"Viral Pathogenesis"

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.

LECTURE

8

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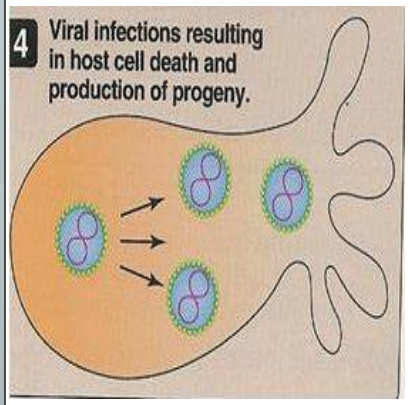
Abbreviations :

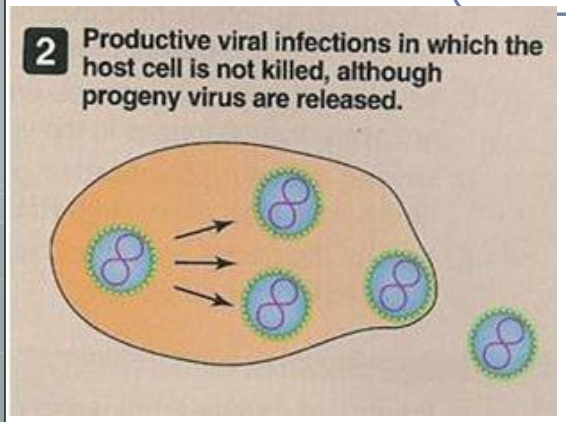
- Vs: Virus
- NA: Nucleic Acid
- INFs: Interferons
- CPE: Cytopathic effect
- HSV: Herpes Simplex Virus
- EBV: Epstein-Barr Virus
- HPV: Human Pappilomavirus
- HTLV: Human T-lymphotropic Virus
- IP: Incubation Period
- AB: Anti Body
- APC: Antigen Presenting Cells
- NK: Natural Killer
- VICs: Virus Infected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

Viral pathogenesis

b)Productive

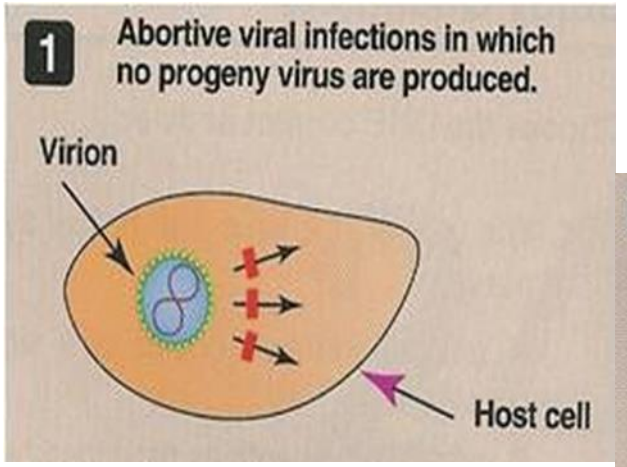
- Ctolytic
  Vs produced
- Non-cytolytic
  Vs produced





