MEDICINE
KING SAUD UNIVERSITY

microbiology

LECTURE:

PATHOGENESIS OF VIRAL INFECTION

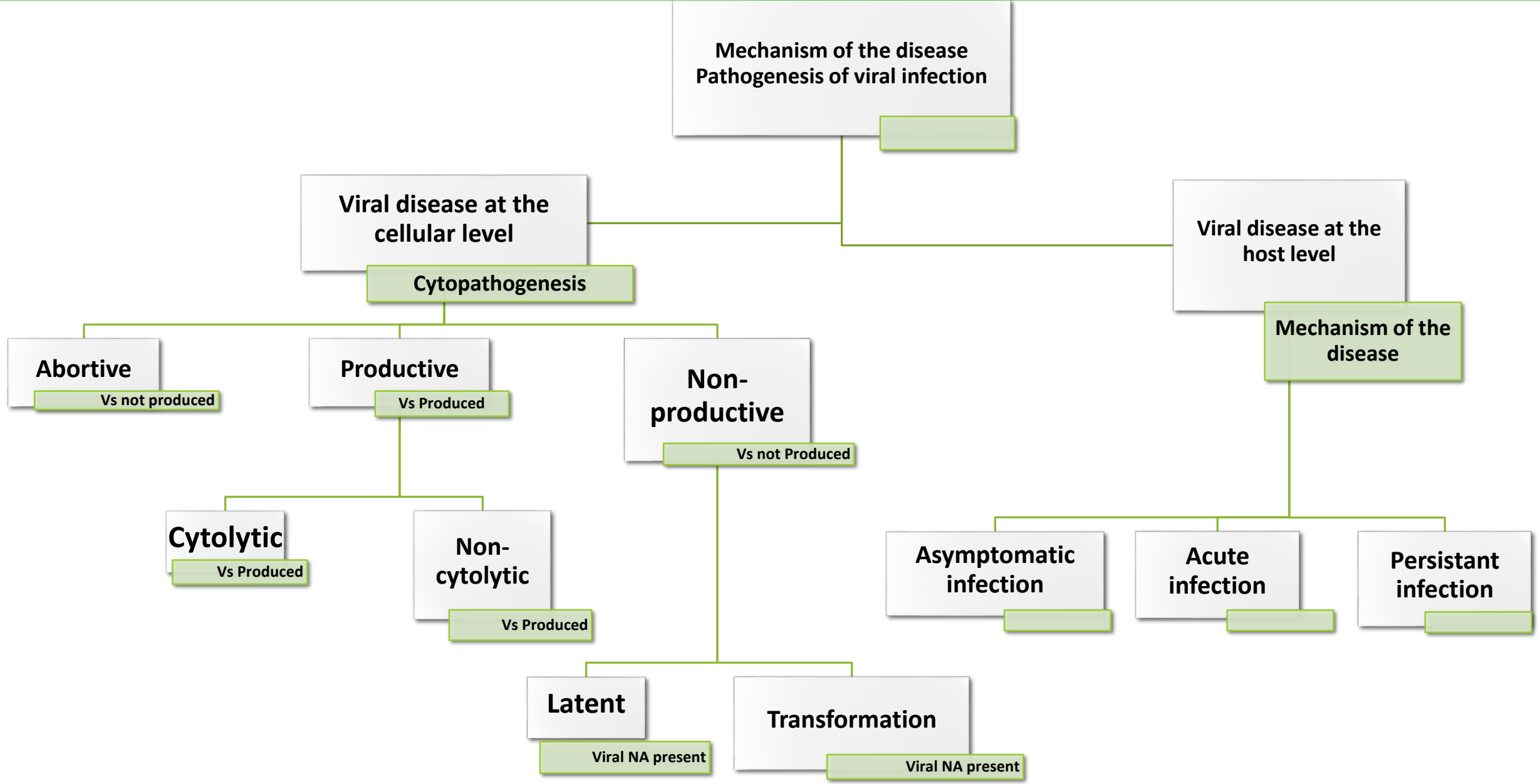
IMPORTANT.
DOCTORS NOTES.
EXTRA INFORMATION.

OBJECTIVE:

- Definition and levels of viral pathogenesis.3
- Types of viral infections at cellular level.(3- 10)
- Pathogenesis at host level. 14
- The immune response to viral infection .(16+18)
- The stages of viral infection. 18
- The types of viral infections at host level. 19

للرموز

Vs= Virus
RSV = Respiratory syncytial virus
HAV = Hepatitis A virus
HBV = Hepatitis B virus.
HCV = Hepatitis C virus
HIV = Human immunodeficiency virus
HPV = Human papillomavirus
HSV = Herpes simplex virus
HTLV = The human T-lymphotropic (leukemia) virus
YFV = Yellow Fever Virus
VZV = Varicella zoster virus
IP= Incubation Period


Mechanism of the disease
Pathogenesis of viral infection
Viral disease at the cellular level
Cytopathogenesis
Abortive
Vs not produced
Productive
Vs Produced
Non-productive
Vs not Produced
Cytolytic
Vs Produced
Non-cytolytic
Vs Produced
Latent
Viral NA present
Transformation
Viral NA present
Viral disease at the host level
Mechanism of the disease
Asymptomatic infection
Acute infection
Persistant infection

