Poltava State Medical University
Department of Microbiology, Virology and Immunology

DNA genomic viruses. General characteristics. Adeno- and Herpesviruses

For two-way communication

between the lecturer and students during the lecture, please contact the following e-mail address:

v.fedorchenko@pdmu.edu.ua

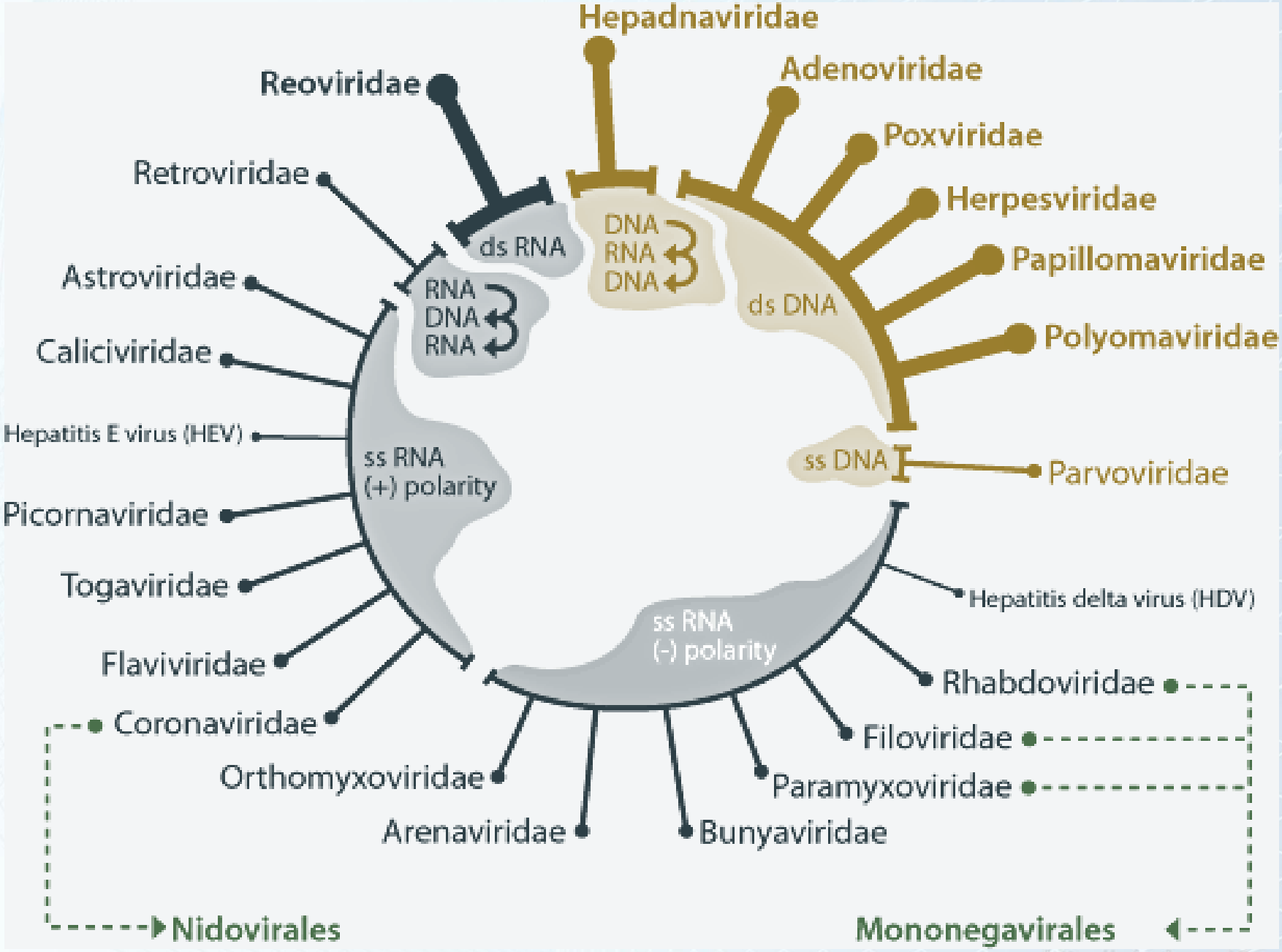
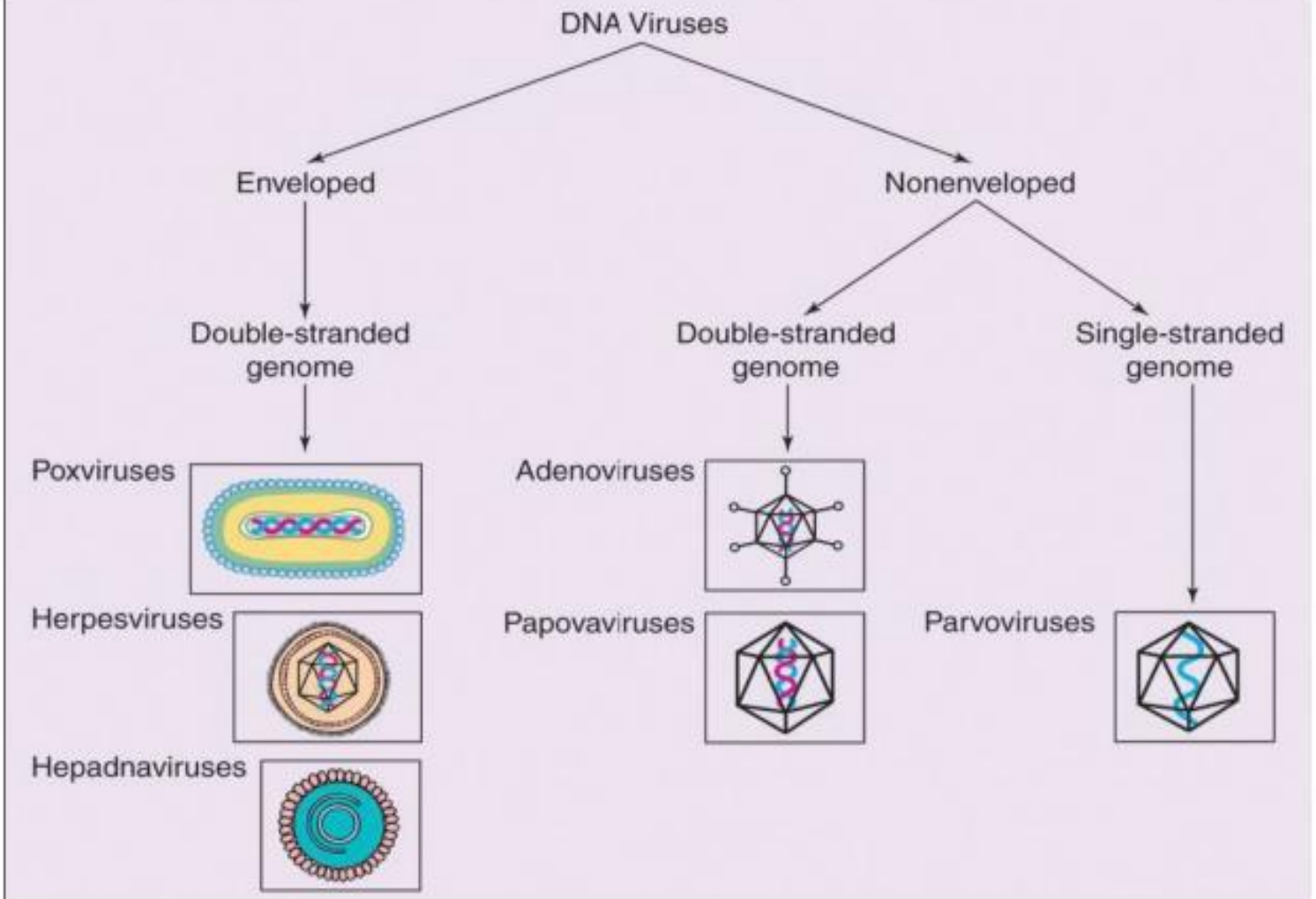

Hepadnaviridae
Reoviridae
Adenoviridae
Poxviridae
Retroviridae
Herpesviridae
DNA
RNA
DNA
ds RNA
Papillomaviridae
Astroviridae
RNA
DNA
RNA
ds DNA
Caliciviridae
Polyomaviridae
Hepatitis E virus (HEV)
ss RNA
(+) polarity
ss DNA
Parvoviridae
Picornaviridae
Hepatitis delta virus (HDV)
Togaviridae
ss RNA
(-) polarity
Rhabdoviridae
Flaviviridae
Filoviridae
Coronaviridae
Paramyxoviridae
Orthomyxoviridae
Arenaviridae
Bunyaviridae
Nidovirales
Mononegavirales