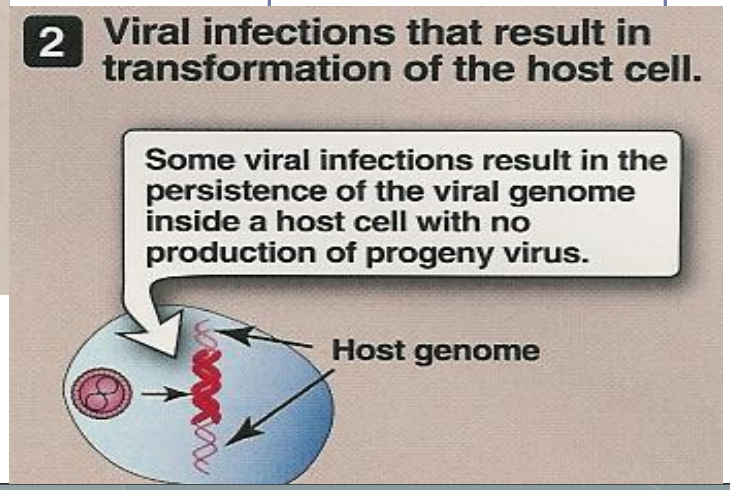
a)Abortive

- Vs not produced



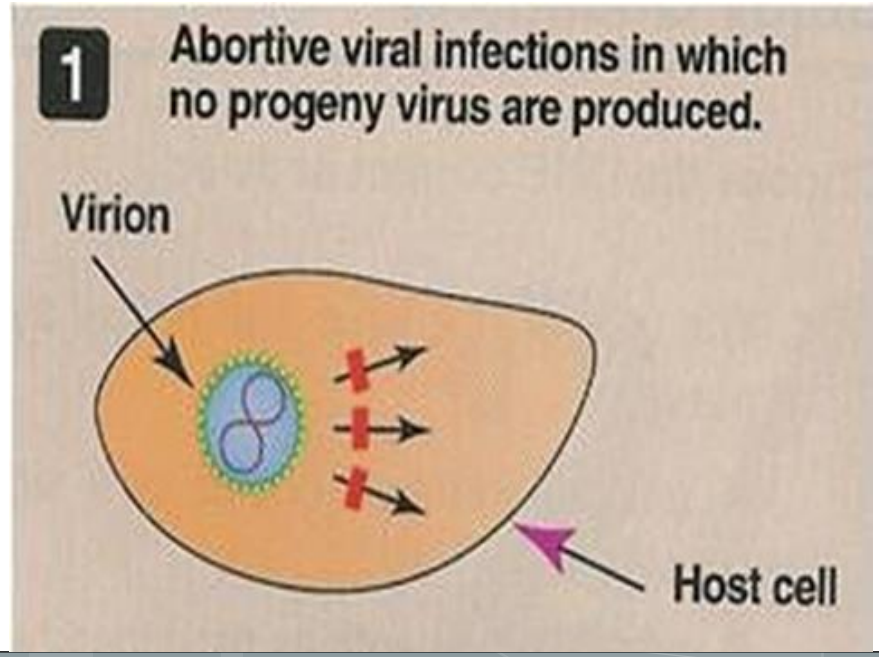
c)Non-productive

- Latent
  Vs NA present
- Transformation
  Vs NA present

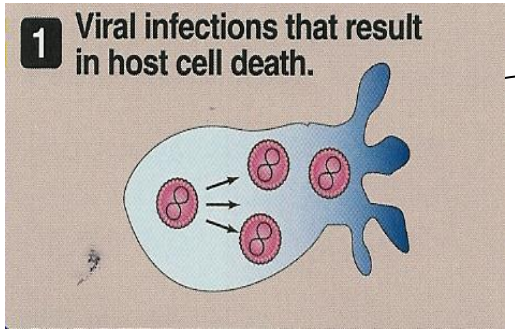


a) Abortive infections : (asymptomatic infection)

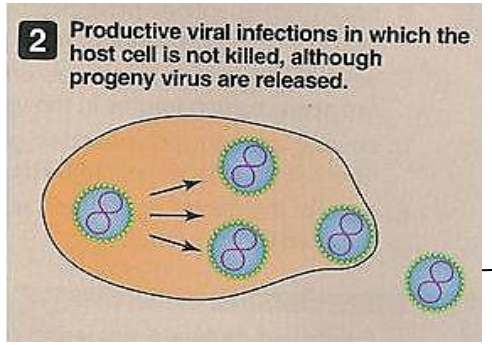
- Vs are not produced at all
  - ➢ Due to
    1-to mutation,
    2-defective interfering particles
    3- the action of IFNs



The types of viral infections at cellular level



(B) Productive Infections



Cytolytic Infections

- Viruses replicate & produce progeny
- Cell death & Cytopathic effects [CPE]
- Inhibition of cellular protein & NA synthesis
- Mostly non-enveloped Vs

Non-cytolytic infections

- Viruses replicate & produce progeny
- Viruses released by cell budding & little or no CPE
- Identified by hemadsorption & direct IF

c)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:

- *Persistent infection b/c* : there is limited expression of viral genes.

