# Introduction to Microbiology

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Lecture 32

# Viral classification

- Knowledge of the structural **(size and morphology)** and genetic **(type and structure of nucleic acid)** features of a virus provides insight into how the virus replicates, spreads, and causes disease.

- *The most consistent and current means of classification is by physical and biochemical characteristics, such as size, morphology (e.g., presence or absence of a membrane envelope), type of genome, and means of replication*

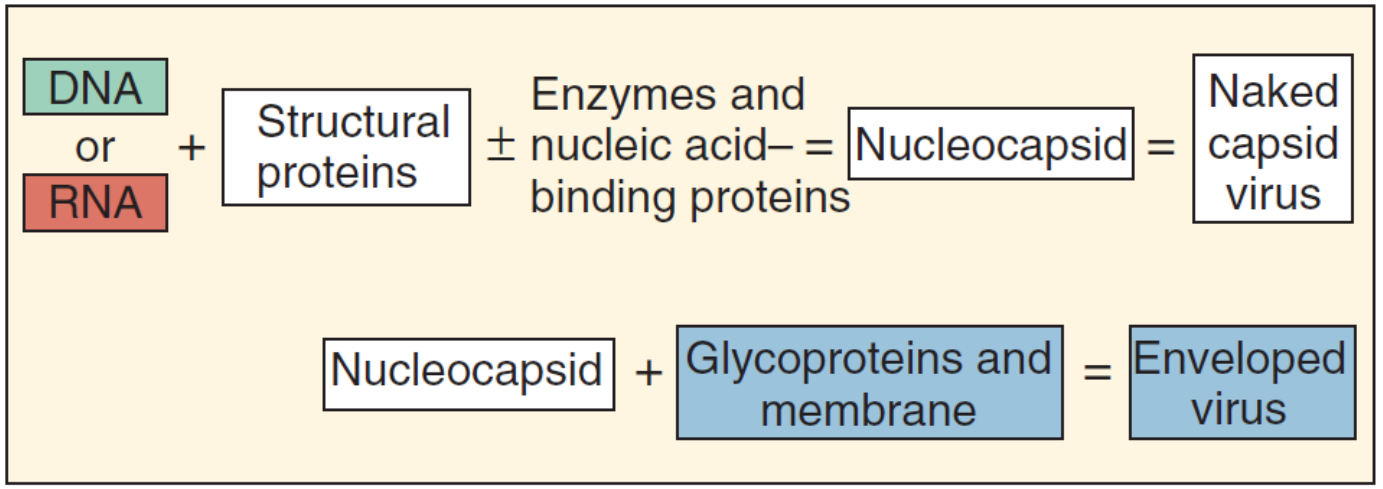
**Box 36-3 Means of Classification and Naming of Viruses**

Structure: size, morphology, and nucleic acid (e.g., picornavirus [small RNA], togavirus)
Biochemical characteristics: structure and mode of replication*
Disease: encephalitis and hepatitis viruses, for example
Means of transmission: arbovirus spread by insects, for example
Host cell (host range): animal (human, mouse, bird), plant, bacteria
Tissue or organ (tropism): adenovirus and enterovirus, for example

*This is the current means of taxonomic classification of viruses.

# Viral structure

- The **virion** (the virus particle) consists of a nucleic acid **genome** packaged into a protein coat **(capsid)** or a membrane **(envelope)** The clinically important viruses range from 18 nm (parvoviruses) to 300 nm (poxviruses)



# Viral structure

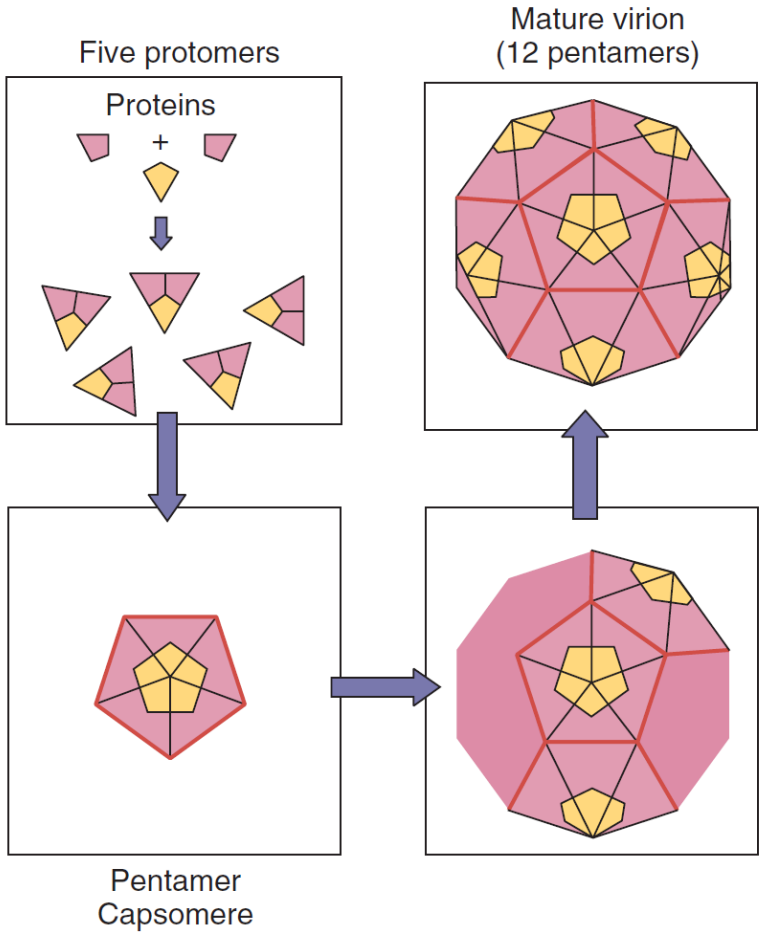



**FIGURE 36-5** Capsid assembly of the icosahedral capsid of a picornavirus. Individual proteins associate into subunits, which associate into protomers, capsomeres, and an empty procapsid. Inclusion of the (+) RNA genome triggers its conversion to the final capsid form.

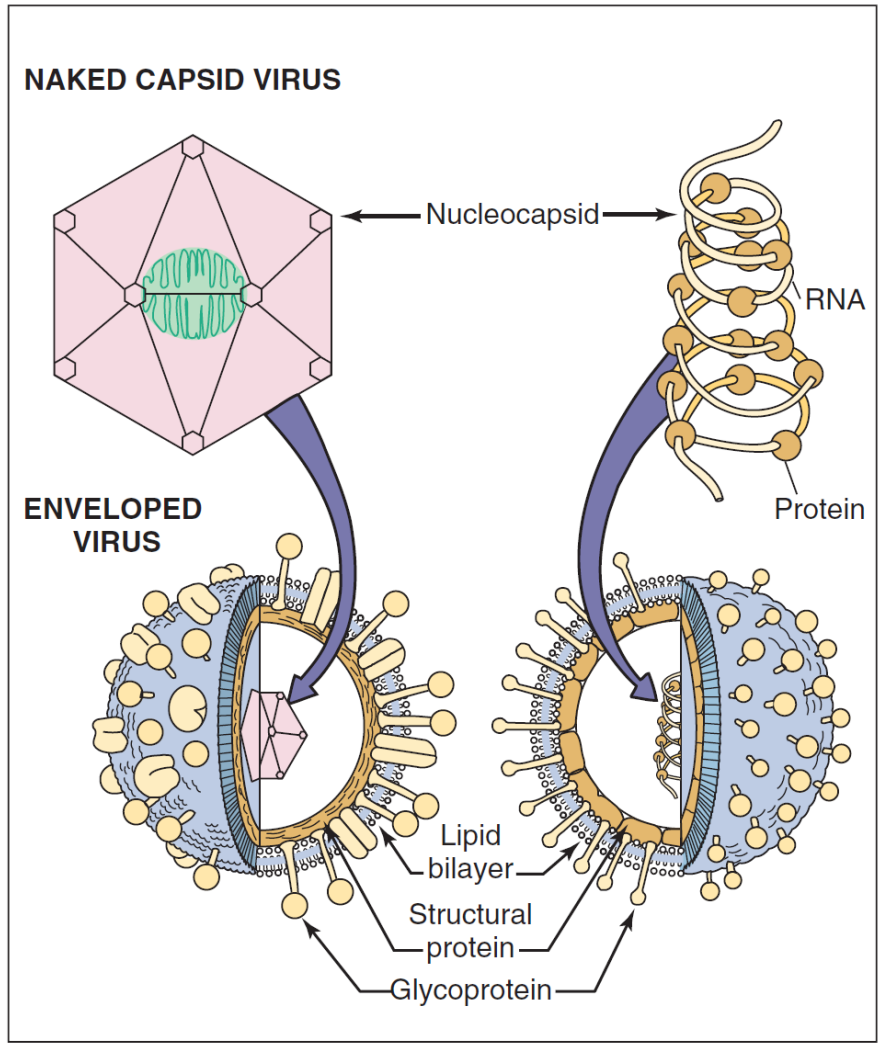



**FIGURE 36-4** The structures of a naked icosahedral capsid virus *(top left)* and enveloped viruses *(bottom)* with an icosahedral *(left)* nucleocapsid or a helical *(right)* ribonucleocapsid. Helical nucleocapsids are always enveloped for human viruses.

