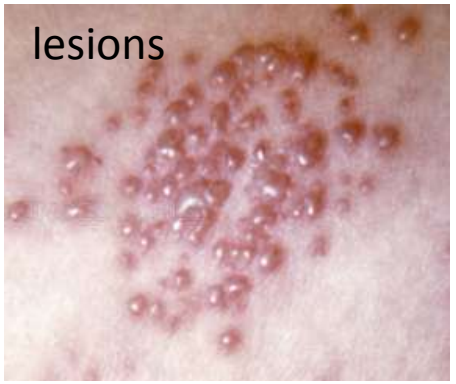
23.1.21

Viral diseases:
Herpes

Microbiology III

Herpes

- The term *herpes* Greek: *to creep*
- Occur as spreading cutaneous lesions of varied causes.
- **Herpes simplex** is a viral infection caused by the herpes simplex virus (HSV).
- Infections are categorized based on the part of the body infected.
- Oral herpes – HSV-1
- Genital herpes - HSV-2



Herpes viruses (HSV)

- The HSV are a unique group of enveloped DNA viruses that affect humans & animals.
- The HSV family includes over a 100 species.
- They show great diversity in pathology and biology.
- The only common feature is their property of establishing latent infection.

Classification of HSV:

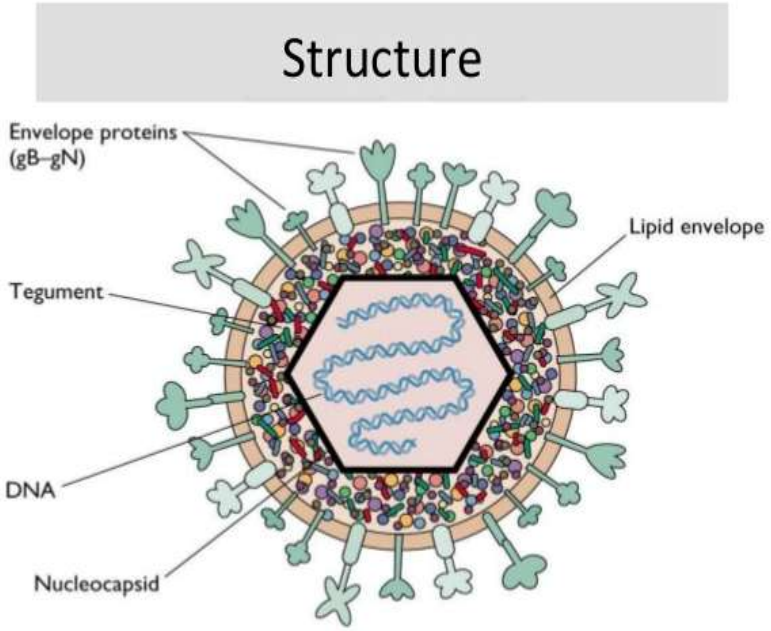
- The family *Herpesviridae* has been divided into three subfamilies:
  1. *Alpha herpesvirinae (*e.g. *Herpes simplex virus).*
  2. *Beta herpesvirinae (*e.g. *Cytomegalovirus).*
  3. *Gamma herpesvirinae (*e.g. *Epstein-Barr virus)*.

- Eight different HSV are known – primary host are humans.

Table 64–1. Human herpesviruses

Designation	*Subfamily*	*Common name*	*Abbreviation*
Human herpesvirus 1	Alpha	Herpes simplex virus type 1	HSV-1
Human herpesvirus 2	Alpha	Herpes simplex virus type 2	HSV-2
Human herpesvirus 3	Alpha	Varicella-zoster virus	VZV
Human herpesvirus 4	Gamma	Epstein-Barr virus	EBV
Human herpesvirus 5	Beta	Human cytomegalovirus	CMV
Human herpesvirus 6	Beta	Human B cell lymphotropic virus	HHV-6
Human herpesvirus 7	Beta	RK virus	HHV-7

Morphology of Herpesviruses



- Icosahedral capsid
- Size: 120-200nm in diameter
- Genome: linear ds DNA
- Enveloped with spikes
- Tegument: amorphous region btw envelope & capsid
- Replication and assembly occur in nucleus of infected cell

