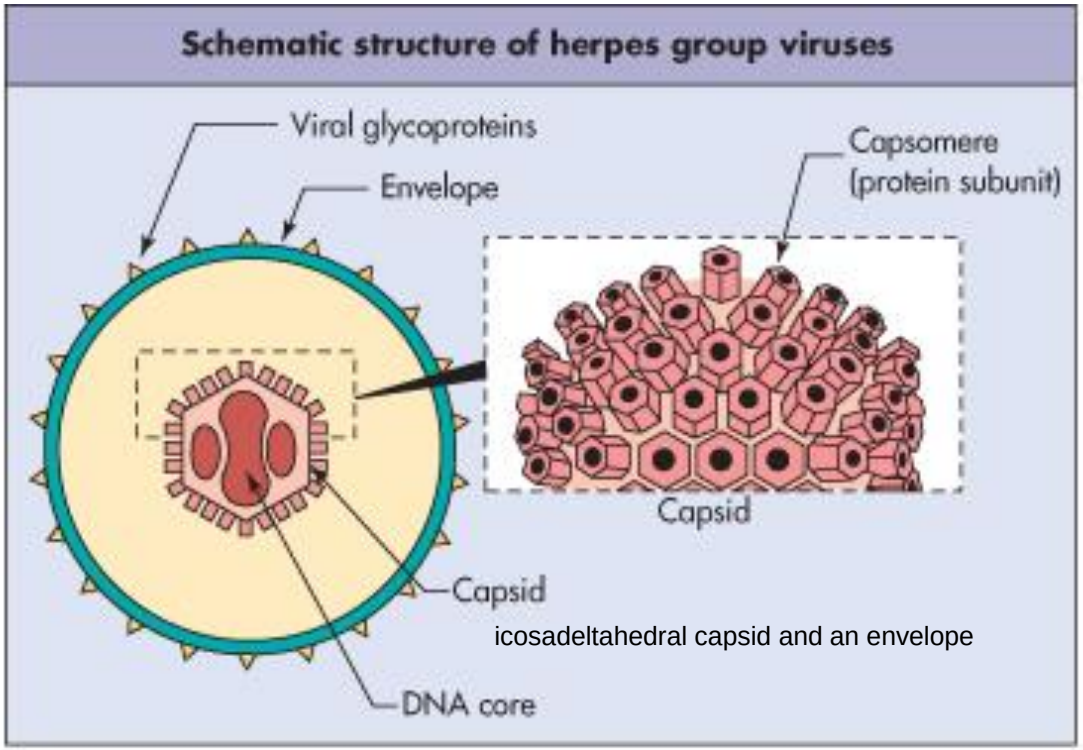
***Human herpesvirus 5 Cytomegalovirus CMV***

***Human herpesvirus 6Herpes lymphotropic virus HHV-6***

***Human herpesvirus 7 Human herpesvirus 7 HHV-7***

## Herpesviruses

| Subfamily | Virus | Primary Target Cell | Site of Latency | Means of Spread |
|---|---|---|---|---|
| **Alphaherpesvirinae** | | | | |
| Human herpesvirus 1 | Herpes simplex type 1 | Mucoepithelial cells | Neuron | Close contact |
| Human herpesvirus 2 | Herpes simplex type 2 | Mucoepithelial cells | Neuron | Close contact (sexually transmitted disease) |
| Human herpesvirus 3 | Varicella-zoster virus | Mucoepithelial cells | Neuron | Respiratory and close contact |
| **Gammaherpesvirinae** | | | | |
| Human herpesvirus 4 | Epstein-Barr virus | B cells and epithelial cells | B cell | Saliva (kissing disease) |
| Human herpesvirus 8 | Kaposi's sarcoma-related virus | Lymphocyte and other cells | B cell | Close contact (sexual), saliva? |
| **Betaherpesvirinae** | | | | |
| Human herpesvirus 5 | Cytomegalovirus | Monocyte, lymphocyte, and epithelial cells | Monocyte, lymphocyte, and ? | Close contact, transfusions, tissue transplant, and congenital |
| Human herpesvirus 6 | Herpes lymphotropic virus | T cells and ? | T cells and ? | Respiratory and close contact? |
| Human herpesvirus 7 | Human herpesvirus 7 | T cells and ? | T cells and ? | ? |

