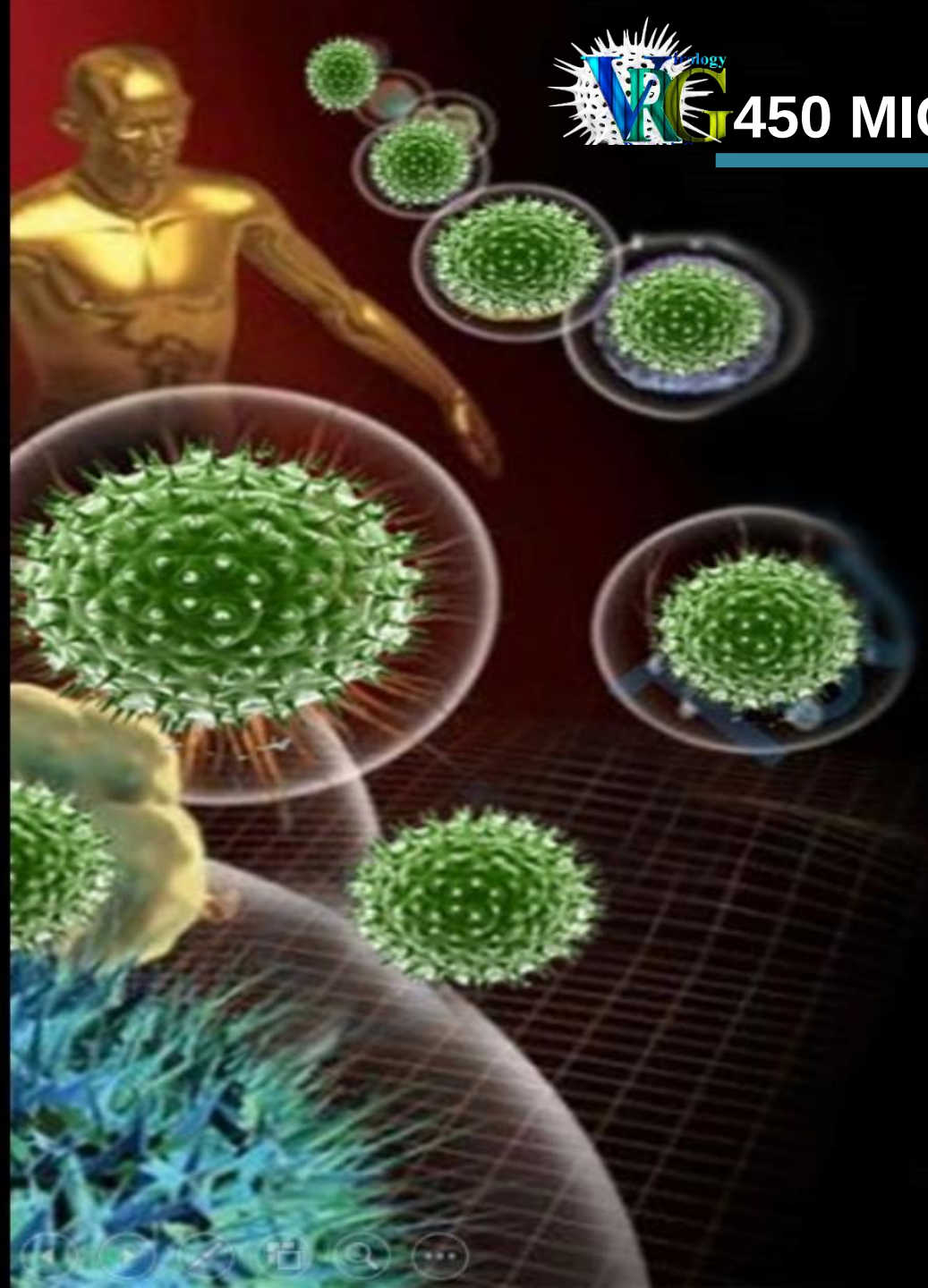


Lecture six

Mechanisms of Virus Infection and Spread

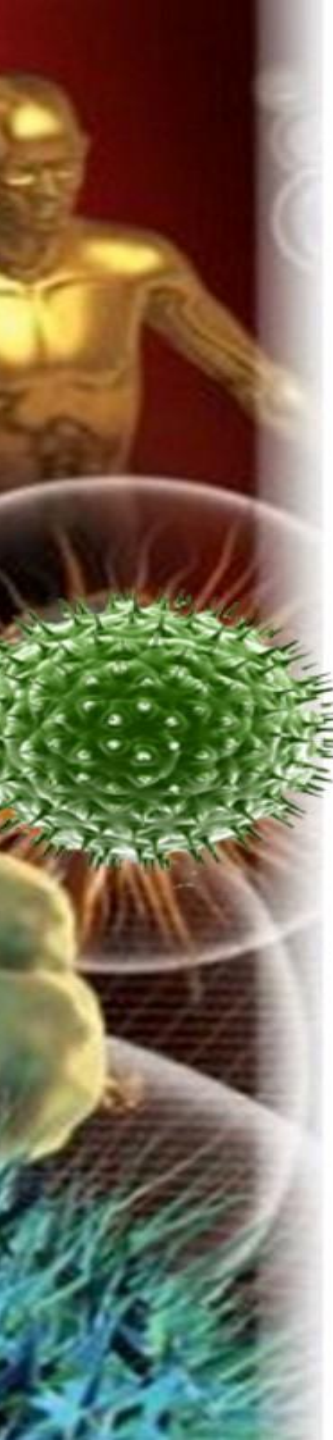
B-Virus Spread

By

Dr. Mohamed A. Farrag

Assistant professor of Virology

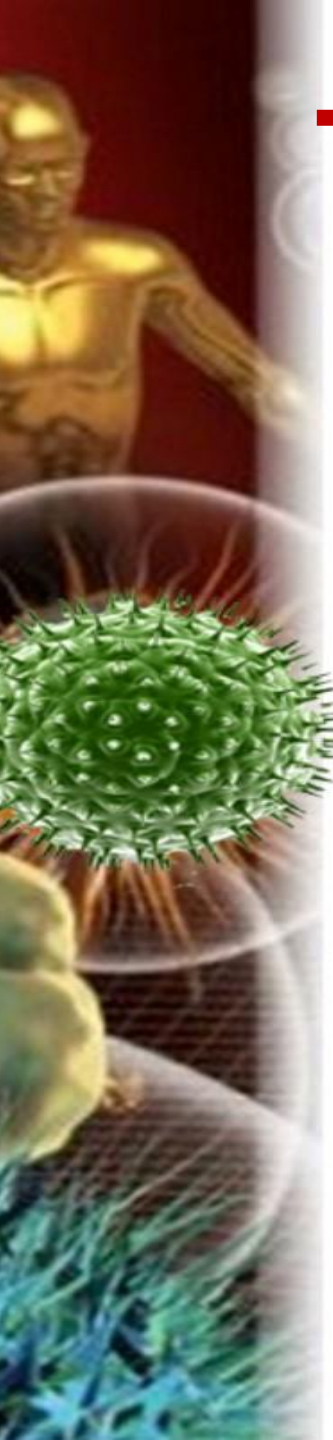
Botany and Microbiology Dept., KSU



Learning outcomes

By the end of this lecture students should

- Recognize the sequential steps of virus infection and spread. √
- Recognize different portals of virus entry into human body. √
- Define viremia and its sources and types.
- Recognize different portals of virus shedding.