# Viral structure

## Box 36-4 Virion Structure: Naked Capsid

**Component**

Protein

**Properties***

Is environmentally stable to the following:

- Temperature
- Acid
- Proteases
- Detergents
- Drying

Is released from cell by lysis

**Consequences***

Can be spread easily (on fomites, from hand to hand, by dust, by small droplets)

Can dry out and retain infectivity

Can survive the adverse conditions of the gut

Can be resistant to detergents and poor sewage treatment

Antibody may be sufficient for immunoprotection

*Exceptions exist.

## Box 36-5 Virion Structure: Envelope

**Components**

Membrane

Lipids

Proteins

Glycoproteins

**Properties***

Is environmentally labile—disrupted by the following:

- Acid
- Detergents
- Drying
- Heat

Modifies cell membrane during replication

Is released by budding and cell lysis

**Consequences***

Must stay wet

Cannot survive the gastrointestinal tract

Spreads in large droplets, secretions, organ transplants, and blood transfusions

Does not need to kill the cell to spread

May need antibody and cell-mediated immune response for protection and control

Elicits hypersensitivity and inflammation to cause immunopathogenesis

*Exceptions exist.

# Pathogenesis of Viral Diseases

- The outcome of a viral infection is determined by the nature of the **virus-host interaction** and the **host's response** to the infection.

- Viruses encode activities **(virulence factors)** that promote the efficiency of viral **replication**, viral **transmission**, access and **binding** of the virus to target tissue, or **escape** of the virus from host defences and immune resolution.

- A particular disease may be **caused by several viruses** that have a common tissue preference. (hepatitis—liver, encephalitis—CNS)

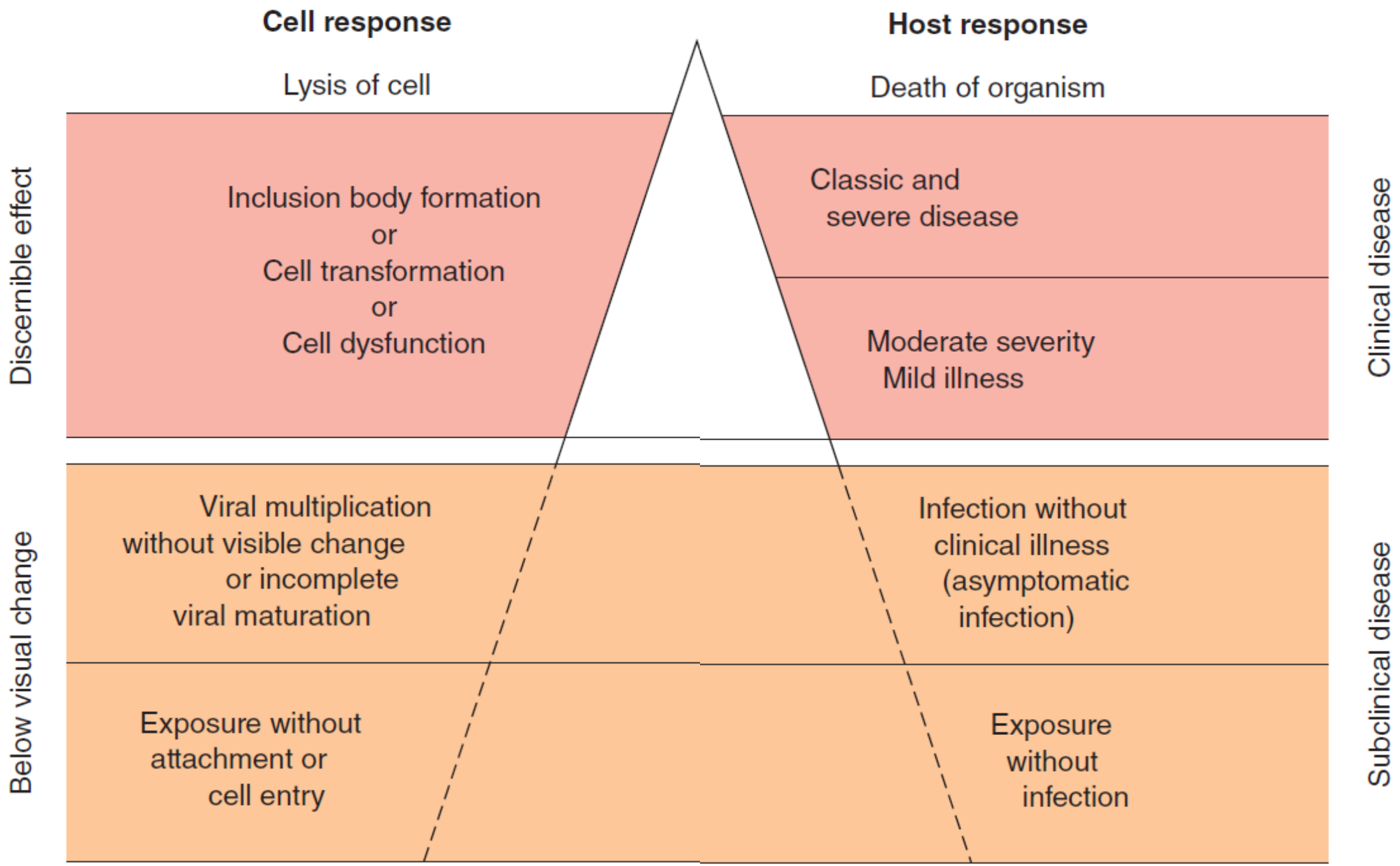
- A particular virus may cause **several different diseases** herpes simplex virus type 1 (HSV-1) can cause gingivostomatitis, pharyngitis, herpes labialis (cold sores), genital herpes.

- A particular virus **may cause no symptoms at all**.

The outcome of a viral infection is determined by the nature of the **virus-host interaction** and the **host's response** to the infection.

| Nature of the Disease |
| --- |
| Target tissue |
| Portal of entry of virus |
| Access of virus to target tissue |
| Tissue tropism of virus |
| Permissiveness of cells for viral replication |
| Pathogenic activity (strain) |

| Severity of Disease |
| --- |
| Cytopathic ability of virus |
| Immune status (naïve or immunized) |
| Competence of the immune system |
| Prior immunity to the virus |
| Immunopathology |
| Virus inoculum size |
| Length of time before resolution of infection |
| General health of the person |
| Nutrition |
| Other diseases influencing immune status |
| Genetic makeup of the person |
| Age |


Cell response
Lysis of cell
Host response
Death of organism
Discernible effect
Below visual change
Inclusion body formation
or
Cell transformation
or
Cell dysfunction
Classic and
severe disease
Moderate severity
Mild illness
Viral multiplication
without visible change
or incomplete
viral maturation
Infection without
clinical illness
(asymptomatic
infection)
Exposure without
attachment or
cell entry
Exposure
without
infection
Clinical disease
Subclinical disease