- *The cell retains its normal properties.*

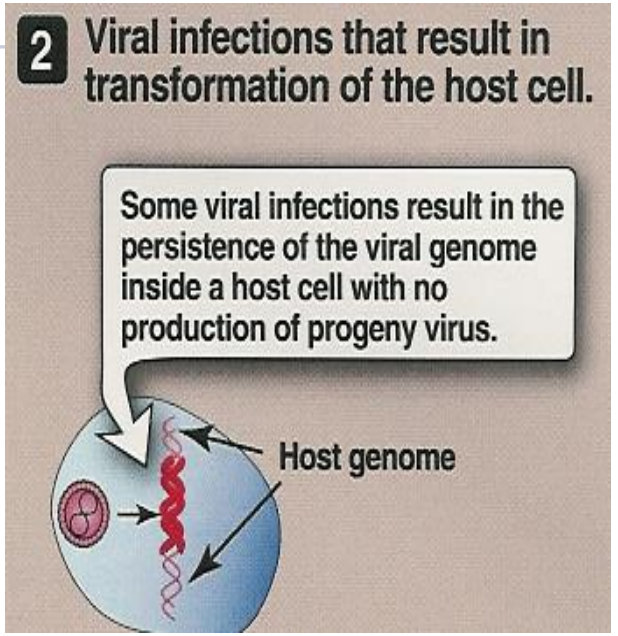
Ex: HSV

- Transformation:

Cause tumor in animals & humans and can transform cell culture.

Ex: EBV, HPV and HTLV

Vs can stimulate uncontrolled cell growth causing transformation by alternating the balance between growth activators & growth suppressors gene products.

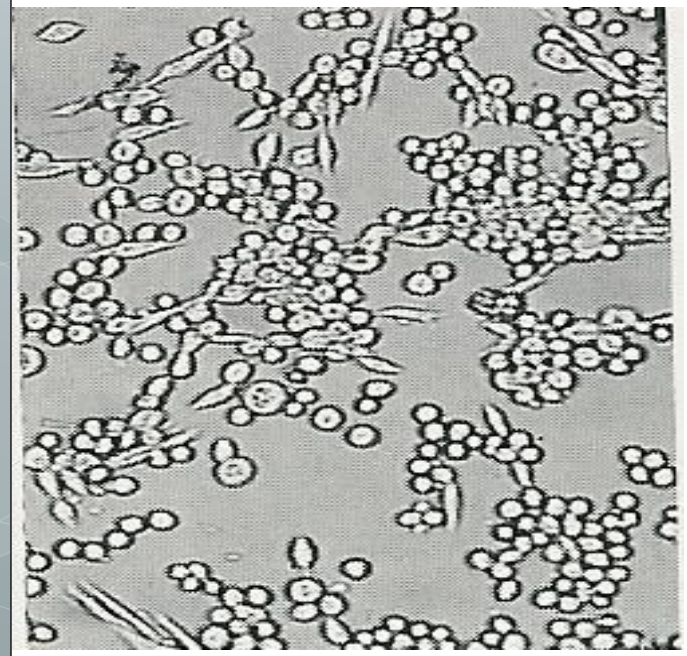


Cytopathic effects(cpe)

