MED437
KING SAUD UNIVERSITY

MICROBIOLOGY
437

Microbiology – Lecture 9
Viral pathogenesis

TEAM 437

Red: important
Green : doctor notes
Black : original slides
Grey: extra information

In this link, you will find any corrections or notes unmentioned in the team's work. Please check the link below frequently.

https://docs.google.com/presentation/d/1yIQt3G8UDFG6xYMRhXkTk-dS54NeTfhJaPe_y0M-kjk/edit?usp=sharing

Objectives:

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- 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.

Word abbreviations to know:

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

Pathogenesis of viral infection

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Viral Disease At The Cellular Level (Cytopathogenesis)

- Abortive (Virus NOT Produced)
- Productive Virus produced
- Non-productive (virus NOT produced)
  - Only viral nucleic acid is present, the virus itself is not produced and that is why it is called non-productive.

Viral Disease At The Host Level: Mechanisms of infection

- Asymptomatic Infection (Most Common)
- Persistent Infection
  - Late Complication Of Acute Infection
  - Chronic Infection
  - Latent infection
- Acute Infection

Cytopathogenesis at cellular level

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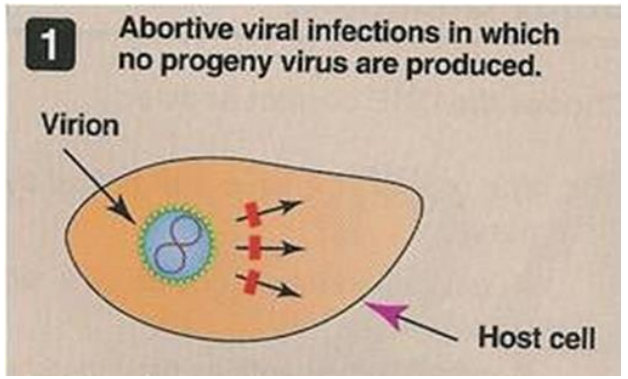
I. Abortive infection

- Viruses don't complete the replication cycle
- Due to mutation, defective interfering particles and the action of interferons(proteins released by animal cells, usually in response to the entry of a virus, which has the property of inhibiting virus replication.)



II. Productive Infections: Viruses continue the replication cycle

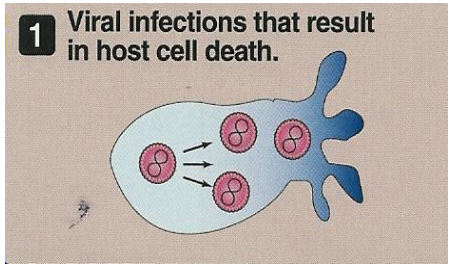
Cell isn't killed because virus is enveloped

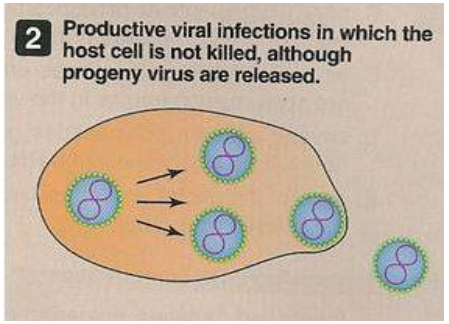
Cytolytic infections

- Viruses Replicate & Produce Progeny
- Cause Of Cell Death & Cytopathic Effects causes morphologic changes
- Inhibition Of Cellular Protein & NA Synthesis

Non cytolytic infections

- Viruses replicate & produce progeny
- Viruses Releases By Cell Budding & Little Or No CPE
- Identified By Hemadsorption(adherence of red blood cells to other cells) & Direct Immunofluorescence





The types of viral infections at cellular level

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III. Non-Productive infection virus is only present in genome

- 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 episomer or both.

1. Latent Infection: (Persistent infection)

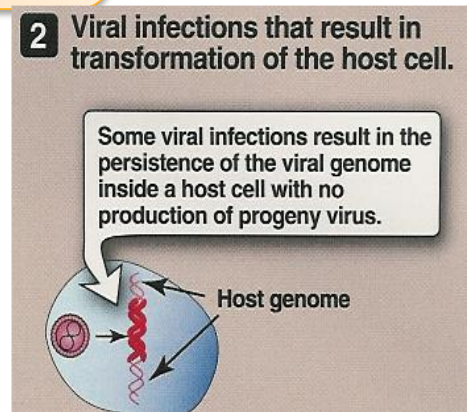
The cell retains its normal properties

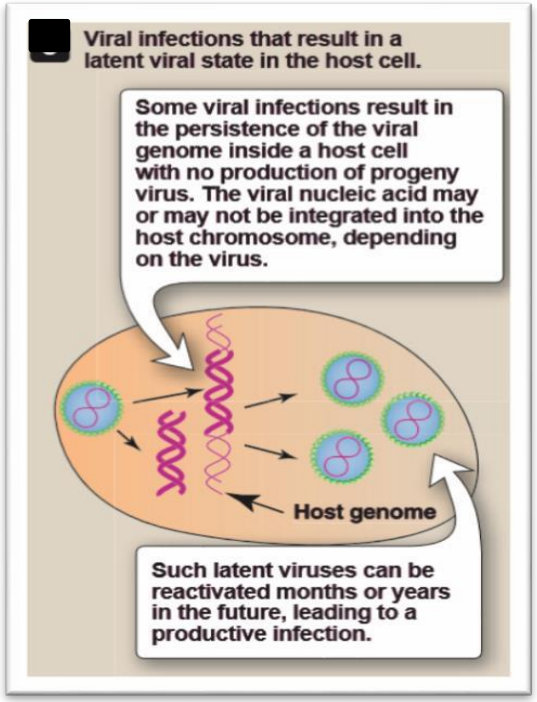
There is limited expression of viral genes
e.g. HSV