# Steps in Viral Pathogenesis

A. **Entry and Primary replication**

B. **Viral Spread and Cell Tropism**

C. **Cell Injury and Clinical Illness**

D. **Recovery from Infection**

E. **Virus Shedding**

**Box 37-2 Progression of Viral Disease**

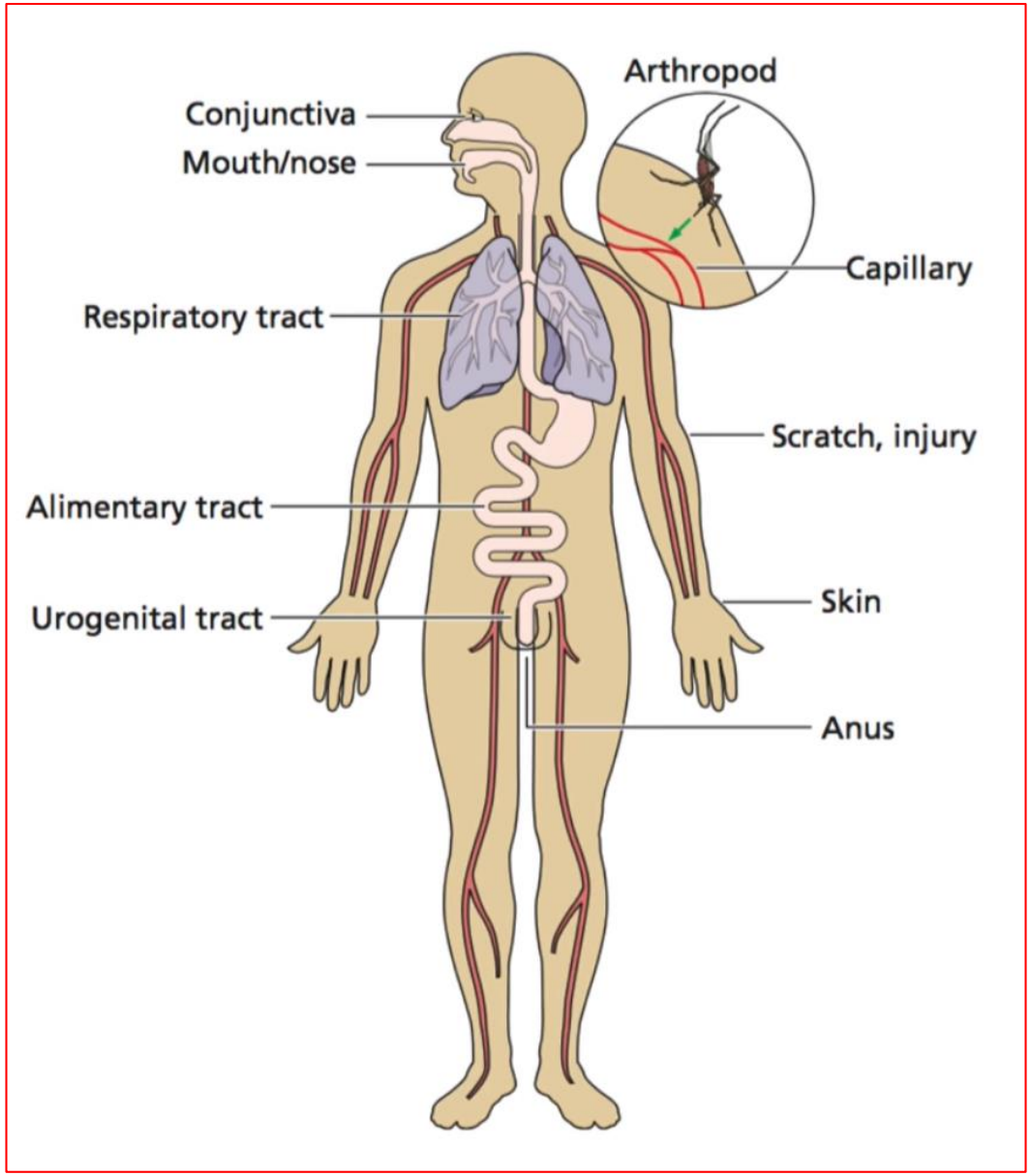
1. **Acquisition** (entry into the body)
2. Initiation of infection at a primary site
3. Activation of innate protections
4. An **incubation period,** when the virus is amplified and may spread to a secondary site
5. Replication in the **target tissue,** which causes the characteristic disease signs
6. **Host responses** that limit and contribute (immunopathogenesis) to the disease
7. Virus production in a tissue that releases the virus to other people for **contagion**
8. **Resolution** or **persistent infection/chronic disease**

# A. Entry and Primary replication

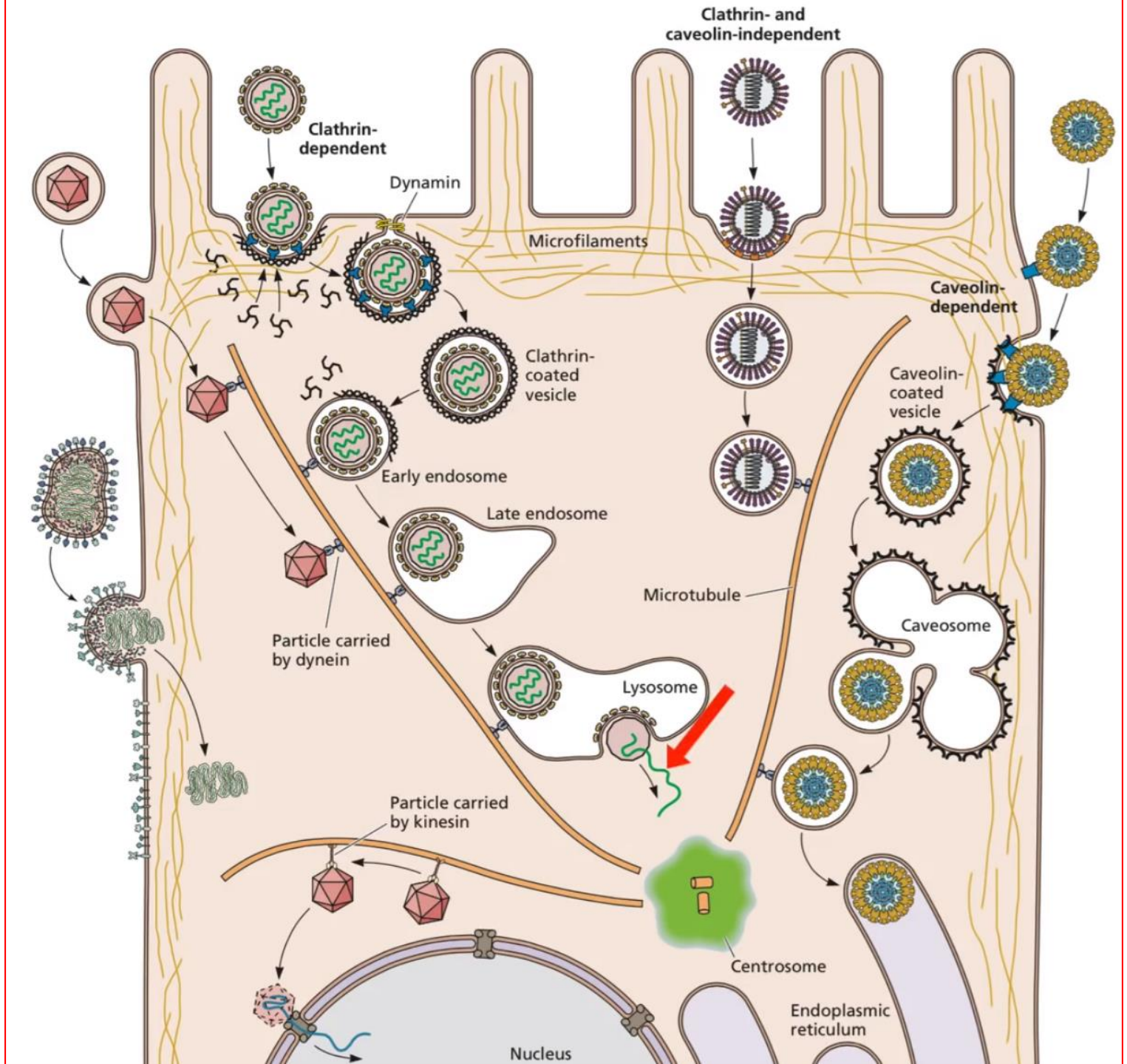
- The virus gains **entry into the body** through breaks in the **skin** (cuts, bites, injections) or across the **mucoepithelial membranes** that line the orifices of the body (eyes, respiratory tract, mouth, genitalia, and gastrointestinal tract). ***Inhalation*** *is probably the most common route of viral infection*.

