

Lecture 7



Viral Pathogenesis

- Additional Notes
- Important
- Explanation
- Examples

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.

ABBREVIATIONS

- Vs: Virus
- NA: Nucleic Acid
- INFs: Interferons
- CPE: Cytopathic effect
- HSV: Herpes Simplex Virus
- EBV: Epstein-Barr Virus
- HPV: Human Pappilomavirus
- HTLV: Human T-lymphotropic Virus
- IP: Incubation Period
- AB: Anti Body
- APC: Antigen Presenting Cells
- NK: Natural Killer
- VICs: Virus Infected Cells
- IL: Interleukin
- CMI: Cell-Mediated Immunity
- IR: Insulin Resistance
- CTCs: Cytotoxic T Cells
- IF: Immunofluorescence
- HAV: Hepatitis A Virus

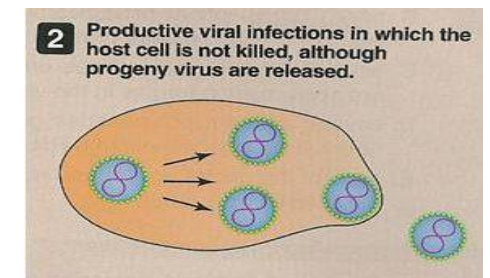
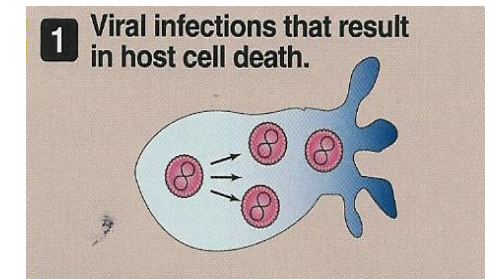
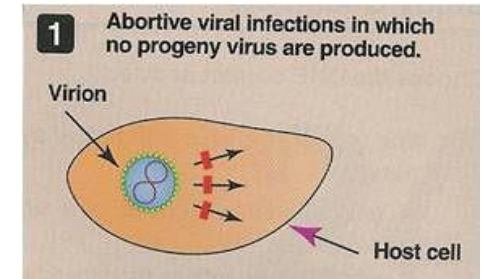
Pathogenesis of viral infection:

Viral disease level can be divided into:

- Viral disease **at the cellular level:**
 - ✓ Abortive “Vs not produced”
 - ✓ Productive “Vs Produced”
 - ✓ Non-productive “Vs not produced, but Viral NA present”
- Viral disease **at the host level:**
 - ✓ Asymptomatic infection “Most common”
 - ✓ Acute infection
 - ✓ Persistent infection:
 - Late complication of acute infection
 - Latent infection
 - Chronic infection

Viral infection at the cellular level:

- Abortive infection:
 - Virus don't complete the replication cycle.
 - Due to: mutation, defective interfering particles & the action of INFs.
- Productive infection:
 - ✓ Cytolytic Infections:
 - Virus replicate & produce progeny “small virus”
 - Cause of cell death & CPE
 - Inhibition of cellular protein & NA synthesis
 - Mostly cause by naked Virus “Not enveloped”
 - ✓ Non-cytolytic Infections:
 - Viruses replicate & produce progeny.
 - Viruses releases by cell budding & little or no CPE
 - Identified by hemadsorption⁽¹⁾ & direct IF



⁽¹⁾ The ability of cell infected with an enveloped virus containing glycoprotein substance to absorb RBCs

Viral infection at the cellular level:

- Non-productive Infections:
 - Viruses infect cells that restrict or lack the machinery for transcribing viral genes.
 - Viral genome is found either integrated into cell DNA or as a circular episome or both.
 - ✓ Latent infection:
 - The cell retains its normal properties.
 - There is limited expression of viral genes.
 - Ex: HSV
 - ✓ Transformation:
 - Cause tumor in animals & human and it can transform cell culture
 - Ex: EBV, HPV & HTLV
- **REMEMBER:** Virus can stimulate uncontrolled cell growth causing transformation by: alternating the balance between growth activators & growth suppressors gene products.

Cytopathic Effects: CPE

- CPE can take several forms:
 1. Cell lysis “cell disintegration”
 2. Cell rounding
 3. Syncytium formation “Cell fusion”
Ex: Herpes Paramyxo Vs.
 4. Inclusion bodies formation:

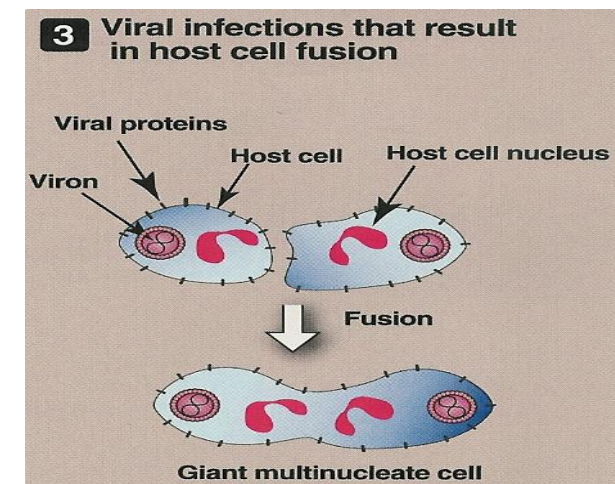
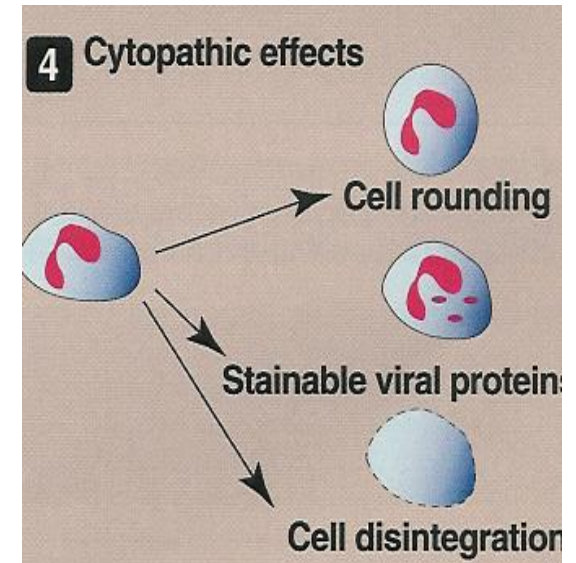
✓Take place in:

- Intranuclear (DNA Vs): Protein synthesis and multiplication accrue in the nucleus. Ex: Herpes Vs
- Intracytoplasmic (RNA Vs): Protein synthesis and multiplication accrue in the cytoplasm.

Ex: Rabies Vs. → it causes Negri bodies

✓Take several forms:

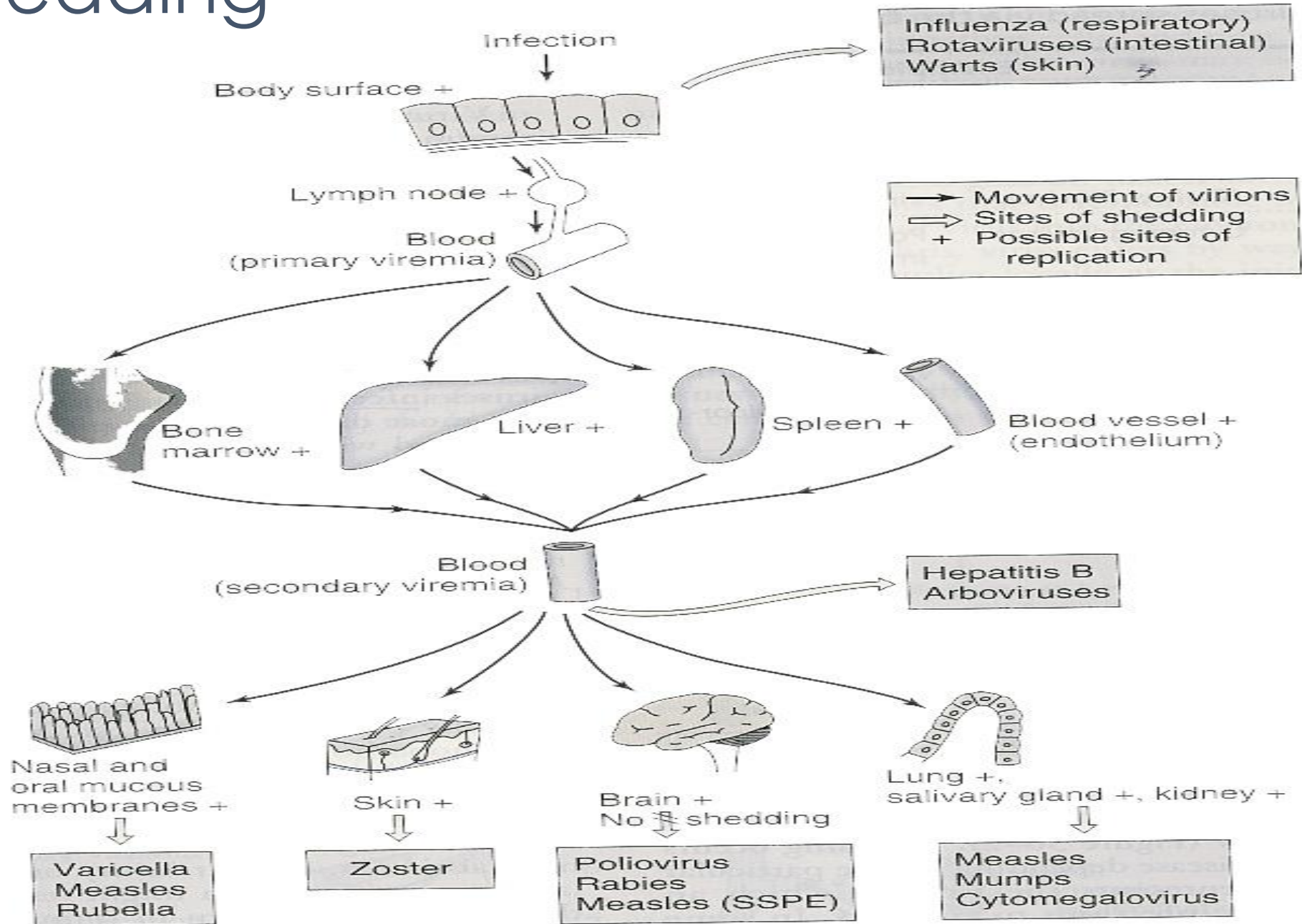
1. Single/multiple
2. Small/large
3. Round/irregular



