Viral Pathogenesis & Host–Virus Interaction

Summer Term
Lecture no. 4

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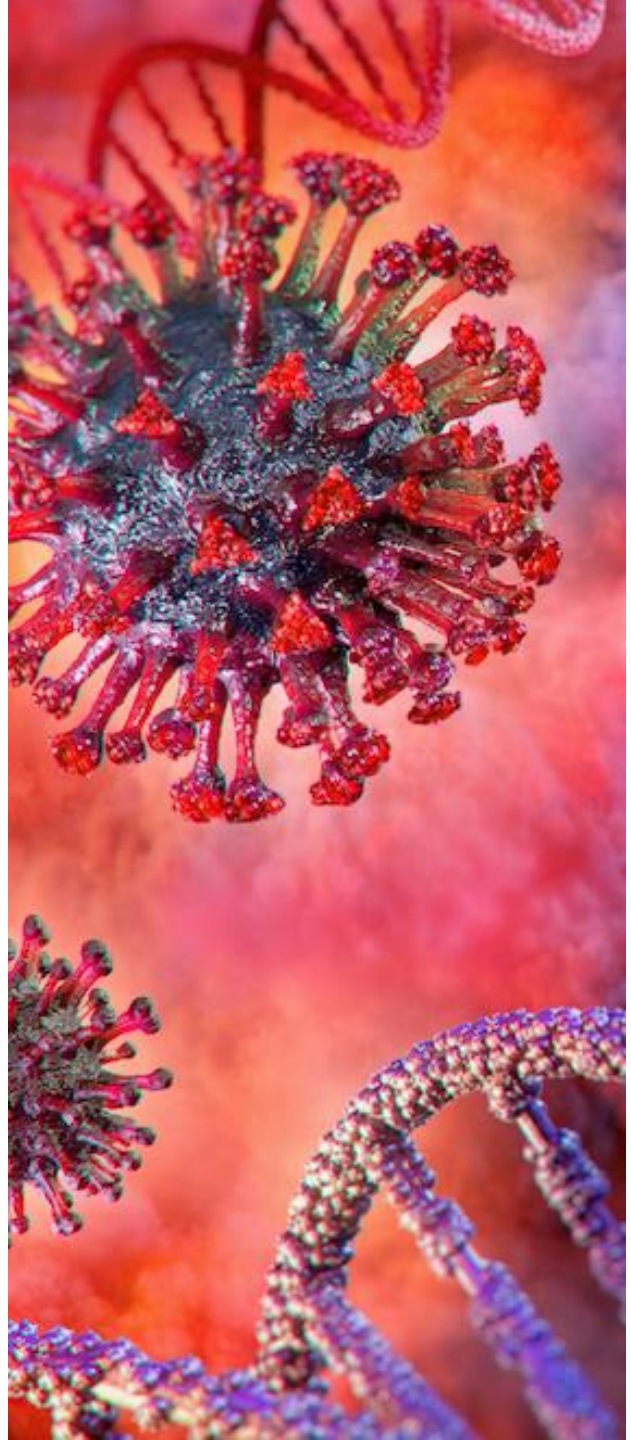
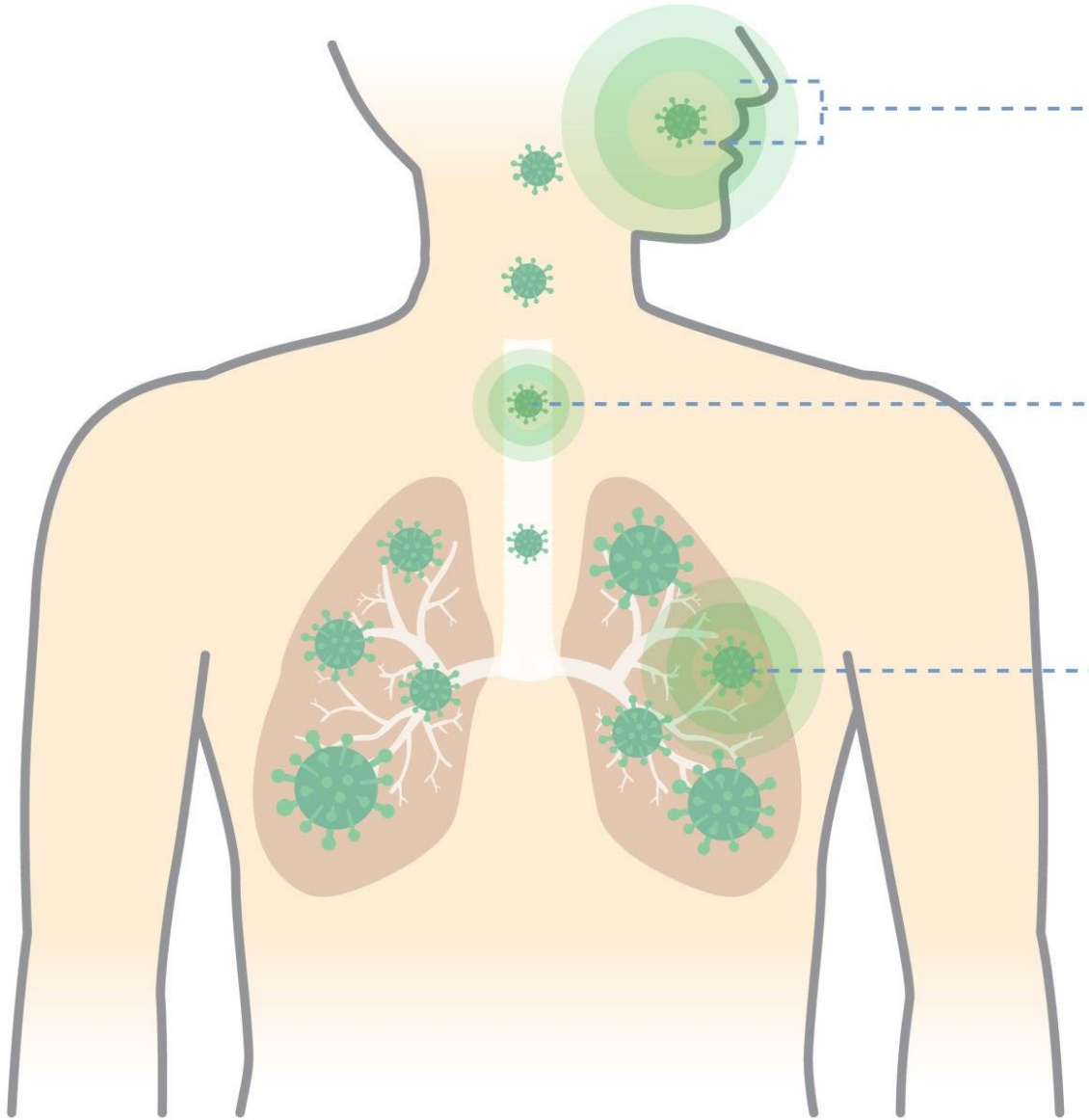