Cytopathogenesis

Infection	Types ,Ex	Cause	Result
Abortive Infections		-Mutation. -Defective interfering particles. -The action of IFNs (Interferons)	Viruses don't complete the replication cycle
Productive infection غالباً تظهر الأعراض	**Cytolytic Infections:**	-Viruses replicate & produce progeny. -Inhibition of cellular protein & NA synthesis	Cell death & Cytopathic effects [CPE]
	Non- Cytolytic infection (Persistant) = فيروس ماكث في الجسم	-Viruses replicate & produce progeny. (enveloped viruses) -Identified by hemadsorption & direct IF	Vs released by cell budding & little or no CPE.
Non-productive infection: غالباً تظهرلا الأعراض	**Latent infection (pt)**	-Vs infect cells that restrict or lack the machinery for transcribing viral genes. -The cell retains its normal properties	-Viral genome is found either integrated into cell DNA or as a circular episome or both.
	Transformation (pt)	Vs 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.

Pathogenesis of viral infection:

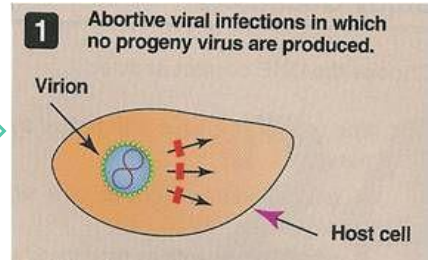
❖Viral disease at the cellular level:

1.Cytopathogenesis: (**The types of viral infections at cellular level):**

Abortive Infections

:Viruses don’t complete the replication cycle Due to

- Mutation
- Defective interfering particles
- The action of IFNs (Interferons)



Pathogenesis of viral infection:

❖Viral disease at the cellular level:

1.Cytopathogenesis: **(The types of viral infections at cellular level):**

➢**Productive infection(Two types)**:

- ❑ Cytolytic
- ❑ Non-cytolytic

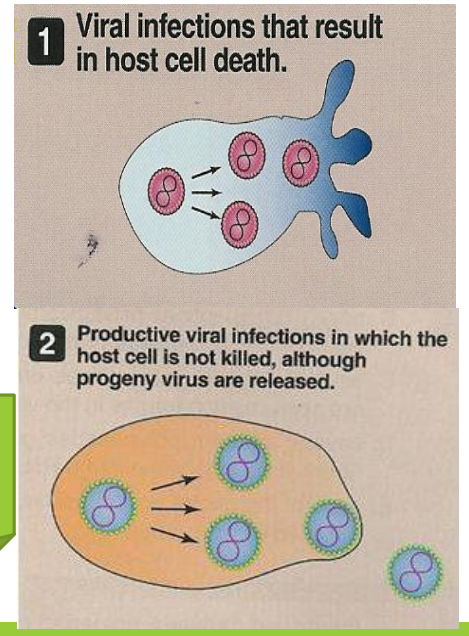
Cytolytic Infections:

- **Viruses replicate & produce progeny.**
- **Cell death & Cytopathic effects [CPE]**
- Inhibition of **cellular protein & NA synthesis**

Non- Cytolytic infection:

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

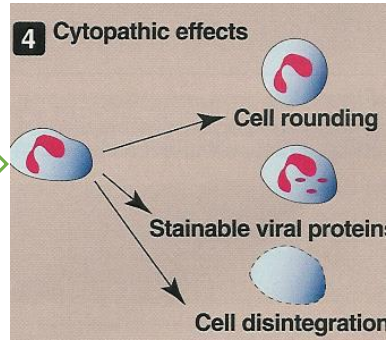
ما يكون واضح إن الخلية مصابة

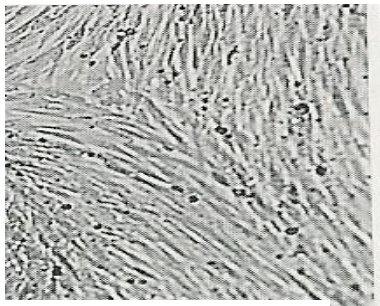


CPE

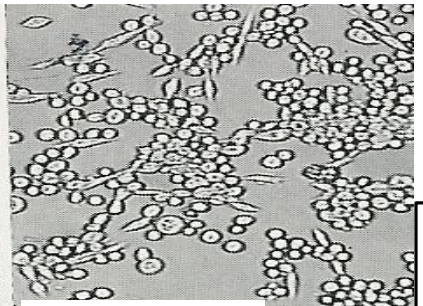
Cytopathic effect (CPE):
Any possible change in the appearance of the infected cell (CPE can take several forms) :

- **Cell lysis.**
- **Cell rounding.**
- **Syncytium formation.**
- **Inclusion body formation**