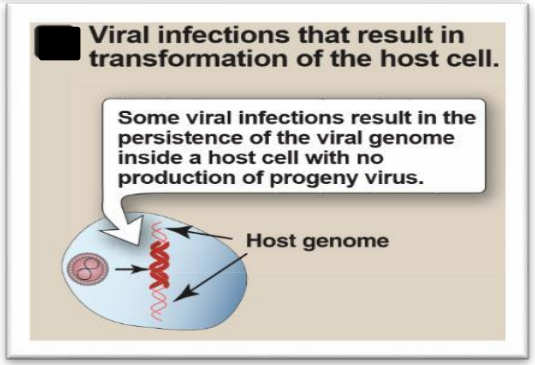
2. Transformation:

Cause tumor in animals & human and it can transform cell culture
e.g. ~~EBV, HPV & HTLV don't memorize them~~

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







structural changes in host cells that are caused by viral invasion

Cytopathic Effects

Defined as any morphologic change detected by LM

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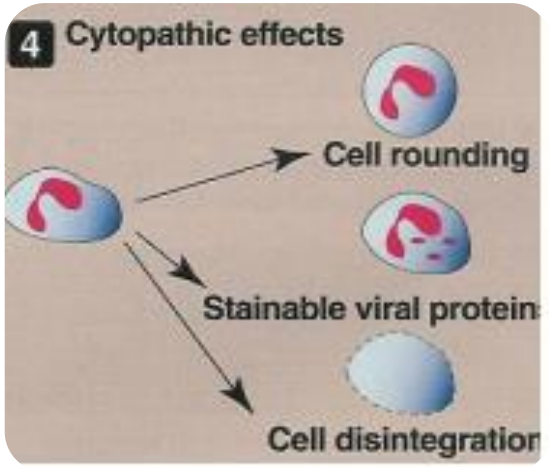
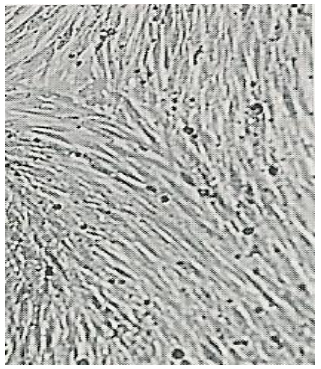
CPE can take several forms:

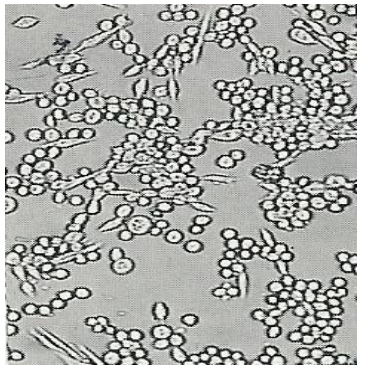
1. Cell lysis: “cell disintegration” (non-enveloped)
2. Cell rounding (enveloped only)
3. Syncytium formation "Cell fusion”
4. Inclusion bodies formation (apoptotic bodies)



Uninfected cc



Cell rounding

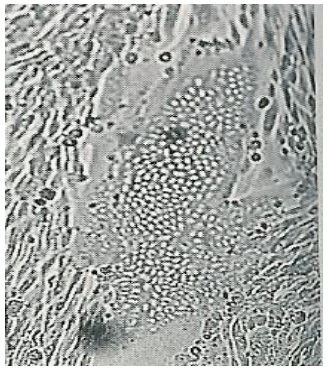


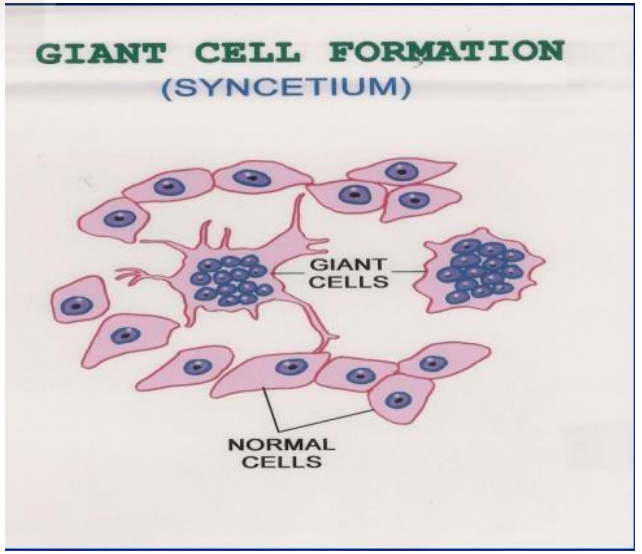
Syncytium formation:

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





Inclusion bodies formation:

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Site:

1. Intranuclear [Herpes V.]
2. Intracytoplasmic [Rabies V.]

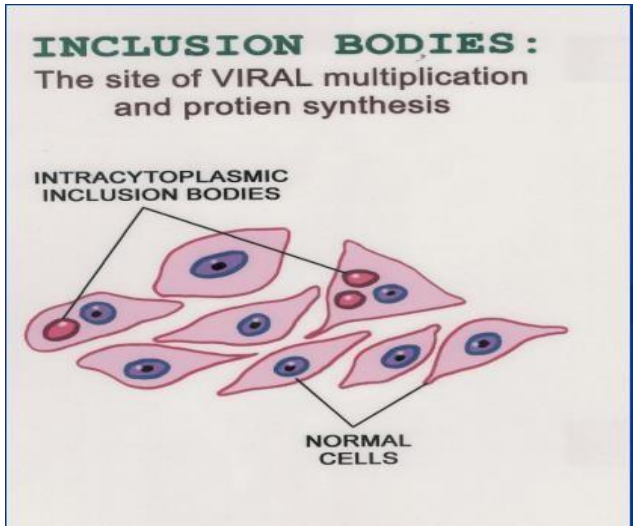
Takes a several forms:

1- Single/multiple

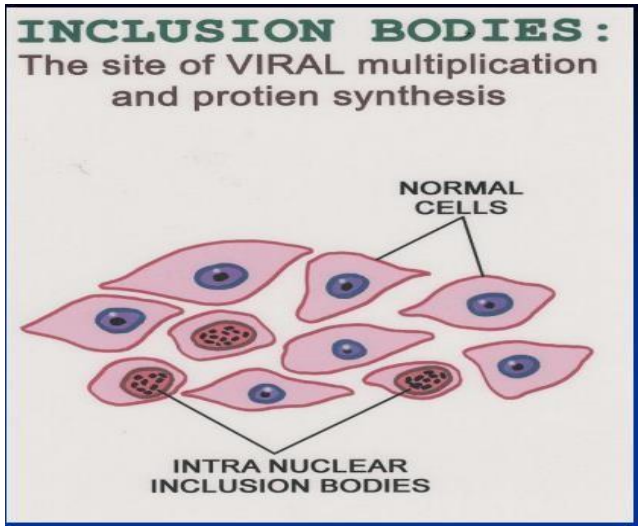
2- Small/large

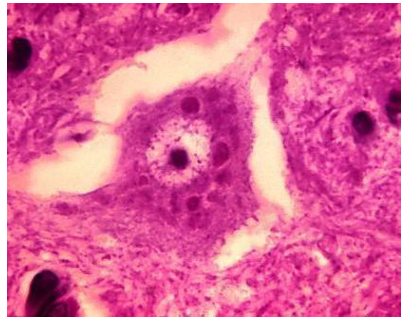
3-Round/irregular

Intracytoplasmic inclusions

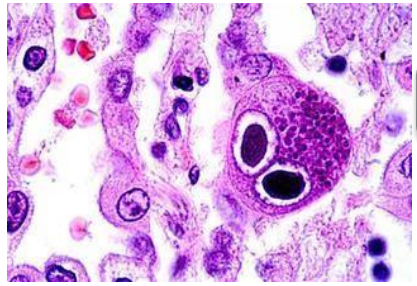


Intranuclear inclusions





Negri bodies caused by Rabie viruses



Owls eye inclusions by CMV VIRUS

Pathogenesis at the host level

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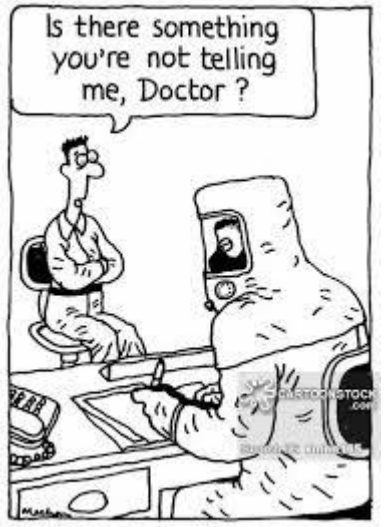
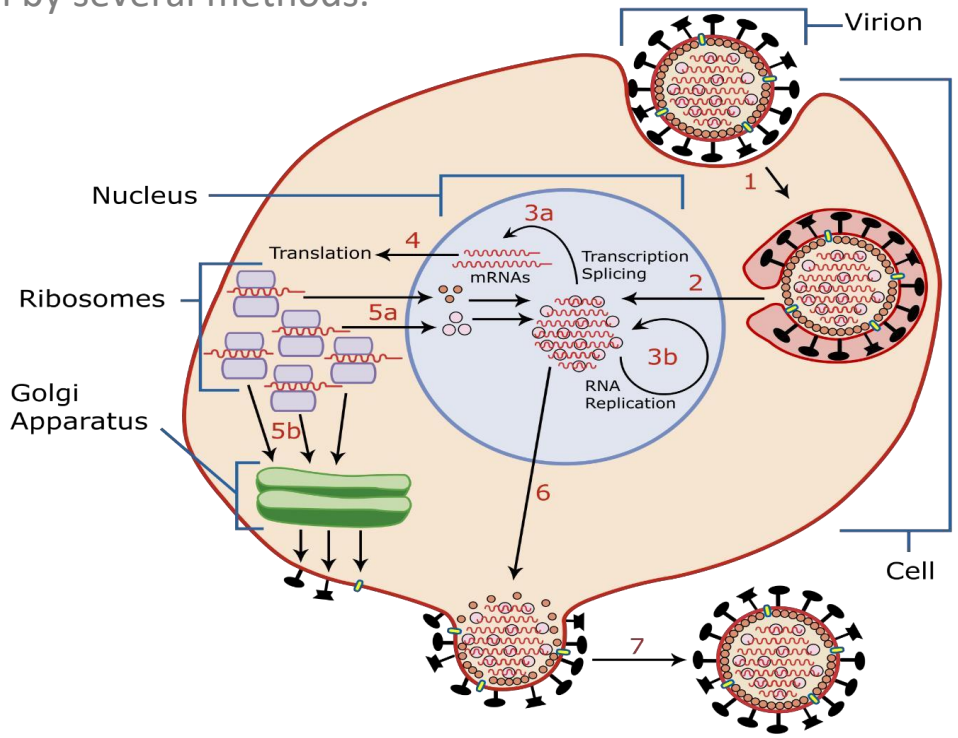
1. Transmission of the virus & its entry into the host.
2. Replication of the virus & damage to cells
3. Vs remain localized or spread to other organs
4. Viral shedding
5. The immune response as :
   - Host defense
   - Immunopathogenesis



Viral shedding:

Viral shedding refers to the expulsion and release of virus progeny following successful reproduction during a host-cell infection.

Once replication has been completed and the host cell is exhausted of all resources in making viral progeny, the viruses may begin to leave the cell by several methods.