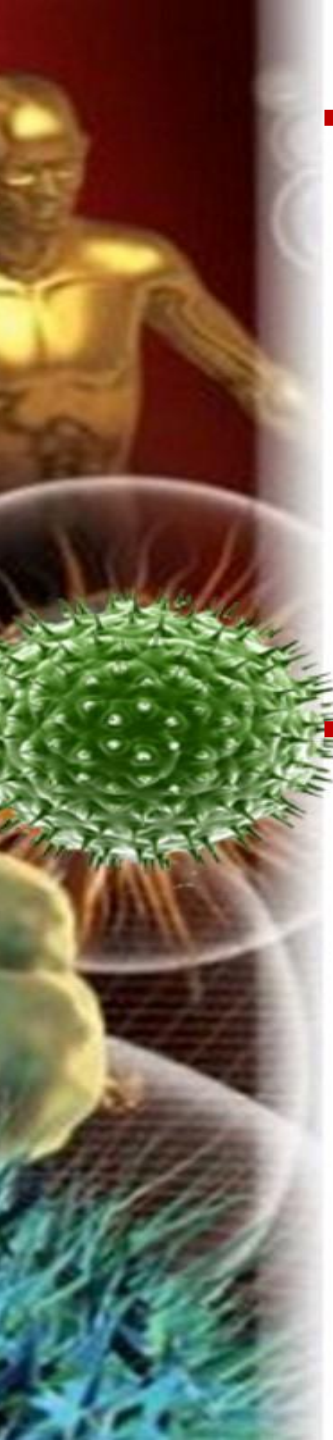


The Sequential Steps in Viral Infection

1. Virus Entry √
2. Virus Spread

   2.1. Viremia, types and sources.

3. Virus Shedding.
4. Virus Transmission



Step 2: Spread

Local Spread

- Local spread occurs by infection of contiguous cells and can result in lesions such as the cold sores produced by herpes simplex virus.

Viremia

- In the blood, a particular virus circulates either free in the plasma or is cell-associated.
- Most viremias are acute, lasting no more than 1–2 weeks, but certain viruses are able to evade immune defenses and persist in the blood for months or years.

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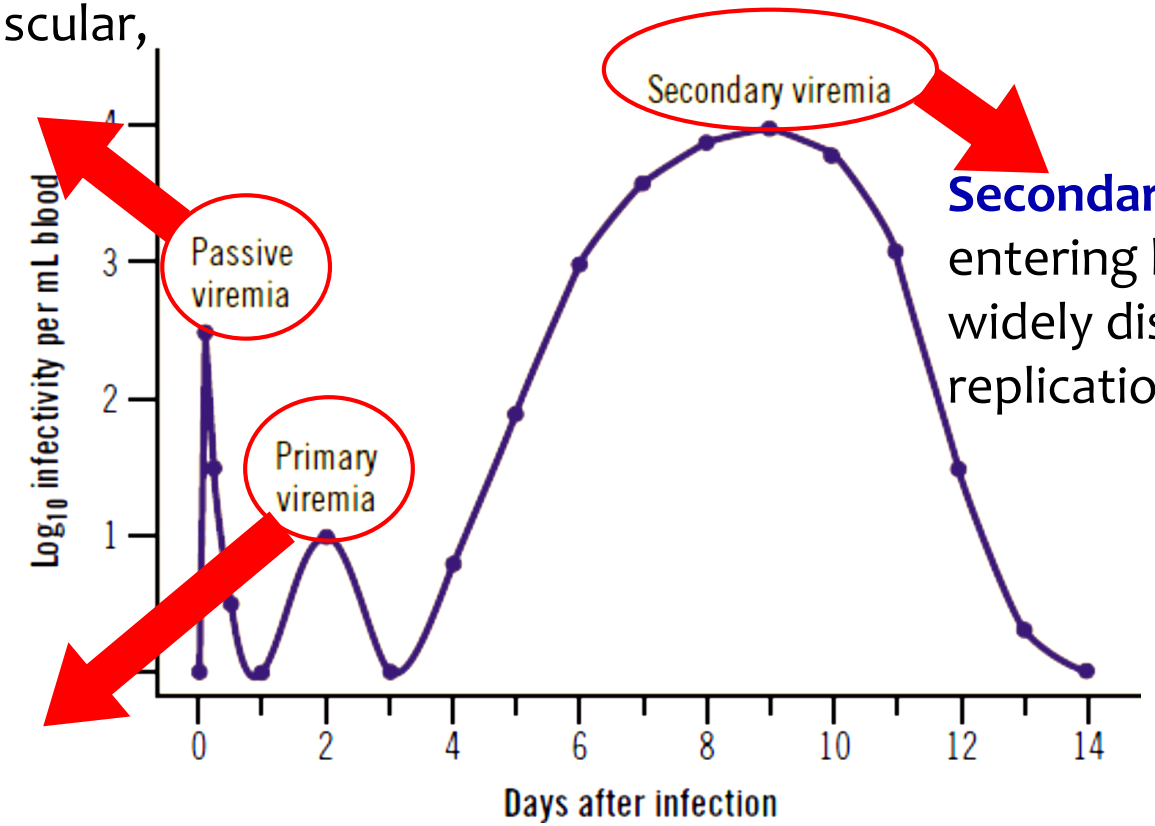
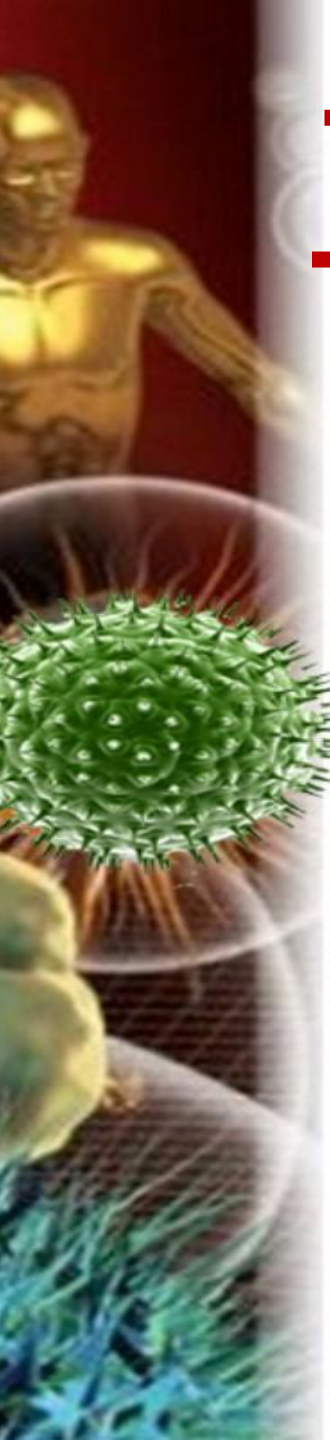
Stages in acute viremia