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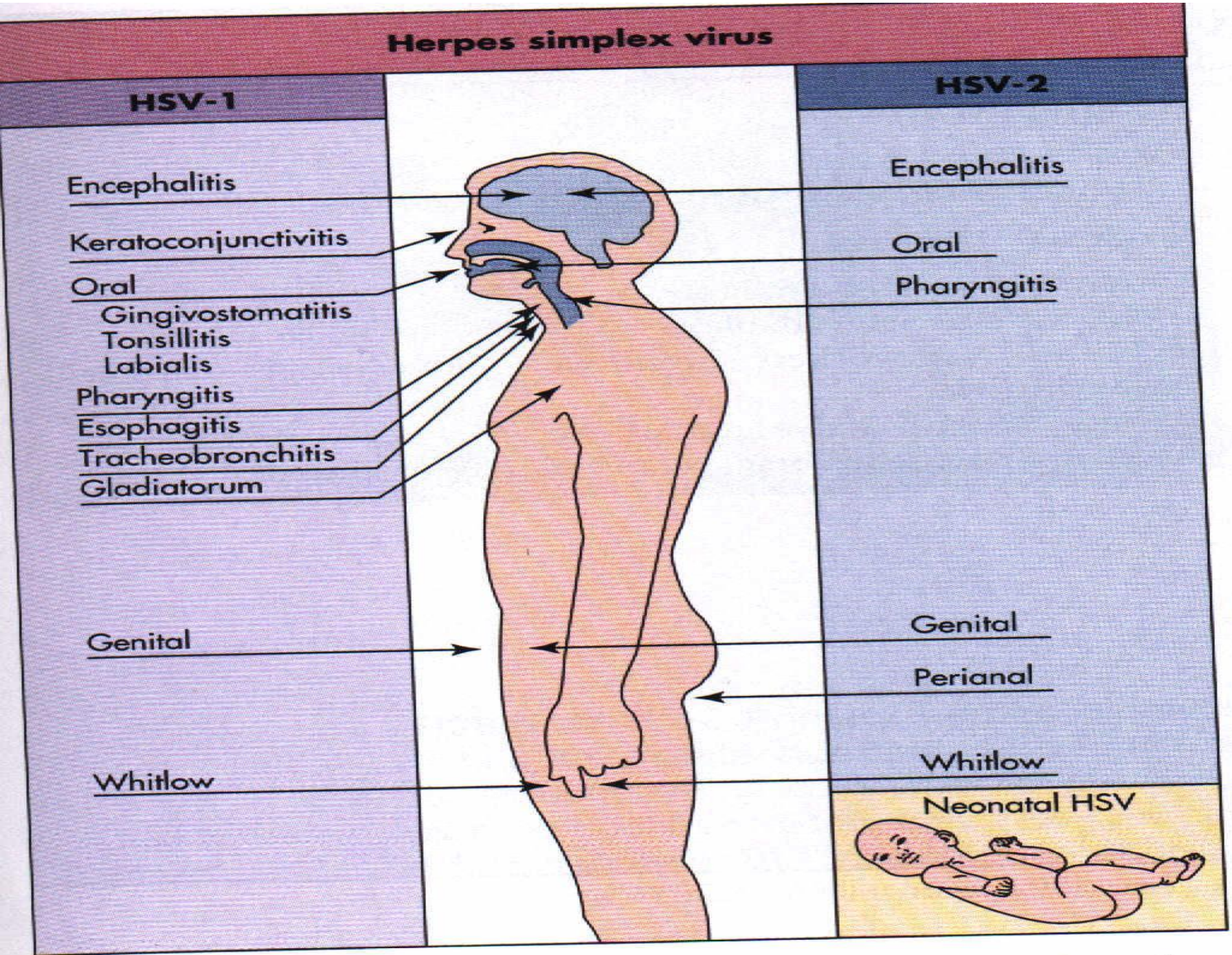
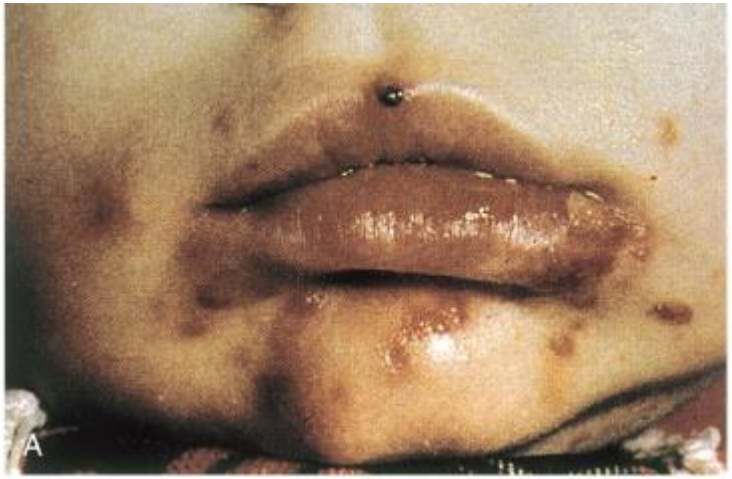
## Disease Mechanisms for Herpes Simplex Viruses

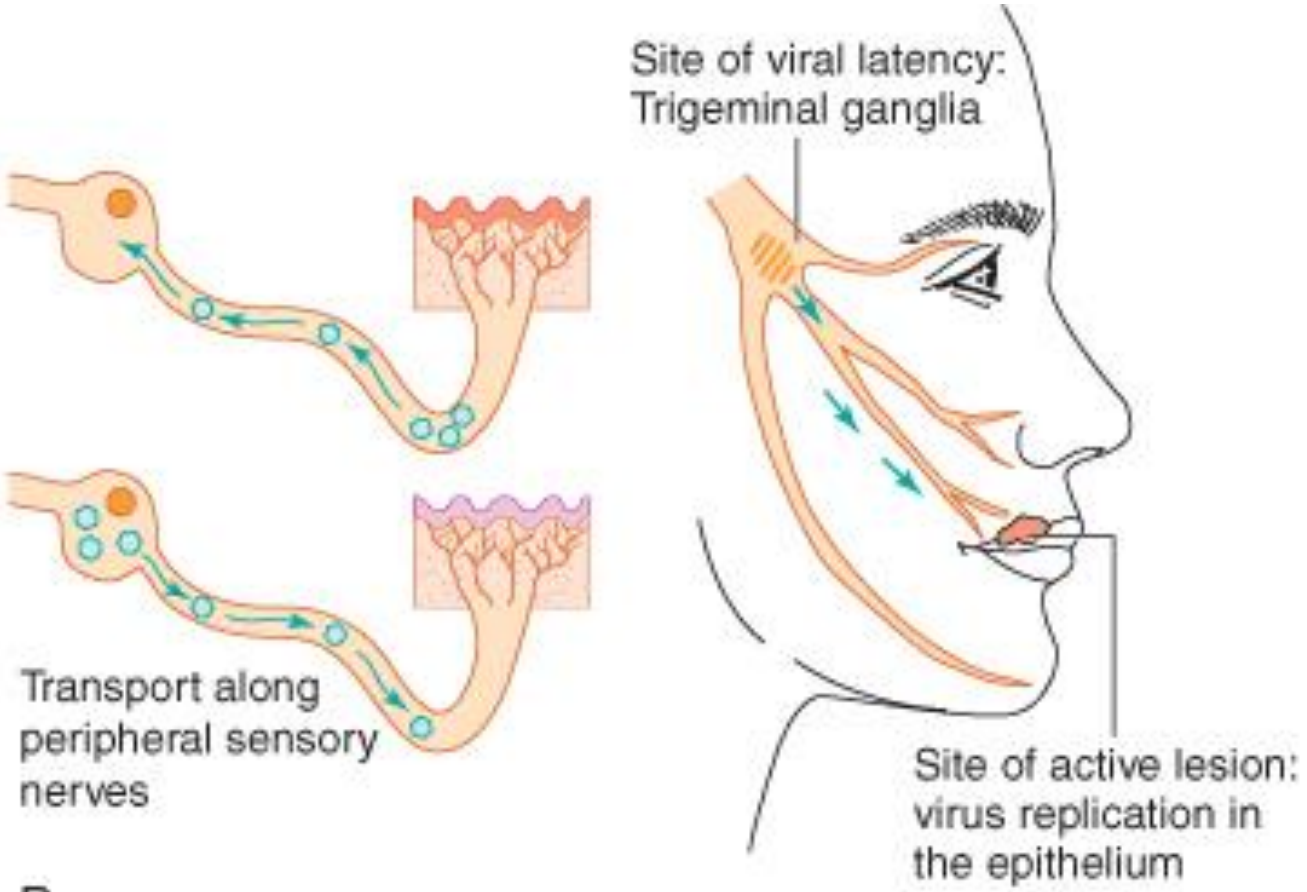
- Disease is initiated by direct contact and depends on infected tissue (e.g., oral, genital, brain).
- Virus causes direct cytopathologic effects.
- Virus avoids antibody by cell-to-cell spread (syncytia).
- Virus establishes latency in neurons (hides from immune response).
- Virus is reactivated from latency by stress or immune suppression.
- Cell-mediated immunity is *required* for resolution with limited role for antibody.
- Cell-mediated immunopathologic effects contribute to symptoms.