Uninfected cc



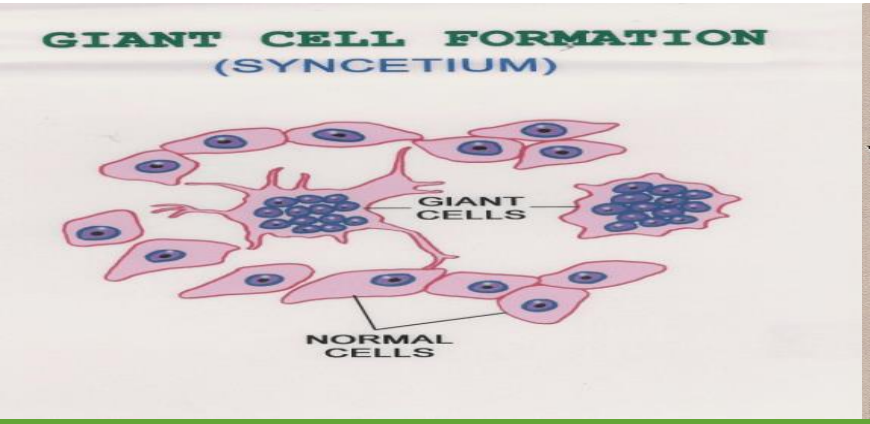
Cell rounding

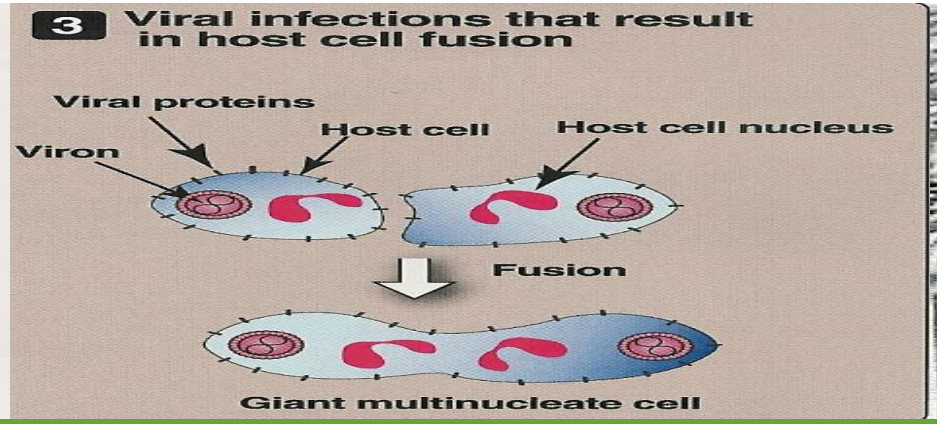
✓ Uninfected cc: Normal cell culture
✓ Cell rounding: it is a cytopathic effect

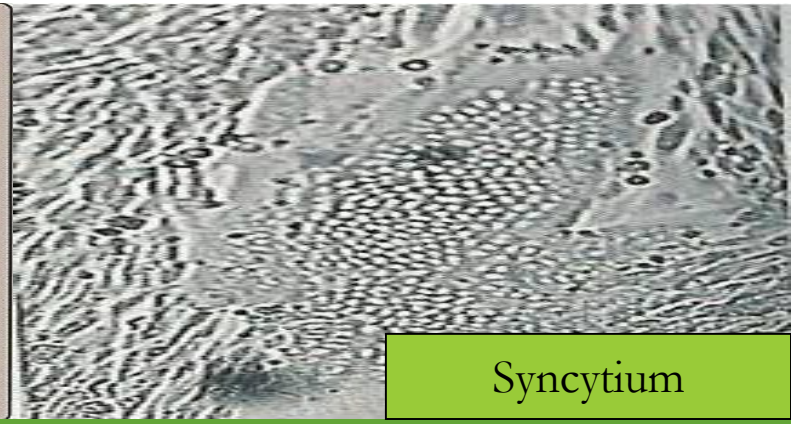
Syncytium formation

Syncytium formation

- This is due to insertion of viral protein in the surface membrane.
- This occurs in membrane of adjacent infected cells that will fuse together to form large cell (giant cell) with multi nuclei .







Syncytium

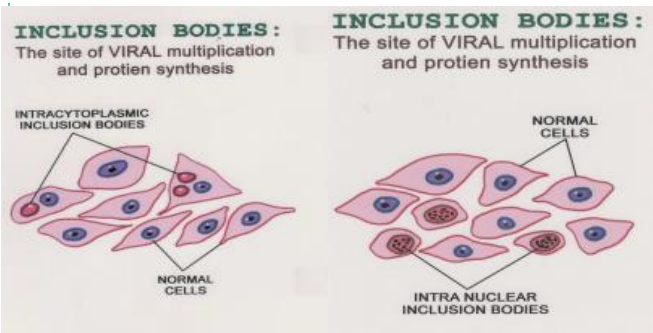
Inclusions bodies formation

✓**Inclusions bodies formation (collection of viral protein or particles inside the cells these particles stay inside the(site):**

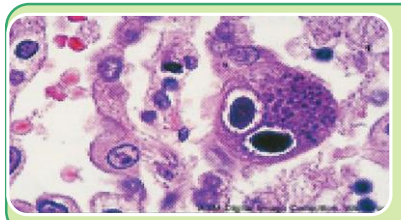
1. Nuclei (Intranuclear inclusion bodies) ex [Herpes V.]
2. Cytoplasm (intracytoplasmic bodies) ex [Rabies V.]