Pathogenesis at Host level

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Transmission of the virus & its entry to the host:

1) Person to person:

Horizontal
- Skin contact.
- Blood Respiratory route.
- Fecal - oral route.
- Genital contact

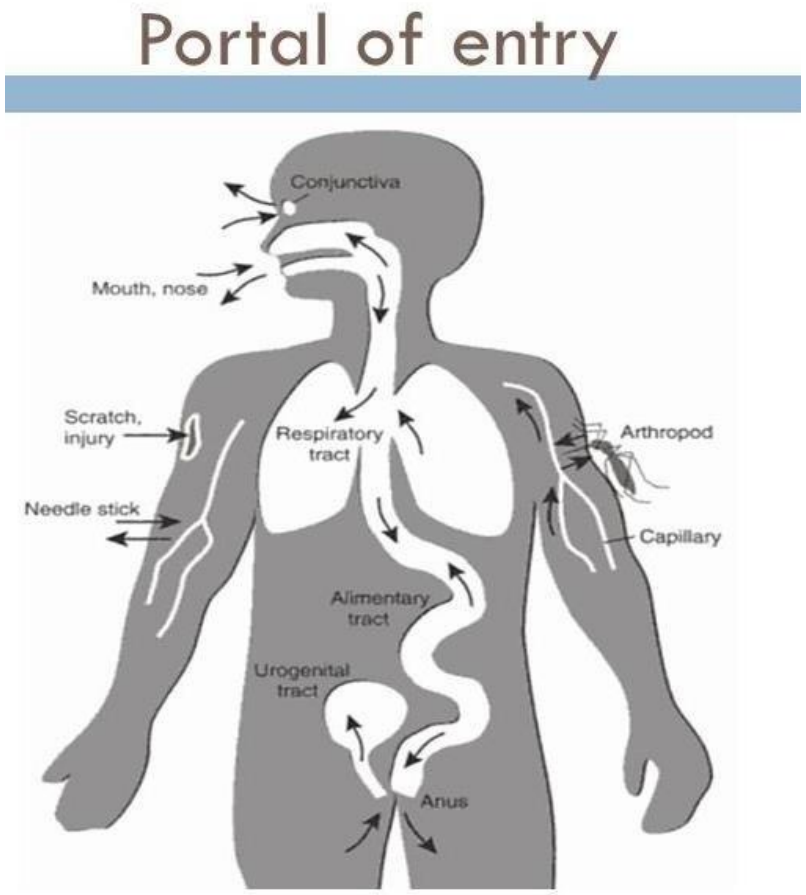
Vertical
- from the mother to her baby.
- During delivery through an infected birth canal.

2) Animal to person

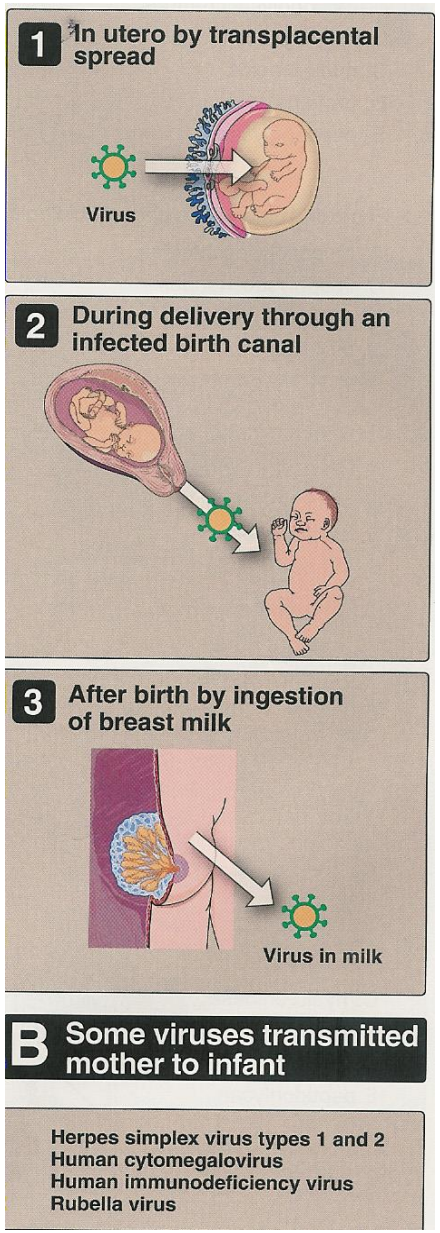
Reservoir —Direct→ Human (Rabies v.)

Reservoir → vector → Human (YFV)

Indirect, uses vectors. E.g. fly for transmission of yellow fever virus



Vertical transmission



Important features of Acute Viral Diseases

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	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***