Passive viremia: un-replicated inoculum entering the circulation after intraperitoneal, intramuscular, or intravenous injection.
Last for only few hours.



Secondary viremia: virus entering blood from widely dispersed sites of replication.

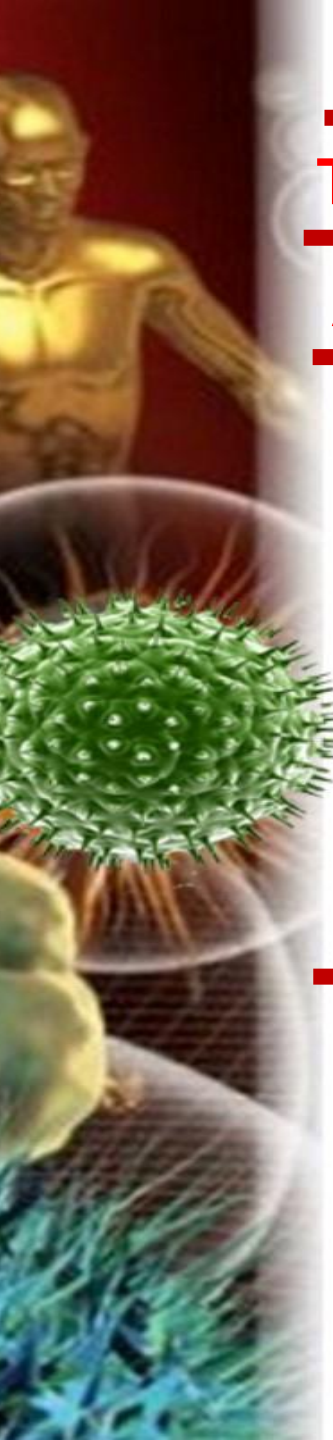
Primary viremia: virus entering blood after local infections. The virus replicates locally at the site of entry or in the draining regional lymph node, then a brief active primary viremia may occur. lasting for 1–2 days.



Step 2: Spread

Sources of viremia

- Those viruses that replicate in regional lymph nodes are shed into efferent lymphatics and are transported via the thoracic duct into the circulation.
- Some viruses replicate in the vascular endothelium and are released directly into the circulation.
- A number of viruses replicate in monocytes, B cells or T cells to create a cell-associated viremia; in some cases, virus may also be released from these cells to produce a concomitant plasma viremia.
- Viruses that replicate in other tissues, such as striated muscle or liver, may enter the vascular compartment by crossing endothelium into capillaries or via the draining lymphatics.