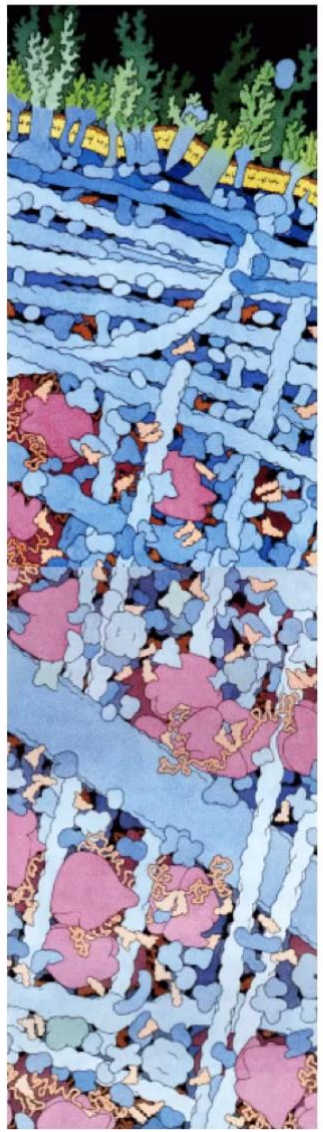
- Viruses usually **replicate at the primary site of entry**. Some, such as influenza viruses (respiratory infections) and noroviruses (gastrointestinal infections), produce disease at the portal of entry and likely have no necessity for further systemic spread.

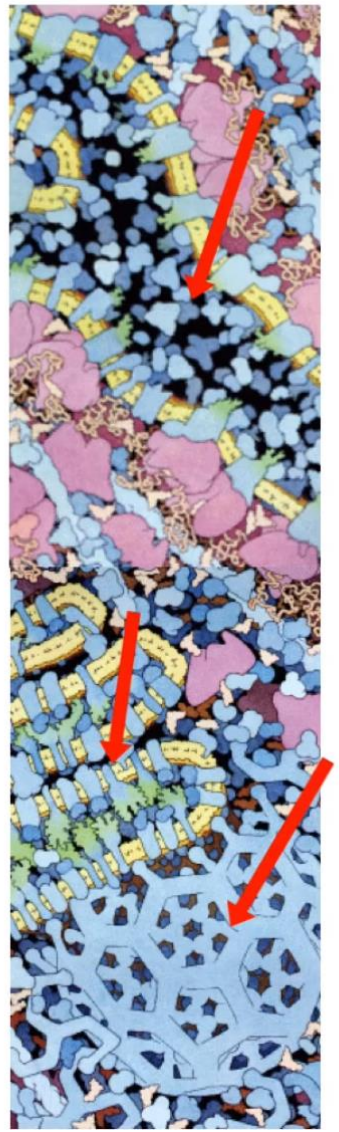
- Some viruses are introduced **directly** into the **bloodstream** by needles (hepatitis B, human immunodefi ciency virus [HIV]), by blood transfusions, or by insect vectors (arboviruses).

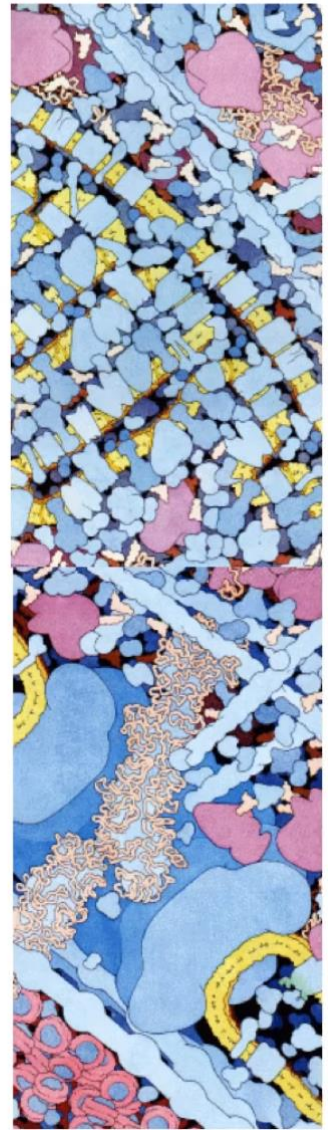


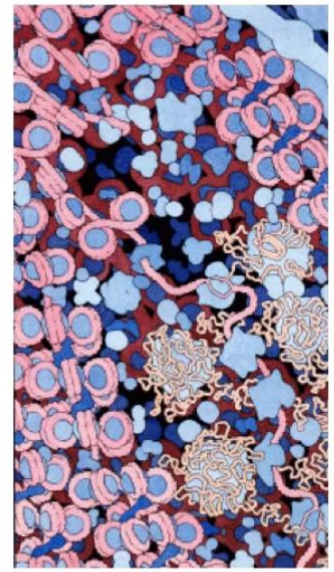
| Route of Entry | Virus Group | Produce Local Symptoms at Portal of Entry | Produce Generalized Infection Plus Specific Organ Disease |
|---|---|---|---|
| Respiratory tract | Parvovirus | | B19 |
| | Adenovirus | Most types | |
| | Herpesvirus | Epstein-Barr virus, herpes simplex virus | Varicella virus |
| | Poxvirus | | Smallpox virus |
| | Picornavirus | Rhinoviruses | Some enteroviruses |
| | Togavirus | | Rubella virus |
| | Coronavirus | Most types | |
| | Orthomyxovirus | Influenza virus | |
| | Paramyxovirus | Parainfluenza viruses, respiratory syncytial virus | Mumps virus, measles virus |
| Mouth, intestinal tract | Adenovirus | Some types | |
| | Calicivirus | Noroviruses | |
| | Herpesvirus | Epstein-Barr virus, herpes simplex virus | Cytomegalovirus |
| | Picornavirus | | Some enteroviruses, including poliovirus, and hepatitis A virus |
| | Reovirus | Rotaviruses | |
| Skin | | | |
| Mild trauma | Papillomavirus | Most types | |
| | Herpesvirus | Herpes simplex virus | |
| | Poxvirus | Molluscum contagiosum virus, orf virus | |
| Injection | Hepadnavirus | | Hepatitis B |
| | Herpesvirus | | Epstein-Barr virus, cytomegalovirus |
| | Retrovirus | | Human immunodeficiency virus |
| Bites | Togavirus | | Many species, including eastern equine encephalitis virus |
| | Flavivirus | | Many species, including yellow fever virus |
| | Rhabdovirus | | Rabies virus |


Clathrin- and caveolin-independent
Clathrin-dependent
Dynamin
Microfilaments
Caveolin-dependent
Clathrin-coated vesicle
Caveolin-coated vesicle
Early endosome
Late endosome
Microtubule
Particle carried by dynein
Caveosome
Lysosome
Particle carried by kinesin
Centrosome
Endoplasmic reticulum
Nucleus