Learning Objectives:

- **Trace the pathway** of viral infection from entry to systemic dissemination.
- Differentiate between **cellular tropism** and host **susceptibility** [defenselessness].
- Contrast direct [**clear differentiation**] viral **cytopathology** with **immunopathology**.
- Categorize **[1]**chronic, **[2]**latent (hidden), and **[3]**persistent (continual) viral infection dynamics.

What coronavirus does to the body?



1. Virus enters through the nose and mouth
2. It then finds a host cell in the respiratory system
3. The host cell then bursts and infects other cells nearby

✔ Infection Pathways & Dissemination Mechanisms

1. Introduction & Terminology_

- **Pathogenicity vs. Virulence:** Pathogenicity is the qualitative ability to cause disease; virulence represents the quantitative degree of pathology.

- **Primary Requirements for Successful Infection:**

[1] Sufficient viral load,
[2] Accessible susceptible/permissive target cells, and
[3] Evasion of initial local intrinsic defenses.

2. Portals of Entry & Transmission Routes

✔ **Respiratory Tract:** Most common portal (e.g., Influenza, SARS-CoV-2). Mucociliary clearance serves as the primary barrier.

✔ **Gastrointestinal Tract:** Exposure to acidic pH, bile salts, and proteolytic enzymes. Unenveloped viruses (e.g., Norovirus, Rotavirus) typically survive better than enveloped viruses.

✔ **Urogenital Tract:** Micro-abrasions facilitate entry (e.g., HSV, HIV, HPV).

✔ **Skin & Mucous Membranes:** Intact stratum corneum (outermost layer of the epidermis) acts as a physical barrier. Entry requires breaches (cuts, bites, vectors like Dengue/Zika via Aedes mosquitoes) or direct inoculation (needles, HBV/HCV).

