Microbiology

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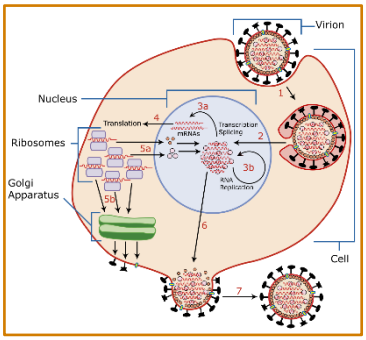
Dr.Saja Ebdah

ARKAN
ACADEMY

Viral Replication and Pathogenesis

- Viral Replication
  - The host cell is absolutely necessary for viral multiplication
    1. Adsorption (attachment)
    2. Entry
    3. Uncoating
    4. Transcription
    5. Synthesis of virus components
    6. Assembly
    7. Release



1. Adsorption (attachment):
   - ✓ Random collision
   - ✓ ***Interaction*** between specific proteins on viral surface and specific receptors on target cell membrane (tropism)
   - ✓ Some viruses may use more than one host cell receptor
   - ✓ Able to infect a limited spectrum of cell types

2. Entry (penetration):
   - ✓ Flexible cell membrane of the host is *penetrated* by the whole virus or its nucleic acid
   - ✓ 2 mechanisms
     - Endocytosis: entire virus engulfed by the cell and enclosed in a vacuole or vesicle
     - The viral envelope can also directly fuse with the host cell membrane

3. Uncoating
   - ✓ *Release* of viral genome
   - ✓ Cell enzymes (lysosomes) strip off the virus protein coat
   - ✓ Virion can no longer be detected; known as the "eclipse period"

4. Transcription/Translation

   A) DNA viruses:
   - ✓ Replicate their DNA in host cell nucleus mediated by viral enzymes
   - ✓ Synthesize capsid and other proteins in cytoplasm using host cell enzymes
   - ✓ New viral proteins move to nucleus where they combine with new DNA to form new viruses

   B) RNA viruses:
   - ✓ "+" sense RNA acts as mRNA - viral proteins are made immediately in cytoplasm mediated by viral enzymes
   - ✓ "-" sense RNA – 1^{st} makes a "+" sense RNA copy via viral enzyme

5. Synthesis
   - ✓ *Protein synthesis* - 2 types
     - Structural
     - Non-structural (enzymes for replication)
   - ✓ *Nucleic acid synthesis*
     - New virus genome
     - Most often by a virus
     - Coded polymerase or replicase; with some DNA viruses a cell enzyme carries this out

6. Assembly
   - ✓ *Mature virus* particles are constructed from the growing pool of parts
   - ✓ May take place in cell nucleus, cytoplasm or (with most enveloped viruses) at the plasma membrane

7. Release
   - ✓ *Non-enveloped* and complex viruses are released when the cell lyses or ruptures
   - ✓ *Enveloped* viruses are liberated by budding or exocytosis
   - ✓ Anywhere from 3,000 to 100,000 virions may be released, depending on the virus
   - ✓ Entire length of cycle- anywhere from 8 to 36 hours

- **Viral Pathogenesis**
  - ➢ The process by which a viral infection leads to disease
  - ➢ The majority of viral infections are subclinical
  - ➢ The consequences of viral infections depend on the interplay between a number of viral and host factors
  - ➢ ***Factors in Viral Pathogenesis:***
    - ✓ Entry into the Host
    - ✓ Course of Infection (Primary Replication, Systemic Spread, Secondary Replication)
    - ✓ Cell/Tissue Tropism
    - ✓ Effects of viral infection on cells (Cellular Pathogenesis)
    - ✓ Cell/Tissue Damage
    - ✓ Host Immune Response
    - ✓ Virus Clearance or Persistence
    - ✓ Viral shedding
  - ➢ ***Steps in Viral pathogenesis***

    1. Viral Entry & Primary Replication
    2. Viral Spread & Cell tropism
    3. Cellular injury & Clinical illness
    4. Recovery from infection
    5. Viral clearance or persistence
    6. Viral shedding

  - ➢ ***Viral Entry***
    - ✓ Skin - through cuts or abrasions, animal bites e.g. Rabies virus
    - ✓ Respiratory tract e.g. Influenza, Parainfluenza virus
    - ✓ Gastrointestinal tract e.g. Rotavirus, Poliovirus
    - ✓ Conjunctiva and other mucous membranes
    - ✓ Genitourinary tract e.g. HIV
    - ✓ Directly into Bloodstream by
      - Needles : HBV, HIV
      - Blood transfusions : HIV, HCV, HBV
      - Insect vectors : Arboviruses

➢ ***Routes of Transmission***

✓ Horizontal transmission:

- Direct contract (secretions, blood etc.)
- Respiratory (aerosol)
- Contaminated inanimate objects
- Insect vector (mosquitoes, ticks, etc.)
- Zoonoses

✓ Vertical transmission:

- Mother to fetus [Transplacental (Congenital), Perinatally]

- **Course of Viral Infection**

➢ ***Primary Replication***

✓ Viruses usually replicate at the site of initial entry into the host.