- Human is only natural host for HSV.
- It is also known as Human Herpesvirus (HHV).
- HSV are of two types:
- HSV1 and HSV2.
- Structurally and morphologically similar.
- Distinguished by:
  - Antigens - using type specific monoclonal Ab
  - Restriction endonuclease pattern of their genome
  - Site of lesions

Mode of transmission:

- Direct contact with lesion fluid or saliva
- Sexual transmission; genital herpes
- Perinatal route; child gets Herpes during birth from infected mother
- Congenital transmission; it is rare

Replication cycle:

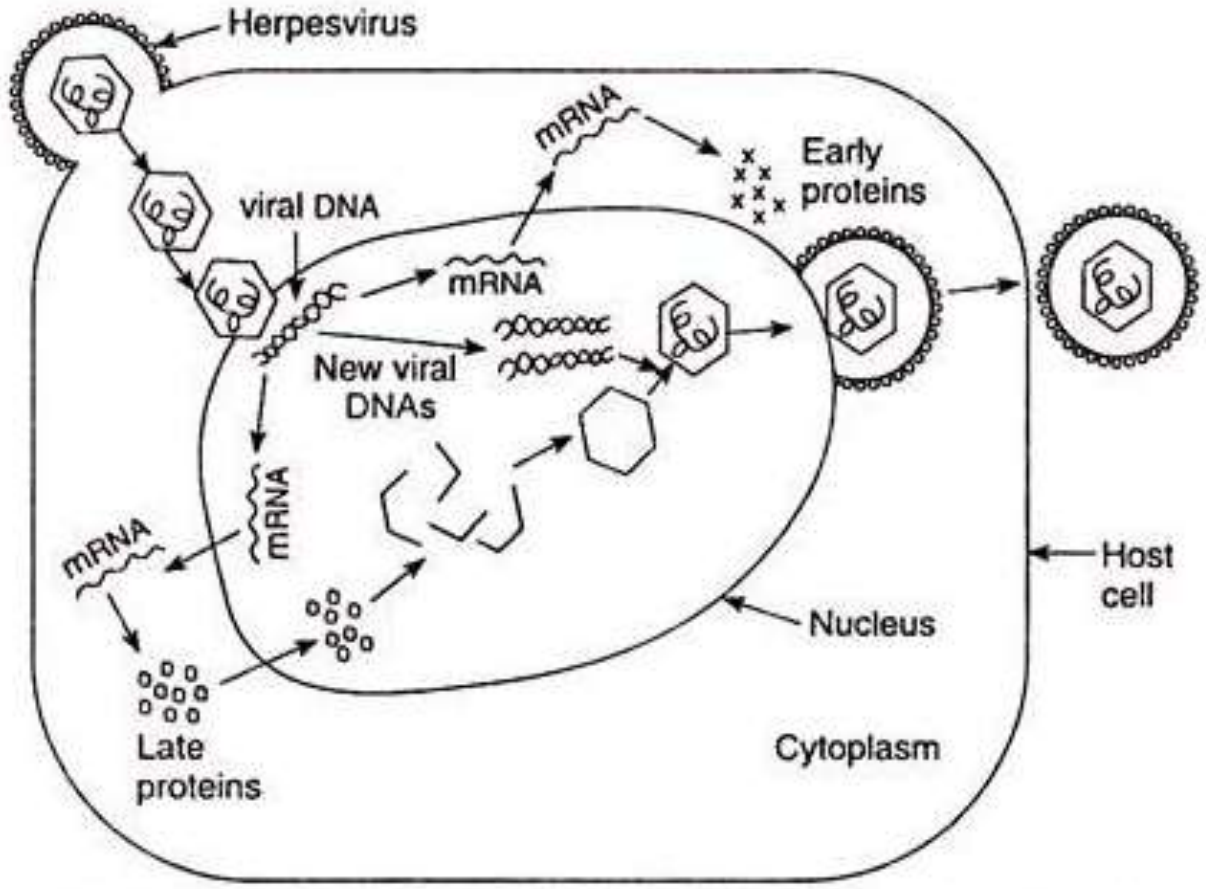


FIG. 14.6. Replication of herpesvirus genome and the formation of new viral particles.