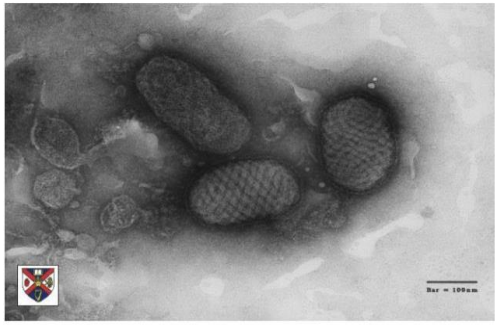
TABLE 24.1

DNA Virus Groups



Pox Virus

- Produce eruptive skin pustules called pocks or pox, that leave scars
- Largest & most complex animal viruses
- Have the largest genome of all viruses
- dsDNA
- Multiply in cytoplasm in factory areas
  - Variola – cause of smallpox
  - Vaccinia – closely related virus used in vaccines
  - Monkey pox
  - Cowpox

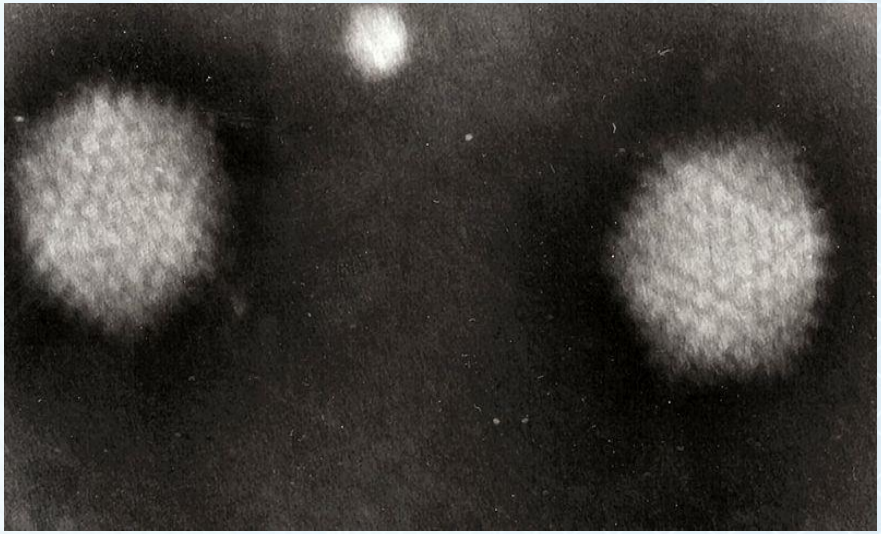


Small Pox

- First disease to be eliminated by vaccination
- Exposure through inhalation or skin contact
- Infection associated with fever, malaise, prostration and a rash.
  - Variola major – highly virulent, caused toxemia, shock and intravascular coagulation.
  - Variola minor – less virulent
- Routine vaccination ended in US in 1972
- Vaccine reintroduced in 2001

Adenoviruses

Adenoviruses are medium-sized (90–100 nm), nonenveloped (without an outer lipid bilayer) icosahedral viruses composed of a nucleocapsid and a double-stranded linear DNA genome. There are 57 described serotypes in humans, which are responsible for 5–10% of upper respiratory infections in children, and many infections in adults as well.



Adenoviruses

Adenovirus infections most commonly cause illness of the respiratory system.

However, depending on the infecting serotype, they may also cause various other illnesses and presentations

Adenoviruses

Besides from respiratory involvement, illnesses and presentations of adenovirus include gastroenteritis, conjunctivitis, cystitis, and rash illness.

Symptoms of respiratory illness caused by adenovirus infection range from the common cold syndrome to pneumonia, croup, and bronchitis.

Adenoviruses

Patients with compromised immune systems are especially susceptible to severe complications of adenovirus infection.

Acute respiratory disease (ARD), first recognized among military recruits during World War II, can be caused by adenovirus infections during conditions of crowding and stress

Adenoviruses

Pharyngoconjunctival fever

Pharyngoconjunctival fever is a specific presentation of adenovirus infection, manifested as:

- high fever that lasts 4-5 days
- pharyngitis (sore throat)
- conjunctivitis (inflamed eyes, usually without pus formation like pink eye)
- enlargement of the lymph nodes of the neck
- headache, malaise, and weakness
- Incubation period of 5-9 days

Diagnosis

- Antigen detection,
- polymerase chain reaction assay,
- virus isolation,
- and serology

*can be used **to identify** adenovirus infections*.

Adenovirus typing is usually accomplished by hemagglutination-inhibition and/or neutralization with type-specific antisera.

Since adenovirus can be excreted for prolonged periods, the presence of virus does not necessarily mean it is associated with disease.

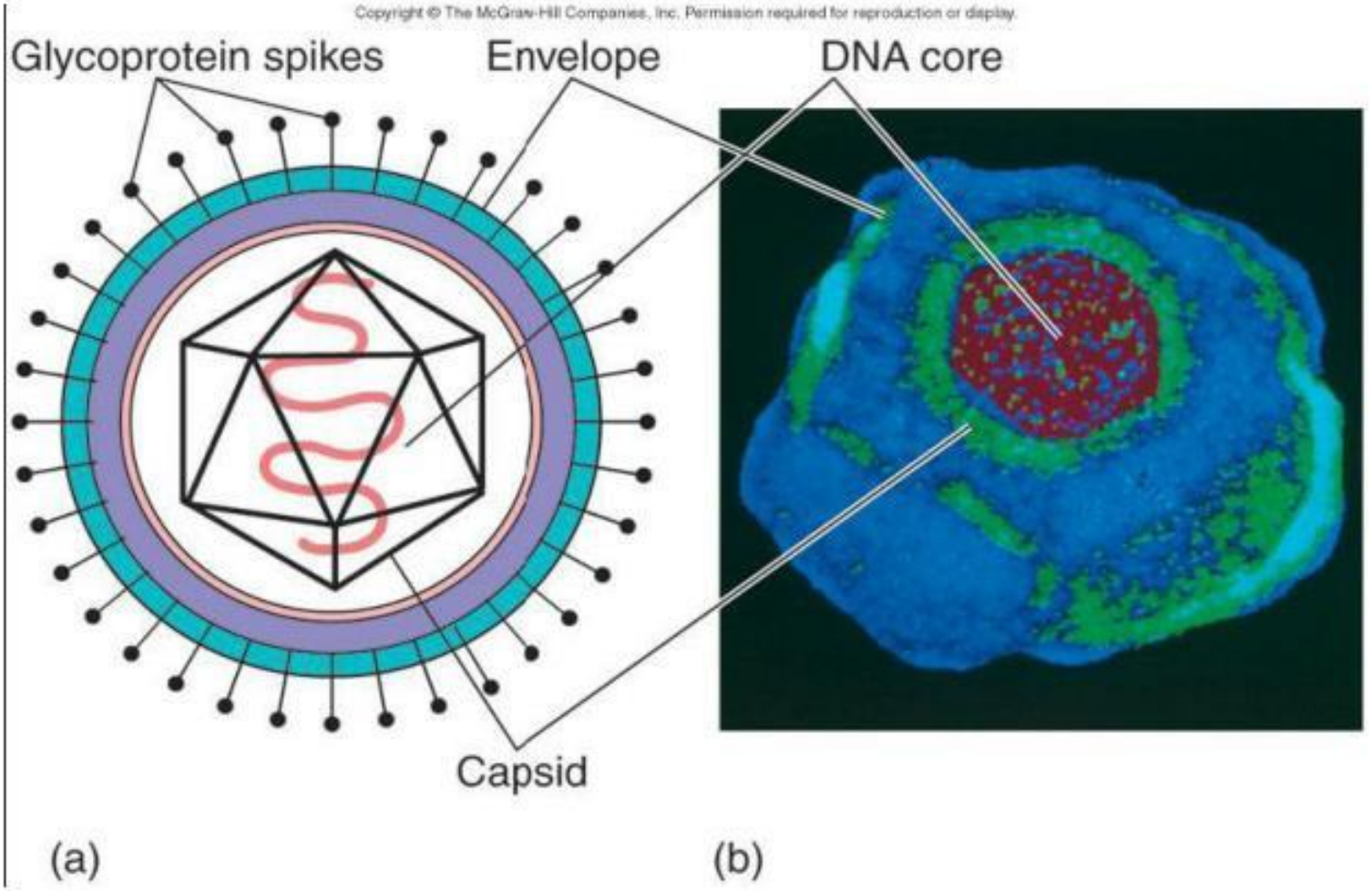
Prevention

Safe and effective adenovirus vaccines were developed for adenovirus serotypes 4 and 7, but were available only for preventing ARD among US military recruits, and production stopped in 1996.

