

Viruses**Lecture Outline**

Feb. 23-26, 2001

I. General characteristics.

1. Virus Structure. Nucleic acid protected by a nucleocapsid with or without a lipid bilayer membrane called a viral envelope.

2. Viral life cycle in host cell to cell transmission.

A. Entry into host cell usually through a viral envelope protein binding to a host cell receptor.

Viral **tropism**: Means viruses will only infect certain cells.

Tropism is usually based on expression of host cell receptor.

B. Replication. Viruses make mRNA to get protein production.

Viruses must also replicate their nucleic acid.

Virus must assemble and release new viral particles.

C. Release from cell. Viruses can bud from membrane or lyse cell to release new virus.

3. Outcome of infection.

A. Lysis of host cell.

B. Persistent infection cell continually makes virus.

C. Latency. Viral DNA is integrated into host cell DNA. No protein production, no viral replication.

4. Viral Transmission.

Primarily horizontal transmission. Many different types of spread e.g. respiratory droplets, fecal-oral, sexual, mosquito vectors, and contact with contaminated tissue.

II. DNA viruses

1. DNA viruses are larger size and encode for many more genes than RNA viruses.

Highly evolved and specialized for infecting mammals.

2. Viral DNA can be integrated into the host genome.

DNA integration is how virus becomes **latent**, can be passed on to daughter cells.

3. DNA viruses can be **oncogenic** (cancer causing).

Many DNA viruses are able to transform or immortalize an infected so that it will be kept alive indefinitely for production of virus. This loss of growth regulation can sometimes cause a tumor or cancerous growth.

Disease Examples of DNA viruses:

Hepatitis B virus (HBV) causes liver disease.

A small percentage of infected people will develop chronic HBV infection and can become an asymptomatic carrier or develop liver cancer and liver failure.

Papillomaviruses many different strains but all cause warts but has also associated with cervical carcinoma.

Herpesviruses.

Epstein Barr Virus (EBV) causes infectious mononucleosis and also lymphomas.

EBV infects epithelial cells and B cells.

Herpes Simplex virus (HSV) causes cold sores and genital herpes.

Virus infects epithelial cells for replication and neurons for latency.

HSV travels up the neuron integrate in to host cell DNA.

Reactivation of HSV causes low level of viral production in neuron and then widespread replication in epithelial cells.

Unclear what causes reactivation but suppression of immune responses a factor.

Pox viruses Smallpox virus caused pox disease in humans.

Vaccinia. Causes cowpox. Used as vaccine for smallpox.

III. RNA viruses--

1. Smaller size and smaller genome. Some RNA viruses make as few as 10 proteins.
2. Few proteins but still must take over cell replication machinery to make mRNA.
3. Fast growth and replication cycle.
4. Often lytic. Usually kill cell to escape.

Disease Examples:

Influenza--flu virus. Infects respiratory epithelium. Fast replicating and lytic to infected cells.

Measles--infects epithelium of respiratory tract. Highly infectious by droplets. Spreads to entire body to give characteristic rash.

Polio. Humans are only reservoir. Must have close contact to get fecal-oral transmission. First infects throat and digestive tract epithelium.

Spreads to entire body and can infect nervous tissue.

Most people have inapparent infection (no disease) but when virus replicates in nervous tissue can cause paralysis. Only 1 percent of infections cause illness.

Coronaviruses and **Rhinoviruses** are the viruses that cause colds. Rapid replication. Lytic.

There are many different types of these viruses and they mutate quickly.

Rabies virus slower growing not as lytic. Infects neurons.

IV. Retroviruses. A unique family of RNA viruses that make DNA copies of their viral RNA. This complementary DNA (cDNA) copy of the viral RNA can be integrated into host genome.

Retroviruses use a special enzyme called **reverse transcriptase** to make DNA from RNA.

These are the only RNA viruses that can be oncogenic.

Human immunodeficiency virus (HIV). HIV-1, HIV-2.

Human T cell leukemia virus (HTLV-I). Infects T cells. Causes T cell lymphoma/leukemia.

IV. Innate immune responses to viruses.

Interferons IFN α and β

Inhibit viral replication. Increase class I MHC expression. Activate NK cells.

NK cells. kill infected cells.

V. Specific Immune response to viruses.**1. Antibody responses to viruses**

- A. Neutralizing antibodies. IgG (IgA) block entry by binding to viral receptor or block attachment and therefore prevent cell to cell spread of infection.
- B. Opsonization IgG. enhance uptake by macrophages and Neutrophils.
- C. ADCC. IgG, IgM, help kill infected cells.

2. Cell mediated immunity

CTLs. CD8⁺ CTLs are most effective for elimination of virally infected cells.

Th cells provide cytokines. Th2 for antibody production. Th1 antiviral IFN- γ .

VI. Immune evasion mechanisms.

Immune evasion is the development of a multiplicity of mechanisms to evade, subvert, deviate or suppress host-protective immune responses.

1. Antigenic variation.

A. Mutate coat proteins so antibodies wont bind. e.g. Influenza.

B. Multiply distinct antigenic varieties. Need to make immune response to new virus subtype.

E. g. rhinoviruses, coronaviruses cause common colds.

These viruses are fast replicating viruses with a short incubation time. They can usually infect cells and cause symptoms before ab/CTL responses kick in. Easily eliminated once you have specific immunity but can take a week to make ab/CTL, by that time virus has replicated and moved on to new host.

2. Immune suppression. By living in immune cells many pathogens can avoid host defenses as well as weaken immune responses by destroying infected immune cells.

E.g. HIV lives in T cells and macrophages. EBV lives in B cells.

3. Viral Protein Inhibitors. Viral proteins that can inhibit IFNs.

Inhibition of Fas expression or class I MHC expression. E.g. herpesviruses.