# Herpes simplex virus

- Two types: HSV-1 and HSV-2
- HSV can infect most types of human cells and even cells of other species.
- Lytic infection of fibroblasts and epitelial cells but latent infection of neurons


Herpes simplex virus
HSV-1
Encephalitis
Keratoconjunctivitis
Oral
Gingivostomatitis
Tonsillitis
Labialis
Pharyngitis
Esophagitis
Tracheobronchitis
Gladiatorum
Genital
Whitlow
HSV-2
Encephalitis
Oral
Pharyngitis
Genital
Perianal
Whitlow
Neonatal HSV



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# Herpes simplex virus

- Initiates infection through mucosal membranes or breaks in the skin
- Virus replicates in the cells at the base of the lession and infects the innervating neurons
- Travels by retrograde transport to the ganglion( trigeminal ganglion for oral HSV, sacral ganglia for genital HSV)

# Herpes simplex virus

- Then turns to initial site of infection
- May be inapparent or vesicular( vesicle fluid contains infectious virons)
- Tissue damage: viral pathology+immunopathology
- Heals without a scar
- Latent infection occurs in neurons

# Epidemiology

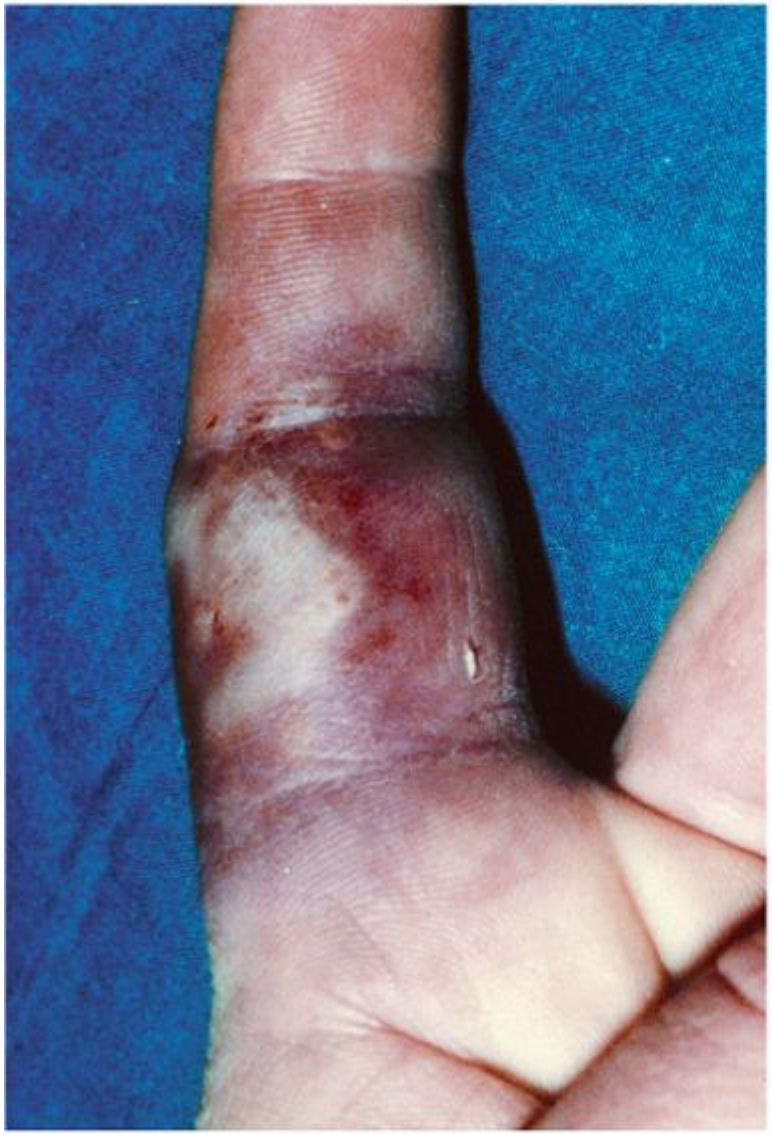
- Virus causes lifelong infection
- Recurrent diseases is source of contagion
- Asymtomatic shedding
- Saliva, vaginal secretion, lesion fluid
- Transmitted orally, sexually, into eye, breaks in skin
- HSV-1 usually orally
- HSV-2 usually sexually