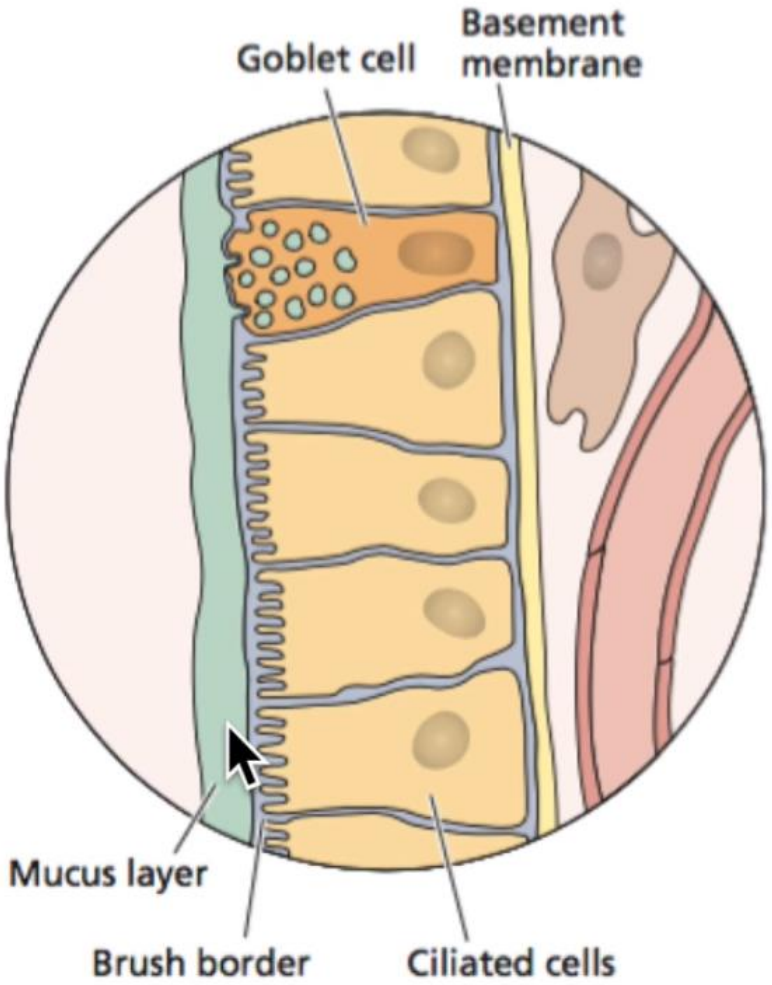


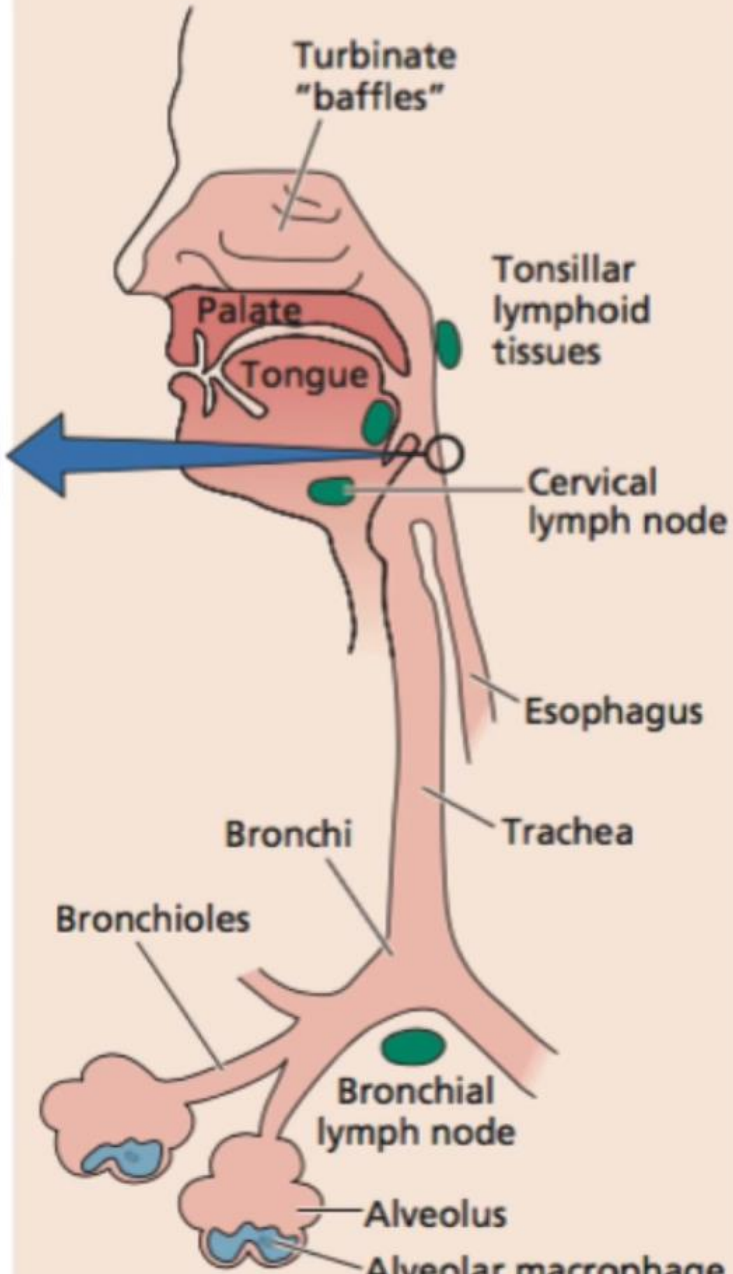




**The cytoplasm is crowded!**

**Movement of large protein complexes will not occur by diffusion!**




| Site of reproduction | Clinical manifestation | Virus |
|---|---|---|
|  | Rhinitis (common cold)<br>Pharyngitis<br>Laryngitis | Rhinovirus<br>Coronavirus<br>Parainfluenza virus<br>Respiratory syncytial virus<br>Influenza virus<br>Adenovirus<br>Herpes simplex virus<br>Epstein-Barr virus |
| | Tracheitis<br>Bronchitis<br>Bronchiolitis<br>Bronchopneumonia | Parainfluenza virus<br>Respiratory syncytial virus<br>Influenza virus<br>Adenovirus<br>Measles<br>SARS<br>MERS |

# B. Viral Spread and Cell Tropism

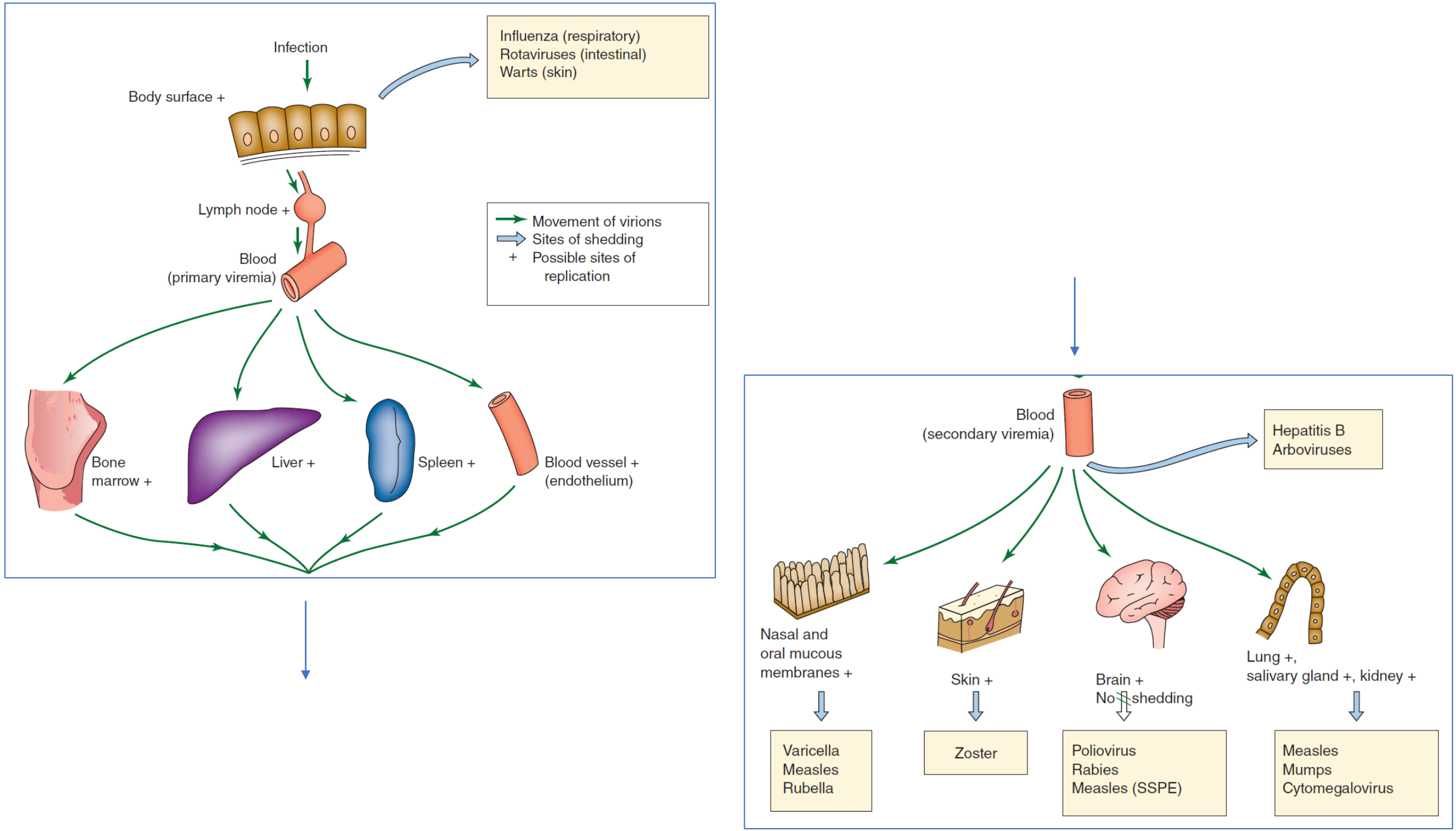
Many viruses produce disease at sites distant from their point of entry, the most common route is via the bloodstream or lymphatics. The presence of virus in the blood is called **viremia** . Virions may be free in the plasma (eg, enteroviruses, togaviruses) or associated with particular cell types (eg, measles virus)

Viruses tend to exhibit organ and cell specificities. Thus, **tropism** determines the pattern of systemic illness produced during a viral infection. (e.g. hepatitis B virus has a tropism for liver hepatocytes).