✓ **These inclusion body have different shapes :**

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

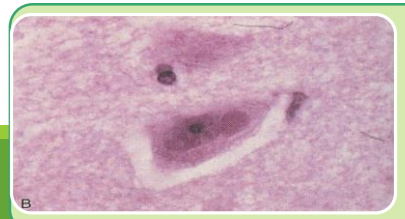


Very important



Owl's eye bodies

- Example **of Intranuclear body** is **owl's eye inclusion** bodies caused by **CMV (cytomegalovirus**).



Negri bodies

- Example **of Intracytoplasmic body** is :**negri bodies** which is caused by **rabies virus .**

❖Viral disease at the cellular level:

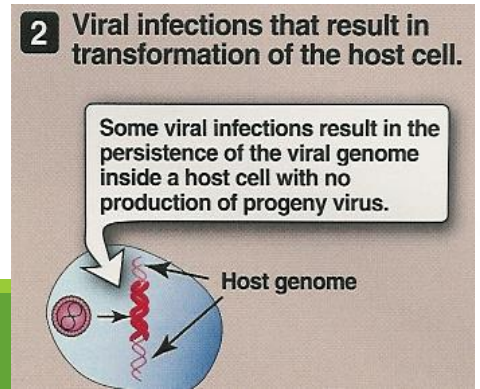
Non- productive infection:

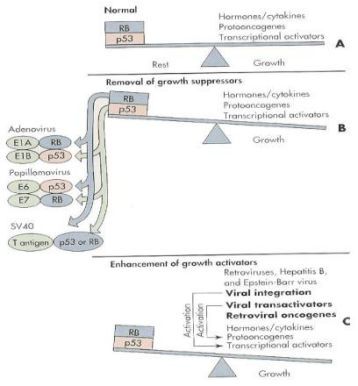
- -Vs infect cells that restrict or lack the machinery for transcribing viral genes.
- -Viral genome is found either integrated into cell DNA or as a circular episome or both.

Non- productive infection have two types

Latent infection : Persistent infection because (there is limited expression of viral genes) Ex: HSV

Transformation :Cause tumor in animals & Human and can transform cell cultureEx ; EBV, HPV and HTLV





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

Doctor's notes

Extra explanation: abortive

Abortive Infections occur when there **is no virus progeny**(سلالة او ذرية) **produced**

The virus infects the cell but → **the virus can't continue its replication cycle** → **Thus, no virus progeny is produced.**

Why did this happen? Due to:

Defective interfering particles is composed of:- **protein**. -**viral genome.**

1- Mutation: viral genome mutation which lead to **the lost of important function of the virus**, therefore the virus can't complete its replication cycle.

2- **Production defective interfering particles** : These particles **are produced during replication**

of the virus and may have:

–mutation in the viral genome. – deletion in the viral genome. –incorrect enzymes.

(Therefore the virus can't continue its replication cycle).

3-interaction of Interferons: Interferons are **cytokines** produced by some cells (infected cells)that **Protect other cells from infection** (or attack) of the same virus.(the virus infect cells but it can't continue replication so no virus produced and no disease.

Doctor's notes

Extra explanation: Cytolytic infection

1- The cell is killed by replication and releasing of the virus from the infected cell.

2- So the replication of the virus will produce **change in the infected cell leading to cell death** or **lysis**, by changing of **structure** and **function** of infected cell this is called **cytopathic effect.**

3-This is mainly due to **inhibition of cellular protein** and **nucleic acid synthesis** Which leads to cell death.

Cytopathic effect is : Any possible change in appearance of the infected cell.

4- (Cell death is due to replication of virus and accumulation of virus protein inside the cell this will cause disturbing of the structure and function of the cell leading to disturb of **lysosomes** resulting to **Autolysis or Apoptosis** which is programed cell death)

Extra explanation: non-Cytolytic infection

Viruses infecting the cell can continue replication cycle

then the viruses is produced or released without damaging the cell because of (enveloped viruses)

Viruses is released gently by budding through the cell membrane This kind of infection have little or no CPE

Doctor's notes

➢ **Extra explanation:** Non- productive infection

When the virus infect the cell, the virus can’t complete its replication cycle

cycle so no virus progeny produced

Because the cell lack machinery to transcribe viral genes

However, the virus maintain inside the cell in the form of its genome either integrated chromosome (to DNA) or non integrated chromosome (in cytoplasm) or both

Pathogenesis at Host Level:(process to tack place in host level)

❖ **Transmission of the virus & its entry into the host.**

1-Person to person :

a) Horizontal transmission:

- Skin contact , Blood, **e.g : cut in the skin**
- Respiratory route , **e.g : inhalation , through the nose**
- Fecal - oral route , **e.g : GIT through food or water**
- Genital contact

b) Vertical transmission

: e.g :from mother to baby through breast feeding or During delivery through an infected birth canal

2-Animal to person :

Reservoir…….Human (Rabies v.) داء الكلب بشكل مباشر ينتقل الى الإنسان

Reservoir…….(vector) Human (YFV) بشكل غير مباشر عن طريق بعوضة

yellow fever virus

❖ **Replication of the virus**

❖ **Vs remain localized or spread to other organs**

❖ **Viral shedding**

❖ **The immune response as:** 1-Host defence

2- Immunopathogenesis (ability of virus to cause disease through immue system)