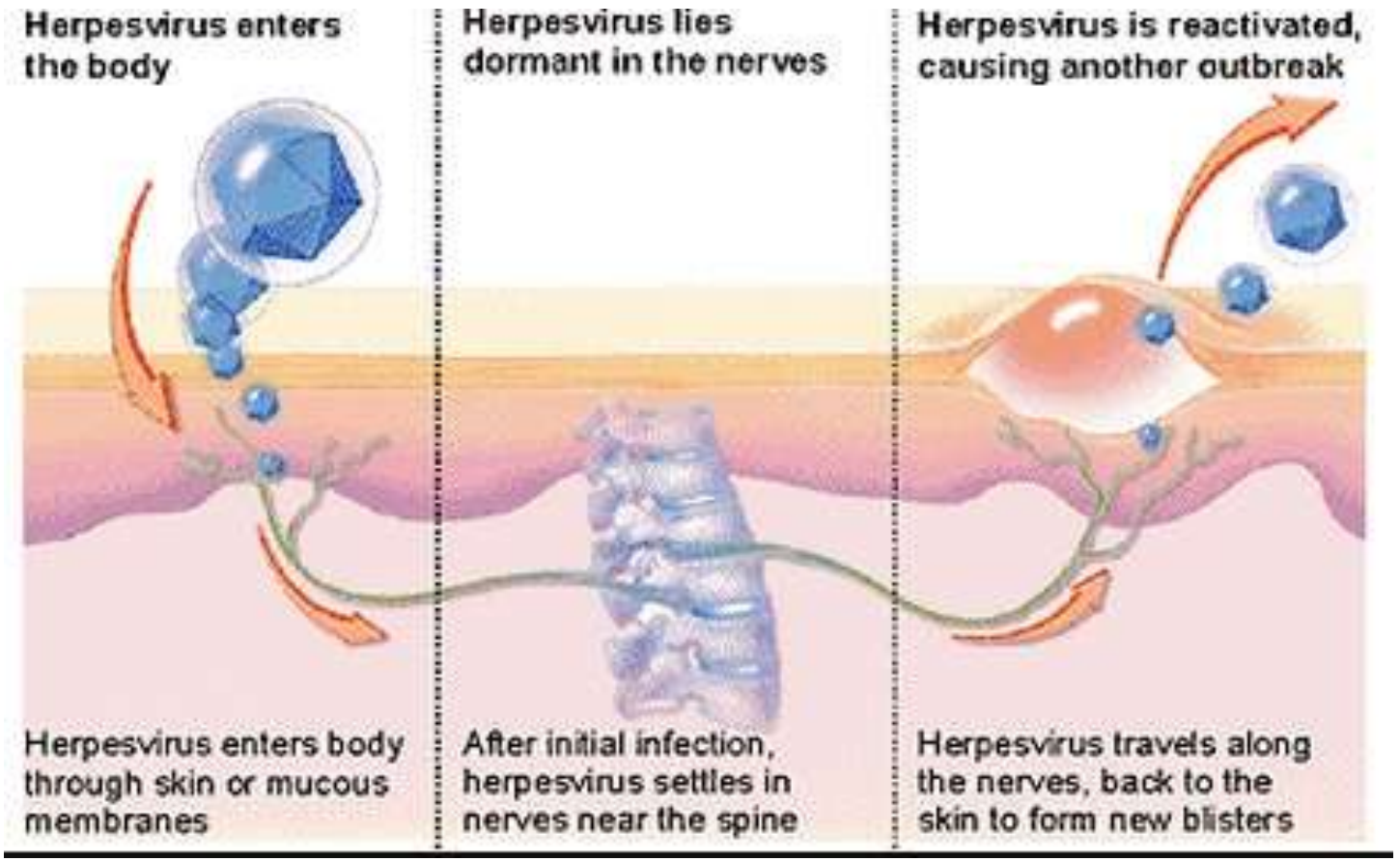
Pathogenesis:

- Virus enter through skin and mucus membrane and multiply locally.
- Virion interacts with specific cell surface receptor through its glycoprotein spike.
- HSV1 and HSV2 have several cell surface receptor
- They uses one of them for entry in host cell.

- Binding of glycoprotein → trigger fusion of viral envelope with host cell membrane
- fusion → release of nucleo-capsid → cytoplasm → transported to nucleus

- Nucleus of host cell ⟶ virus replication occur immediately.
- Viral gene will be transcribed ⟶ virus protein synthesis ⟶ Replication of virus genome ⟶ Assembly of progeny viruses.