Tissue tropism depends mainly on **cell receptors** for attachment and internalization of the virus.

Also **cellular enzymes** can be needed to modify viral proteins and initiate infection, and thus affect tropism.

**Enhancer regions** that show some cell-type specificity may regulate transcription of viral genes. For example, the JC polyomavirus enhancer is much more active in glial cells than in other cell types.


Infection
Body surface +
Influenza (respiratory)
Rotaviruses (intestinal)
Warts (skin)
Lymph node +
Blood
(primary viremia)
Movement of virions
Sites of shedding
+ Possible sites of replication
Bone marrow +
Liver +
Spleen +
Blood vessel +
(endothelium)
Blood
(secondary viremia)
Hepatitis B
Arboviruses
Nasal and
oral mucous
membranes +
Skin +
Brain +
No shedding
Lung +,
salivary gland +, kidney +
Varicella
Measles
Rubella
Zoster
Poliovirus
Rabies
Measles (SSPE)
Measles
Mumps
Cytomegalovirus

# C. Cell Injury and Clinical Illness

- **Destruction of virus-infected cells** in the target tissues and **physiologic alterations** produced in the host by the tissue injury are partly responsible for the development of disease.

- General symptoms associated with many viral infections, such as **malaise** and **anorexia**, may **result from host response** functions such as cytokine production.

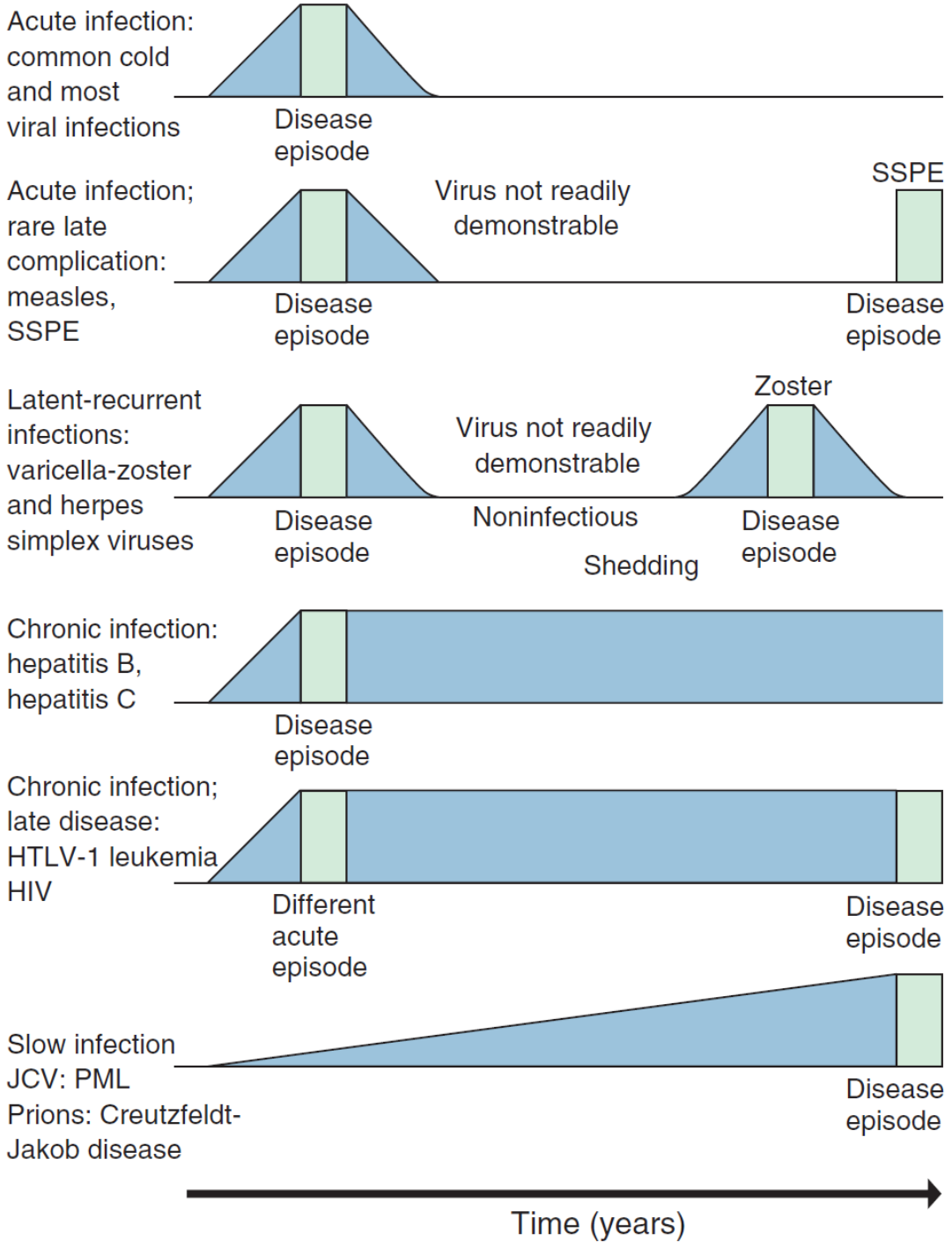
- Inapparent infections by viruses are very common.

**Table 37-2 Mechanisms of Viral Cytopathogenesis**

| Mechanism | Examples |
|---|---|
| Inhibition of cellular protein synthesis | Poliovirus, herpes simplex virus (HSV), togaviruses, poxviruses |
| Inhibition and degradation of cellular DNA | Herpesviruses |
| Alteration of cell membrane structure | Enveloped viruses |
| Viral glycoprotein insertion | All enveloped viruses |
| Syncytia formation | HSV, varicella-zoster virus, paramyxoviruses, human immunodeficiency virus |
| Disruption of cytoskeleton | Nonenveloped viruses (accumulation), HSV |
| Permeability | Togaviruses, herpesviruses |
| Toxicity of virion components | Adenovirus fibers, reovirus NSP4 protein |

# D. Recovery from Infection

- The host either succumbs or recovers from viral infection.
- Recovery mechanisms include both innate and adaptive immune responses. **Interferon** (IFN) and other cytokines, humoral and cell-mediated immunity, and possibly other host defense factors are involved.
- In acute infections, recovery is associated with viral **clearance**. However, there are times when the host remains **persistently** infected with the virus.