Important features of Acute Viral Diseases

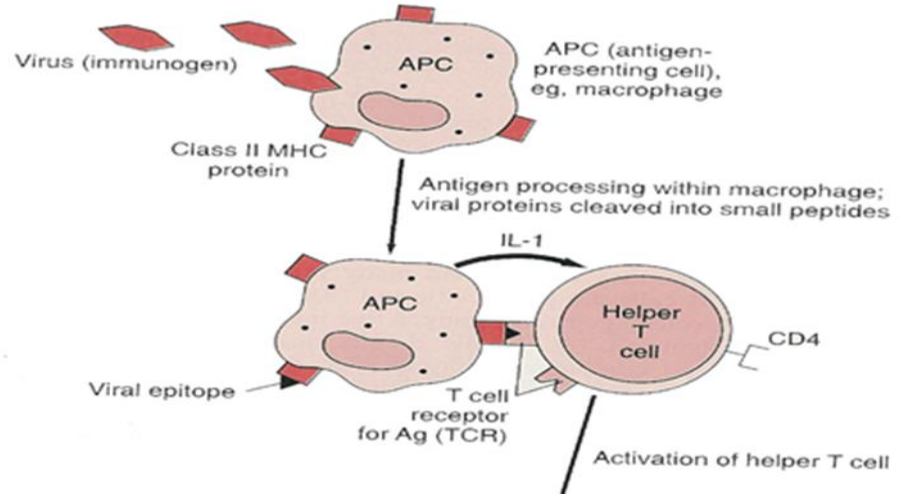
	Local Infections	Generalized (systemic) infections
Example of disease	***Rhinovirus***	الحصبى ***Measles***
Site of Pathology	***Portal of entry***	***Distant site***
IP (incubation period)	***Relatively short***	***Relatively long***
Viremia (presence in the blood)	***Absent***	***Present***
Duration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

Taken from Med433

Note: local mean it will replicate in primary site

The immune response to virus:

- **Macrophages: APC, Phagocytosis and cytokines production.**
- **Natural killer cells: Lysis of VICs**
- **Cytokines:(release from virus infected cell)**

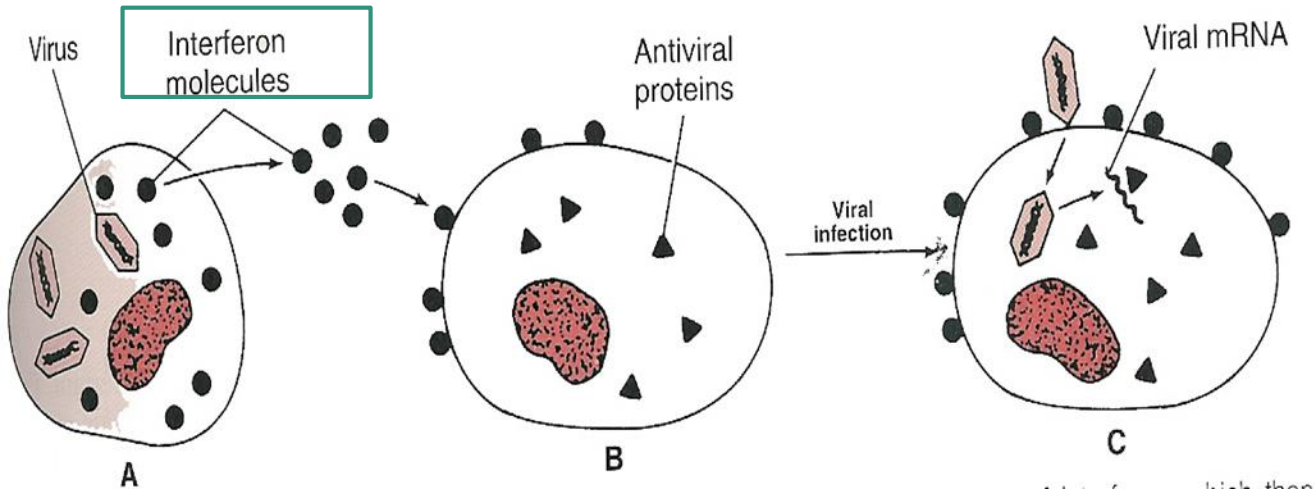


*Interferons "INF":