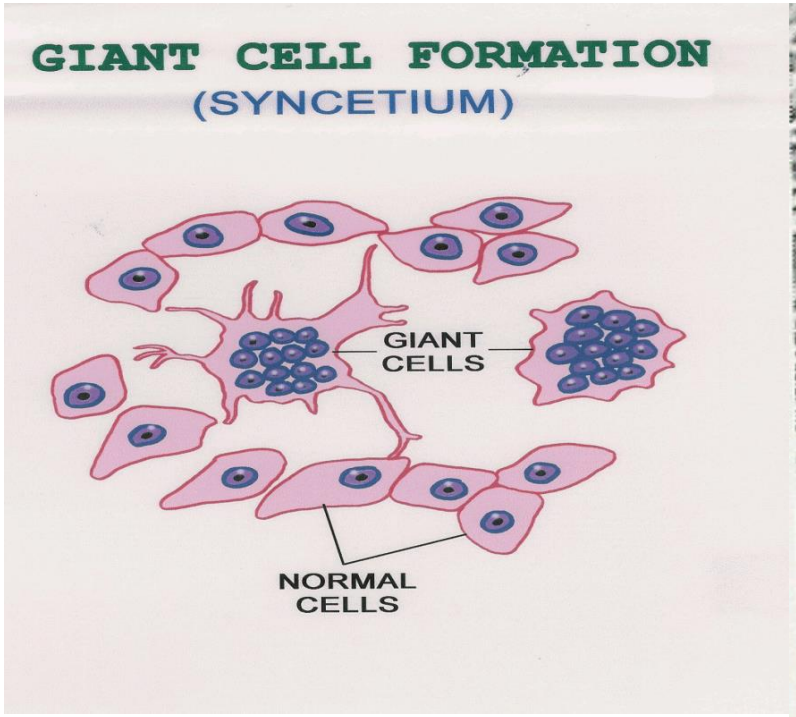
- CPE can take several forms:
  1. Cell lysis(digestion of cell)
  2. Cell rounding
  3. Syncytium formation (cells fuse together)
  4. Inclusion bodies formation(sites of viral production)

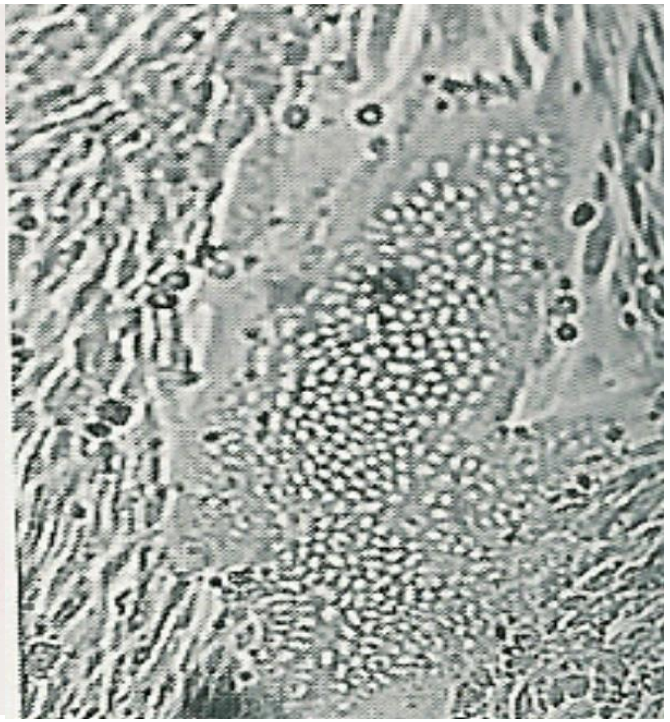
1. cell lysis (the cell is destroyed by viral mechanisms and cell death occur)
2. Cell rounding
3. Synctuim formation (multi nucleated gaint Cells) they are produced when two or more cells fuse together.

Ex: Herpes Paramyxo Vs.