The immune response to virus

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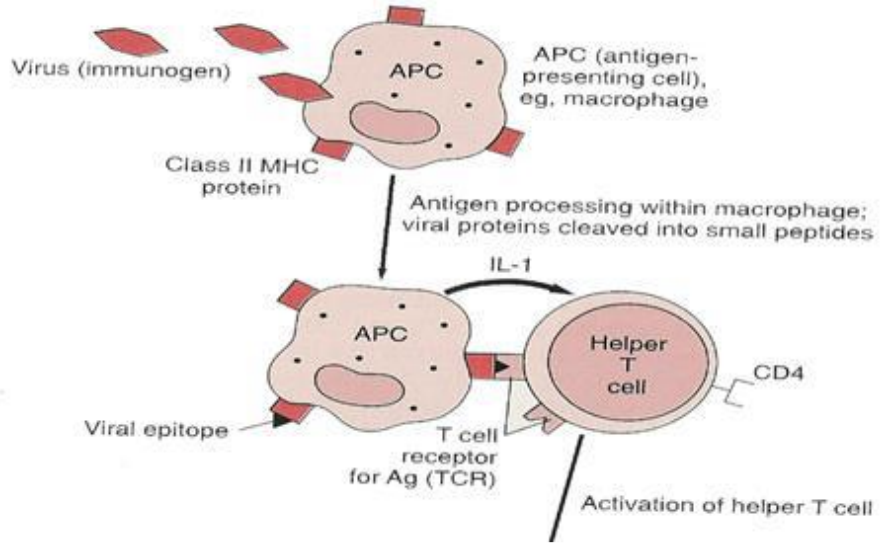
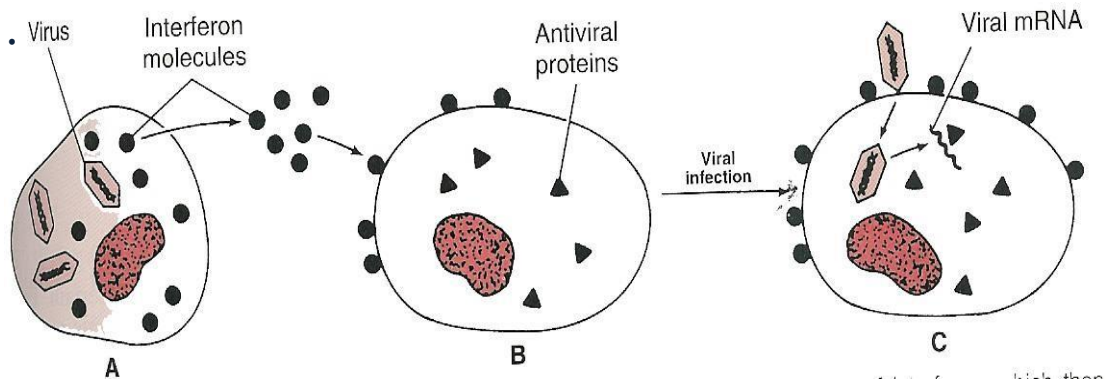
1-Macrophages: Antigen Presenting Cell , Phagocytosis, Cytokines production

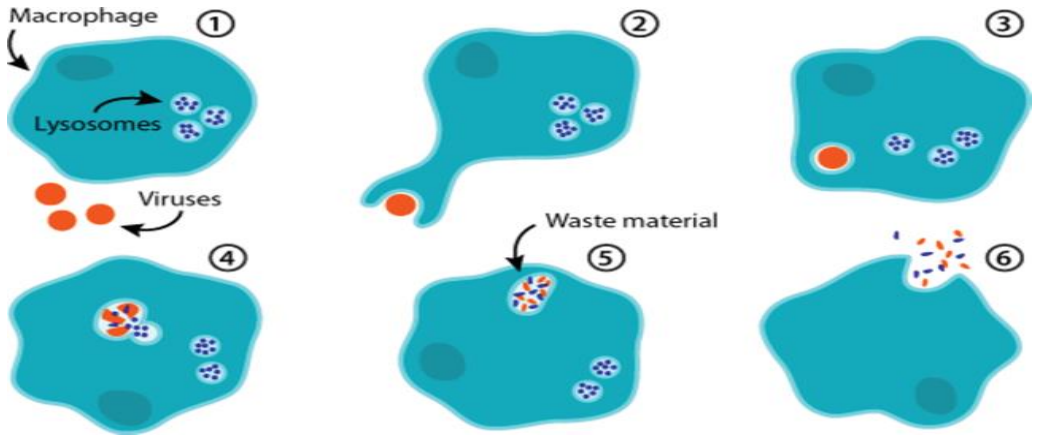
2- Natural killer (NK) cells : lysis of viruses

3- Cytokines: (release from virus infected cell)

Interferons "INF“	Interleukin "IL":
a. α, β IFN: inhibit the viral and the host cell mRNA translation b. γ IFN: stimulate phagocytosis and killing by macrophages and NK cells	a. Stimulate Ab production b. Activate T cells & CMI c. Suppress the IR SAS: stimulate, activate and suppress







For more info

The immune response to virus cont.

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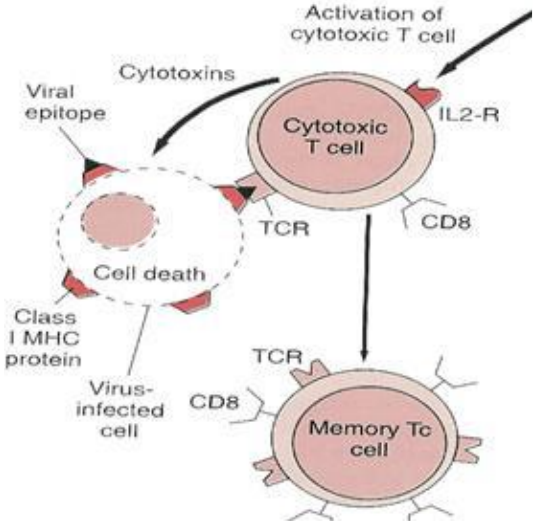
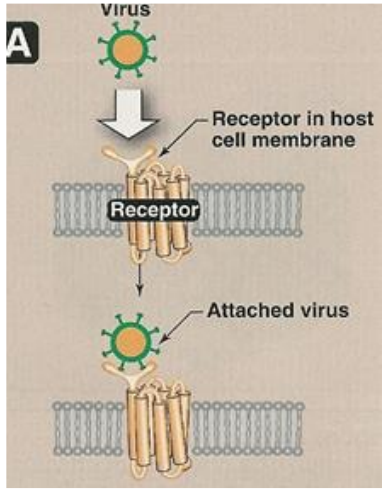
Adaptive immunity:

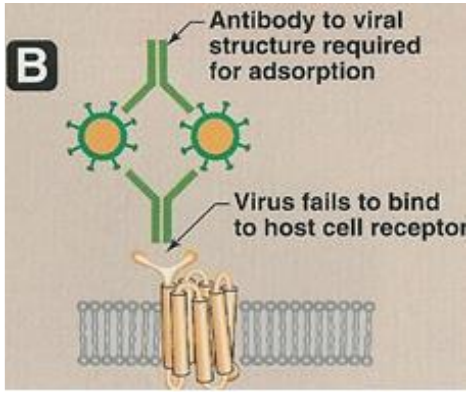
1. Humoral immunity
   - Effective on extracellular viruses [viremia]
   - Neutralization

2. Cell mediated immunity
   - Effective against intracellular viruses
   - Lysis of virally infected cells by CTCs [CD8]

   Faster than humoral immunity







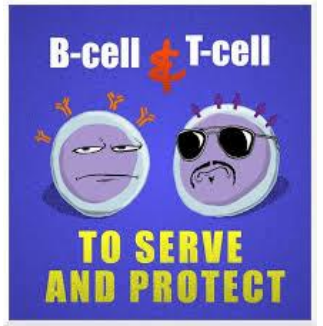
The stages of a typical viral infection:

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:

a. Inhibition of cellular macromolecular synthesis.
b. Immunologic attack “Immunopathogenic”
c. cytotoxic T cells. e.g. hepatitis (HAV.HBV.HCV).