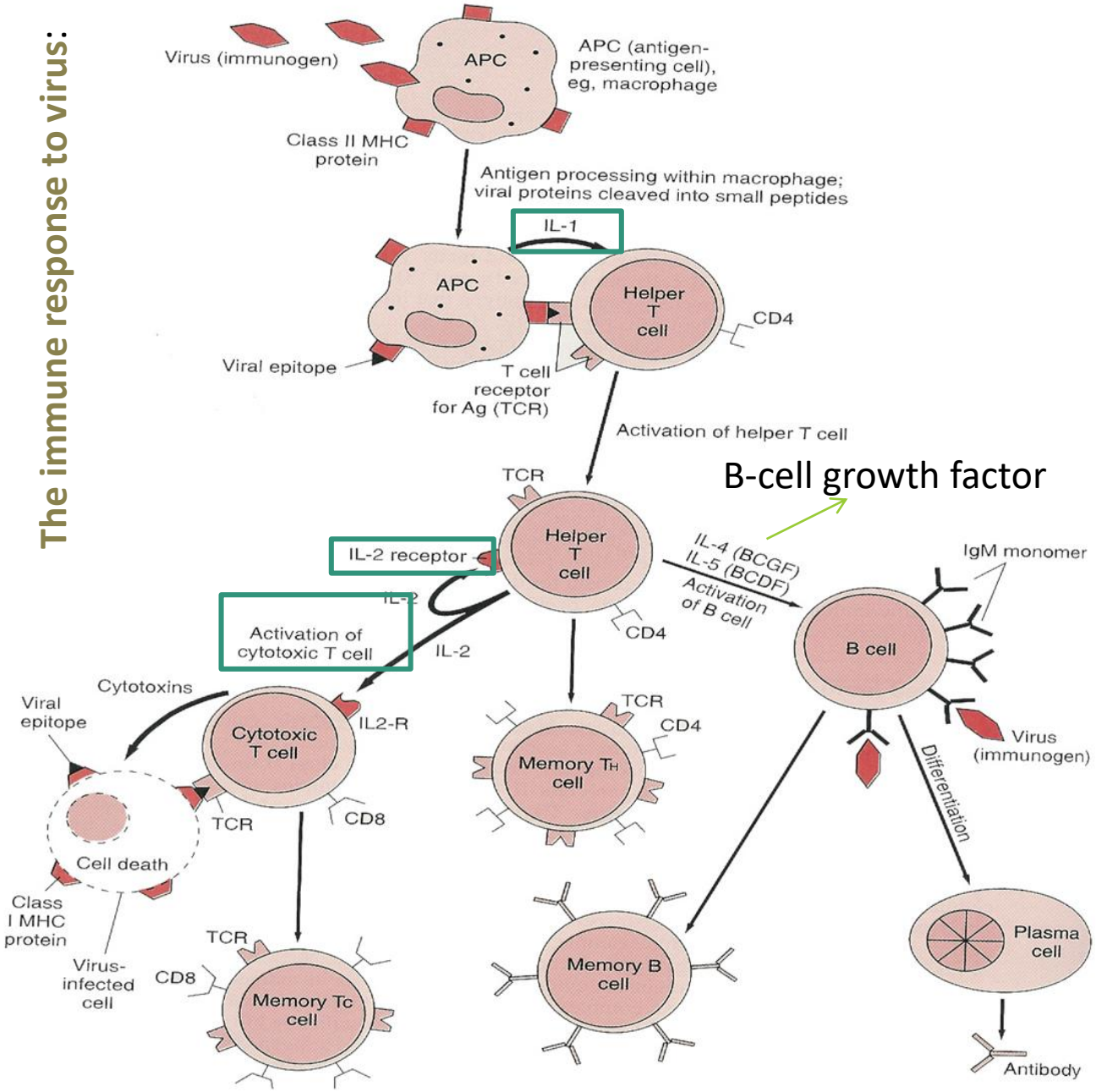
- α, β IFN: inhibit the viral and the host cell mRNA translation
- γ IFN (from lymphocyte) : stimulate phagocytosis and killing by macrophages and NK cells

*Interleukin "IL":

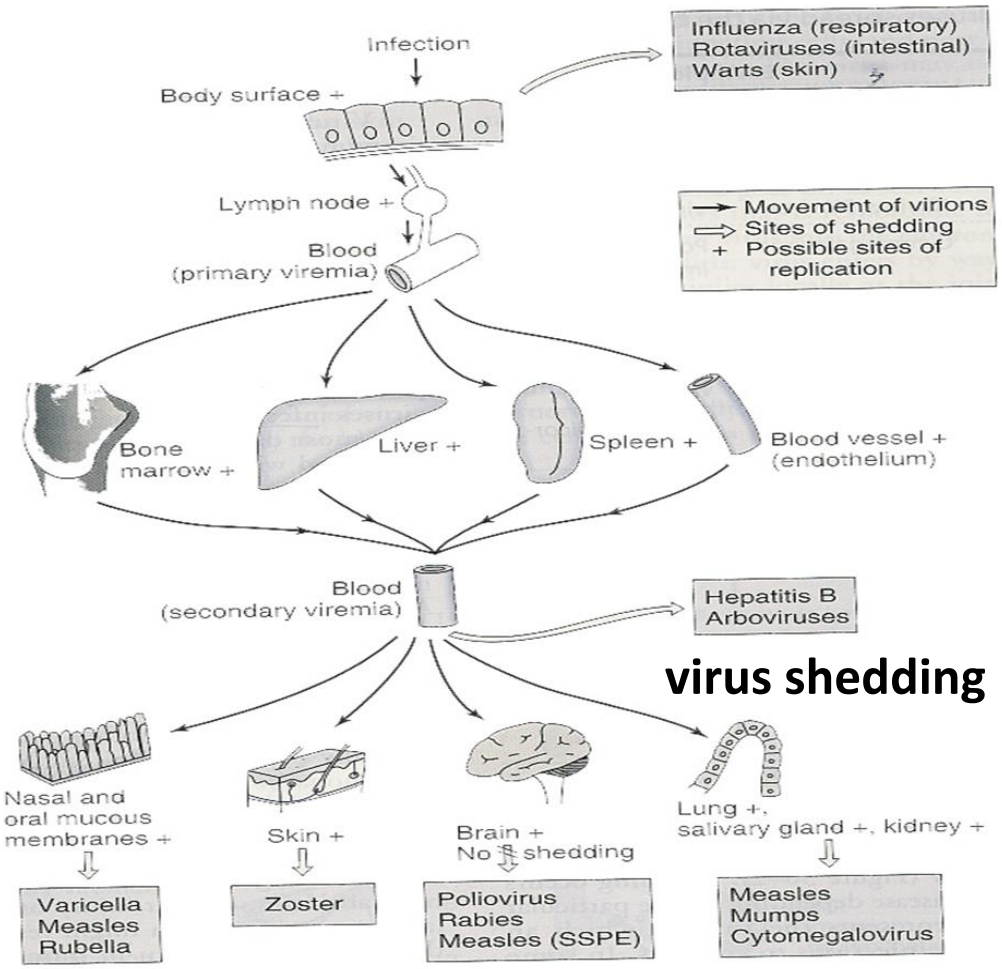
- Stimulates AB production
- Activate T cells & CMI
- Suppress the IR(Insulin Resistance)