Strict attention to good infection-control practices is effective for stopping nosocomial outbreaks of adenovirus-associated disease, such as epidemic keratoconjunctivitis.

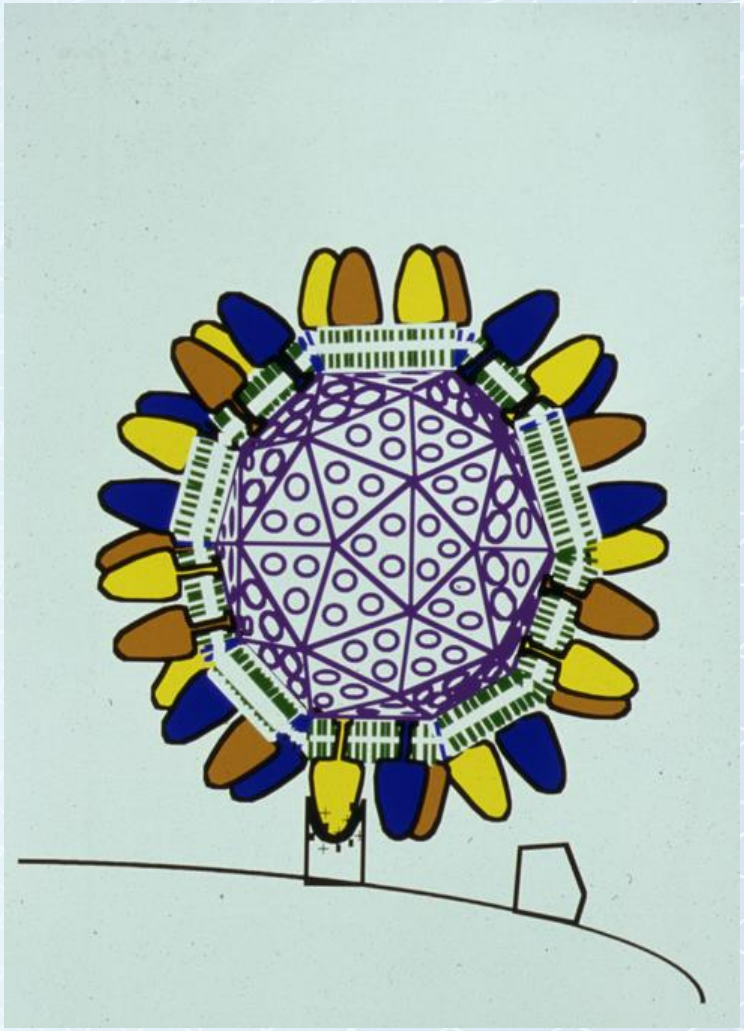
Maintaining adequate levels of chlorination is necessary for preventing swimming pool-associated outbreaks of adenovirus conjunctivitis.

Herpes Virus



Virion structure

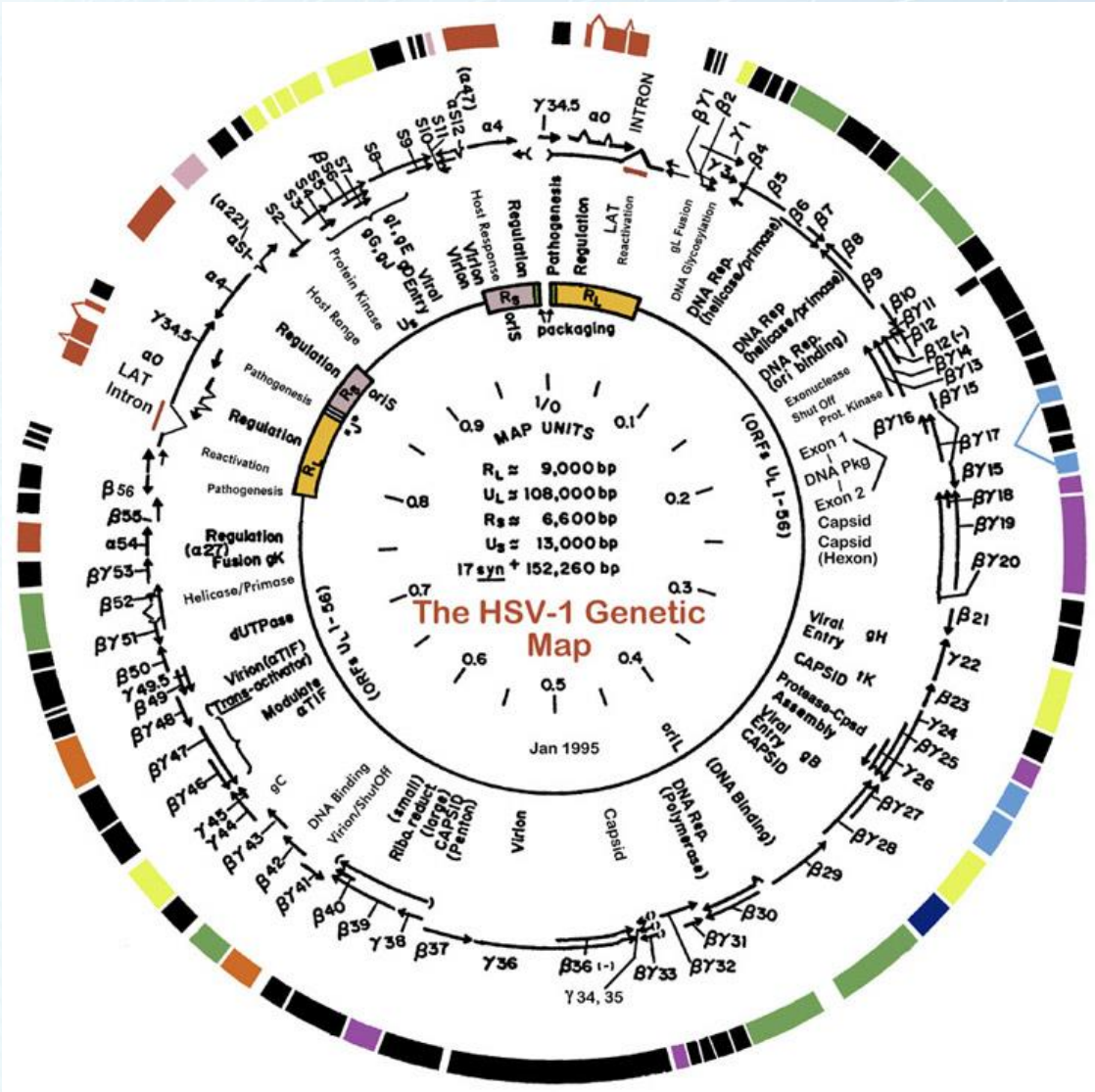
- Enveloped, spherical virion
- Icsoahedral capsid 120 - 200 nm
- >12 virally encoded glycoproteins
- Tegument proteins



Genome structure

- Linear double-stranded DNA
- 120 - 230 kb
- Genetic complexity

→ **# of genes**



Herpes Simplex Virus

- **Enveloped virus**
- **Sensitive to dessication**
- **Easily inactivated by detergents and lipid solvents**

Herpesviruses

Herpes simplex I	(oropharyngeal lesions)
Herpes simplex II	(genital herpes)
Varicella zoster	(chicken pox, shingles)
Cytomegalovirus	(microcephaly, infectious mono)
Epstein-Barr virus	(mononucleosis, nasopharyngeal carcinoma, Burkitt lymphoma,)
Human herpesvirus 6	(Roseola infantum)
Human herpesvirus 8	(Kaposi sarcoma)

Human Herpesviruses

Virus	Subfamily	Disease	Site of Latency
Herpes Simplex Virus I	α	Orofacial lesions	Sensory Nerve Ganglia
Herpes Simplex Virus II	α	Genital lesions	Sensory Nerve Ganglia
Varicella Zoster Virus	α	Chicken Pox Recurs as Shingles	Sensory Nerve Ganglia
Cytomegalovirus	β	Microcephaly/Mono	Lymphocytes
Human Herpesvirus 6	β	Roseola Infantum	CD4 T cells
Human Herpesvirus 7	β	Roseola Infantum	CD4T cells
Epstein-Barr Virus salivary	γ	Infectious Mono	B lymphocytes,
Human Herpesvirus 8 Tissue	γ	Kaposi's Sarcoma	Kaposi's Sarcoma

Herpesviridae

- Latency & recurrent infections
- Complications of latency & recurrent
- Infections become more severe with age, cancer chemotherapy, etc
- Most common & serious opportunists among AIDS patients

Transmission and Seroepidemiology of Herpesviruses That Infect Humans

Table 2.