✓ The infection remains localized at the site of entry

➢ ***Systemic Spread***

✓ Many viruses produce disease at sites distant from point of entry

✓ After primary replication, they spread via blood, neurons or lymphatics to other organs.

✓ Presence of virus in blood is called VIREMIA

✓ Viral spread is determined by its organ & cell specificity – CELL TROPISM

➢ ***Secondary Replication***

✓ Secondary replication takes place at susceptible organs/tissues following systemic spread.

- **Effects of Viral Infection on Cells**

➢ Cells can respond to viral infections in following ways:

✓ No apparent change

✓ Cell death or lysis e.g. poliovirus

✓ Cellular proliferation e.g. Molluscum

✓ Malignant transformation e.g. Oncogenic viruses

✓ Cytopathic effects as in tissue cultures

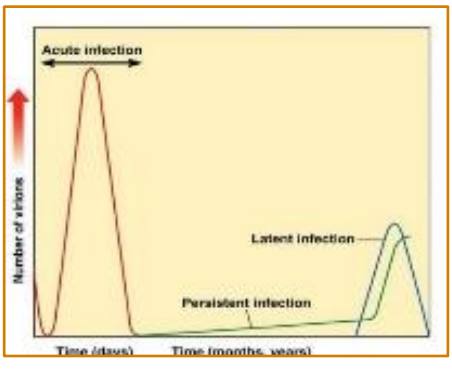
➢ Cytopathic effects- virus-induced damage to the cell that alters its microscopic appearance

➢ Inclusion bodies- compacted masses of viruses or damaged cell organelles

- **Outcome of Viral Infection**

➢ Clinical outcome – subclinical (Inapparent) or clinical (apparent) infections. Clinical infections can be:

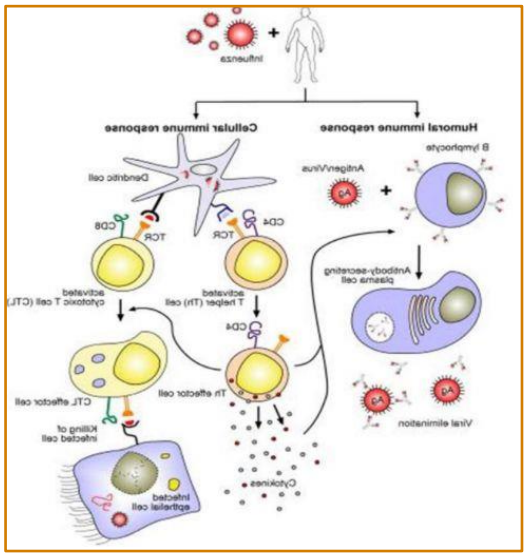
1. ***Acute Infection***
   - ✓ Complete recovery
   - ✓ Recovery with residual effects
   - ✓ Proceed to chronic infection (latency)
2. ***Chronic Infection***
   - ✓ Silent subclinical infection for life
   - ✓ A long silent period before disease
   - ✓ Reactivation to cause acute disease
   - ✓ Chronic disease with relapses and excerbations
   - ✓ Cancers



- **Virus Shedding**
  - Last stage in pathogenesis
  - Necessary step to maintain a viral infection in a population of hosts
  - Usually occurs from the site of entry
  - Occurs at different stages of disease depending on the agent
  - Represents the time at which an infected individual is infectious to contacts
  - In certain cases, shedding does not occur e.g. Rabies

- **Viral Persistence**
  - Majority of viral infections are cleared but certain viruses may cause persistent infections. There are 2 types of persistent infections:
    - ✓ Chronic infections – virus is continuously detected but at low levels
    - ✓ Latent infections - virus remains completely latent following primary infection. Intermittent flare ups of disease

- **Host Responses to Viral Infections**
  - ***Innate immunity*** – Interferons
    - ✓ Humoral response – protects the host against reinfection by same virus
      - IgG & IgM : Blood & tissue
      - IgA : mucosal surfaces of respiratory& gastrointestinal tract
      - Neutralising Abs prevents initiation of infection
  - ***Cellular response*** – recovery from viral infection, destroy viral infected cells
    - ✓ Mostly gives lifelong protection



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www.arkan-academy.com

+962 790408805