Cell rounding





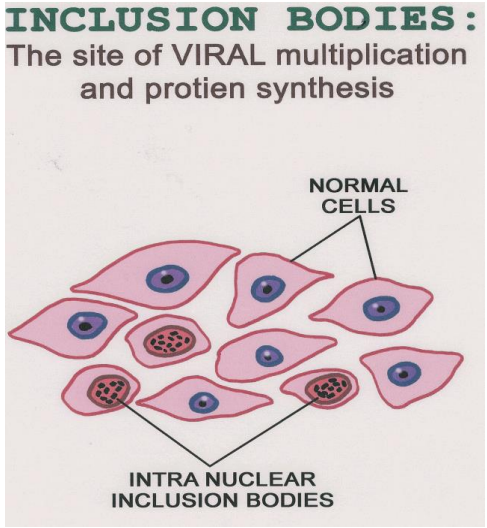
Synctuim formation

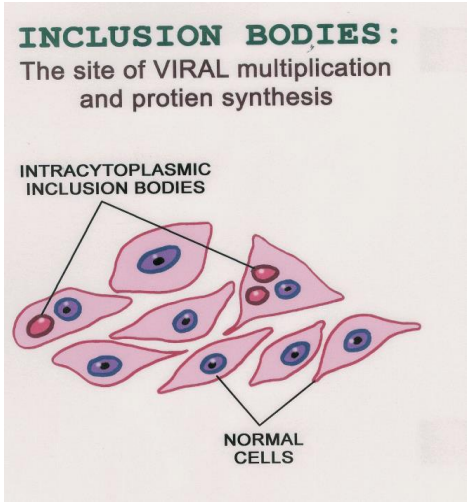
4. Inclusion bodies formation:

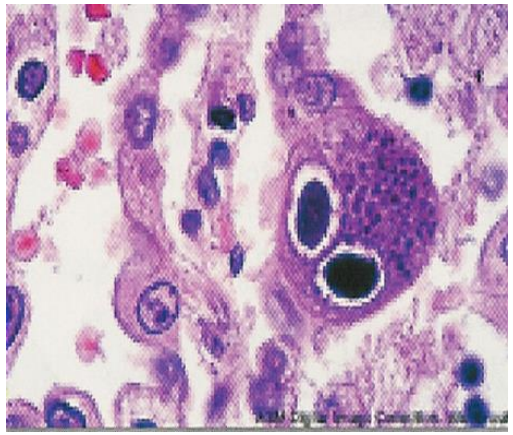
They are the sites of synthesis of viral components(proteins and NA)in the cell, they take place in :

- **in the nucleus:** (Intranuclear)(DNA Vs) Protein synthesis and multiplication accrue in the nucleus. Ex: Herpes Vs
- **In the cytoplasm:** (Intracytoplasmic) (RNA Vs): Protein synthesis and multiplication accrue in the cytoplasm. Ex: Rabies Vs. it causes Negri bodies

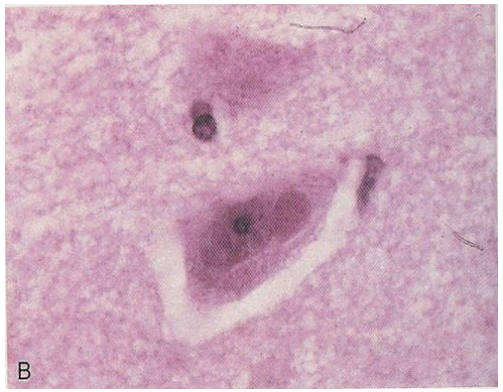
Inclusion bodies Take several forms:
1.Single/multiple 2.Small/large
3.Round/irregular







Owl's eye inclusions caused by CMV



Negri bodies caused by Rabies virus

Pathogenesis at Host Level

1. Transmission of the virus & its entry into the host.

-)Person to person :

a)Horizontal transmission: (between members of the same species that are not in a parent-child relationship)

b) Vertical transmission: transmitted directly from the mother to the fetus baby during pregnancy or childbirth.

- Animal to person

2) Replication of the virus & damage to cells

3) Vs remain localized or spread to other organs

4) Viral shedding: Successful reproduction, expulsion & host-cell infection caused by virus progeny.

