

Lecture 7

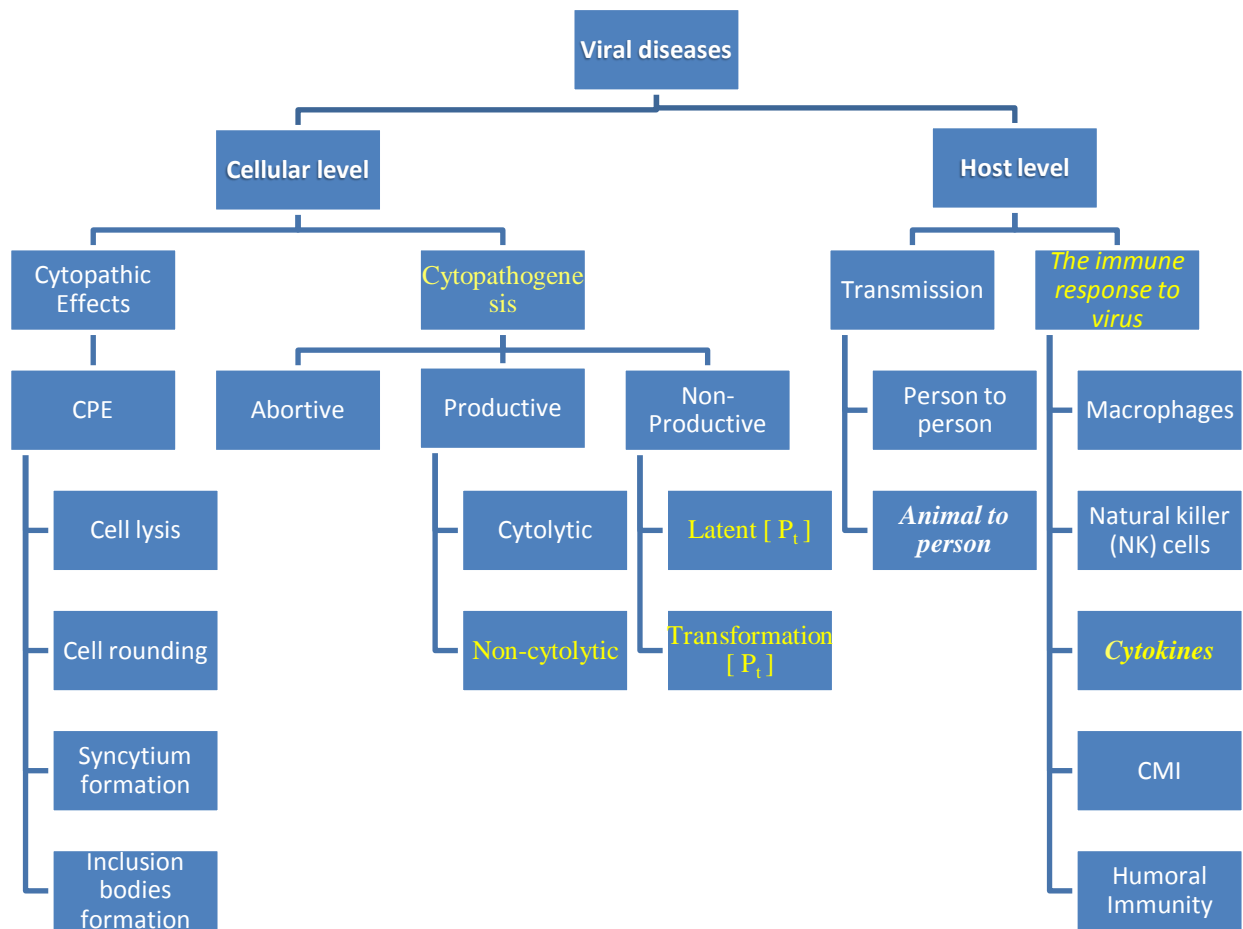
Pathogenesis of viral infections



Done by: أحمد الطايغ

OBJECTIVES

- *Definition and levels of viral pathogenesis.*
- *Types of viral infections at cellular level.*
- *Pathogenesis at host level.*
- *The immune response to viral infection.*
- *The stages of viral infection.*
- *The types of viral infections at host level.*



*cytopathogenesis = the effect of V on a single cell

Types of viral infections:

- **Abortive** : do not replicate due to:
 1. Mutation
 2. Actions of IFNs
 3. Defective interfering practicals.