Virus	Seroprevalence (%) (United States)		Groups of Activities with Higher Risk of Infection
	Healthy Children	Healthy Adults	
Herpes simplex virus 1	20-40	50-70	Frequent intimate contact
Herpes simplex virus 2	0-5	20-50	Frequent intimate contact
Varicella-zoster virus	50-75	85-95	Children in day care
Cytomegalovirus	10-30	40-70	Children in day care promiscuous gay men Transplant or blood recipients
Epstein-Barr virus	10-30	60-90	Frequent intimate contact
Human herpesvirus 6	80-100	60-100	Celluar immune deficiency states
Human herpesvirus 7	40-80	60-100	?

Tissue tropism of HSV-1 and HSV-2

HSV-1:

- Causes 95% of orofacial herpes (remainder caused by HSV-2)
- Causes 10 - 30% of primary genital herpes (but seldom recurs there)

HSV-2:

- Causes primary and recurrent genital herpes infections
- May cause primary oral herpes but, like HSV-1 in genital area, it seldom recurs there

TABLE 24.2

Comparative Epidemiology and Pathology of Herpes Simplex, Types 1 and 2

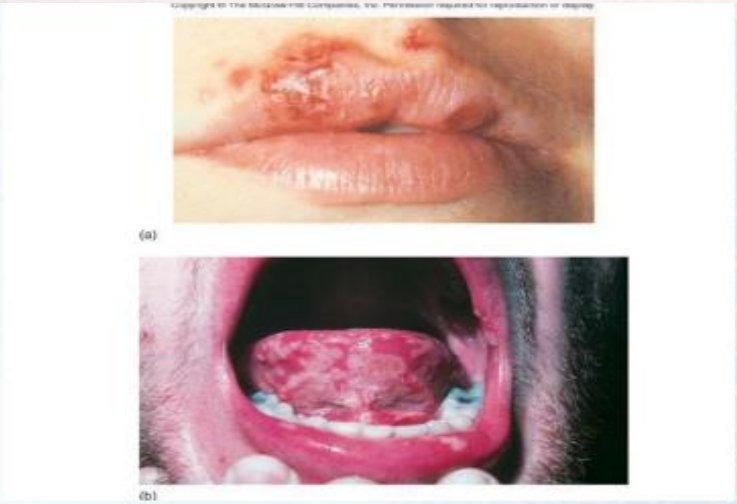
	HSV-1	HSV-2
Usual Etiologic Agent of:	Herpes labialis Ocular herpes Gingivostomatitis Pharyngitis	Herpes genitalis*
Transmission	Close contact, usually of face	Sexual or close contact
Latency	Occurs in trigeminal ganglion	Occurs primarily in sacral ganglia
Skin Lesions	On face, mouth	On internal, external genitalia, thighs, buttocks
Complications		
Whitlows	Among personnel working on oral cavity	Among obstetric, gynecological personnel
Neonatal encephalitis	Causes up to 30% of cases**	Causes most cases

**The other herpes simplex type can be involved in this infection, though not as commonly.*

***Due to mothers infected genitally by HSV-1 or contamination of the neonate by oral lesions.*

DISEASE SYNDROMES INDUCED BY HERPES SIMPLEX VIRUS.

- -*Cold Sores* (not canker sores), on the lip.
- -*Gingivostomatitis*, on the gums and inside of the mouth.
- -*Keratitis*, as ulcers on the cornea.
- -Dentists and oral hygenists are suscepible to HSV on the finger, called *Whitlow*.
- -Wrestlers can acquire HSV along their trunk, called *Herpes Gladiatorum*.
- -HSV-2, and to a lesser extent HSV-1, is transmitted venereally.
- -Anal and perianal infections with HSV-2 are common among sexually active male homosexual populations.



Herpes Simplex Virus type 2

- Infects the genital tract
- Is sexually transmitted
- Complicates childbirth
- 2/3 of the acquisitions of genital herpes come from clinically asymptomatic partners

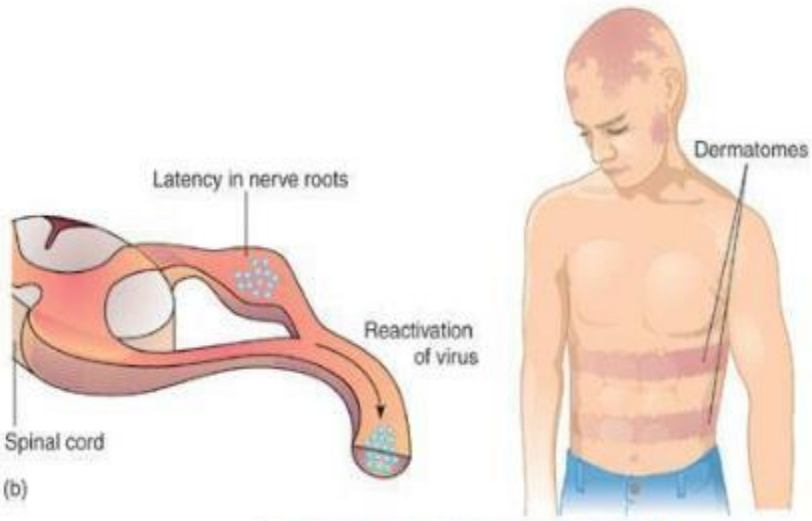
Varicella-Zoster Virus (VZV)

- Causes chickenpox & shingles
- Transmitted by respiratory droplets & contact
- Primary infection – chickenpox – vesicles
- Virus enters neurons & remains latent
- Later, reactivation of the virus results in shingles with
- Vesicles localized to distinctive areas, dermatomes
- Treatment : acyclovir, famciclovir, interferon
- Live attenuated vaccine

Two Unique Features of VZV:

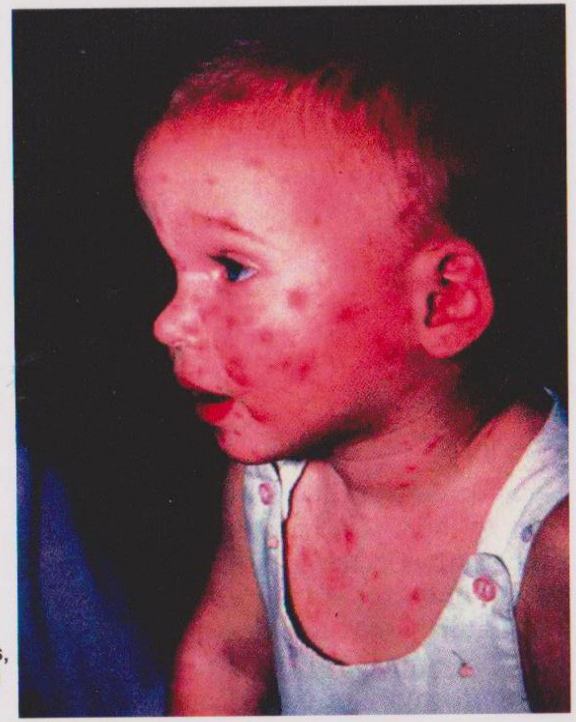
- Airborne spread or skin to skin contact
- More severe infection if primary infection occurs as an adult

(a)



(b)

(c)



Patient with varicella (chicken pox). Characteristically, lesions in various states of evolution are present - macules, papules, vesicles and pustules.

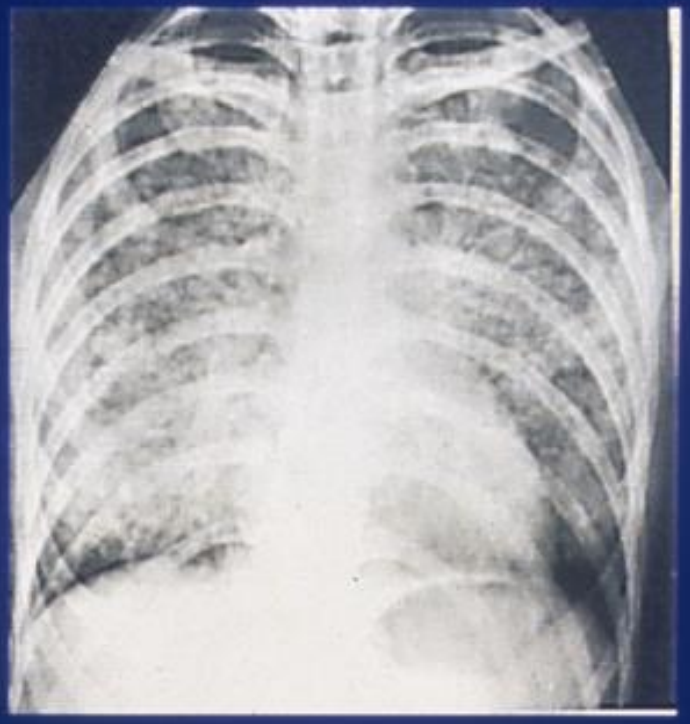
Patient with shingles. The rash mimics that of chicken pox, except that it is limited to a sensory nerve distribution on one side of the body.

