Pathogenesis of viral infections

by:

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Learning Objectives:

Upon the end of this lecture, the student should be able to:

1- list the general steps of pathogenesis and clinical course of viral infection.

2- **Differentiate** between local & systemic acute viral infection

3- **Describe** the mechanisms of cell tropism, types of cell injury during viral infection and mechanisms by which virus can escape from the host.

4- **Explain** the mechanisms of different types of persistent viral infections.

5- **Differentiate** between conventional and non-conventional viral infection.
Pathogenesis:

Refers to the interaction of viral and host factors that lead to a disease production.

- Pathogenic v. :

- Virulent strain : produce more severe disease
ATTACHMENT

Click after each step to view process

PENETRATION

UNCOATING

HOST FUNCTIONS

Transcription

Translation

REPLICATION

ASSEMBLY (MATURATION)

MULTIPLICATION

VIRAL LIFE CYCLE

RELEASE
Steps in viral pathogenesis

- Viral entry (RT, GE, skin, UGT, conjunctiva, blood)
- Primary viral replication
- Viral spread
- Cellular injury
- Cell & tissue tropisms
- Host immune response
- Viral clearance & establishment of persistant inf.
- Viral shedding
Viral entry

- RT
- GE
- Skin
- UGT
- conjunctiva
- blood born: needles,
insect vectors,
blood Transfusion
Mode of transmission

- **Horizontal**: person to person (infl.v., herpes v., HIV)
- **Vertical**: mother to offspring (rubella, HIV, CMV, Hepatitis B & C, parvo B19)
- **Zoonotic**: rabies v.
- **No transmission**: reactivation of latent infection (HSV1, HSV2, CMV)
viral replication

- Localized: infl.v. rotav.
- Disseminated infection: polio v. measles v.
## Features of acute viral diseases

<table>
<thead>
<tr>
<th></th>
<th>Local inf.</th>
<th>Syst. inf.</th>
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</thead>
<tbody>
<tr>
<td><strong>Ex.</strong></td>
<td>rhino v.</td>
<td>Measles v.</td>
</tr>
<tr>
<td><strong>Site of Pathology</strong></td>
<td>portal of entry</td>
<td>distant</td>
</tr>
<tr>
<td><strong>I.P</strong></td>
<td>short</td>
<td>long</td>
</tr>
<tr>
<td><strong>Viremia</strong></td>
<td>_</td>
<td>+</td>
</tr>
<tr>
<td><strong>IgA role</strong></td>
<td>important</td>
<td>not</td>
</tr>
</tbody>
</table>
Viral spread Mechanisms

- blood
- Lymphatics
- Neuronal spread

free Virions in plasma ....entero v., toga v.
Particular types of cells.....measles
Cell tropism

- Organ & cell specificities
  1- cell receptors with viral surface (capsid or envelope)
  2- factors affecting viral gene expression
  3- proteolytic enzymes
  4- specific viral genes
Cell injury

No apparent morphological or functional changes

Cytopathic effect (CPE):
1. Changes in the cell appearance
2. Giant cells
3. Inclusion bodies

Malignant transformation

Cell Death
Some tissue regenerate rapidly, other can’t
Non lethal physiological alteration
Clinical illnesses

- I.P
- Prodromal period
- Specific illness period
- Recovery period
immunopathogenesis

- **Direct** effect
  - polio v. / Ebola v.
- **Indirect** effect (immunological attack)
  - rota v. = cytokines
  - hepatitis A, B & C
  - measles = cytotoxic T-cell
  - HBV,
  - Parvo B19
  - & RSV = v-ab-c’ complex deposition
Evasion of host defences

• **Cytokine decoys:** viral prot. Block host immune mediators (IL1 /TNF)

• **MHC I (HIV/CMV)**

• **Inhibit complement (HSV)**

• **Virokines (HIV/EBV/adeno v.)** RNAs that block phosphorylation of (elf-2), the ability of interferon to block viral protein synthesis.

• **Multiple antigenic types (rhino v./HCV)**
Persistent viral infection

- Intact/subviral component (genome)

Mechanisms of Persistent
- Integration of a DNA provirus into host cell DNA
- Immune tolerance: no NA
- V. – ab complexes formation: infectious
- Location in an immunologically sheltered organ
- Rapid antigenic variations
- Spread from cell to cell: no EC phase
- Immunosuppression (AIDS)
Types of Persistent viral infection

- **Chronic carrier**: pt. infected == viral shedding for long period (HBV/ neonatal rubella & CMV)
- **Latent infections**: pt. infected == recover == no v. production == symptoms recur + production of v.
- **Slow virus infections:**
  - prolonged I.P & disease progression
  - normal growth cycle

**Types of Slow virus infections:**
- Conventional: SSPE/PML
- Non- Conventional: prions
Non-Conventional viruses (transmissible spongiform encephalopathies)

- In human:
  Creutzfelds-Jacob disease
  Kuru
- In animal:
  mad -cow disease
  scrapie - sheep
Infectious particles that are composed solely of protein, no detectable n.a.
E/M: filaments

Resistant to:
• U/V
• Heat
• Formaldehyde
• Nuclease

Inactivated by:
Hypochlorite
Na(OH)2
autoclave
<table>
<thead>
<tr>
<th>Feature</th>
<th>prions</th>
<th>conventional</th>
</tr>
</thead>
<tbody>
<tr>
<td>-N.a.</td>
<td>No</td>
<td>yes</td>
</tr>
<tr>
<td>-Prot.</td>
<td>Encoded by cellular gene</td>
<td>v. gene</td>
</tr>
<tr>
<td>-U/v heat</td>
<td>resist</td>
<td>inactivated</td>
</tr>
<tr>
<td>-E/M</td>
<td>filmentous(amyliod)</td>
<td>icosohedral/helical</td>
</tr>
<tr>
<td>-Ab production</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>-Induce inflammation</td>
<td>no</td>
<td>yes</td>
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</tbody>
</table>
Viral shedding

- Last stage
- Maintain viral infection in population
- Occurs from body surface involved in v. entry
- pt. is infectious to contact

Dead-end infection in human (no v. shedding)
- Rabies
- Poliomyelitis
- SSPE
Summary

• Virulent viral strain is more pathogenic

• Common viral entry through RT and GIT, while common viral spread is through blood and lymphatic.

• Cell injury: Direct or due immunopathogenesis

• Many mechanisms causing viral persistent; chronic, latent and slow viral infection.