Pathogenesis at Host level:

- Transmission of the virus & its entry to the host:
 1. Person to person:
 - Horizontal: Ex: Skin contact
 - Vertical: “from the mother to her baby”
Ex: During delivery through an infected birth canal.
 2. Animal to person
- Replication of the virus & damage to cells
- Viruses remain localized or spread to other organs
- Viral shedding
 - Successful reproduction, expulsion & host-cell infection caused by virus progeny.
- The immune response acts as:
 1. Host defense
 2. Immunopathogenesis

Viral Shedding

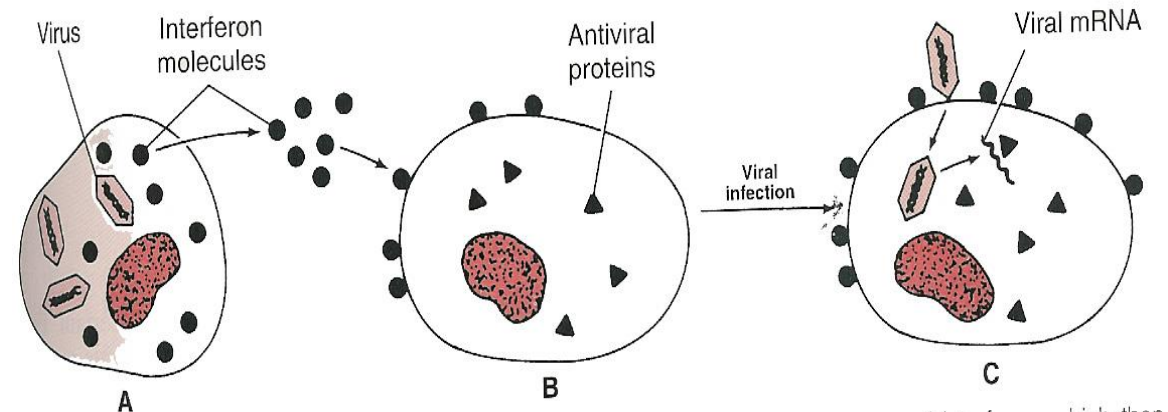


Important features of acute viral diseases

	Local Infections	Generalized (systemic) infections
Example of disease	<i>Rhinovirus</i>	<i>Measles</i>
Site of Pathology	<i>Portal of entry</i>	<i>Distant site</i>
IP (incubation period)	<i>Relatively short</i>	<i>Relatively long</i>
Viremia (presence in the blood)	<i>Absent</i>	<i>Present</i>
Duration of immunity	<i>Variable- may be short</i>	<i>Usually life long</i>
Role of secretory AB (anti bodies) [IgA] in resistance	<i>Usually important</i>	<i>Usually not important</i>

The immune response to virus:

- Macrophages: APC, Phagocytosis and cytokines production.
- Natural killer cells: Lysis of VICs
- Cytokines:
 - ✓ Interferons “INF”:
 - α , β IFN: inhibit the viral and the host cell mRNA translation
 - γ IFN: stimulate phagocytosis and killing by macrophages and NK cells
 - ✓ Interleukin “IL”:
 - Stimulates AB production
 - Activate T cells & CMI
 - Suppress the IR



The immune response to virus:

- Cell-mediated Immunity “CMI”:
 - Effective against **intracellular** viruses
 - Lysis of virally infected cells by CTC [CD8]
- Humoral Immunity:
 - Effective on **extracellular** viruses “viremia”
 - Usually by neutralization⁽¹⁾
- **P.S:** The cellular immunity is **faster** than the Humoral immunity

⁽¹⁾ Binding to the virus’s receptors so it cannot attach to the host cell.