Step 2: Spread

Types of Viremia

A – Plasma viremia

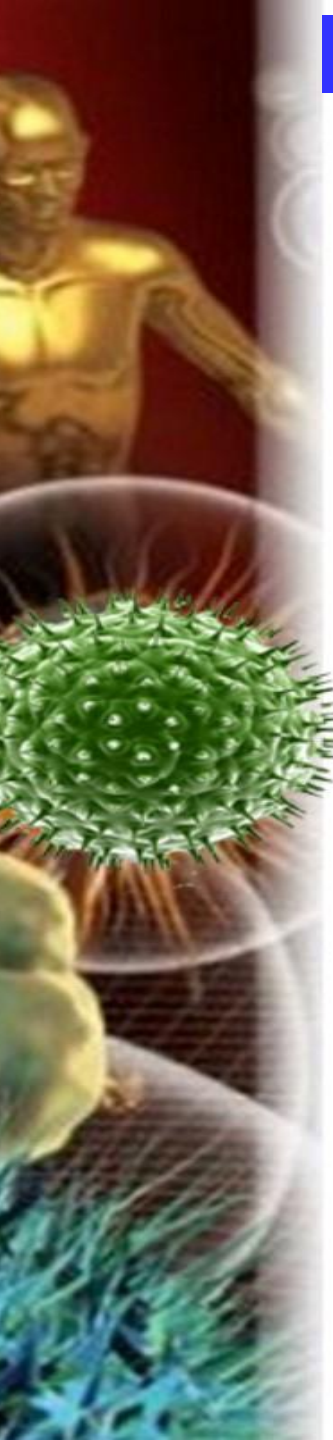
- It often appears within a week after infection, lasts for 1–2 weeks and comes to an abrupt termination concomitant with the appearance of circulating antibody.

- Plasma viremia is dynamic: virus continually enters the circulation and is continually being removed. Viral clearance is mediated primarily by the sessile macrophages of the liver, spleen and lung, which monitor the circulation for foreign particulates.

B – Cell-associated viremia

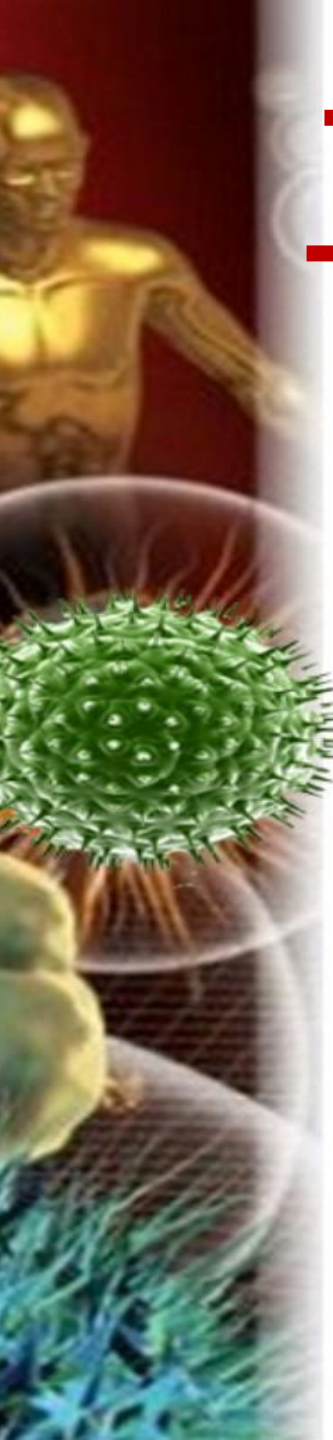
- Cell-associated viremias may persist over months to years, although the virus titers are often low.

- In such case, viral genome is latent or is so poorly expressed. Consequenlty, virus-infected cells in the blood cannot be recognized by the immune system.



Representative viruses that replicate in blood cells

Cell type	Virus family	Representative example	Duration of viremia
Monocytes	Flaviviridae	Dengue viruses	Acute
	Togaviridae	Rubella virus	Acute
	Coronaviridae	Mouse hepatitis virus	Acute
	Orthomyxoviridae	Influenza viruses	Acute
	Paramyxoviridae	Measles virus	Acute
	Arenaviridae	LCMV	Persistent
	Retroviridae	HIV	Persistent
	Herpesviridae	Cytomegalovirus	Persistent
	Poxviridae	Ectromelia virus	Acute
B lymphocytes	Retroviridae	Murine leukemia virus	Persistent
	Herpesviridae	Epstein-Barr virus	Persistent
T lymphocytes	Retroviridae	HIV	Persistent
		HTLV-I	Persistent
	Herpesviridae	Human herpes viruses 6, 7	Acute
Erythroblasts	Reoviridae	Colorado tick fever virus	Acute