Pathogenesis



1. Primary infection
2. latent infection
3. Recurrent infection

Primary infection:

- HSV1 infection:
- are usually limited to oropharynx
- transmitted by respiratory droplet or saliva whereas
- HSV2 infection:
- usually transmits by genital route.

- Primary infection of Herpes results -
- Vesicle formation under the layer of keratinized squamous epithelium cell.
- Vesicle – filled with fluid – contains:
  - multinucleated giant cells
  - eosinophilic intranuclear inclusions bodies
  - inflammatory cell
  - cellular debris

- After primary infection – virus invades – local nerve ending
- Travel from retrograde intra axonal flow to sensory root ganglia where they further multiply.
- The virus settle within neuron in sensory ganglia and remain latent.

Latent infection:

- During latency – no viral particles are produced.
- Does not causes any demonstrable damage in neuron.
- This latency phase – reactivated periodically in some individuals
- Causes recurrent oral and genital lesion.

Recurrence herpes:

- The virus travels back – neuron and multiply – mucosal epithelial cell – producing lesion at the same spot each time.
- They are less severe, more localized and of shorter duration than that of primary infection due to presence of past immune response.

Clinical manifestation:

- Cutaneous or skin infection
- Mucosal or Oropharyngeal infection
- Ophthalmic or eye infection
- Nervous system infection
- Visceral herpes
- Genital herpes
- Congenital herpes

❑ Cutaneous or skin infection:

- It is characterized by fever blister on face, cheeks, chin, around mouth and forehead.

❑ Mucosal or Oropharyngeal infection: (mouth)

- It is characterized by vesicular lesion on oral mucosa, tongue and lips.
- The lesions subsequently rupture and coalesce together leaving behind ulcerated plaques.
- Pharyngitis and tonsillitis manifests with fever, malaise, headache and sore throat.

- Ophthalmic or eye infection:
  - Follicular conjunctivitis
  - Corneal blindness
- Nervous system infection:
  - Herpes encephalitis; caused by HSV-1
  - Herpes meningitis; caused by HSV-2
- Visceral herpes:
  - Pneumonitis
  - Hepatitis

- Genital herpes:
  - Mostly caused by HSV-2
  - Primary genital herpes is asymptomatic caused by both HSV-1 and HSV-2.
  - Recurrent is more frequent in HSV-2
  - Characterized by fever, pain, dysuria, mucoid urethral discharge with enlarged inguinal lymph node
- Congenital herpes:
  - Caused by HSV-2
  - Manifested as infection of eye, mouth, skin and more commonly a disseminated infection with multiple organ involvement.

Laboratory diagnosis:

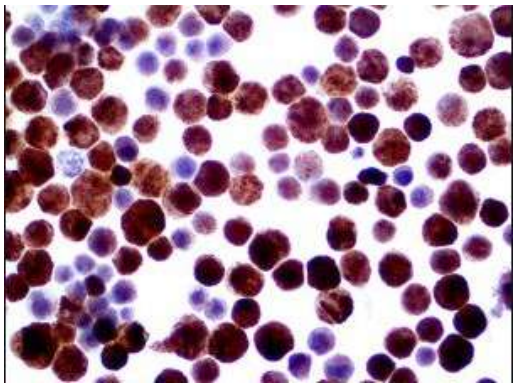
Specimens:

- Saliva
- vesicle fluids
- conjunctival fluids
- corneal scrapping
- skin swab
- CSF

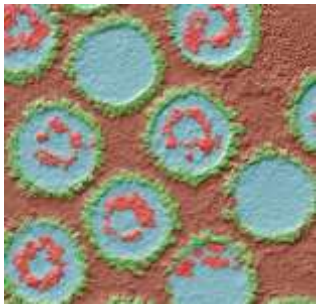
- Depends upon site of infection

Microscopy:

- Tzanck smear preparation:
- Smear is prepared from lesion and stained with 1% aqueous solution of toluidine blue for 15 seconds.
- Multinucleated giant cells are visualized in positive smear.
- Giemsa stain can also be used to see inclusion bodies.