Complications of Varicella

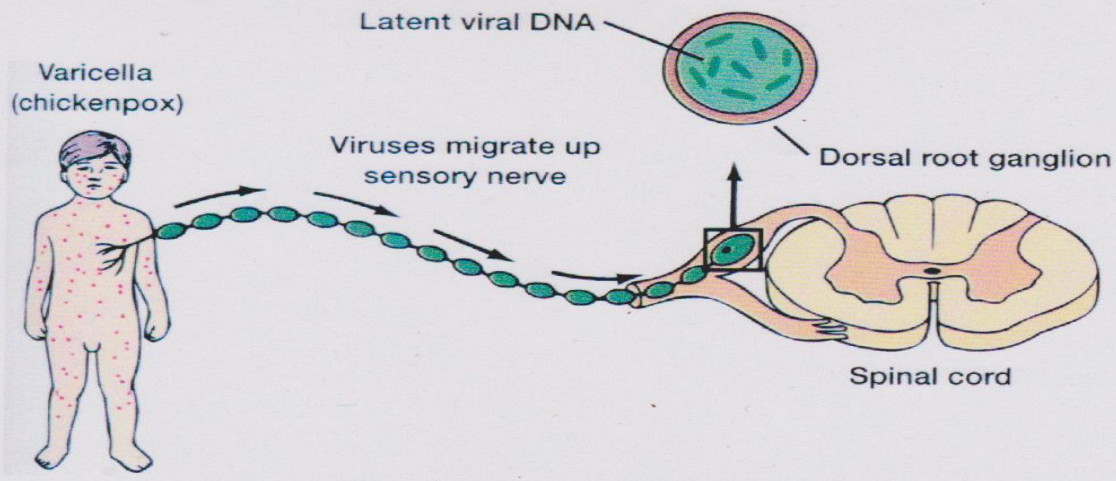
- Bacterial Superinfection of lesions (more common in younger patients)
- Varicella pneumonia
- Neonatal varicella - disseminated, 30% mortality

Bacterial superinfection of chickenpox lesions

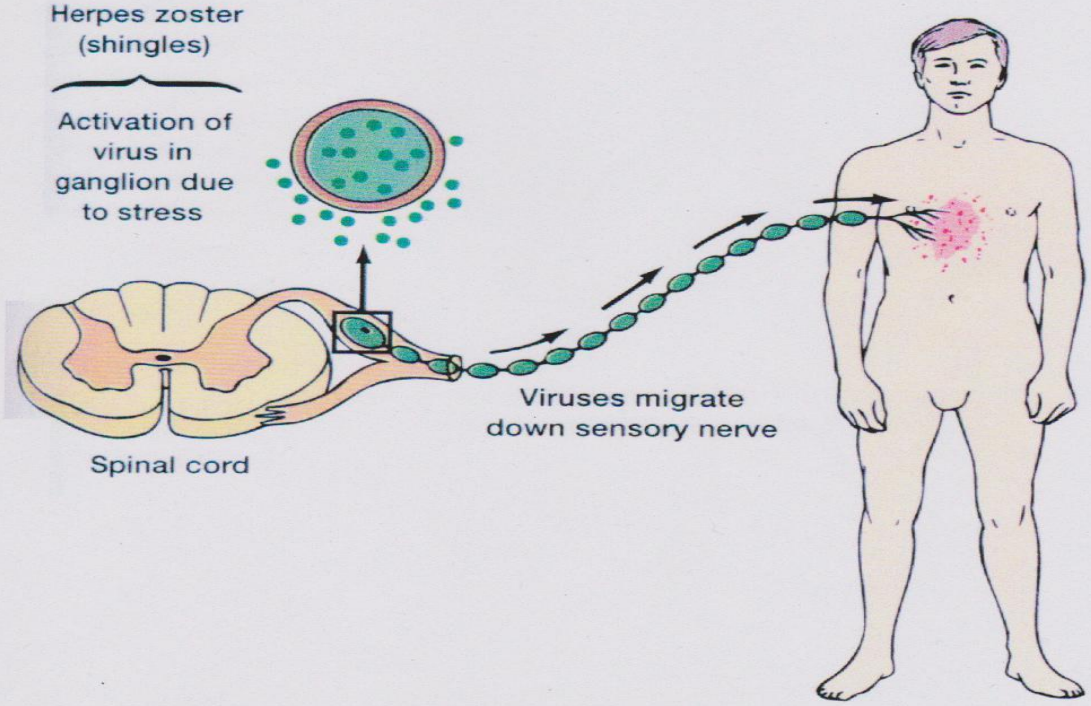
Chickenpox pneumonia



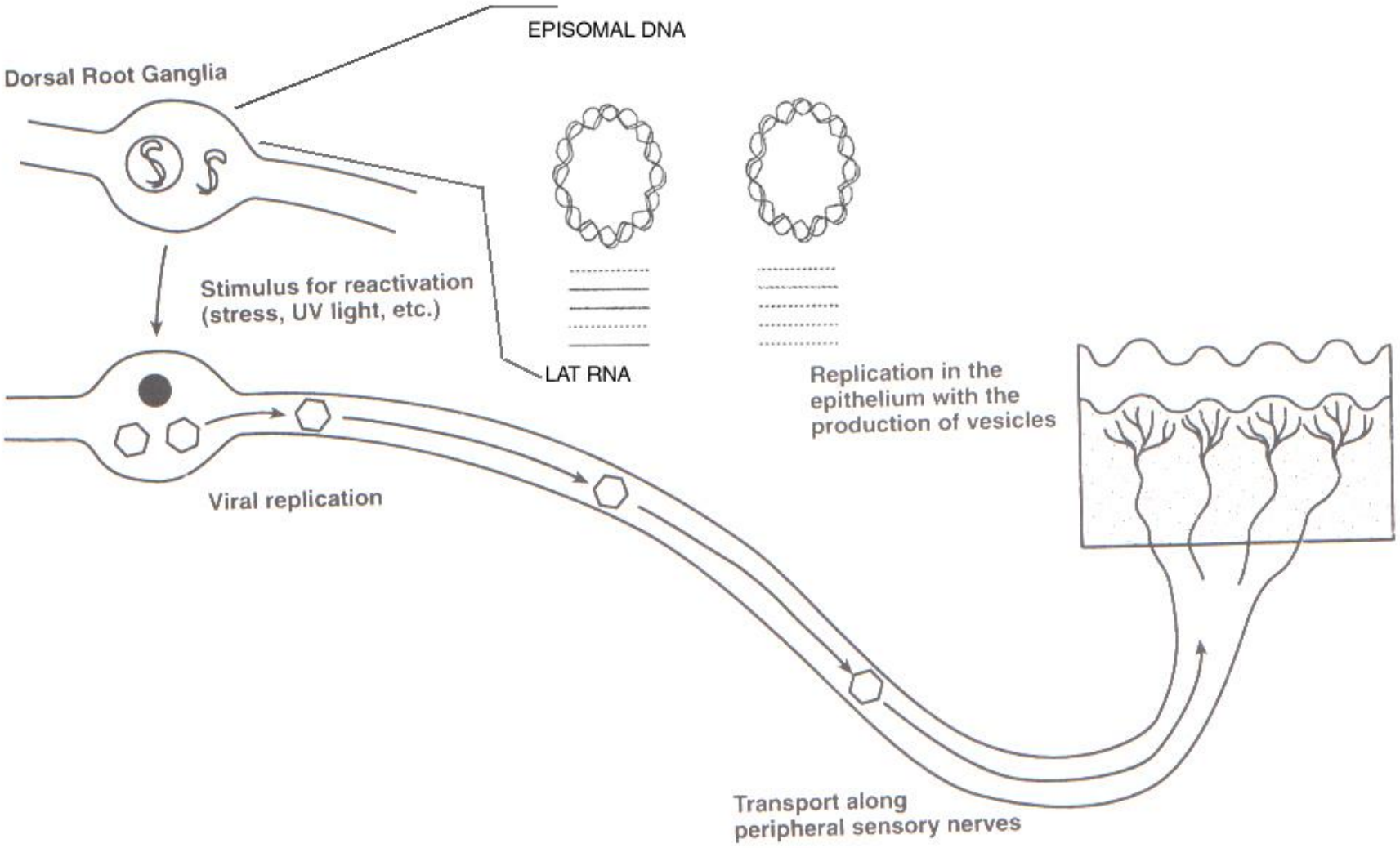
Neonatal Varicella



(a) **Primary infection**



(b) **Recurrence**


EPISOMAL DNA
Dorsal Root Ganglia
Stimulus for reactivation
(stress, UV light, etc.)
LAT RNA
Replication in the
epithelium with the
production of vesicles
Viral replication
Transport along
peripheral sensory nerves

