CHAPTER 13
VIRAL PATHOGENESIS

WHY IS THIS IMPORTANT?

- Most infections are caused by viruses.
- Health care professionals must understand the pathogenic mechanisms used by these pathogens.

OVERVIEW
**PATTERNS OF VIRAL INFECTION**

- Viral infections can be:
  - **Acute** (rapid and self limiting)
  - **Persistent** (long term)
  - **Latent** (extreme versions of persistent infections)
  - **Slow or transforming** (complicated types of persistent infections)

- Cytopathic viruses produce virions and kill host cells rapidly (cytopathology).
- Noncytopathic viruses produce virions but do not cause cytopathology.
- Some viruses do not produce virions or cause cytopathology but still cause infection.

- Incubation periods vary for different viruses.
  - Some are as short as days.
  - Some are as long as years.
During the incubation period:
- The virus is replicating.
- The host is beginning to respond.

**PATTERNS OF VIRAL INFECTION**

- Characterized by rapid production of virions and elimination of infection
  - Virions can be missed and can spread to other tissues.
  - This can then cause re-infection.
  - Re-infection is seen with varicella-zoster (chicken pox).
ACUTE INFECTIONS

Acute viral infections are severe public health problems.
- They are usually associated with epidemics.
- The main problem is the short incubation period.
- This causes a delay in identifiable symptoms until the virus has already spread.

ACUTE INFECTIONS

- Acute infection epidemics are often seen in crowded populations.
  - Schools
  - Military bases
  - Nursing homes
ACUTE INFECTIONS: Antigenic Variation

- Hosts that survive acute infections are immune to re-infection for life.
- Some diseases escape this immunity.
  - Re-infection occurs because of antigenic variation – changes in virion structure.
  - Antigenic variation is due to the specificity of the immune response.
    - The new structure is not recognized by the immune system memory.

ACUTE INFECTIONS: Antigenic Variation

- There are two forms of antigenic variation:
  - Antigenic drift
    - Involves small changes in virion structure
    - Results from mutations
    - Occurs after the infection has begun

ACUTE INFECTIONS: Antigenic Variation

- There are two forms of antigenic variation:
  - Antigenic shift
    - Involves major changes in virion structure
    - Is due to the acquisition of new genes
    - This is through co-infection or recombination
PERSISTENT INFECTIONS

- Caused when host defenses are either modulated or completely bypassed.
- Virions are produced for months or even years.
- There are two variations of persistent infections:
  - Chronic infection – the infection is eventually cleared
  - Latent infection – the infection lasts for life

PERSISTENT INFECTIONS: Killing Of Cytotoxic T Lymphocytes

- One host defense mechanism against viral infection is cytotoxic T cells.
  - They must be given the signal to begin killing infected cells.
  - Some viruses can kill them first.

PERSISTENT INFECTIONS: Killing Of Cytotoxic T Lymphocytes

- Some viruses escape killing by infecting tissues that have reduced immunosurveillance.
  - Skin
  - Central nervous system
PERSISTENT INFECTIONS: Latent Infections

- Three general characteristics:
  - No large-scale production of virions
  - Reduced or absent immune response
  - Persistence of an intact viral genome so infections can reoccur
- Latent viruses can be reactivated years after entry into host.

PERSISTENT INFECTIONS: Slow Infections

- Slow infections are lethal.
  - They are usually associated with brain infections.
  - Signs may not be seen until years after the primary infection.
  - Once signs and symptoms appear, death usually follows very quickly.

DISSEMINATION AND TRANSMISSION OF VIRAL INFECTION

- Viral infections are disseminated within the host and transmitted from one host to another.
- There are three basic requirements for successful infection:
  - Sufficient number of viruses present
    - The number depends on the type of virus, the site of infection, and the age and health of the host.
  - Access to susceptible and permissive host cells
  - An ineffective host immune response
VIRAL DISSEMINATION

- Viral dissemination refers to spread of virus within an infected body.
- There are common sites for viruses to enter into the body.

The three main entry points are:
- Respiratory system
- Digestive tract
- Urogenital tract

VIRAL DISSEMINATION: Respiratory Tract

- The most common portal of entry into the human body.
  - It is always exposed to large numbers of potential pathogens.
  - Viruses easily disseminate from here into other areas of the body.
VIRAL DISSEMINATION: Respiratory Tract

- Nasal cavity
- Throat
- Lungs

VIRUS
- Rhinovirus
- Coronavirus
- Influenza virus
- Adenovirus
- Herpes simplex virus
- Epstein-Barr virus

VIRAL DISSEMINATION: Digestive Tract

- The digestive tract is the second most common portal of entry.
- Many viruses use this portal of entry.
  - They must be resistant and resilient to harsh environments in order to survive.