- **Non-productive:** Vs. genes integrated in to cell's DNA or appear as a circular episome or both. This happened when vs. infect cells lack the machinery for transcribing viral genes. It is divided to:

1. **Latent:** The cell return to its normal properties ex: HSV
2. **Transformation:** cause tumour and stimulate uncontrolled cell growth.

- **Productive:**

1. Cytolytic:

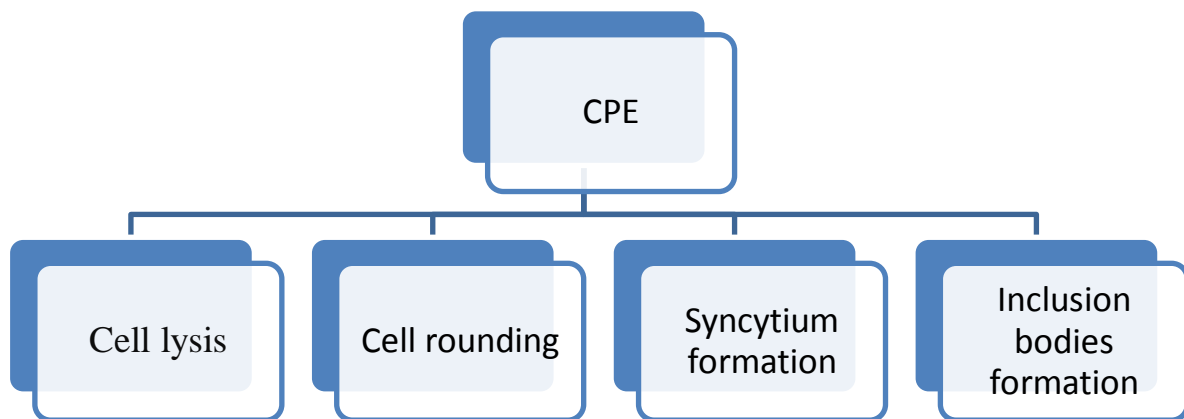
- Vs. replicate and produce progeny
- Inhibition of cellular protein and NA(nucleic acid) synthesis
- Mostly caused by naked viruses (not enveloped).
- Lead to cell death, cytopathic effects:
 - **Cell lysis**
 - **Syncytium formation** (giant cell formation, fusion of host's cells).
 - **Inclusions bodies formation:** It take several forms: single / multiple, small / large. round / irregular and has two sites:
 1. **Intracytoplasmic:** protein synthesis and multiplication accrue in the cytoplasm. Ex, Rabies which cause Negri bodies.
 2. **Intranuclear:** protein synthesis and multiplication accrue in the nucleus. Ex, herpes.

2. Non cytolytic:

- Vs. replicate and produce progeny.
- On or little cytopathic effects.
- Vs. released by budding.
- Identified by: Direct immunofluorescence, Hemadsorption.

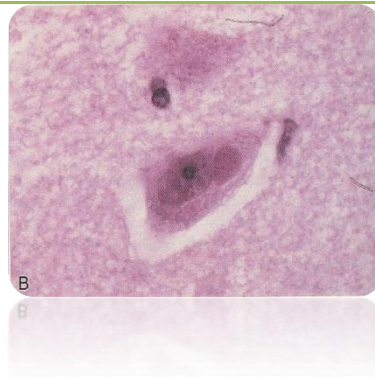
Some viral infections at cellular level cause cytopathic effects (CPE)

- CPE can take several forms

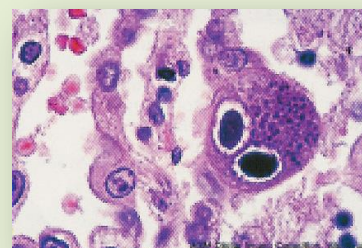


Examples of inclusion bodies :

Negri bodies caused by Rabies virus



Owl's eye inclusions caused by Cytomegalo virus (CMV/ it is also known as herpesvirus) (intranuclear)



Pathogenesis at host level

The mechanism:

1. The virus is transmitted and enter the host cell
2. The virus replicate and damage the host cell
3. Viruses remain localized or spread to other organs (generalized)
4. Viral shedding
5. The immune response acts as :
 - a. Host defense
 - b. Immunopathogenesis

