**Medical microbiolo**gy

**Virology**

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**Pathogenesis lec.2**

**Viral pathogenesis** is the process that occurs when a virus infects a cell and causes cellular changes.

**Disease** **pathogenesis** is a subset of events during an infection that results in disease manifestation in the host.

**Steps in Viral Pathogenesis**

Specific steps involved in viral pathogenesis are the following: viral entry into the host, primary viral replication, viral spread, cellular injury, host immune response, viral clearance or establishment of persistent infection, and viral shedding.

**A. Entry and Primary Replication**

Most viral infections are initiated when viruses attach and enter cells of one of the body surfaces—skin, respiratory tract, gastrointestinal tract, urogenital tract, or conjunctiva.

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**B. Viral Spread and Cell Tropism**

Some viruses, such as influenza viruses (respiratory infections) and noroviruses (gastrointestinal infections), **produce disease at the** **portal of entry and typically do not spread systematically**. Others can spread to distant sites (eg, cytomegalovirus [CMV], HIV, rabies virus) and cause additional disease manifestations . **Mechanisms of viral spread vary, but 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 may multiply within those cells (eg, Epstein-Barr virus [EBV] is lymphotrophic.**

**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.

Some tissues, such as intestinal epithelium, can rapidly regenerate

and withstand extensive damage better than others, such as the brain.

**D. Recovery from Infection**

Following a viral infection, the host will succumb, recover, or establish a chronic infection. Recovery mechanisms include both innate and adaptive immune responses. Interferon (IFN) and other cytokines and possibly other host defense factors are involved. The relative importance of each component differs with the virus and the disease.

**E. Virus Shedding**

The last stage in pathogenesis is the shedding of infectious virus into the environment. This is a necessary step to maintain a viral infection in populations of hosts. Shedding usually occurs from the body surfaces involved in viral entry**.**

**Viral Virulence**

Virulence refers **to the capacity of a virus to cause disease in an infected host**. It is a quantitative statement of the degree or extent of pathogenesis. In general, a **virulent** virus causes significant disease, whereas an **avirulent** or **attenuated** virus causes no or reduced disease, respectively.

**Virulence depends on**

-Dose

-Virus strain (genetics)

- Inoculation route - portal of entry

-Host factors - eg. Age SV in adult neurons goes persistent but is lytic in young

**Measuring Viral Virulence**

Virulence can be quantified in a number of ways. One approach is to determine **the concentration of virus** that causes **death or disease in 50% of the infected animals. This parameter is called the 50% lethal dose (LD50),** **the 50% paralytic dose (PD50), or the 50% infectious dose (ID50), depending on the parameter that is measured.**

**Other measurements of virulence include :**

-mean time to death or appearance of symptoms

- measurement of fever or weight loss.

**Virus-induced tissue damage can be measured directly by** :

-examining histological sections or the blood.

The safety of live attenuated poliovirus vaccine is determined by assessing the extent of pathological lesions in the central nervous system in experimentally inoculated monkeys.

- The reduction in blood concentration of CD4+ lymphocytes caused by human immunodeficiency virus type 1 infection is another example. **Indirect measures of virulence include assays for liver enzymes (alanine or aspartate amino-transferases) that are released into the blood as a result of virus-induced liver damage.**