# Herpes simplex virus

- Recurrence: stress, trauma, fever, sunlight)
- The virus travels back down the nerve causing lessions at the dermatome
- Recurrences are less severe and more localized

# Clinical Syndromes

- Primary herpetic gingivostomatitits
- Recurrent mucocutaneous HSV(cold sores, fever blister)
- Herpes pharyngitis
- Herpetic keratitis: corneal damage leading to blindness
- Herpetic whitlow
- Eczema herpeticum
- Genital herpes mostly by HSV-2



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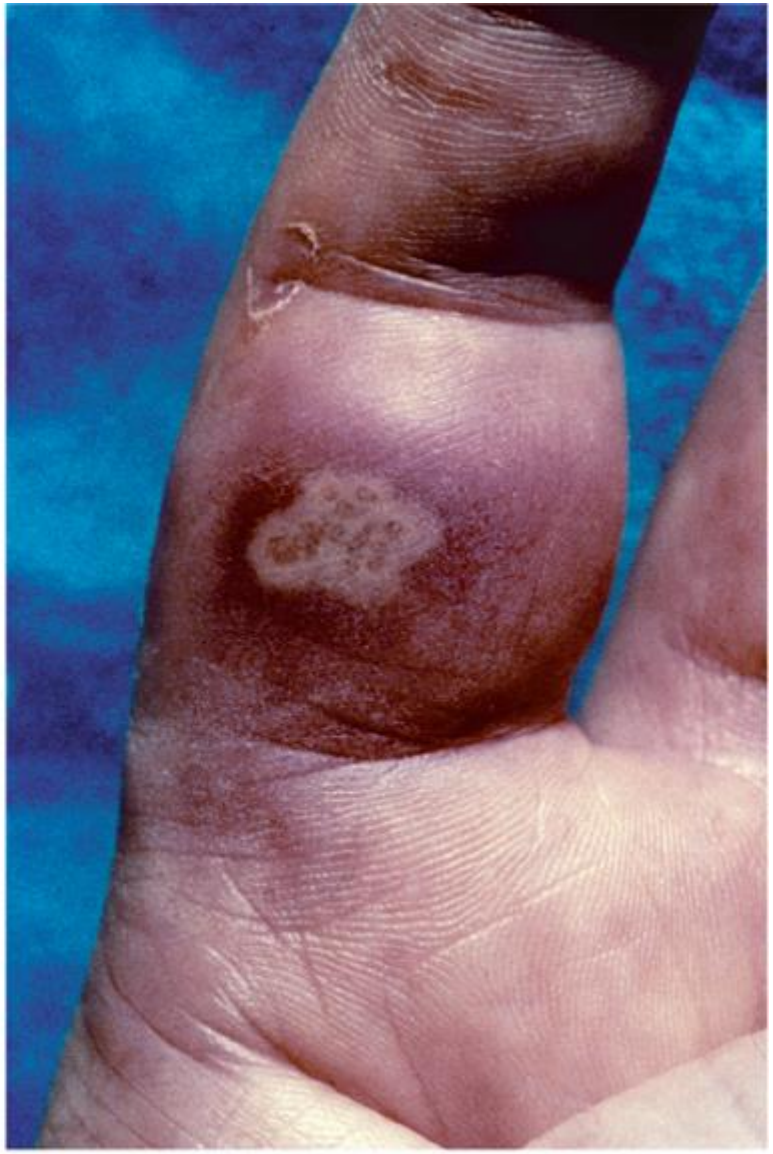

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# Clinical Syndromes

-Herpes encephalitis: usually by HSV-1,the most common viral cause of sporodic encephalitis.Mortality is high.

At all age, at any time of year

-HSV meningitis: complication of genital HSV-2

-Neonatal infection: HSV-2, usually fatal

## FDA-Approved Antiviral Treatments for Herpesvirus Infections

**Herpes Simplex 1 and 2**
- Acyclovir
- Penciclovir
- Valacyclovir
- Famciclovir
- Adenosine arabinoside
- Iododeoxyuridine
- Trifluridine

**Varicella-Zoster Virus**
- Acyclovir
- Famciclovir
- Valacyclovir
- Varicella-zoster immune globulin
- Zoster immune plasma
- Live vaccine