Step 2: Spread

Spread of virus from blood into tissues

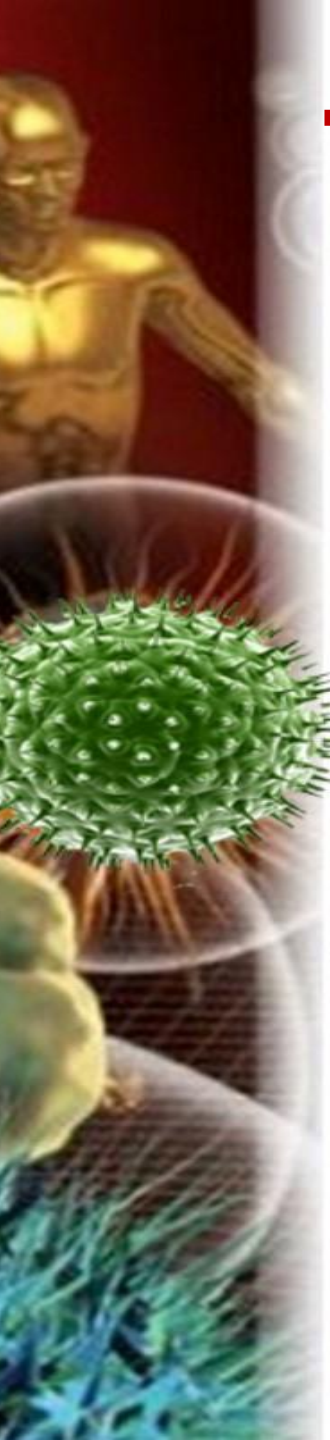
- Capillary fenestration, certain blood-borne viruses, such as mumps, LCMV and visna viruses, probably cross the blood into the cerebrospinal fluid by this pathway.

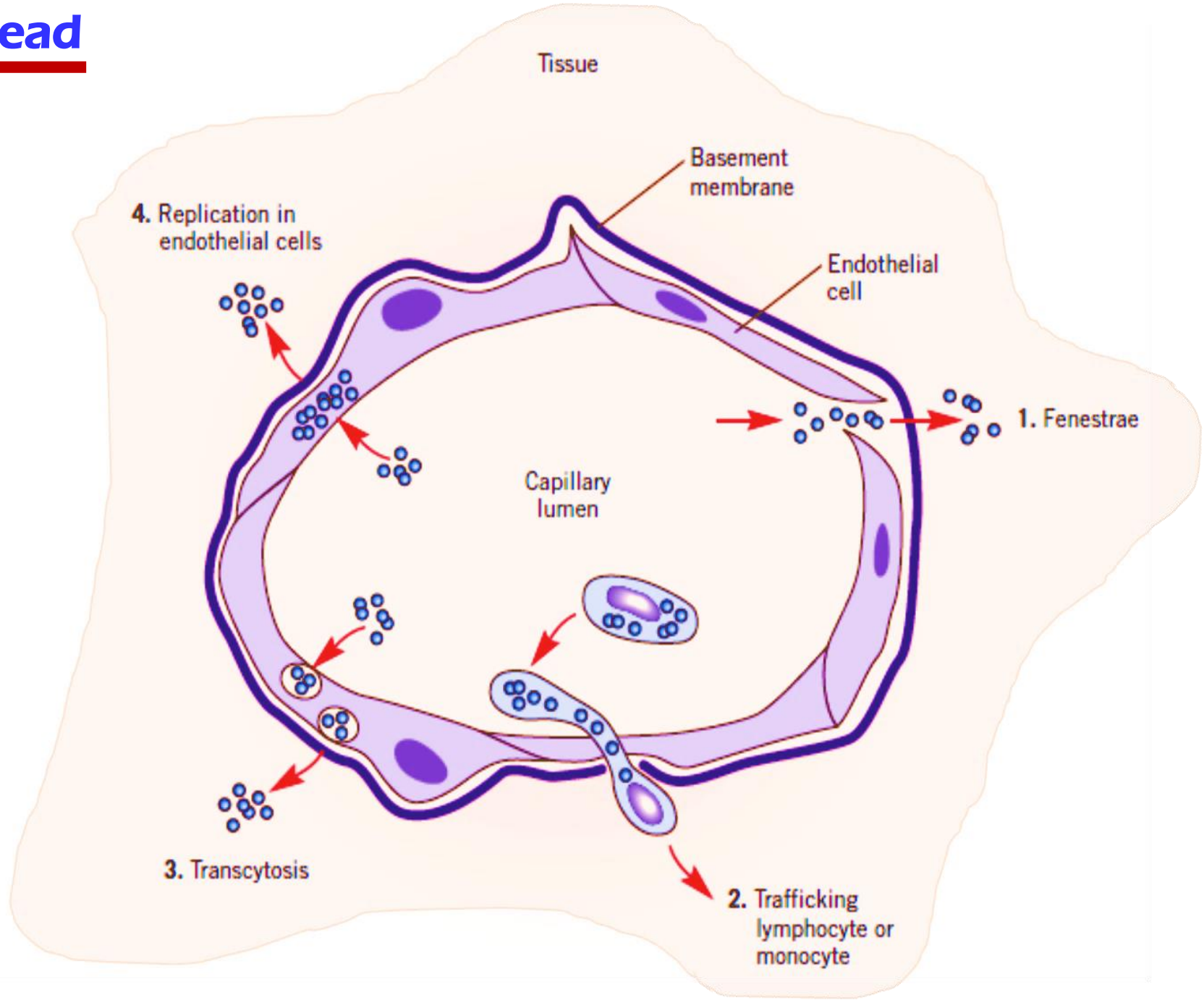
- Some viruses have been visualized to transit the endothelial cell lining of capillaries by a process of endocytosis, transcytosis and exocytosis, to be released from the basal surface of endothelial cells.