VARICELLA ZOSTER

RECURRENT INFECTION

(SHINGLES)

2. Infections are unilateral, painful vesicular eruptions localized to the dermatome, usually in the head or upper trunk
3. Severe systemic infections are observed in immune suppressed individuals

Zoster

Complications of Zoster

- **Postherpetic Neuraligia**
  - Affects 25 - 50% of zoster patients over 50
  - Pain may persist for months or even years

Varicella Vaccine

- Prevents 40 - 70% of chickenpox occurrence
- Greatly reduces the severity in the rest
- Attenuated virus
- Can still establish latency and reactivate

Diagnosis of Herpes Simplex Virus Infections:

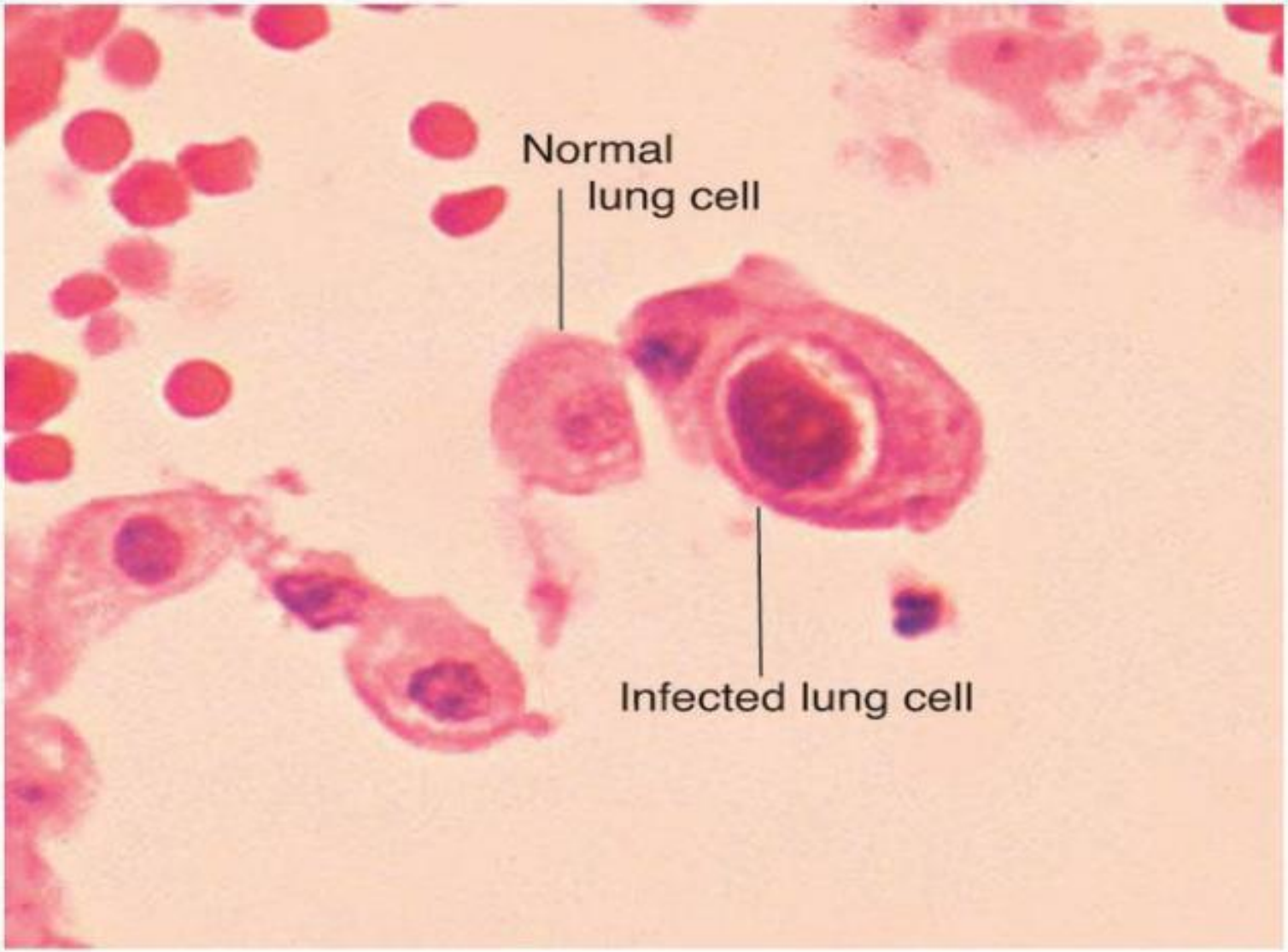
- Viral Culture
- Culture with monoclonal antibody staining
- Serology
- Polymerase chain reaction (PCR)
- ELISA

Cytomegalovirus (CMV)

- Produce giant cells with nuclear & cytoplasmic inclusions
- Transmitted in saliva, respiratory mucus, milk, urine, semen, cervical secretions & feces
- Commonly latent in various tissues
- Most infections are asymptomatic
- 3 groups develop a more virulent form of disease: fetuses, newborns, immunodeficient adults

CMV

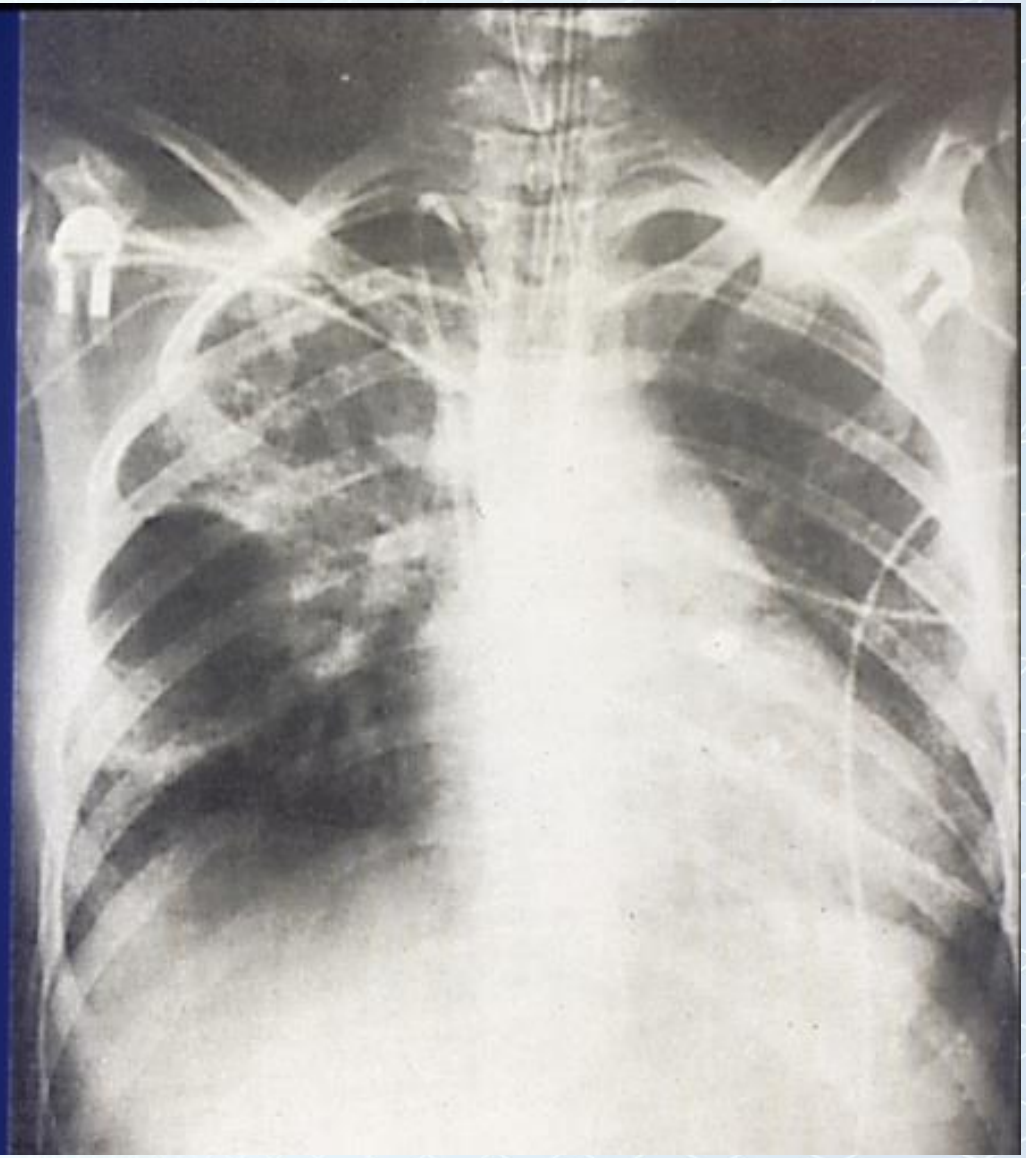
- **Normal Host:**
  - Asymptomatic in the majority of cases
  - Infectious mononucleosis
- **Congenital CMV:**
  - Primary CMV infection during pregnancy of a seronegative mother
- **Immunocompromised:**
  - Pneumonitis in bone marrow transplants
  - Retinitis in AIDS patients