**Epstein-Barr Virus**
- None

***Cytomegalovirus***
- Ganciclovir*
- Valganciclovir*
- Foscarnet*
- Cidofovir*

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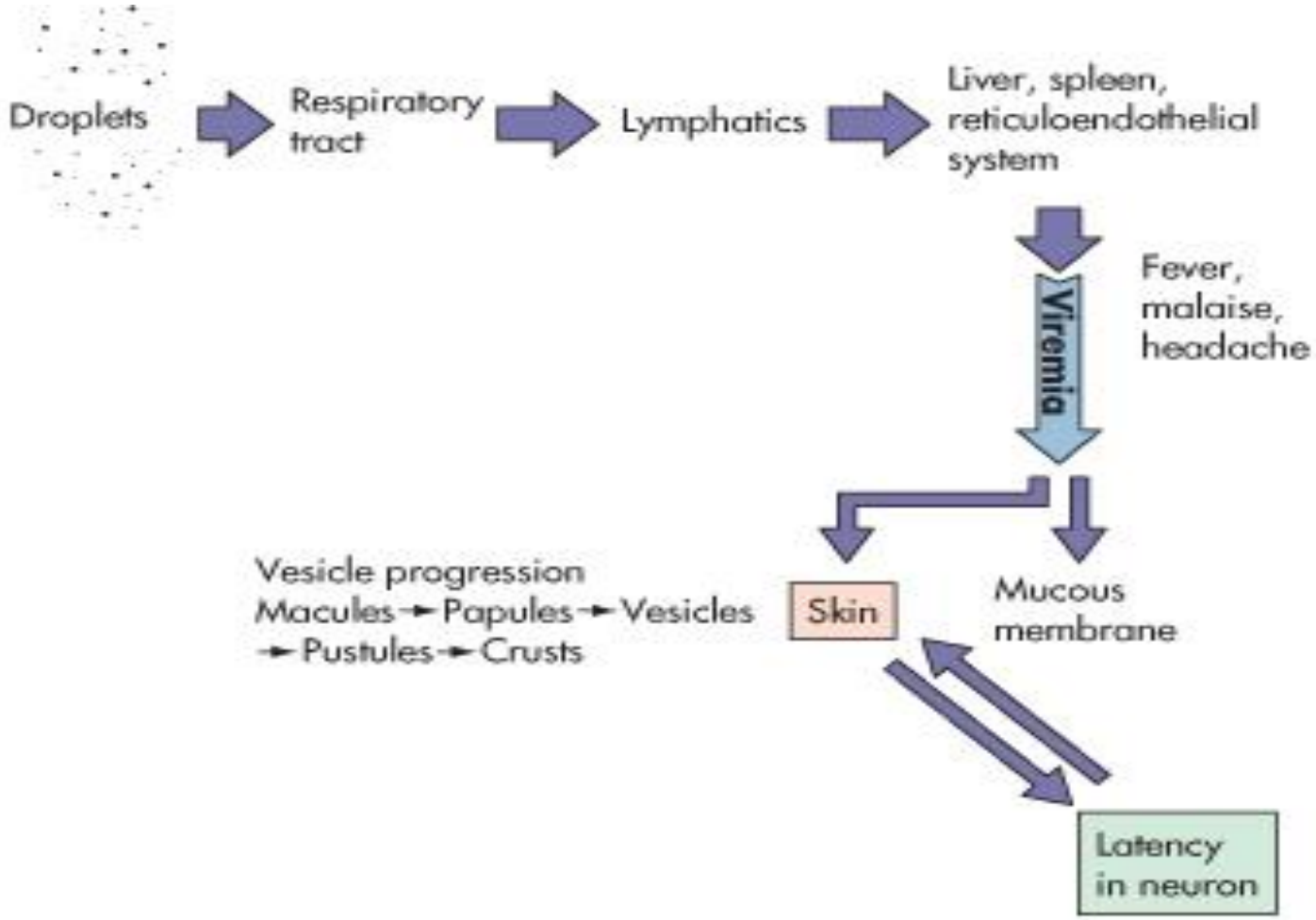
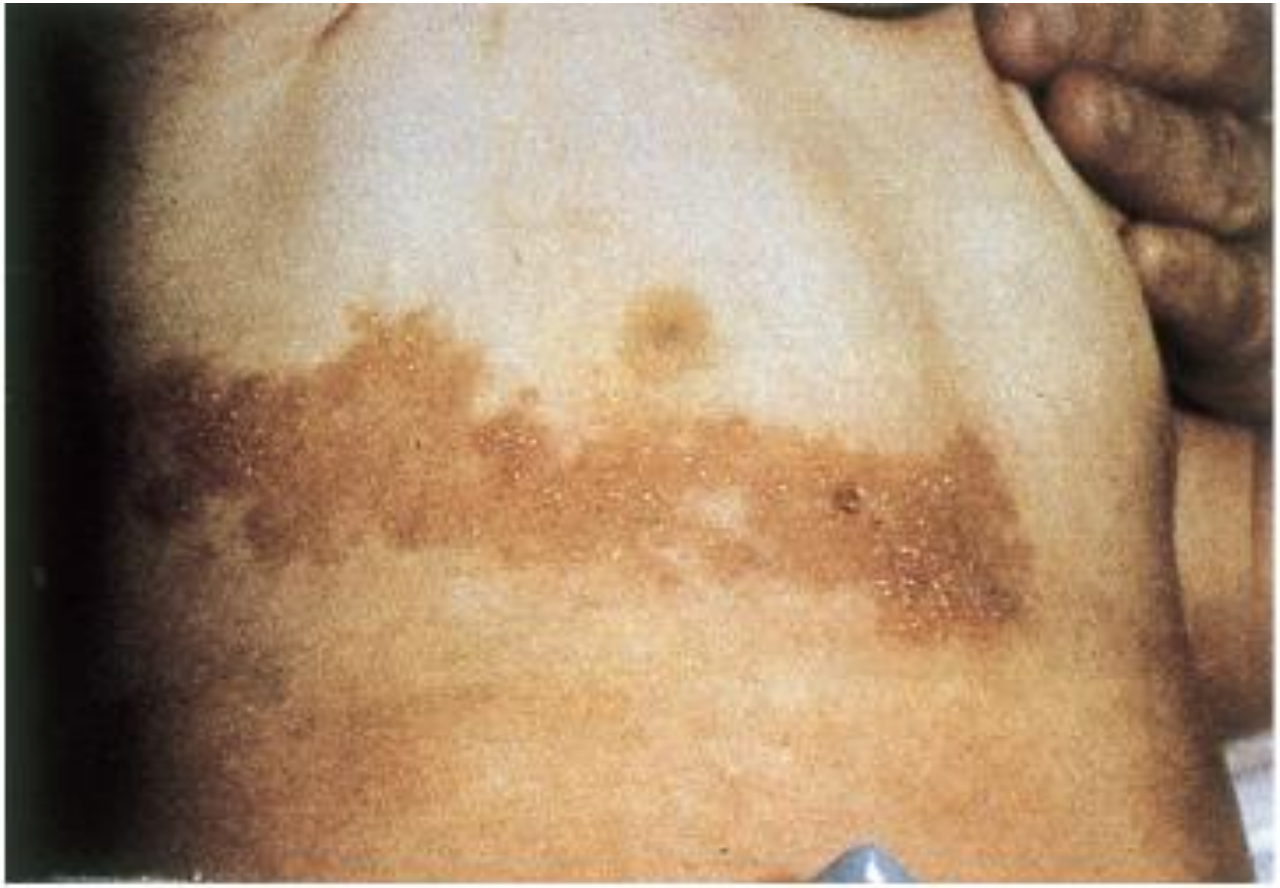
# Varicella-Zoster