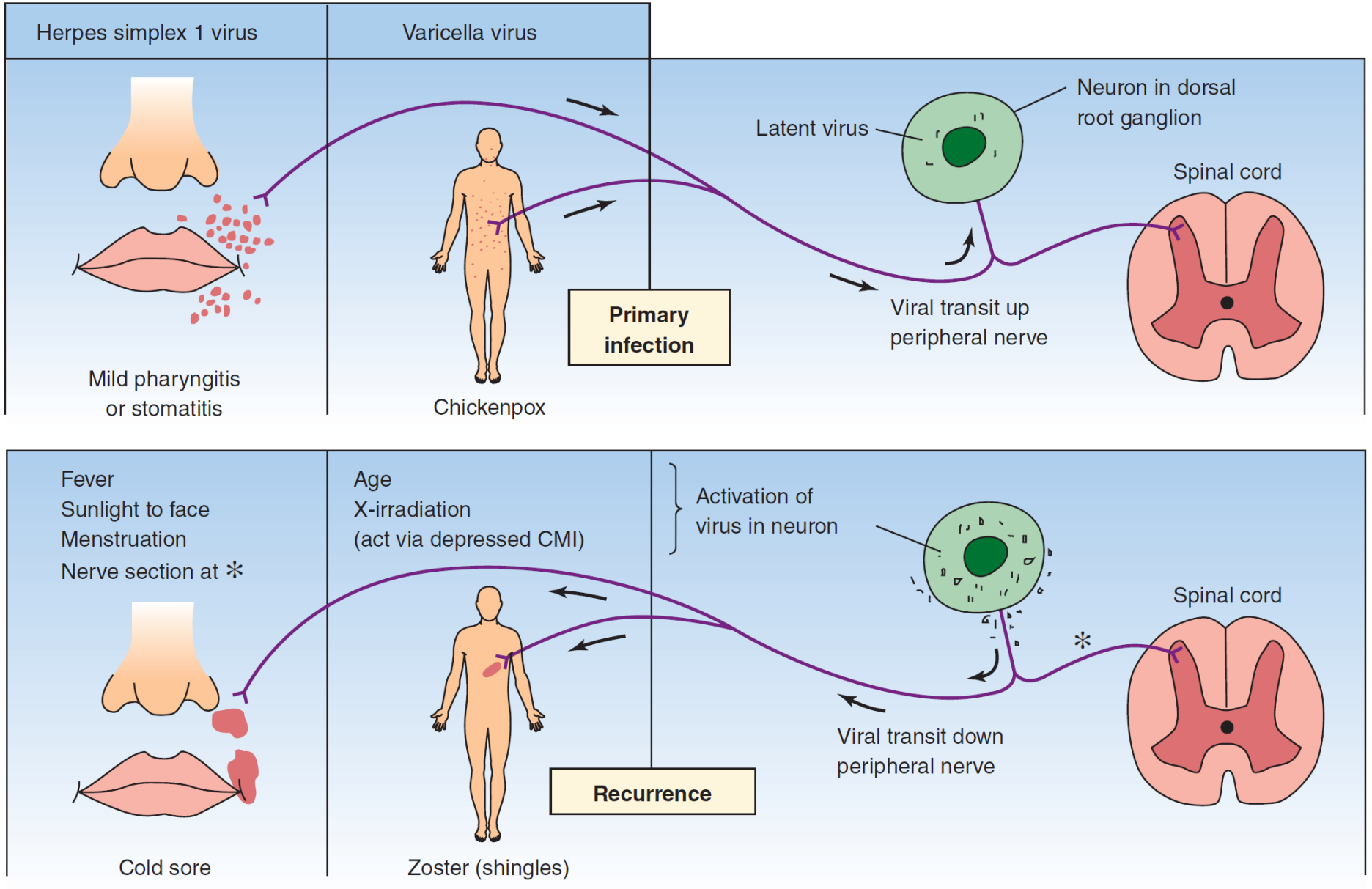
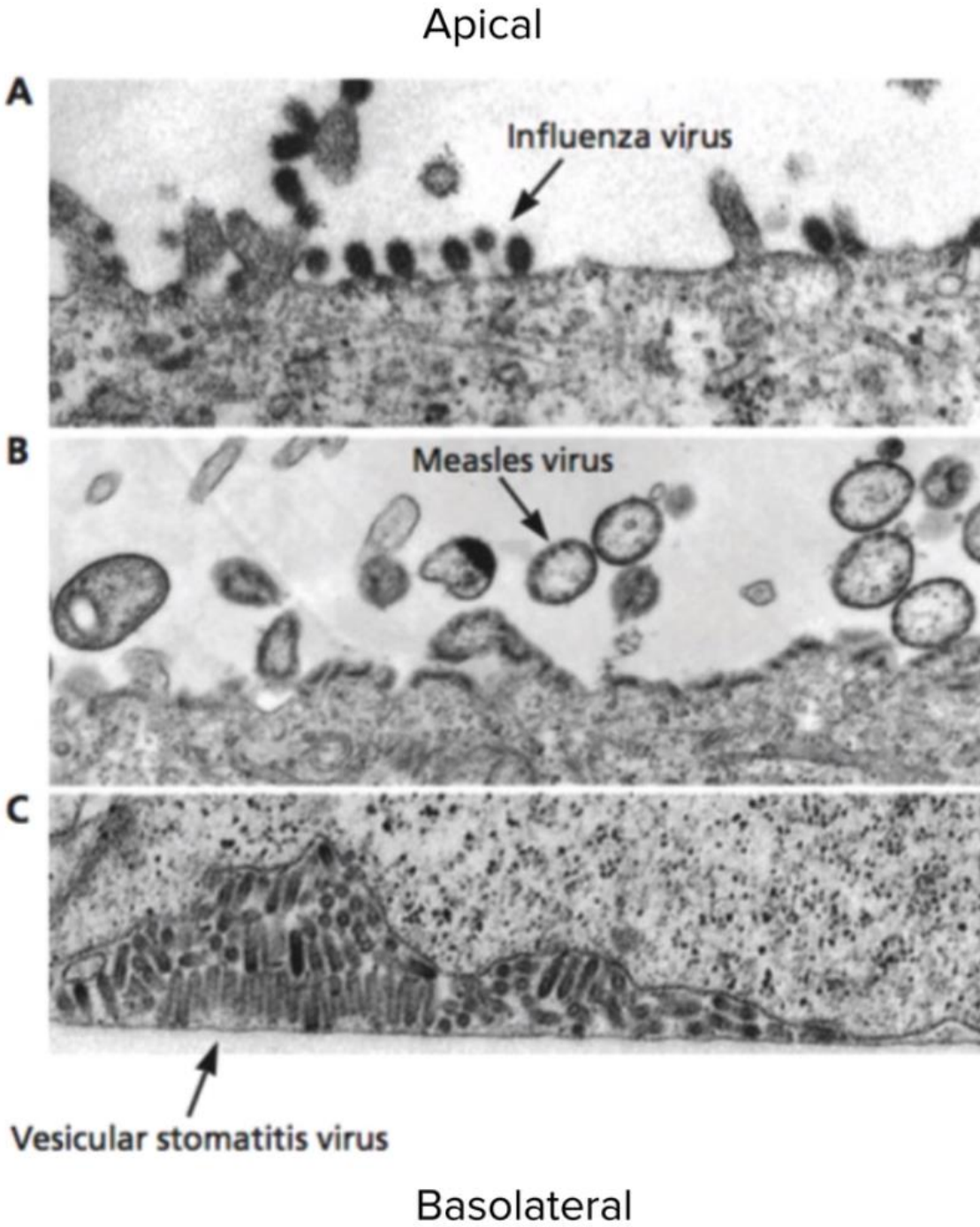