The immune response to virus:



Mechanisms of spread of virus through the body:



The immune response to virus:

❖ CMI: (t-cell)

Effective against intracellular viruses Lysis of virally infected cells by CTCs [CD8]

❖ Humoral Immunity: (b-cell)

Effective on extracellular viruses [viremia]
- Neutralization(Binding to the virus's receptors so it cannot attach to the host cell)

*Note:The cellular immunity is **faster** than the Humoral immunity

The stages of a typical viral infection:

1. The incubation period
2. Prodromal period → Non-specific illness (general symptom)
3. The specific-illness period:

The signs & symptoms of viral diseases are the result of

Cell killing by:

A) Inhibition of cellular macromolecular synthesis

B) Immunologic attack (Immunopathogenesis)

Cytotoxic T cells e.g. Hepatitis (HAV, HBV,HCV)

4-The recovery period

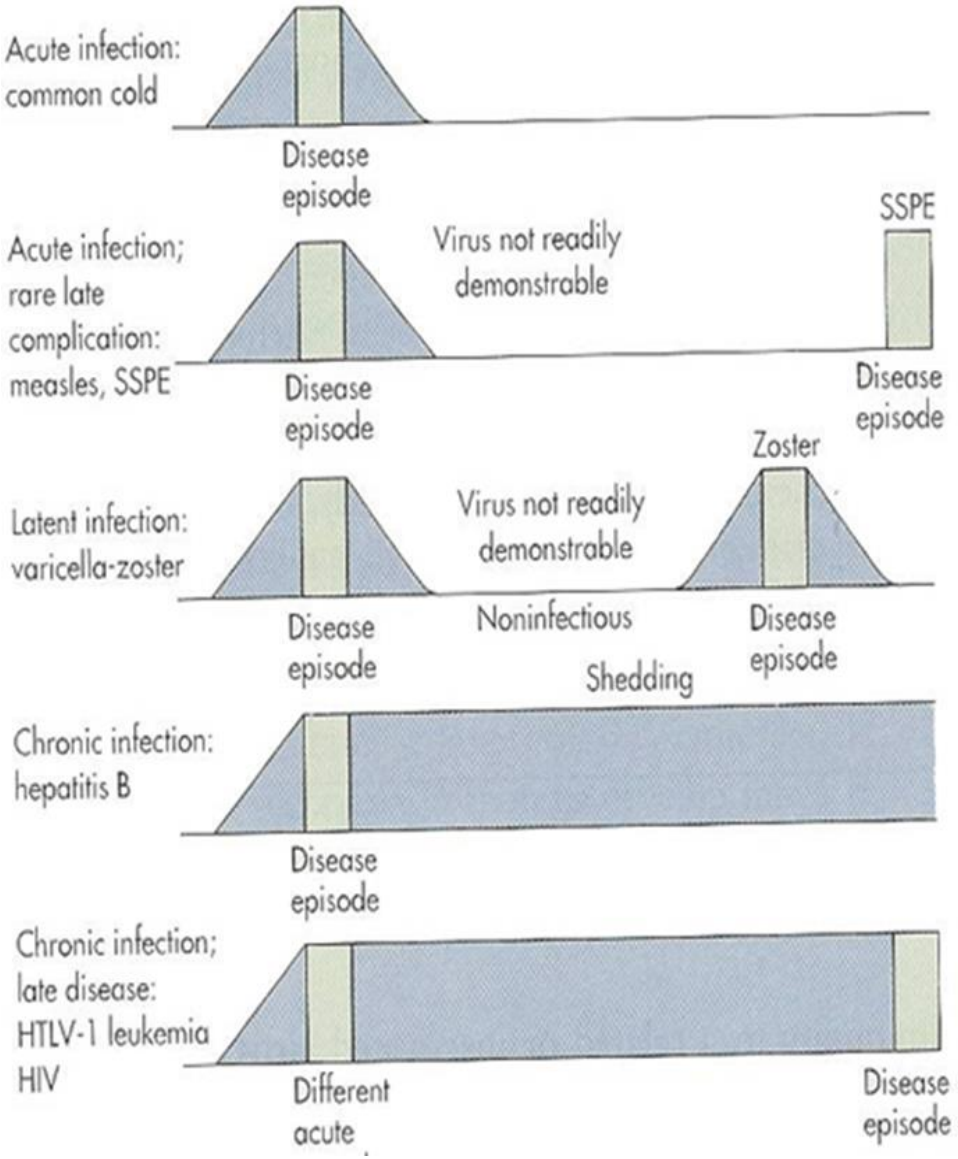
Types of viral infections at host level:

1. Asymptomatic infection (the most common one)
2. Acute infection (like common cold)
3. Persistant infection:

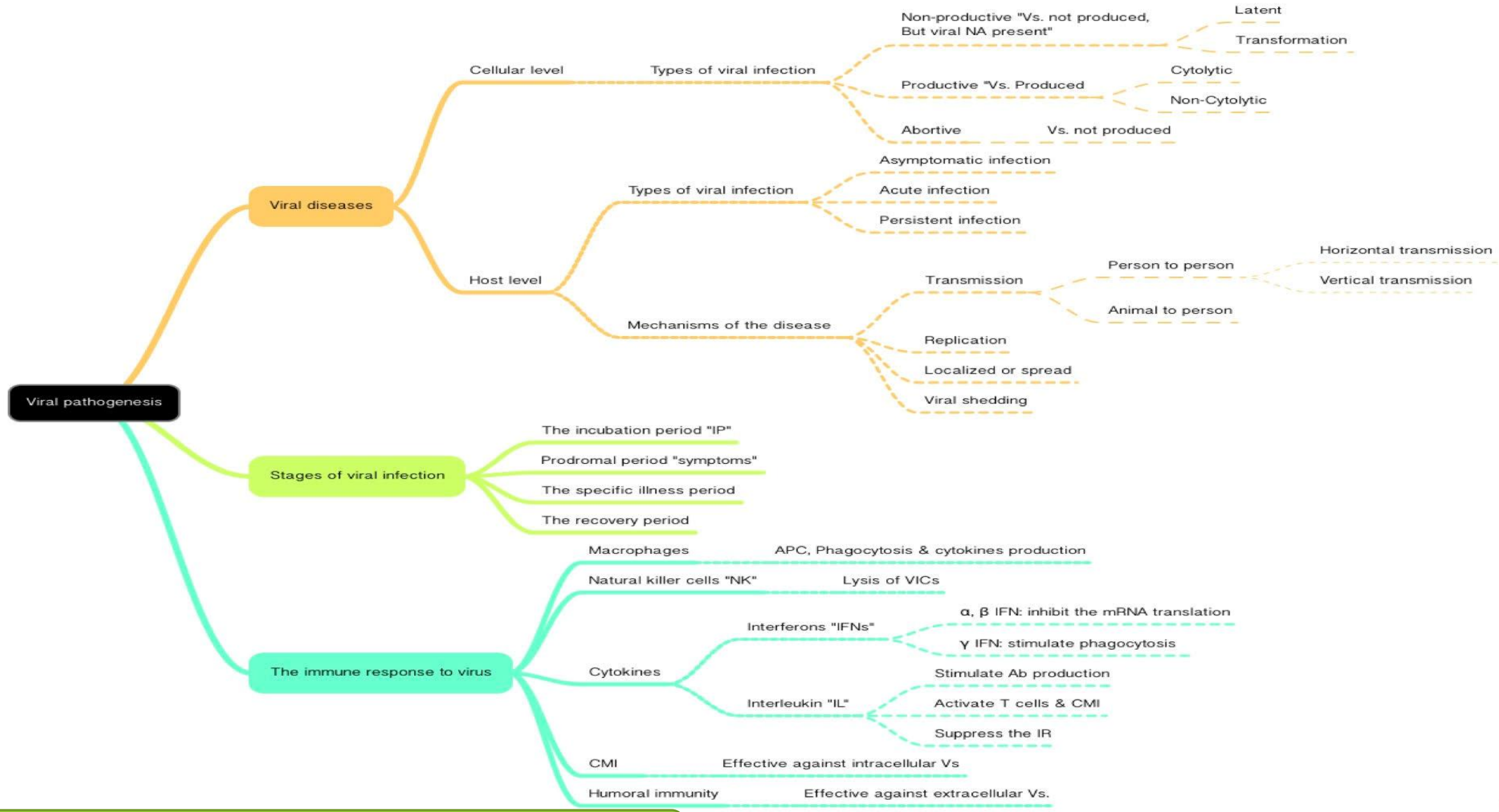
***Late complication of acute infection**

***Latent infection(خامل)(herpes virus)**

***Chronic infection (like HBV)**



Summary from 434 team



Online quiz: https://www.onlineexambuilder.com/microbiology-l7/exam-106264

quiz

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

a-mechanisms of the disease
b-cytopthogenesis
c-viremia

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

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

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

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

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

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

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

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

12.Negri bodies is caused by:

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

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

a) T b) F

1)a 2)a 3)b 4)b 5)c 6)e 7)b 8)C 9) D 10) B 11) A 12) A 13) a

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