- Chickenpox(varicella)
- With recurrence :herpes zoster-shingles:zona
- Primary target cell: mucoepitelial cell
- Site of latency: neuron
- Means of spread: respiratory and close contact
- Viremia occurs after local replication :skin lessions over the entire body



# Varicella-Zoster

- Extremely communicable
- Rates of infection exceeds 90% among household contact
- Contagious before and during symptoms.
- HZ develops in 10-20% of people infected with VZV and contains viable virus.



# Epstein-Barr Virus

- Heterophile antibody-positive infectious mononucleosis
- Chronic disease
- Associated with endemic Burkitt's lymphoma, Hodgkin's disease, nasopharyngeal carcinoma, B-cell lymphomas in patients with acquired or congenital immunodeficiencies.
- Hairy oral leukoplakia
- Mitogen for B cells and immortalizes them

# Epstein-Barr Virus

Gammaherpesvirinae:

Primary target cell: B cells and epitelial cells

Site of latency: B cell

Means of spread: saliva (kissing disease)

# EBV

- The diseases of EBV result from either an overactive immune response (infectious mononucleosis) or

- the lack of effective immune control (lymphoma and hairy cell leukoplakia).

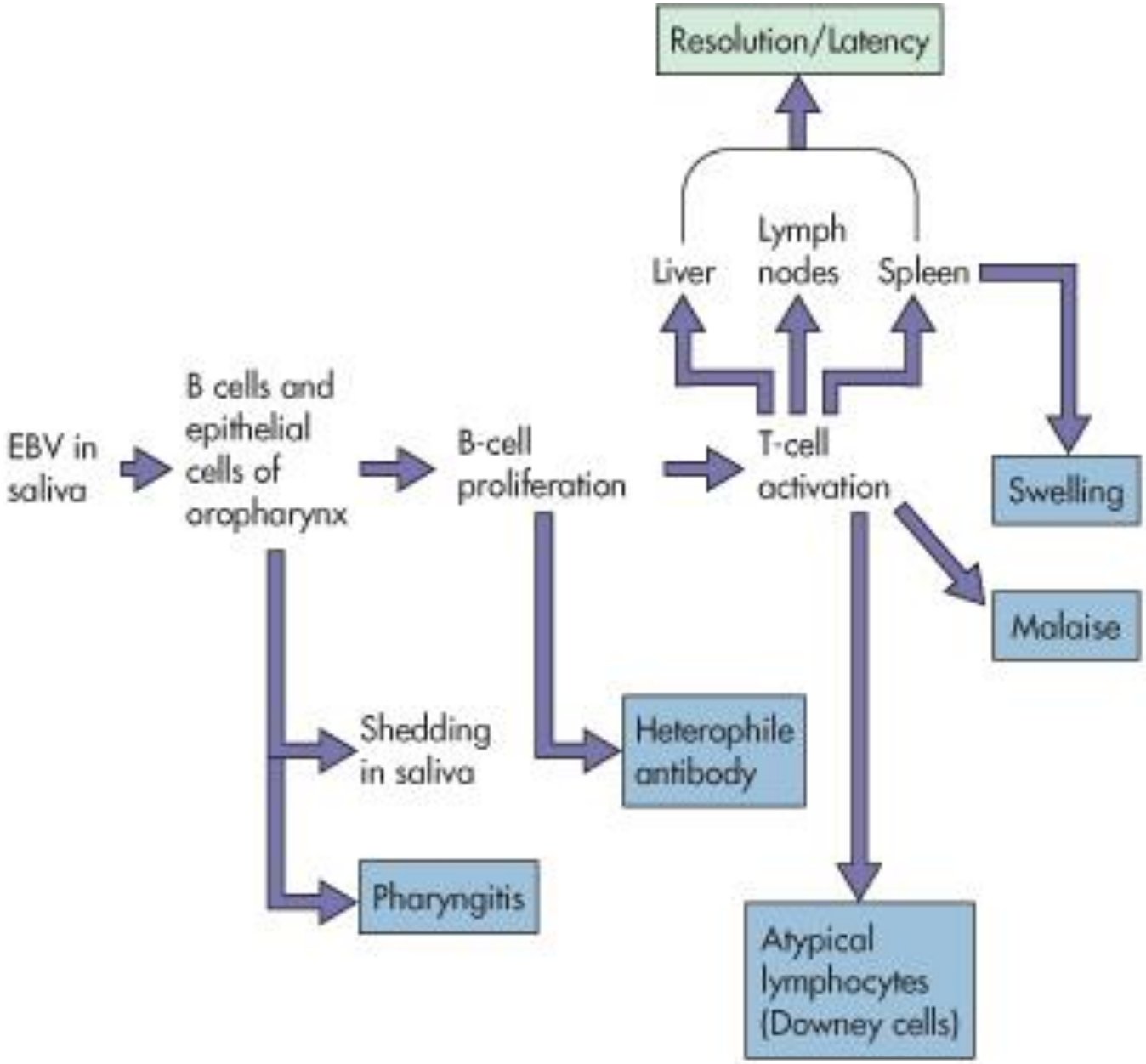
# Epstein-Barr Virus

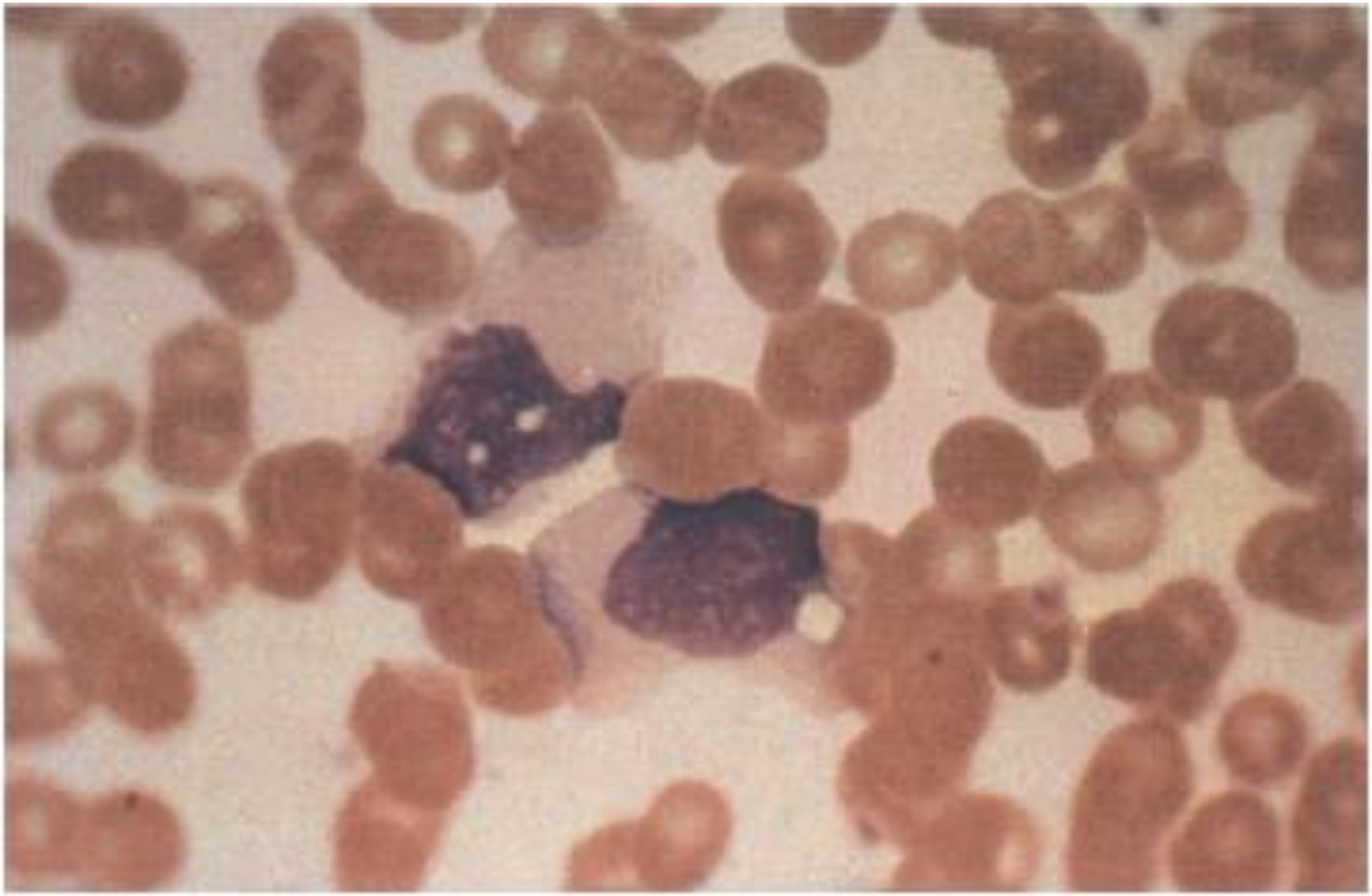
EBV activate B-cell growth and prevents apoptosis(programmed cell death)