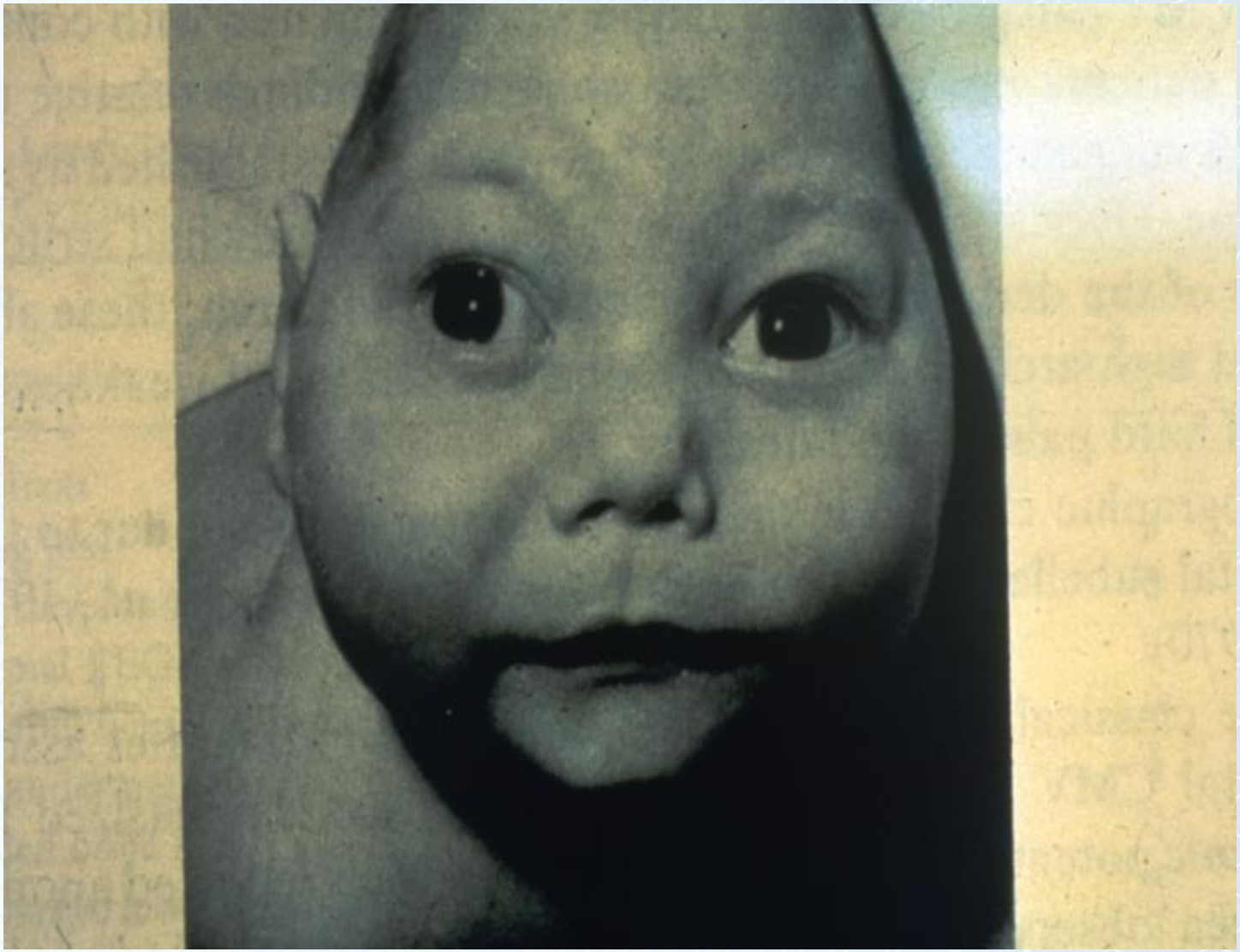
CMV

- Newborns may exhibit **enlarged** liver & spleen, jaundice, capillary bleeding microcephaly, & ocular inflammation, may be fatal
  - Babies who survive develop neurological sequelae; hearing, visual disturbances & mental retardation
- perinatal CMV infection – mostly asymptomatic, or pneumonitis, & a mononucleosislike syndrome
- AIDS patients – CMV mononucleosis, disseminated CMV, retinitis.
- Transplant patients pneumonitis, hepatitis, myocarditis, meningoencephalitis
- Treatment: ganciclovir, valvcyclovir, foscarnet

Cytomegalovirus
Pneumonia
in an
Immunocompromised
Host



Microcephaly



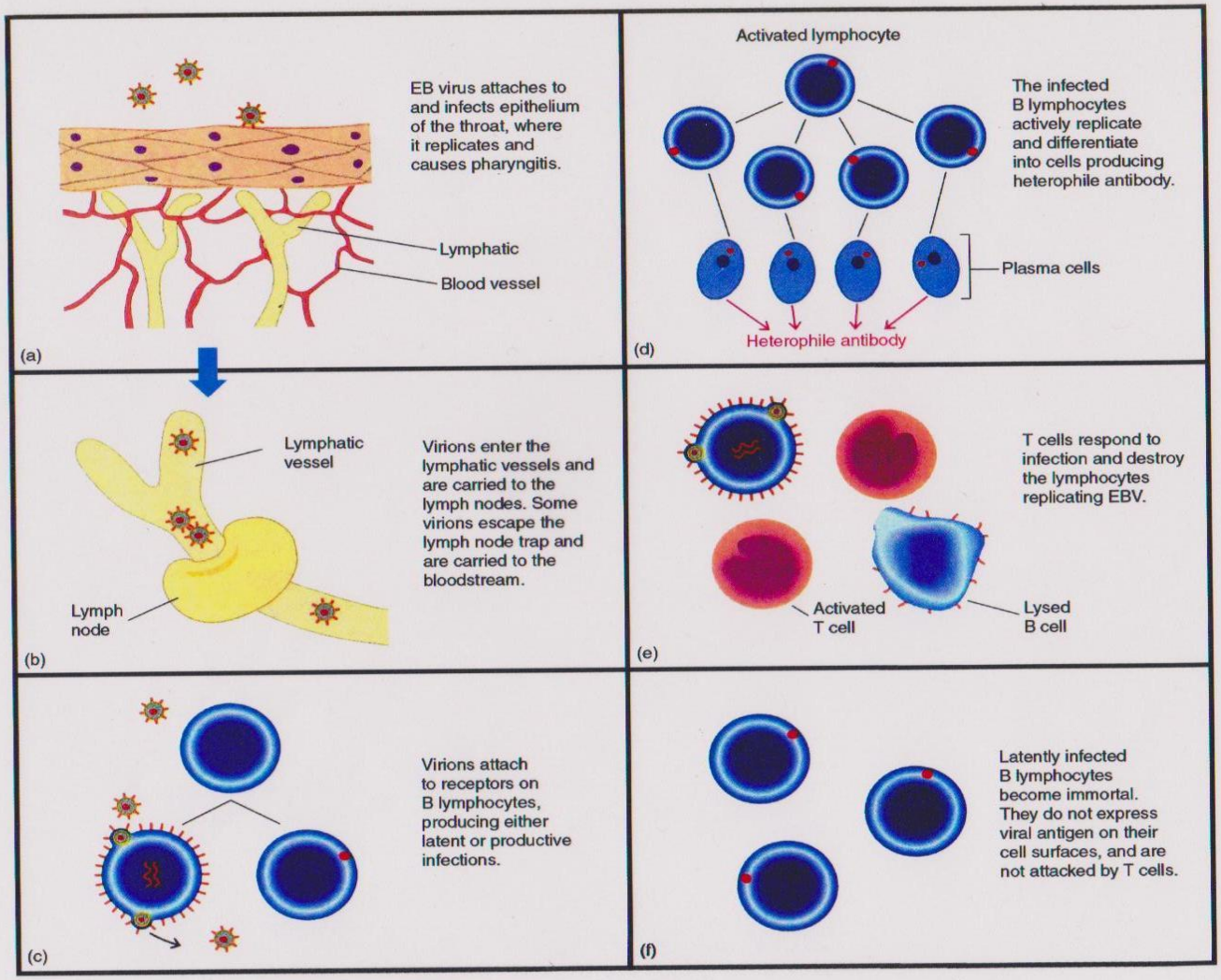
Transmission of CMV

- In utero
- Early childhood (saliva, etc.)
- Venereal in young adults
- Blood transfusion
- Organ transplantation

EPSTEIN-BARR VIRUS (EBV)

(Gamma Herpesvirus)

1. Infectious mononucleosis
2. Associated with Burkitt's lymphoma (Africa)
3. Associated with Nasopharyngeal carcinoma (China)



Pathogenesis of infectious mononucleosis.

