CHAPTER 13
VIRAL INFECTION

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

- Incubation period is the time between initial pathogen exposure and onset of symptoms and signs

PATTERNS OF VIRAL INFECTION

- Incubation periods vary for different viruses
  - Some (influenza, cold viruses) are as short as days
  - Some (HIV) are as long as years

<table>
<thead>
<tr>
<th>Disease</th>
<th>Incubation period</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza</td>
<td>1-3 days</td>
</tr>
<tr>
<td>Common cold</td>
<td>3-5 days</td>
</tr>
<tr>
<td>Rubeola (measles)</td>
<td>7-10 days</td>
</tr>
<tr>
<td>Measles</td>
<td>7-14 days</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>3-10 days</td>
</tr>
<tr>
<td>Rubella</td>
<td>1-2 weeks</td>
</tr>
<tr>
<td>Rabies</td>
<td>30-90 days</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>3-4 years</td>
</tr>
<tr>
<td>Hepatitis A</td>
<td>15-45 days</td>
</tr>
<tr>
<td>Hepatitis B (HBV)</td>
<td>2-6 months</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>3-6 months</td>
</tr>
<tr>
<td>Hepatitis E</td>
<td>2-3 weeks</td>
</tr>
<tr>
<td>AIDS</td>
<td>&gt;10 years</td>
</tr>
</tbody>
</table>
PATTERNS OF VIRAL INFECTION

- Viral infections can be:
  - **Acute** (rapid and self-limiting)
  - **Persistent** (long term)
    - **Chronic** (continuous long-term production of virions)
    - **Latent** (no virion production between outbreaks)
    - **Slow** (long incubation period and progressive disease)

ACUTE INFECTIONS

- Characterized by rapid production of virions and elimination of infection
- 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
  - Prisons
  - 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

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 never cleared from the host
- There are three variations of persistent infections:
  - Chronic infection
  - Latent infection
  - Slow infections

PERSISTENT INFECTIONS: Killing Of Cytotoxic T Lymphocytes

- One host defense mechanism against viral infection is cytotoxic T lymphocytes (CTLs)
- Cytotoxic T lymphocyte escape mutants avoid CTLs
- Some viruses escape CTLs by infecting tissues that have reduced immunosurveillance
  - Outer skin layer
  - Vitreous humor of the eye

PERSISTENT INFECTIONS: Chronic Infections

- Long-term illness
- Continuous, long-term production of virions
- Example: hepatitis C
PERSISTENT INFECTIONS:
Latent Infections

- Three general characteristics:
  - No large-scale production of virions between episodic outbreaks
  - Reduced or absent immune response
  - Persistence of an intact viral genome so infections can recur
- Latent viruses can be reactivated years after entry into host
- Example: varicella-zoster (chickenpox/shingles)

PERSISTENT INFECTIONS:
Slow Infections

- Prolonged incubation period followed by progressive disease state, and increased virion production
- Slow infections are usually associated with fatal 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 basic requirements for successful infection:
  - Access to susceptible and permissive host cells
  - 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
PORTALS OF ENTRY

- The three main portals of entry are:
  - Respiratory tract
  - Gastrointestinal tract
  - Genitourinary tract

PORTALS OF ENTRY: Respiratory Tract

- The most common portal of entry into the human body
  - It is always exposed to large numbers of potential pathogens
  - Viruses disseminate from here into other areas of the body
PORTALS OF ENTRY: Gastrointestinal Tract

- The gastrointestinal tract is a common route for infection
- Many viruses use this portal of entry
  - They must be resistant and resilient to harsh environments in order to survive

PORTALS OF ENTRY: Gastrointestinal Tract

- Viruses are collected by M cells in the intestinal epithelium
- Some viruses stay in the M cells and eventually destroy them
  - This causes inflammation of the digestive tract and diarrhea

PORTALS OF ENTRY: Genitourinary Tract

- The primary entry point for sexually transmitted viruses
  - Some remain in this tract and cause local infections, e.g., genital warts
  - Some gain access to underlying tissues and disseminate throughout the body
PORTALS OF ENTRY:
Urogenital Tract

PORTALS OF ENTRY:
Eyes

Some viruses enter through the sclera and inner surface of the eyelids
- Tears and eye secretions make it difficult for virions to cause infections
- Scratches of the cornea can allow herpes infections of the eye
PORTALS OF ENTRY: Skin

- 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

- Viral dissemination refers to spread of virus within an infected body
**VIRAL DISSEMINATION:**

**Bloodstream**

- Systemic viruses can disseminate via the bloodstream – hematogenous dissemination
  - Viremia – virions in blood
  - Active viremia – virion replication in blood
  - Most viruses spend little time in the blood

**VIRAL DISSEMINATION:**

**Nervous System**

- Some viruses can disseminate via the nervous system
  - They can disseminate throughout the entire body
  - Some target neurons
  - Some go through neurons to get to their preferred target area

**VIRAL DISSEMINATION:**

**Internal Organs**

- Systemic viruses can disseminate via the liver, spleen, other organs, and bone marrow
- Viruses that enter the brain can disseminate throughout the central nervous system
VIRAL TRANSMISSION

- Viral transmission refers to the spread of the virus from one host to another
- Two general patterns of viral transmission:
  - Transmission within a single species
    - Human to human, e.g., measles
  - Transmission between species
    - Animal to human, e.g., rabies

VIRAL TRANSMISSION

- Viruses can be transmitted in several ways:
  - Respiratory tract – via sneezing, coughing
  - Epidermis – via skin lesions
  - Bodily fluids – via sexual activity, needles
  - Fecal-oral route – via contaminated food and water
  - In utero – to fetus via infected mothers
VIRAL TRANSMISSION

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

VIRULENCE

- How harmful a pathogen is to its host
- Virulence is affected by host immune system
- Virulence can be reduced by genetic mutations

VIRULENCE

- There are three ways to measure viral virulence:
  - LD₅₀ – how much virus is required to kill 50% of infected individuals
  - ID₅₀ – how much virus is required to infect 50% of infected individuals
  - PD₅₀ – how much virus is required to paralyze 50% of infected individuals
VIRULENCE

- Virulence varies among 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

VACCINE DEVELOPMENT

- Vaccination is the most effective way to deal with viral infections
  - It allows for long-term or even lifelong 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’ 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 – an antiviral product, such as antibody, is administered

RECOMBINANT DNA VACCINES

- Vaccines made from genetic material from multiple sources
- Quicker, cheaper, and safer than traditional methods of producing vaccines
- Dual immunological response – both antibodies and T cells produced in animals given recombinant DNA vaccine
VIRAL CULTURE

- Cultured cell lines are used to grow viruses
  - Primary cell lines – new organs or tissues used for each batch of cells in which viruses are cultured
  - Semi-continuous cell lines – cells grown for several generations until new organs or tissues are again needed
  - Continuous cell lines – cells grown for many generations from an original organ or tissue

VIRUSES AND CANCER

- Some viruses are implicated in cancer in humans and can cause cancer in laboratory animals
  - An estimated 20% of human cancers involve viruses
  - Oncoviruses – cancer-causing 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 defenses
- A battle wages between the host immune system and these modifications