Transmission:

1. Person to person

A. Horizontal transmission: can be transmitted through:

- ❖ Skin contact, blood
- ❖ Respiratory route
- ❖ Genital contact

B. Vertical transmission, from mother to baby:

- ❖ In utero by transplacental spread
- ❖ During delivery through an infected birth canal
- ❖ After birth by ingestion of breast milk

2. Animal to person: Ex: dogs transmit Rabies

Mechanisms of the spread of the virus through the body: Generalized infections :

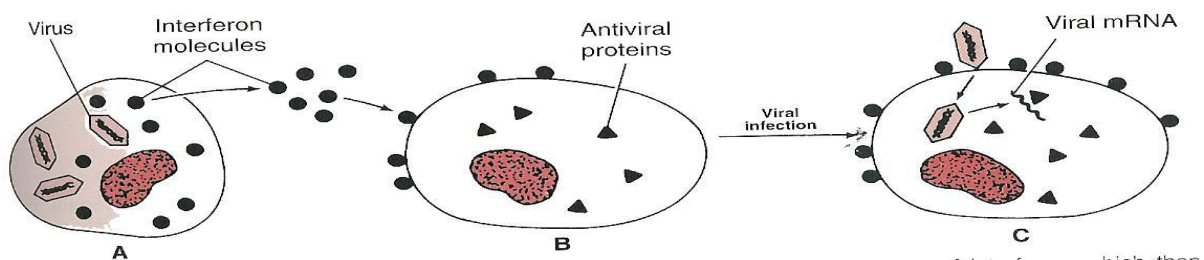
VIRAL SHEDDING

IMPORTANT FEATURES OF ACUTE VIRAL DISEASES :

	Local infections	Generalized (systemic) infections
Example of disease	Rhinovirus	Measles
Site of pathology	Portal of entry	Distant site
IP (incubation period)	Relatively short	Relatively long
Viremia (when the virus is present in the blood)	Absent	Present
Duration of immunity	Variable – may be short	Usually life long
Role of secretory AB (anti bodies) [IgA] (immunoglobulin A) in resistance	Usually important	Usually not important

The immune response to virus

- **Macrophages:** APC (antigen presenting cells), phagocytosis and cytokines production
- **Natural killer (NK) cells:** Lysis of VICs (Virus Infected Cells)
- Cytokines
- **Interferons (IFNs):** shut down the mRNA translation in the host cell and the virus (stop the protein synthesis)
- **α, β IFN** inhibit viral translation
- **γ IFN** stimulates phagocytosis and killing by macrophages and NK Cells.



- *Interleukin (IL)*
 - *Stimulate Ab production*
 - *Activate T cells & CMI*
 - *Suppress the IR*

The Cellular immunity is faster than the Humoral immunity

CMI (Cell-mediated immunity):

1. Affective against intracellular viruses
2. Lysis of virally infected cells by CTC (cytotoxic T cells)[CD8] or macrophages

Humoral Immunity:

1. Effective on extracellular viruses (viremia)
2. Usually by neutralization (binding to the virus's receptors so it cannot attach to the host cell)

The stages of a typical viral infection.

1. The incubation period:

From the time of infections until the symptoms appear

2. Prodromal period:

The period of non-specific symptoms

3. The specific-illness period:

The signs and symptoms of viral diseases are the result of cell killing by:

- Inhibition of cellular macromolecular synthesis.
- Immunologic attack (immunopathogenesis) by cytotoxic T cells (CTC)
Ex: Hepatitis (HAV, HBV, HCV)

4. The recovery period

Types of viral infections at host level:

1. Asymptomatic infection (the most common) .
2. Acute infection
3. Persistent infection:
 - Late complications of acute infection
 - Latent infection
 - Chronic infection

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More information to help you understand more

IFNs: the name "interferon" was given after they were recognized by their ability to interfere with viral infection.

1. Interferons are natural cellular products released from infected host cells in response to viral or other foreign nucleic acids. They are detectable as early as 2 h after infection.
2. They are host specific but not virus specific.
3. Normal cells do not synthesize Interferons until induced to do so.
4. They are considered as the first line defence against viral infection.
5. It last only for few days.

Recourse: <http://www.microrao.com/micronotes/interferon.htm>