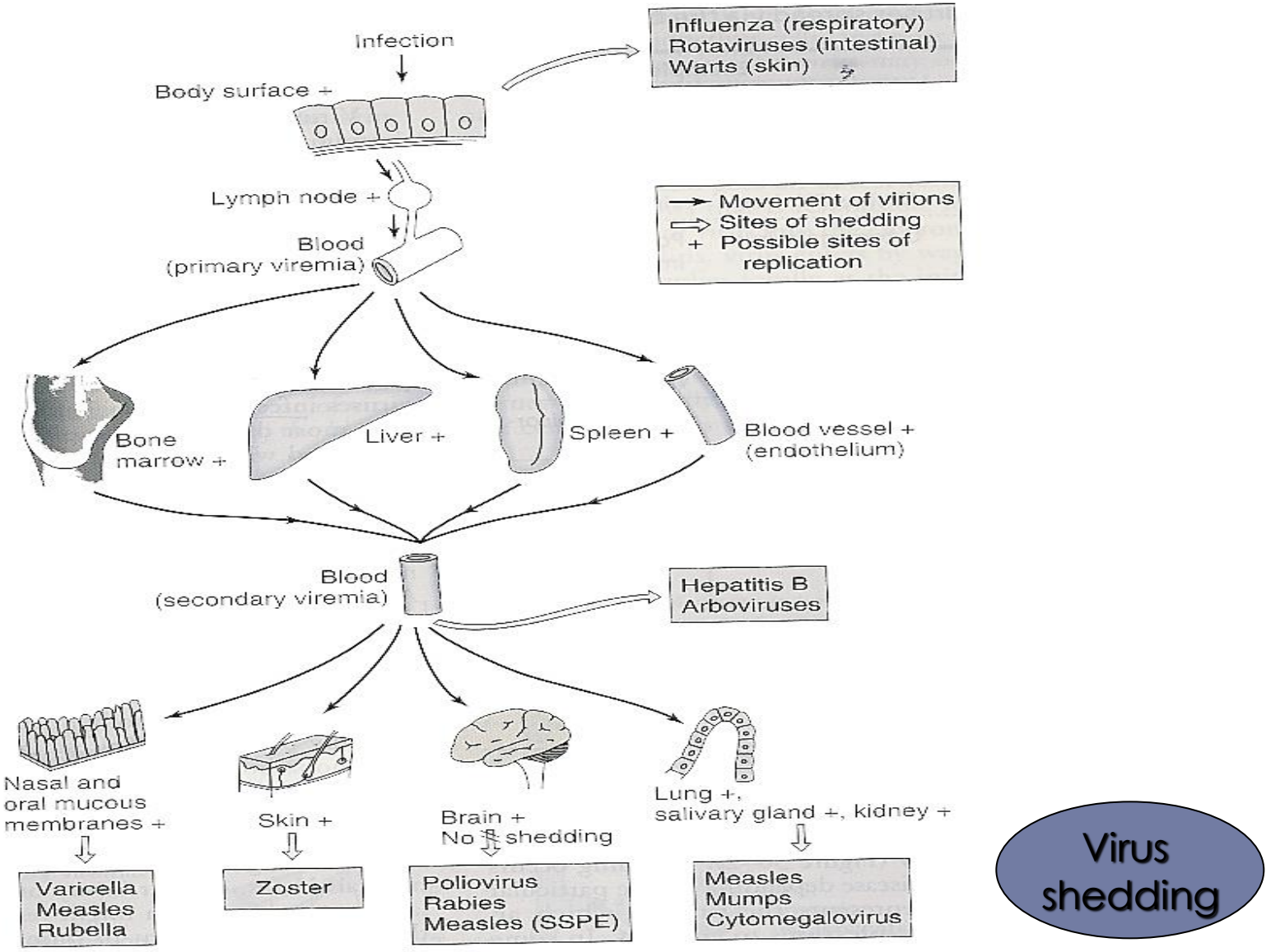
5) The immune response acts as

a) host defence b)immunopathogenesis

Common Routes of Human Infection by Viruses

Route of Entry	Virus	Disease (L/G)
Skin		
Mild Trauma	HPV	Warts (L)
Injection (Blood)	HBV,HCV, HIV	Hepatitis B, Hepatitis C ,AIDS (G)
Bite of insect animal	Yellow fever virus Rabies virus	Yellow fever (G) Rabies (G)
Respiratory tract	▪HSV-1 ▪Rhinovirus ▪RSV ▪Adenovirus ▪VZV ▪Measles virus	Gingivostomatitis (L) (URT) Common cold (L) (URT) Bronchiolitis (L) (LRT) Pneumonia (L) (LRT) Chickenpox (G) Measles (G)
GIT	Rotavirus HAV Poliovirus	Diarrhea (L) Hepatitis A (G) Poliomyelitis (G)
Genital tract	HSV-2 HBV HIV	Genital herpes (L) Meningitis (G) Encephalitis (G) Hepatitis B (G) AIDS(G)