- Viruses that infect lymphocytes or monocytes can be carried by these cells to distant organs, a process called “Trojan horse” mechanism.

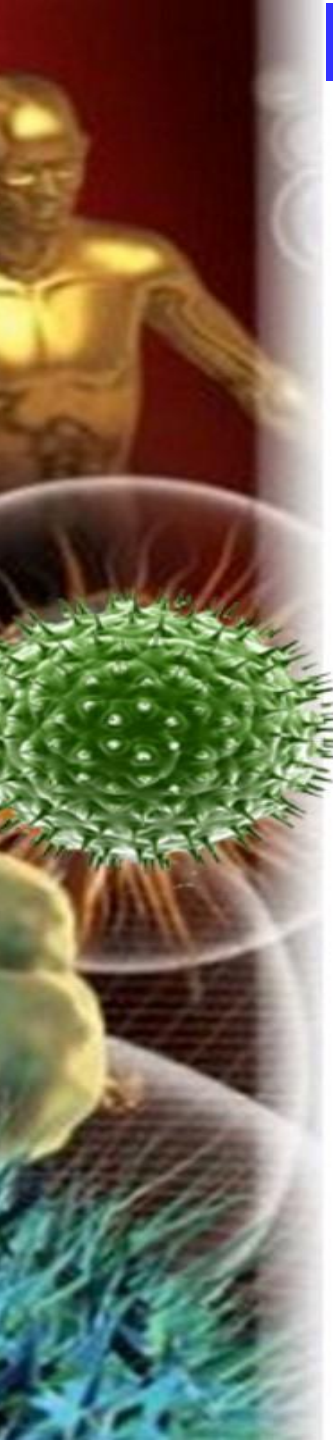
- Example: HIV is carried into the central nervous system by CD4+ lymphocytes or monocytes with subsequent infection of the microglia, which are the resident macrophages of the brain.