3. Viral Tropism

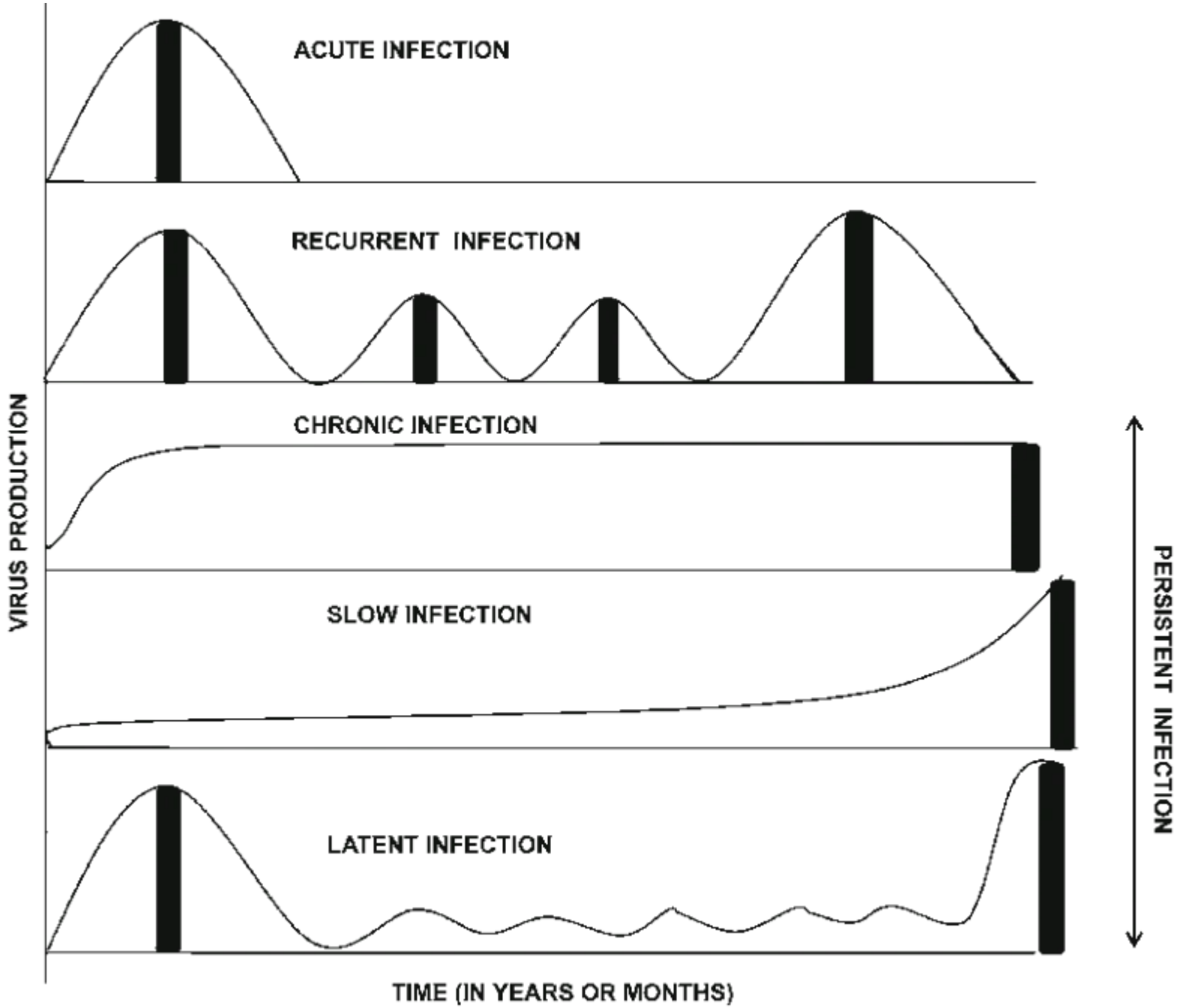
- **Definition:** The specificity of a virus for a particular cell type, tissue, or host species.
- **Determinants of Tropism:**
  - **Cellular Receptors:** Expression of specific surface receptors (e.g., SARS-CoV-2 Spike binding ACE2).
  - **Intracellular Factors:** Transcriptional factors and host proteases required for cleavage (e.g., HA cleavage by furin).
  - **Permissiveness:** The internal cell environment's capacity to support viral replication.

→ **Transcription factors** are specialized proteins that bind to specific DNA sequences to turn genes on or off by controlling how fast transcription happens.

4. Viral Dissemination & Systemic Spread

- **Localized *vs.* Systemic Infections:** Localized (e.g., Rhinovirus restricted to upper airway) *vs.* Systemic (spread beyond primary site).
- **Viremia:**
  - *Primary Viremia:* Initial entry into the bloodstream via lymphatics.
  - *Secondary Viremia:* Higher-titer viral release into blood following replication in distant organs.
- **Neural Spread:** Retrograde/anterograde axonal transport via peripheral nerves to the CNS (e.g., Rabies virus, HSV, Varicella-Zoster Virus).