- Some viruses use transcytosis through M cells to enter the body.
- Some viruses stay in the M cells and eventually destroy them.
  - This causes inflammation of the digestive tract and diarrhea.
VIRAL DISSEMINATION: Urogenital Tract

- The primary point for sexually transmitted viruses to enter the body.
  - Some remain in this tract and cause local infections e.g. genital warts.
  - Some gain access to underlying tissues and disseminate throughout the body.

VIRAL DISSEMINATION: Other Portals of Entry

- Viruses also use other portals of entry.
- Some viruses enter through the eyes.
  - An example of this is an ophthalmic herpes infection.
**VIRAL DISSEMINATION: Other Portals of Entry**

Some viruses enter through the skin.
- Usually by vector transmission from biting insects
- If they remain in the epidermis, a localized, acute infection occurs.
- If they get into the dermis, a systemic infection can occur.

**VIRAL DISSEMINATION: Skin**

- Some viruses can enter the body through the nervous system.
  - They can disseminate throughout the entire body.
  - Some target neurons.
  - Some use neurons to get to their preferred target area.
VIRAL DISSEMINATION: Organs

- Viruses released from the apical surface host cells cause localized limited infection.
- Viruses released from the basement membrane of host cells can spread systemically.
- The bloodstream is the best route for systemic viral infection.
  - Referred to as hematogenous dissemination
  - Viremia refers to virus replicating in the blood

VIRAL DISSEMINATION

VIRAL TRANSMISSION

- Viral transmission refers to the spread of the virus from one host to another.
- There are two patterns of viral transmission:
  - Transmission within a single species
    - Human to human.
  - Transmission between species
    - Animal to human
VIRAL TRANSMISSION

- Viruses can be transmitted in several ways:
  - Via fomites or inanimate objects
  - Via poor techniques employed by health care workers:
    - This type of transmission is referred to as iatrogenic transmission.
    - Fecal-oral route – the digestive tract

VIRAL TRANSMISSION

- Viruses can be transmitted in several ways:
  - Respiratory tract – the sneeze is best form of transmission
  - Viruria – transmission via urine
  - Urogenital tract – sexual transmission
  - Contact with skin
VIRAL TRANSMISSION

- Viral transmission can be geographically or seasonally influenced.
- Most acute viral infections are seasonal.
  - Respiratory tract infections are higher in winter.
  - Digestive tract infections are higher in summer.

VIRAL TRANSMISSION: Fetal Infection

- Viremia in pregnant women can expose the fetus to infection.
  - The fetal infection rate for rubella during the first trimester is more than 80%.
  - About 1 in 5 babies can be infected by HIV in utero from infected mothers.
- Some virus transmission can occur during breast feeding.

VIRULENCE

- The capacity of an infectious organism to cause disease.
- Virulent viruses cause significant disease.
- Nonvirulent (attenuated) viruses cause little or no disease.
VIRULENCE

There are three ways to measure viral virulence:
- \( LD_{50} \) – how much virus is required to kill 50% of a subject population
- \( ID_{50} \) – how much virus is required to infect 50% of a subject population
- \( PD_{50} \) – how much virus is required to paralyze 50% of a subject population.

VIRULENCE

- Virulence varies between viruses.
- Virulence can be directly affected by:
  - Route of entry
  - Age and health of host
  - The gender of the host

VIRULENCE AND HOST SUSCEPTIBILITY

- There are two types of host:
  - Susceptible – can be infected and can also transmit the infection
  - Immune – cannot be infected.
- Gender may play a role in some infections:
  - Males are more susceptible to viral infection than females.
VACCINE DEVELOPMENT

- Vaccination is the most effective way to deal with viral infections.
  - It allows for life-long immunity from a particular infection.
  - It increases herd immunity.

VACCINE DEVELOPMENT

- There are three groups of vaccines:
  - Live attenuated vaccine – made of intact virions rendered non-infectious
  - Inactivated or killed vaccine – composed of killed or dead virions
  - Subunit vaccine – composed of immunogenic parts of virions.

VACCINE DEVELOPMENT

- Vaccination causing immunization can be either active or passive.
  - Active immunization – antigen is administered and causes the onset of the immune response
  - Passive immunization – a preformed antiviral product, such as antibody, is administered.
**VIRUSES AND CANCER**

- Some viruses can cause cancer in animals.
  - An estimated 20% of human cancers involve viruses.
  - Retroviruses can inactivate genes responsible for suppressing tumor formation.

**VIRUSES AND CANCER**

- Viruses associated with human cancers include:
  - Epstein-Barr virus
  - Hepatitis B and C viruses
  - HPV

**HOST DEFENSE AGAINST INFECTION**

- Viral genomes code for many products that modify or block host defense.
- A battle wages between the host immune system and these modifications.