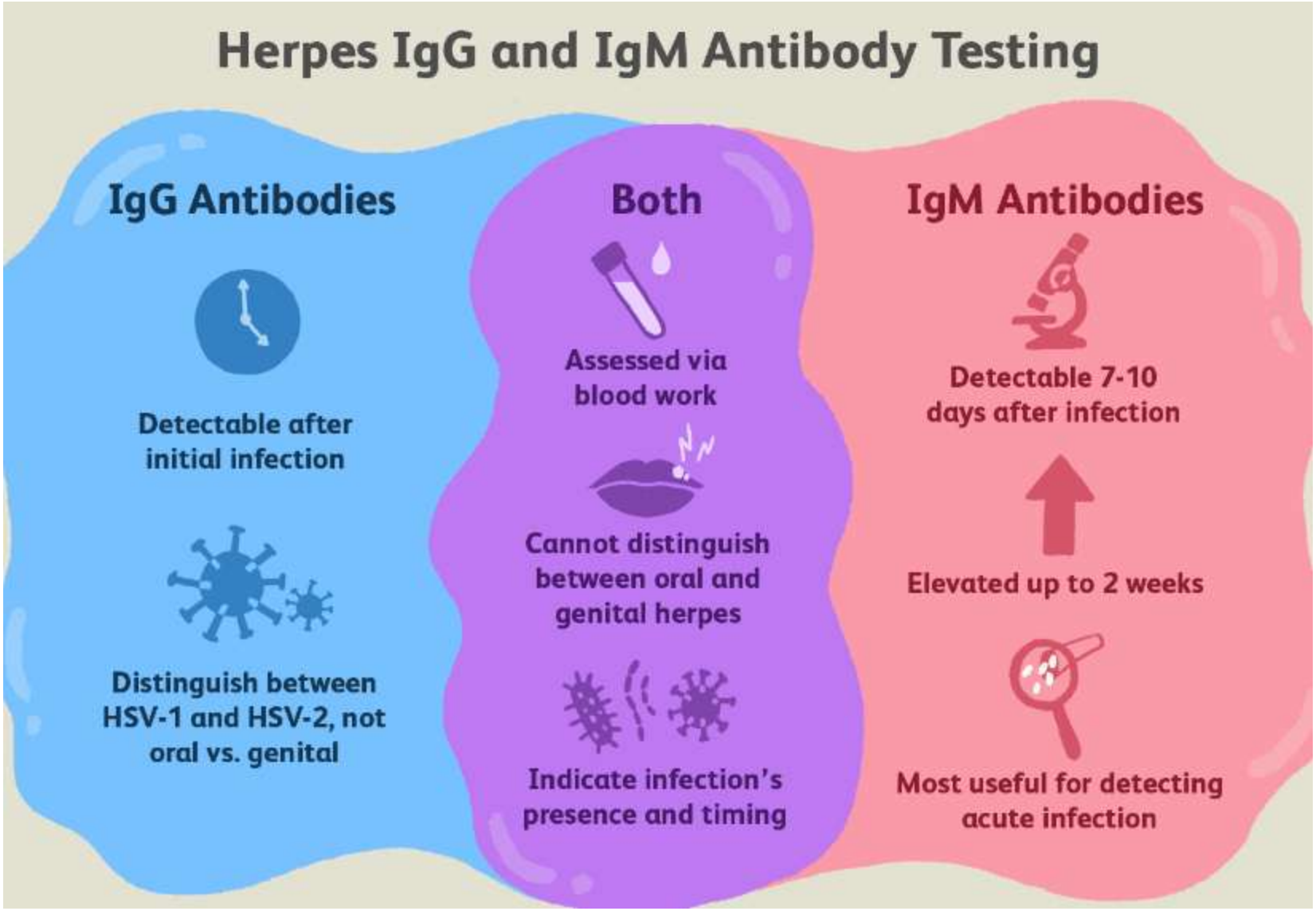


Electron microscope



- Virus Culture:
  - Primary human embryonic kidney cell line culture
  - Hela cell
  - Human amnion
  - Hep2
- Cytopathic effect should be visualized within 1-3 days.
- Serology:
  - ELISA
  - Neutralization test
  - Complement fixation test (CFT)
  - Immunofluorescent test

Serology test



- Molecular diagnosis:
- **PCR**, DNA probe

❑Treatment:

- Acyclovir: orally or parenteraly
  - Ganciclovir
  - Viderabine
  - Famiciclovir

  } orally
- Idoxuvidine: topically
  - eye
  - skin infection

Thank you