EBV mononucleosis

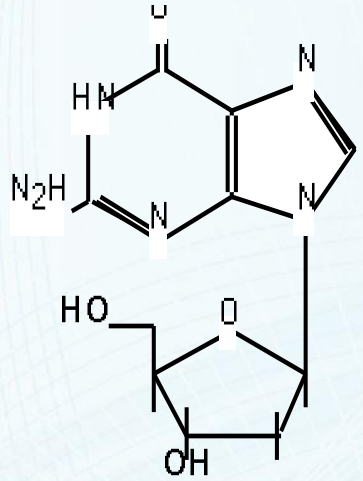
Kaposi's sarcoma caused by HHV-8

Burkitt's lymphoma

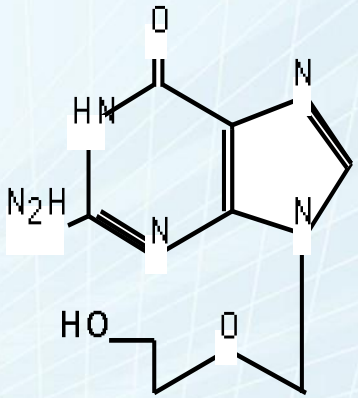
Heterophile Antibody (IM)

- EBV induces many cellular proteins
- An antibody against one of these new cellular proteins is able to agglutinate sheep red blood cells
- EBV mononucleosis is *heterophile antibody positive*
- CMV mono is *heterophile antibody negative*

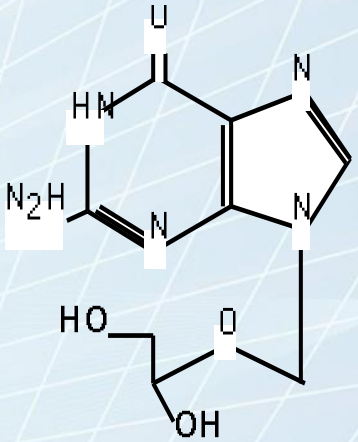
Antiviral therapy



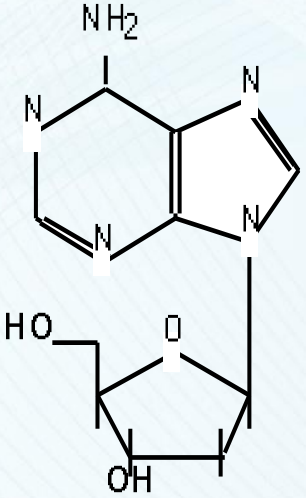
Deoxyguanosine



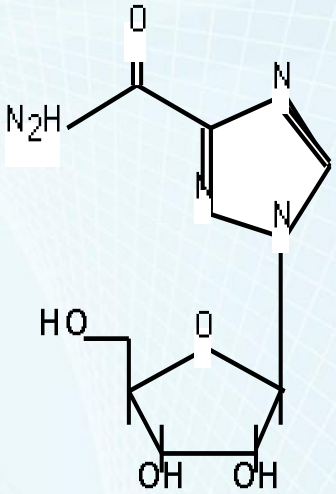
Acyclovir



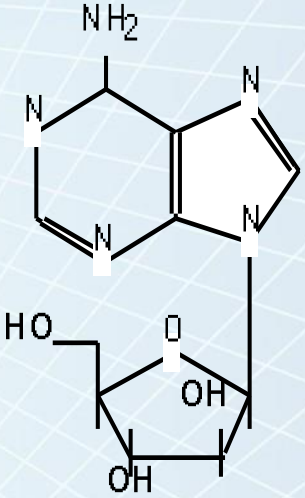
Ganciclovir



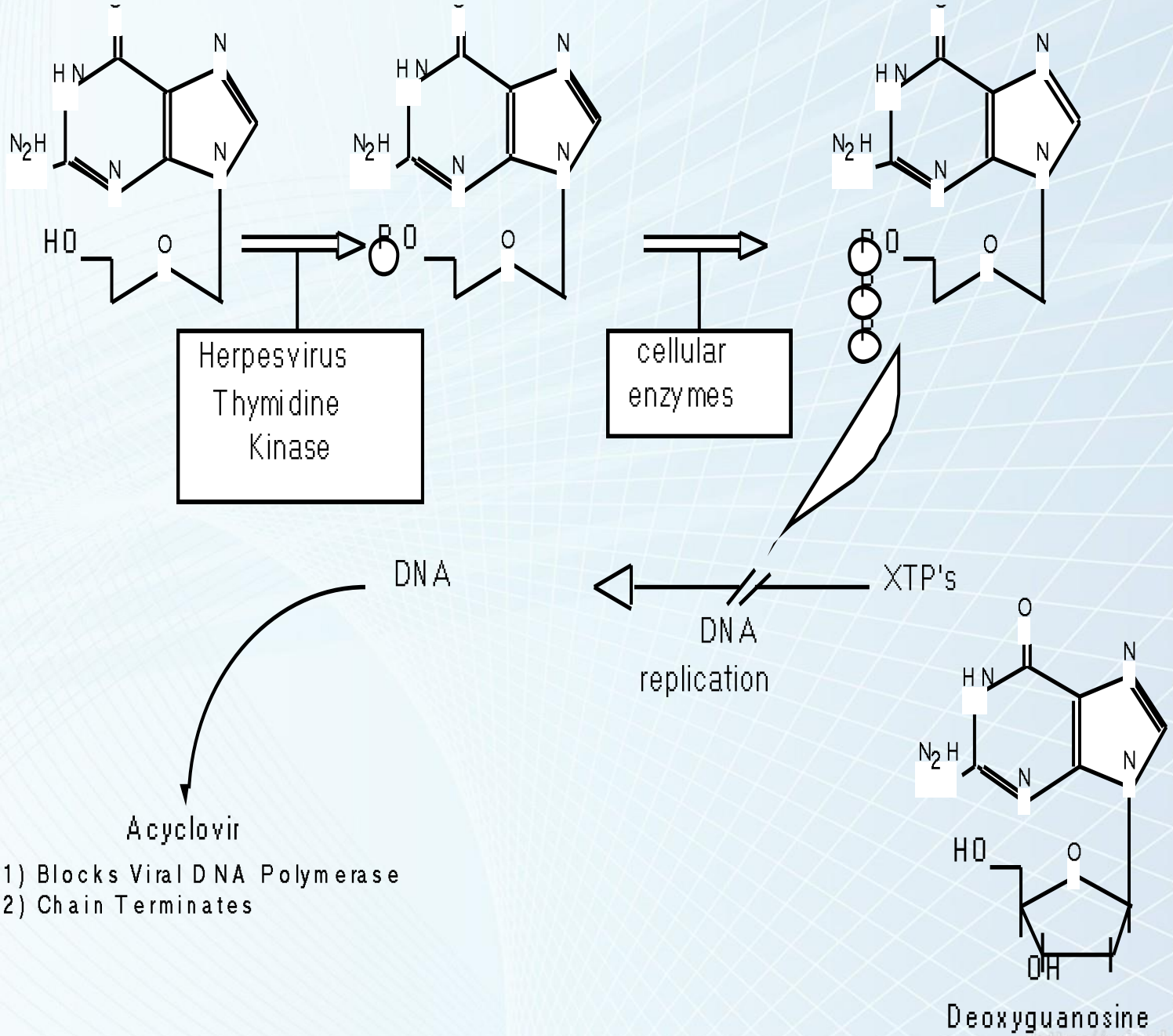
Deoxyadenosine



Ribavirin



Vidarabine


Herpesvirus
Thymidine
Kinase
cellular
enzymes
DNA
XTP's
DNA
replication
Acyclovir
1) Blocks Viral DNA Polymerase
2) Chain Terminates
Deoxyguanosine