Mechanisms of spread of virus through the body



Virus shedding

Important features of Acute Viral Diseases

	Local Infections	Systemic Infections
Ex. of specific Disease	Rhinovirus	Measles
Site of Pathology	Portal of entry	Distant site
IP	Relatively short	Relatively long
Viremia	Absent	Present
Duration of Immunity	Variable- may be short	Usually life long
Role of Secretory AB [IgA] in resistance	Usually important	Usually not important

The immune response to viruses

- **Macrophages :**

Function: antigen presenting cells, phagocytosis, and cytokines production

- **Natural killer cells:** responsible for the lysis of viral infected cells
- **Cytokines:**

1- interferons: α , β inhibit the viral and the host cell mRNA translation
γ stimulate phagocytosis and killing

2-interleukin: stimulate antibody production, activation of t-cells, and suppress the immune response.

- **Cellular mediated immunity:** (effective against intracellular viruses)

Main function: lysis of the virally infected cells by cytotoxic T cell (CTC)(CD8)

- **Humoral immunity:** (effective against extracellular viruses,viremia)

Main function is neutralization

The stages of a typical viral infection:

1- The incubation period

2- The prodromal period

3- The specific-illness period :the signs and symptoms of the viral disease are the result of cell killing by inhibition of cellular synthesis or by an immunologic attack (CTC)