- **Viral dynamics in acute *vs.* persistent (continuous) infections.**



✔ Host Response, Pathology & Infection Dynamics

1. Host Immune Responses & Evasion

- **Innate Response:**
  - Detection via Pattern recognition receptors _**PRRs** (TLR3, TLR7/8, RIG-I-like receptors).
  - Type I Interferon (IFN-alpha\beta) induction establishing an antiviral state in neighboring cells.
  - Natural Killer (NK) cell clearance of MHC-I downregulated cells.
- **Adaptive Response:**
  - Cytotoxic T Lymphocytes (CTLs, CD8+) destroying infected target cells.
  - Neutralizing Antibodies (Abs) blocking viral attachment and entry.

- **Viral Evasion Strategies:** 1Antigenic drift/shift, 2MHC-I downregulation, 3blockade of IFN signaling pathways, and 4immune privilege site hiding.

2. Tissue Damage & Mechanisms of Disease

- **Direct Cytopathic Effects (CPE):**
  - Cell lysis and membrane disruption.
  - Syncytia formation (cell-cell fusion, e.g., RSV, Measles).
  - Inclusion body formation and cytoskeletal rearrangement.
  - Apoptosis and inhibition of host protein synthesis ("shut-off").

- **Immunopathology (Indirect Damage):**
  - Cytokine storm syndrome (excessive systemic inflammatory release).
  - Immune-complex deposition (e.g., Type III hypersensitivity in HBV).
  - Antibody-Dependent Enhancement (ADE) (e.g., Dengue virus secondary infection).

Dynamics of Infection: Acute vs. Persistent

Infection Type	Viral Production	Genome Persistence	Primary Example
Acute	**Rapid** onset, **high** titer, cleared **rapidly**	No	Influenza, Rotavirus
Latent	**Intermittent** reactivation spikes	Yes	HSV-1, VZV, EBV
Chronic	**Continuous** low/high level shedding	Yes	Hepatitis B (HBV), Hepatitis C (HCV)
Slow/Transforming	**Long** incubation, **progressive** escalation	Yes	HIV, HTLV-1, Oncogenic HPVs

1.Which of the following best defines a virion?

A. A free-living microorganism capable of independent metabolism
B. A complete, infectious viral particle containing genetic material within a protein coat
C. A misfolded protein responsible for infectious disease
D. A host cell containing viral proteins

2.What are the protein subunits that make up a viral capsid called?

A. Glycoproteins
B. Capsomeres
C. Peplomers
D. Polymerases

3.Which of the following viruses has icosahedral symmetry?

A. Influenza virus
B. Rabies virus
C. Poliovirus
D. Ebola virus

4.Which statement about helical symmetry is correct?

A. It is found only in non-enveloped human viruses
B. Viral protein subunits bind directly to nucleic acid and coil into a spiral
C. It consists of 20 triangular faces and 12 vertices
D. It is characteristic of poxviruses

5.Which of the following is a characteristic of enveloped viruses?

A. They are highly resistant to detergents
B. Their envelope is derived from host cellular membranes
C. They are more resistant to drying than naked viruses
D. They are released only by cell lysis

6.Which type of viral genome can function directly as mRNA after entering the host cell?

A. dsDNA
B. -ssRNA
C. +ssRNA
D. dsRNA

7.Why must negative-sense RNA viruses carry RNA-dependent RNA polymerase (RdRp) inside the virion?

A. Their genome can directly function as mRNA
B. Their genome must first be transcribed into positive-sense RNA (mRNA)
C. They use reverse transcriptase to produce DNA
D. They cannot synthesize viral proteins

8.The Baltimore classification system categorizes viruses primarily according to their:

A. Capsid shape
B. Host range
C. Mechanism of mRNA synthesis
D. Size and morphology

9.Which Baltimore class includes +ssRNA viruses whose genome can act directly as mRNA?

A. Class II
B. Class III
C. Class IV
D. Class V

10.Which virus is an example of a Baltimore Class V virus?

A. Poliovirus
B. Influenza virus
C. Adenovirus
D. Hepatitis B virus

11.Which enzyme converts the RNA genome of retroviruses into DNA?

A. RNA polymerase II
B. DNA polymerase
C. Reverse transcriptase
D. Integrase

12.What is the first stage of the lytic replication cycle?

A. Uncoating
B. Assembly
C. Attachment (Adsorption)
D. Release

13.Which viral protein binds to the ACE2 receptor during SARS-CoV-2 attachment?

A. Hemagglutinin (HA)
B. GP120
C. Spike (S) protein
D. Reverse transcriptase

14.Which mechanism is typical for the release of enveloped viruses?

A. Lysis
B. Budding
C. Binary fission
D. Sporulation

15.Which of the following is an example of a cytopathic effect (CPE)?

A. Normal cell division
B. Syncytia formation
C. Increased cellular adherence
D. No morphological changes in infected cells

Thank You!