4. The recovery period.



The immune response to virus:

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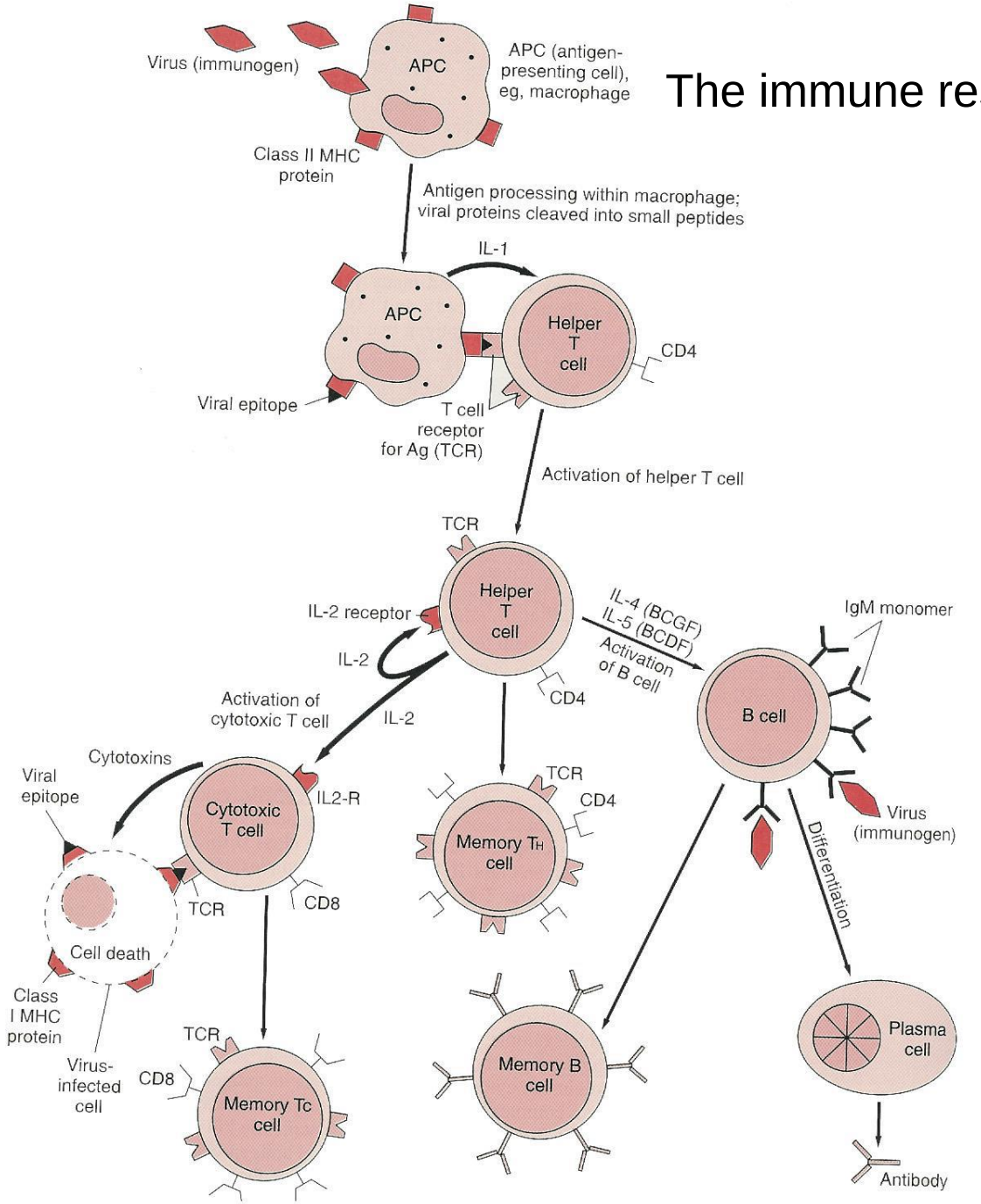