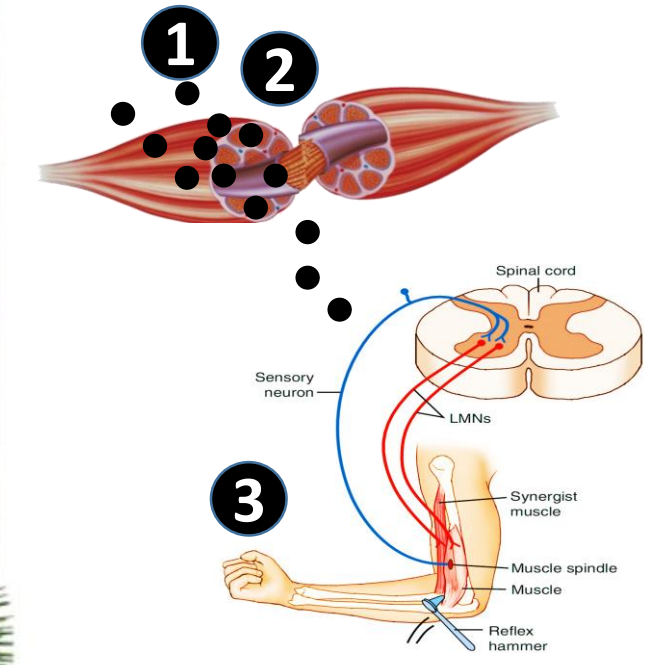
Step 2: Spread

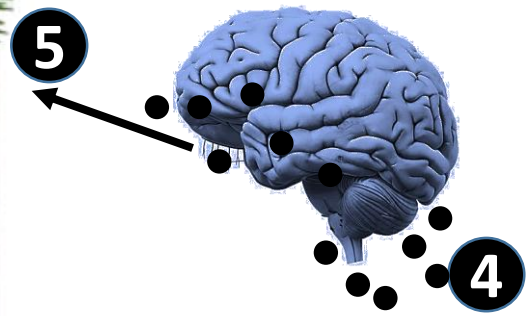


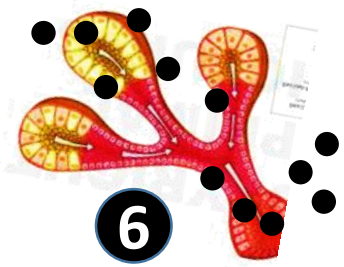


The spread of Rabies virus, an example of a virus that spreads by the neural route only.









Day 0

1. Virus entry

- by bite of rabid animal
- infected saliva is injected.

Day 1-60

2. Striated muscle

- virus replicates in myocytes

Day 10-60

3. Peripheral nerves

- virus enters nerve ending.
- nucleocapsid carried by fast axoplasmic flow to spinal cord

Day 12-70

4. Central nervous system

- virus travels along neural processes, spreads and replicates
- neuronal dysfunction.
- clinical rabies, death

Day 30-70

5. Peripheral nerves

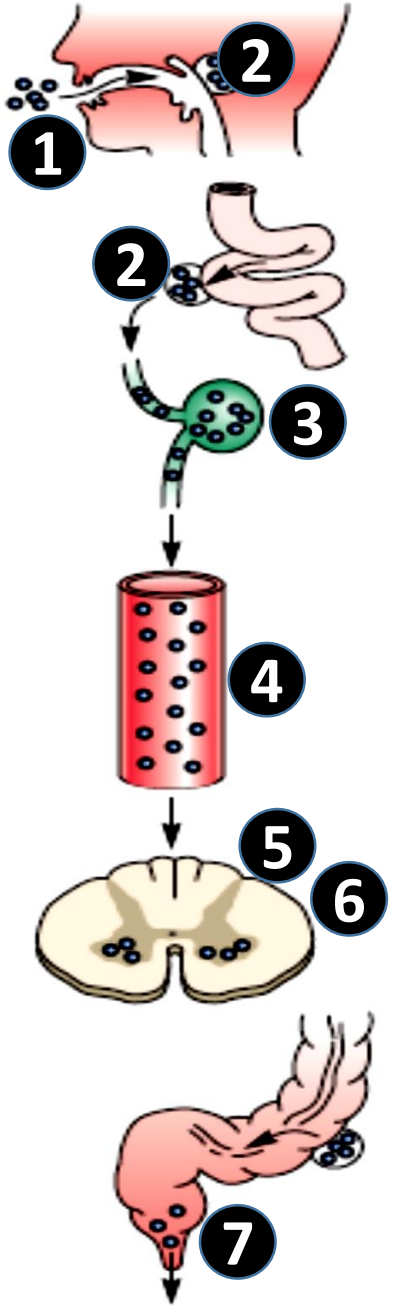
- virus travels along peripheral nerves from CNS.
- invades salivary gland

Day 40-70

6. Salivary gland

- virus replicates in acinar cells.
- virus is discharged in saliva

The spread of Poliovirus, an example of a virus that disseminates via the blood.



Day 0

1. Virus ingested

Day 0-3

2. GUT ASSOCIATED LYMPHOID TISSUE

• tonsils, Peyer's patches. • virus invades (via M cells?) • replicates in monocytes

Day 3-5

3. REGIONAL LYMPH NODES

• replicates in monocytes

Day 3-5

4. BLOOD

• plasma viremia

Day 8-12

5. BLOOD BRAIN BARRIER

• virus crosses endothelium

Day 10-30

6. SPINAL CORD

• virus replicates in anterior horn cells
• cell destruction
• paralysis

Day 5-45

7. GUT

• virus excreted in feces


Thank
You