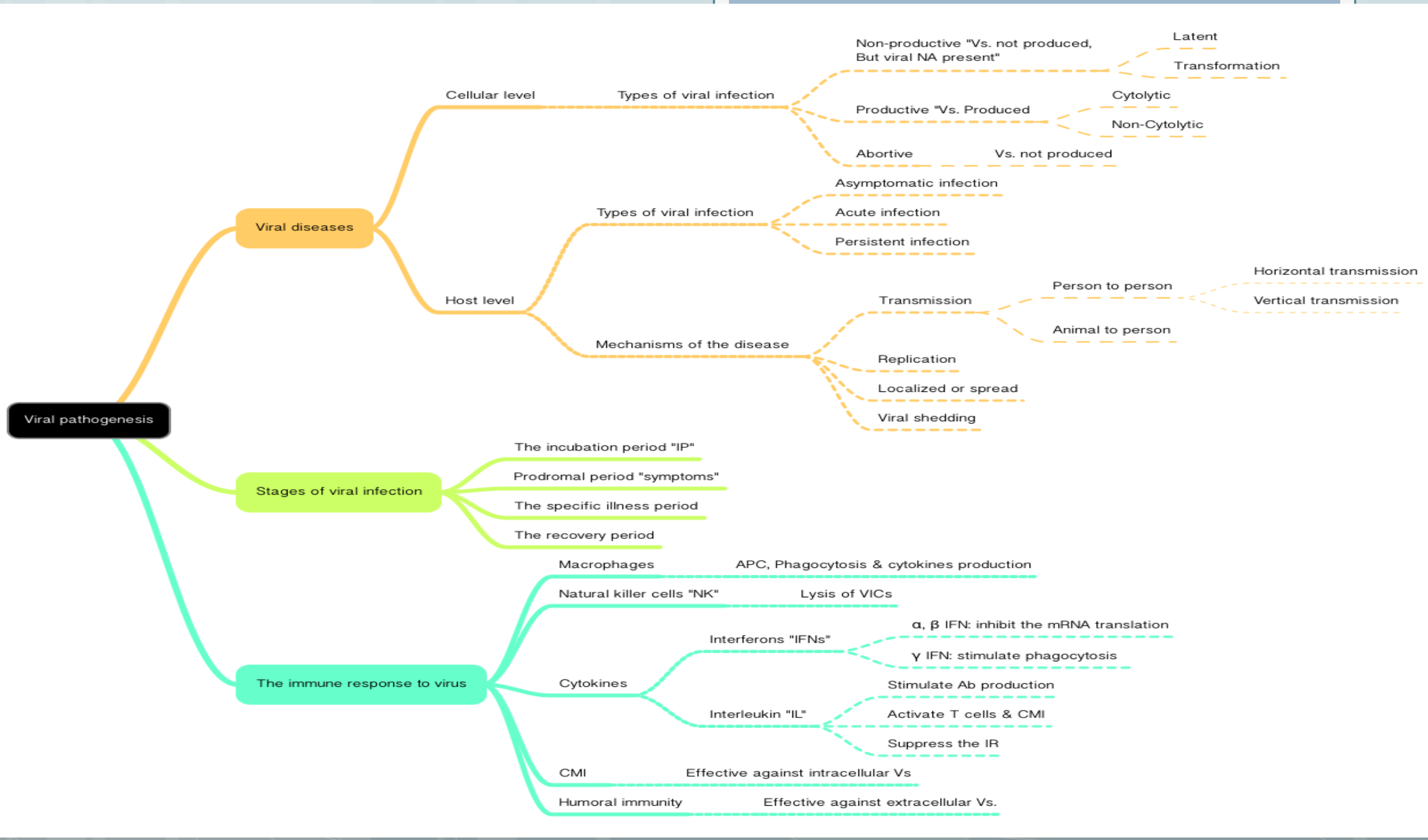
4- the recovery period

Types of viral infection at host level

1- asymptomatic infection

2- acute infection

3- persistent infection (latent, chronic ,or late complication of acute infection)


Viral pathogenesis
Viral diseases
Cellular level
Types of viral infection
Non-productive "Vs. not produced, But viral NA present"
Latent
Transformation
Productive "Vs. Produced
Cytolytic
Non-Cytolytic
Abortive
Vs. not produced
Host level
Types of viral infection
Asymptomatic infection
Acute infection
Persistent infection
Mechanisms of the disease
Transmission
Person to person
Horizontal transmission
Vertical transmission
Animal to person
Replication
Localized or spread
Viral shedding
Stages of viral infection
The incubation period "IP"
Prodromal period "symptoms"
The specific illness period
The recovery period
The immune response to virus
Macrophages
APC, Phagocytosis & cytokines production
Natural killer cells "NK"
Lysis of VICs
Cytokines
Interferons "IFNs"
α, β IFN: inhibit the mRNA translation
γ IFN: stimulate phagocytosis
Interleukin "IL"
Stimulate Ab production
Activate T cells & CMI
Suppress the IR
CMI
Effective against intracellular Vs
Humoral immunity
Effective against extracellular Vs.

MCQ'S

1-which of the following is related to viral disease at host level ?

a-mechanisms of the disease

b-cytopthogenesis

c-virimia

2-which of the following types viruses don't complete their cycles ?

a-Abortive

b- productive

c- non-productive

e-a and c

3-non-cytoletic infections cause noticeable Cytopathic effect

a-true

b-false

4-disease transmitted from by mother to newborn

a-horizontal transmission

b-vertical transmissi

MCQ'S

5-when the virus is found in the blood (viremia) that means the infection is : a-local infection

b-metastatic

c-generalized or systemic

6- inhibition of the viral and the host cell mRNA translation is by :

a- α IFN b- β IFN

c- γ IFN d- a and c e- a and b

7- persistent infection develop into an early complication :

a-true b-false

8- The signs & symptoms of viral diseases are the result of Cell killing:

a-incubation period

b- Prodromal period

c- The specific- illness period

d- The recovery period

Microbiology

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-حنان خشيم
-منال الحمدان
-وجدا الهذلان
-الجوهرة العمران
-أمل أفراح
-الهنوف المهنا

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1)a	2)a	3)b
4)b	5)c	6)e
7)b		8)c