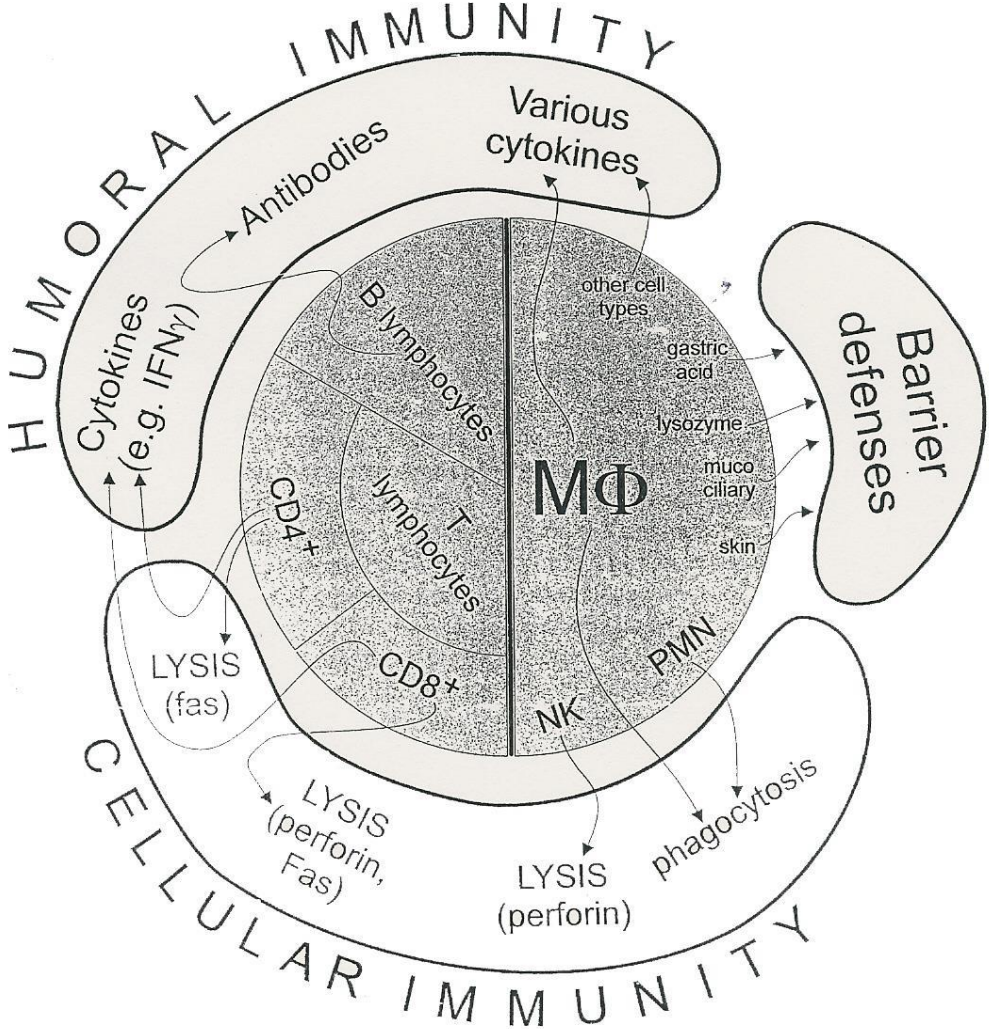

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Doctor's notes

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

Types of viral infections at host level:

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

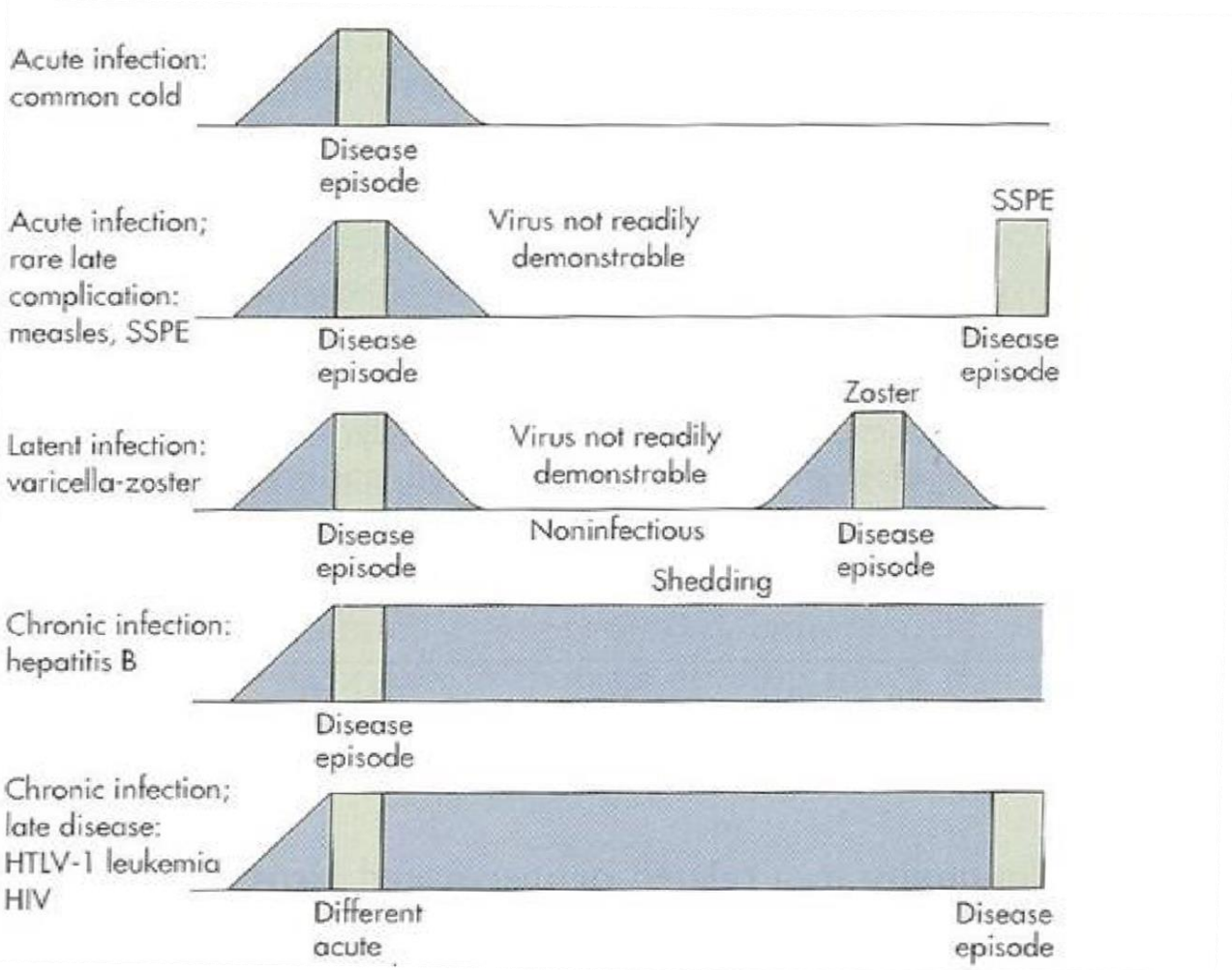
✓ Late complication of acute infection

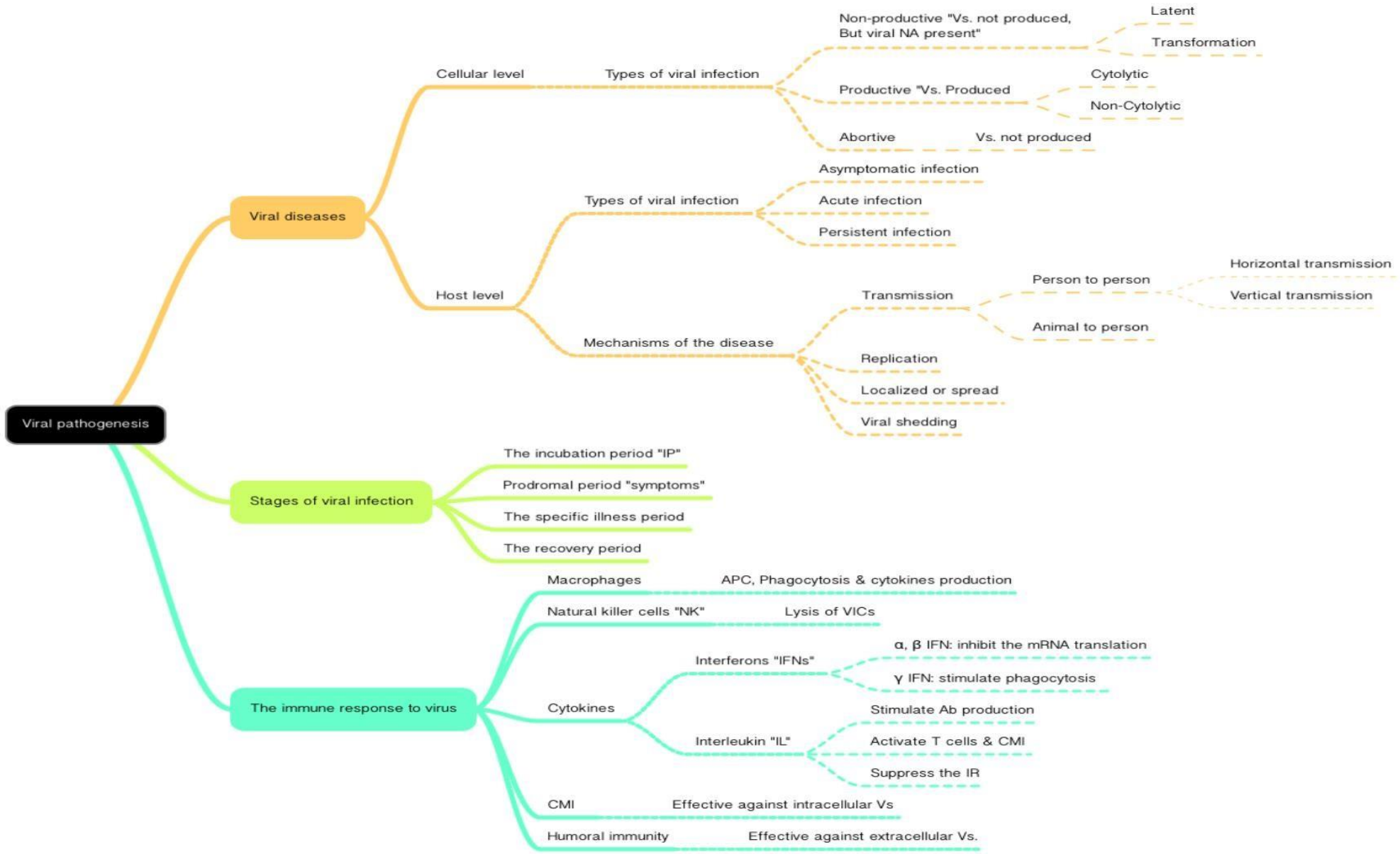
(associated with symptoms)

✓ Latent infection(خاملherpes virus)

(no symptoms until AFTER activation)

✓ Chronic infection (like HBV)





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Questions

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1- The type of viral infections which doesn't produce viruses?

a) *Abortive* *b) Productive* *c) Non-productive* d) both a&c

2-Negri bodies are caused by?

a) CMV b) Rabies Virus c)HIV d) Herpes

3- Stimulates phagocytosis?

a) a IFN b) β IFN c) γ IFN

4-Identified by hemadsorption & direct IF?

a) Cytolytic Infection b)Latent Infection c) Chronic Infection
d) Non-Cytolytic Infection

5- Syncytium formation is a part of the cytopathic effects

a) True b) False

6- The number of stages for a typical viral infection?

a) 4 b) 5 c) 3 d)4

7- Viremia is absent in systemic infections

a) True b) False

1-D 2-B 3-C 4-D 5-A 6-A 7-B

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Team members:

داود إسماعيل	فهد الفايز	الهام العلامي
عمر الفوزان	سعد الهداب	رناد المقرن
عبدالله الزهراني	خالد الدوسري	هديل عورتاني
معن شكر	خالد المطيري	اسراء النزاوي
عبدالمجيد الوردي	أنس السيف	لمياء القويز
محمد إبراهيم	عبدالجبار اليماني	شوق القحطاني
عمر السحيباني	عبدالله السرجاني	نورة القاضي
سيف المشاري	عبدالعزيز الدخيل	افنان المصطفى
سعد العقيلي	عادل العريني	رهف الشمري
حسين علامي	محمد الدويغري	الهنوف الجلعود

Team leaders:

غادة الحيدري ، علي شحادة

For any corrections, suggestions or any useful information please contact us at:
Micro.437@hotmail.com