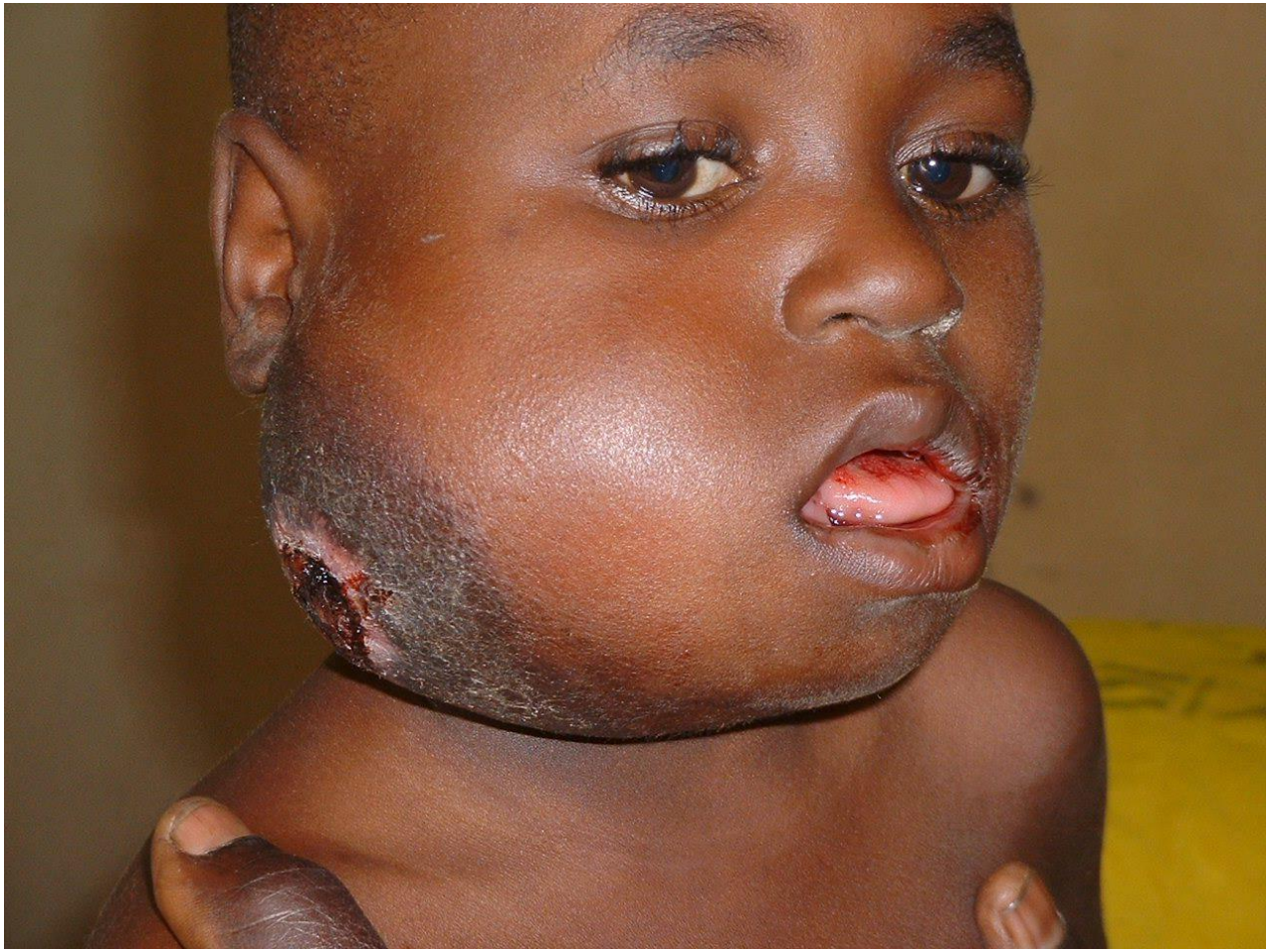
T cell response (lymphocytosis) :atypical Lymphocytosis:Downey cells account for 10-80% of total white blood cells during the second week

Lymph glands,spleen and liver swells

Mild in children







## Box 53-9. Epidemiology of Epstein-Barr Virus

### Disease/Viral Factors

- Virus causes lifelong infection.
- Recurrent disease is cause of contagion.
- Virus may cause asymptomatic shedding.

### Transmission

- Transmission occurs via saliva, close oral contact ("kissing disease"), or sharing of items such as toothbrushes and cups.

### Who Is at Risk?

- Children experience asymptomatic disease or mild symptoms.
- Teenagers and adults are at risk for infectious mononucleosis.
- Immunocompromised people are at highest risk for life-threatening neoplastic disease.

### Geography/Season

- Infectious mononucleosis has worldwide distribution.
- There is causative association with African Burkitt lymphoma in malarial belt of Africa.
- There is no seasonal incidence.

### Modes of Control

- There are no modes of control

# Cytomegalovirus(CMV)

- Betaherpesvirnae: lymphotropic
- Primary target cell: monocyte, lymphocte, epitelial cell
- Site of latency: monocyte, lymphocyte
- Means of spread: close contact, transfusions, tissue transplant and congenital

# Sources of infection

- Neonate: transplacental transmission, intrauterine infection, cervical secretion
- Baby or child: body secretions, breast milk, saliva, tears, urine
- Adult: sexual transmission(semen), blood transfusion, organ graft

# CMV

- the most common viral cause of **congenital defects**
- particularly important as an **opportunistic pathogen in immunocompromised patients**

# CMV immunsupressed patients

- CMV disease of the lung (**pneumonia and pneumonitis**) is a common outcome in immunosuppressed patients
- Retinitis (%10-15 AIDS patients)
- Interstitial pneumonia and encephalitis
- **colitis or esophagitis** may develop in as many as 10% of patients with AIDS

## . Epidemiology of Cytomegalovirus Infection

**Disease/Viral Factors**
•Virus causes lifelong infection.
•Recurrent disease is source of contagion.
•Virus may cause asymptomatic shedding.
**Transmission**
•Transmission occurs via blood, organ transplants, and all secretions (urine, saliva, semen, cervical secretions, breast milk, and tears).
•Virus is transmitted orally and sexually, in blood transfusions, in tissue transplants, in utero, at birth, and by nursing.
**Geography/Season**
•Virus is found worldwide.
•There is no seasonal incidence.
**Who Is at Risk?**
•Babies.
•Babies of mothers who experience seroconversion during term: At high risk for congenital defects.
•Sexually active people.
•Blood and organ recipients.
•Burn victims.
•Immunocompromised people: Symptomatic and recurrent disease.
**Modes of Control**
•Antiviral drugs are available for patients with acquired immune deficiency syndrome.
•Screening potential blood and organ donors for cytomegalovirus reduces transmission of virus.

# Laboratory tests

- Antigen in peripheral leucocytes
- DNA by PCR
- Cell culture: Human diploid fibroblasts
- Serology: primary infection

# Treatment

- Ganciclovir
- Foscarnet
- Valganciclovir
- Cidofovir
- No vaccine

# Other mononucleosis causes

- EBV
- CMV
- HIV
- Toxoplasma gondii