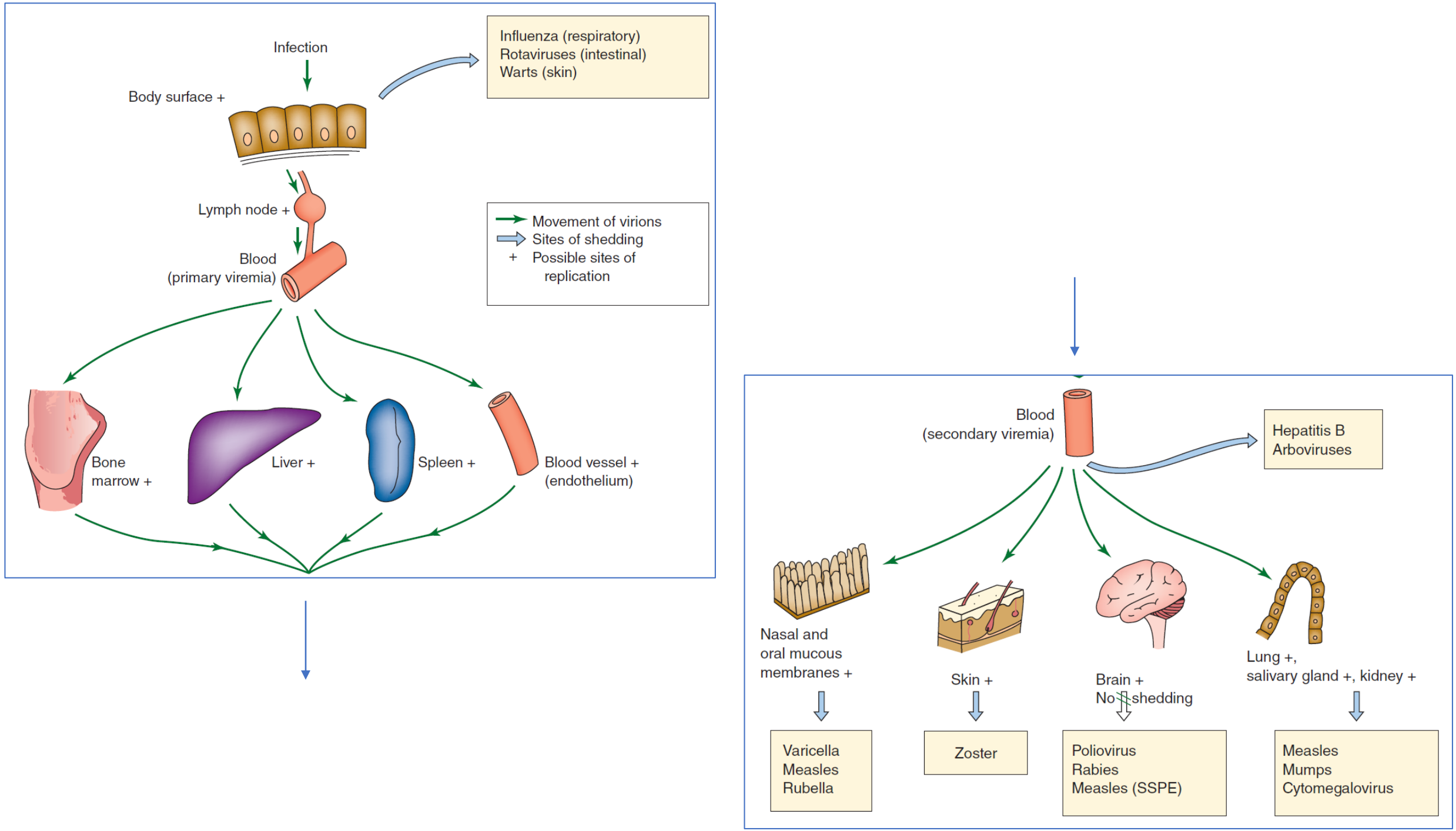

**FIGURE 30-4** Latent infections by herpesviruses. Examples are shown for both herpes simplex and varicella-zoster viruses. Primary infections occur in childhood or adolescence, followed by establishment of latent virus in the cerebral or spinal ganglia. Later activation causes recurrent herpes simplex or zoster. Recurrences are rare for zoster. CMI, cell-mediated immunity. (Reproduced with permission from Mims CA, White DO: *Viral Pathogenesis and Immunology*. Blackwell, 1984.)

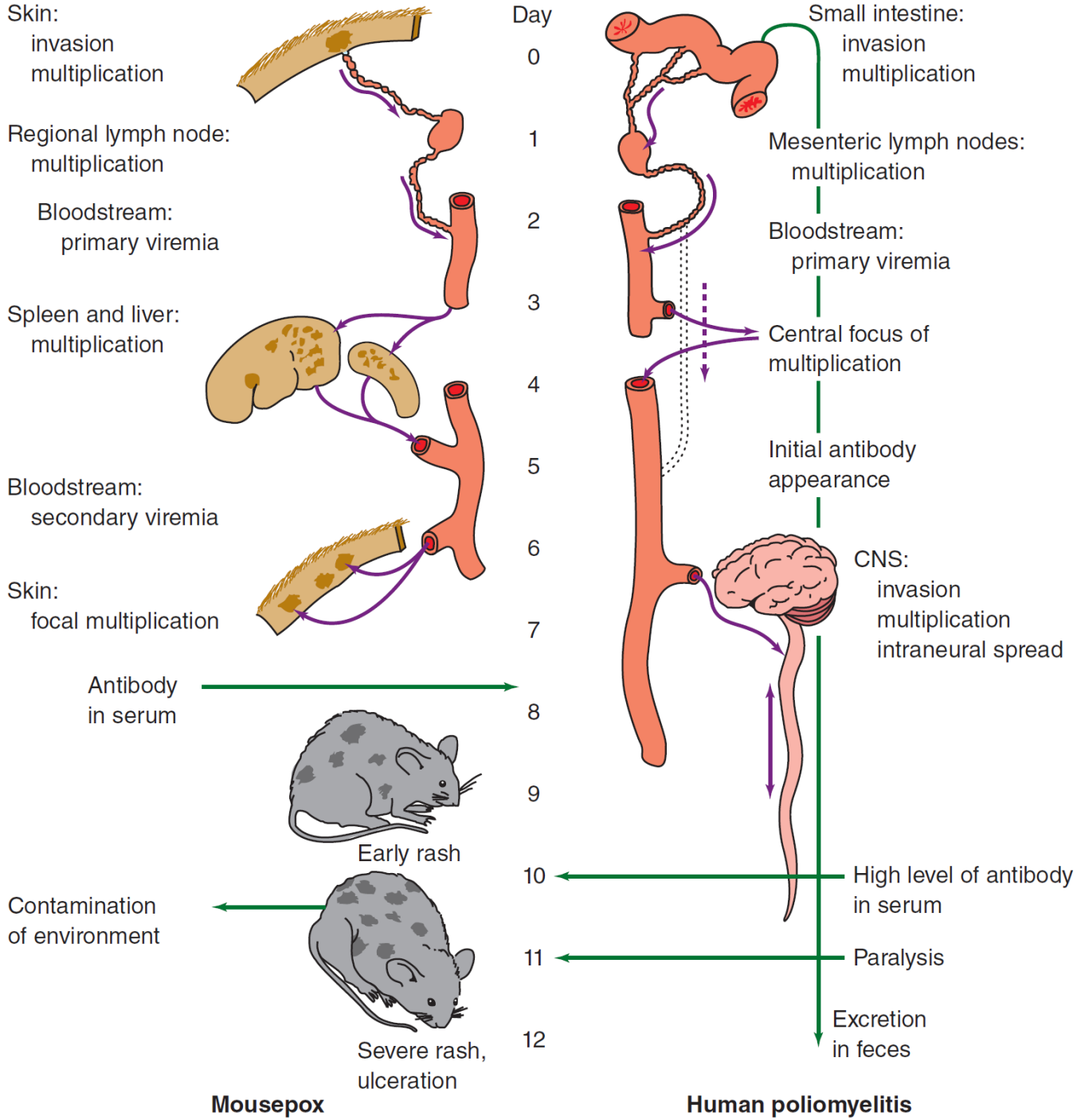
# E. Virus Shedding

- Shedding occurs at different stages of disease depending on the particular agent involved, It represents the time at which an infected individual is infectious to contacts.

- Shedding is important to maintain a viral infection in populations of hosts. In some viral infections, such as rabies, humans represent dead-end infections, and shedding does not occur.




Infection
Body surface +
Influenza (respiratory)
Rotaviruses (intestinal)
Warts (skin)
Lymph node +
Blood
(primary viremia)
Movement of virions
Sites of shedding
+ Possible sites of replication
Bone marrow +
Liver +
Spleen +
Blood vessel +
(endothelium)
Blood
(secondary viremia)
Hepatitis B
Arboviruses
Nasal and
oral mucous
membranes +
Skin +
Brain +
No shedding
Lung +,
salivary gland +, kidney +
Varicella
Measles
Rubella
Zoster
Poliovirus
Rabies
Measles (SSPE)
Measles
Mumps
Cytomegalovirus


Skin:
invasion
multiplication
Regional lymph node:
multiplication
Bloodstream:
primary viremia
Spleen and liver:
multiplication
Bloodstream:
secondary viremia
Skin:
focal multiplication
Antibody
in serum
Early rash
Contamination
of environment
Severe rash,
ulceration
Mousepox
Day
0
1
2
3
4
5
6
7
8
9
10
11
12
Small intestine:
invasion
multiplication
Mesenteric lymph nodes:
multiplication
Bloodstream:
primary viremia
Central focus of
multiplication
Initial antibody
appearance
CNS:
invasion
multiplication
intraneural spread
High level of antibody
in serum
Paralysis
Excretion
in feces
Human poliomyelitis

# Further reading and material:

- Murray - Medical Microbiology 8th Edition
  Section 5: Virology
  Chapter 37
  Chapter 38
- Jawetz, Melnick & Adelberg's Medical Microbiology, 26th edition-
  Section 4: Virology
  Chapter 30
- Youtube:

Channel: Vincent Racaniello
Videos : Virology Lectures 2018 #11 + #12 + # 15