
15.13 Mechanisms of Viral Pathogenicity

Viral disease results from the interaction of:

1. Viral tropism
2. Viral replication strategy
3. Direct cytopathic effect
4. Host immune response
5. Immune evasion
6. Ability to establish latency, chronicity, or oncogenesis

15.13.1 Cell Tropism and Receptor Binding

Viruses infect only cells that provide:

- Suitable receptor
- Entry cofactor
- Intracellular replication environment

- Required host enzymes or transcription factors

Examples of tropism logic:

Tropism	Clinical result
Respiratory epithelium	Cough, coryza, pneumonia
Enterocytes	Diarrhea, vomiting
Hepatocytes	Hepatitis, jaundice
Neurons	Encephalitis, paralysis, rabies-like syndromes
Lymphocytes	Immunodeficiency or immune dysregulation
Endothelium	Vascular leak, hemorrhage, shock
Fetal tissues	Congenital malformation

Exam pearl:

A virus causes disease where it can enter, replicate, and injure tissue—or where the immune response injures infected tissue.

15.13.2 Direct Cytopathic Injury

Viruses may directly damage infected cells by:

- Shutting down host protein synthesis
- Producing inclusion bodies
- Causing cell lysis
- Disrupting cell membranes
- Inducing apoptosis
- Causing metabolic stress
- Forming syncytia

Examples of cytopathic patterns:

Pattern	Clinical meaning
Cell lysis	Acute tissue destruction
Syncytia	Cell-to-cell spread and tissue dysfunction
Inclusion bodies	Diagnostic histopathologic clue
Apoptosis	Tissue loss and immune activation

15.13.3 Immune-Mediated Injury

Many viral diseases are caused not only by viral replication but also by host immune response.

Mechanisms:

- Cytotoxic T-cell killing of infected cells
- Cytokine-mediated inflammation
- Immune complex deposition

Important consequences:

- Chronic inflammation
- Fibrosis
- Organ dysfunction
- Viral shedding
- Immune exhaustion
- Cancer risk in selected viruses

Examples:

- Chronic hepatitis B
- Chronic hepatitis C
- HIV infection
- Some congenital infections

15.13.6 Viral Oncogenesis

Some viruses promote cancer by:

- Inserting viral genes into host cells
- Producing oncogenic proteins
- Blocking tumor suppressor pathways
- Driving chronic inflammation
- Causing immune suppression
- Promoting cell proliferation

Important oncogenic viruses:

Virus	Associated malignancy
HPV	Cervical, anogenital, oropharyngeal cancers
HBV, HCV	Hepatocellular carcinoma
EBV	Burkitt lymphoma, nasopharyngeal carcinoma, some lymphomas
HTLV-1	Adult T-cell leukemia/lymphoma
HHV-8	Kaposi sarcoma
Merkel cell polyomavirus	Merkel cell carcinoma

Exam pearl:

Viral oncogenesis may be direct, as with viral oncogenes, or indirect, as with chronic inflammation and regeneration.

15.14 Host Immune Response to Viral Infection

The host response depends on:

- Site of infection
- Viral replication pattern
- Innate immune recognition
- Interferon response
- NK-cell activity
- CD8 T-cell killing
- Neutralizing antibodies
- Mucosal immunity
- Immune memory