Stages of a typical viral infection:

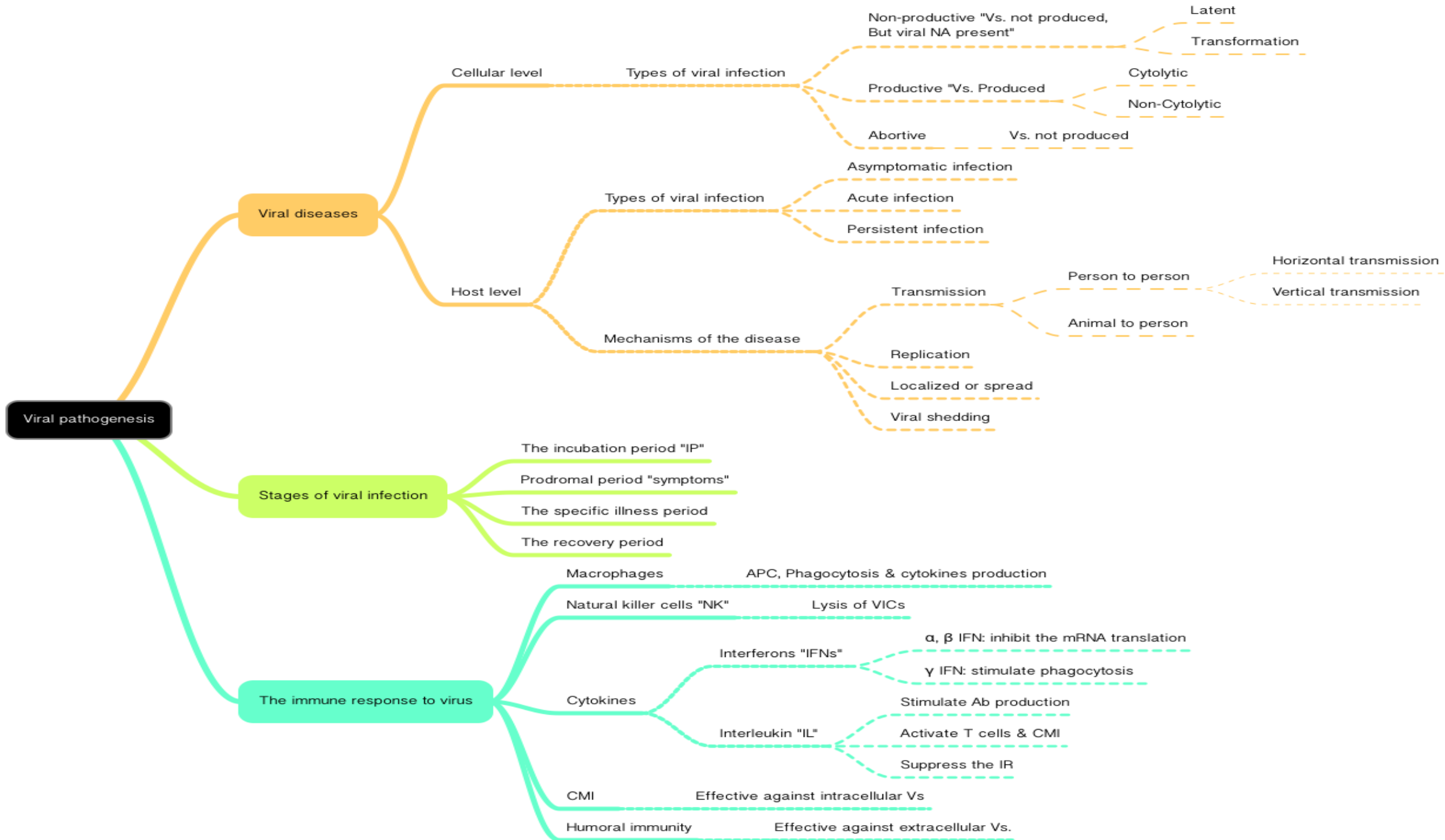
1. The incubation period “IP”
2. Prodromal period “General symptoms”
3. The specific-illness period:

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

- Inhibition of cellular macromolecular synthesis
- Immunologic attack “Immunopathogenesis” cytotoxic T cells

Ex: hepatitis (HAV.HBV.HCV)

4. The recovery period



Quiz

1. Which one is a type of infection at cellular level?

- a) Abortive b) Productive c) Non-productive d) All of the above

2. The number of stages of a typical viral infection is:

- a) 6 b) 4 c) 3 d) 2

3. What is the most common viral infection at host level?

- a) Asymptomatic infection b) Acute infection c) Persistent infection

4. Negri bodies is caused by:

- a) Rabies Virus b) Herpes Virus c) Herpes paramyxo Virus

5. The duration of generalized "systemic" infection is usually life long:

- a) T b) F