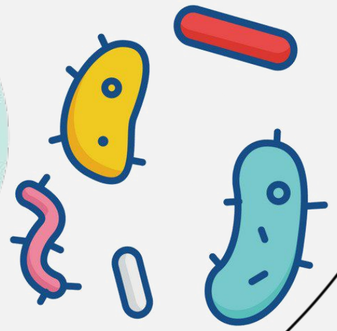

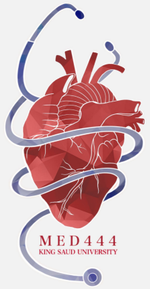

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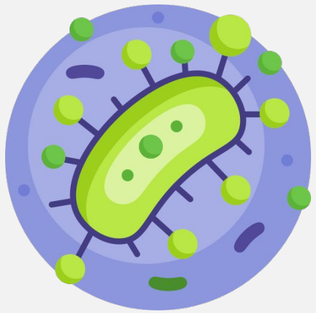
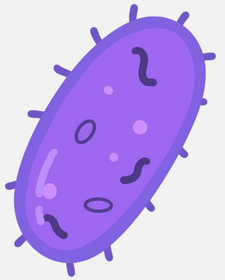
Viral Pathogenesis





index:

- Main text.
- Important.
- In boys slides only.
- In girls slides only.
- Doctors notes.
- Extra info.

OBJECTIVES

- Definition and levels of viral pathogenesis
- Types of viral infection 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.

Definition:

Cytopathogenicity

Viral disease at cellular level (cause cell damage or death)

Cytopathic/ Cytopathogenic Effect(CPE)

Viral disease at the host level caused by viral invasion.

Mechanism of diseases

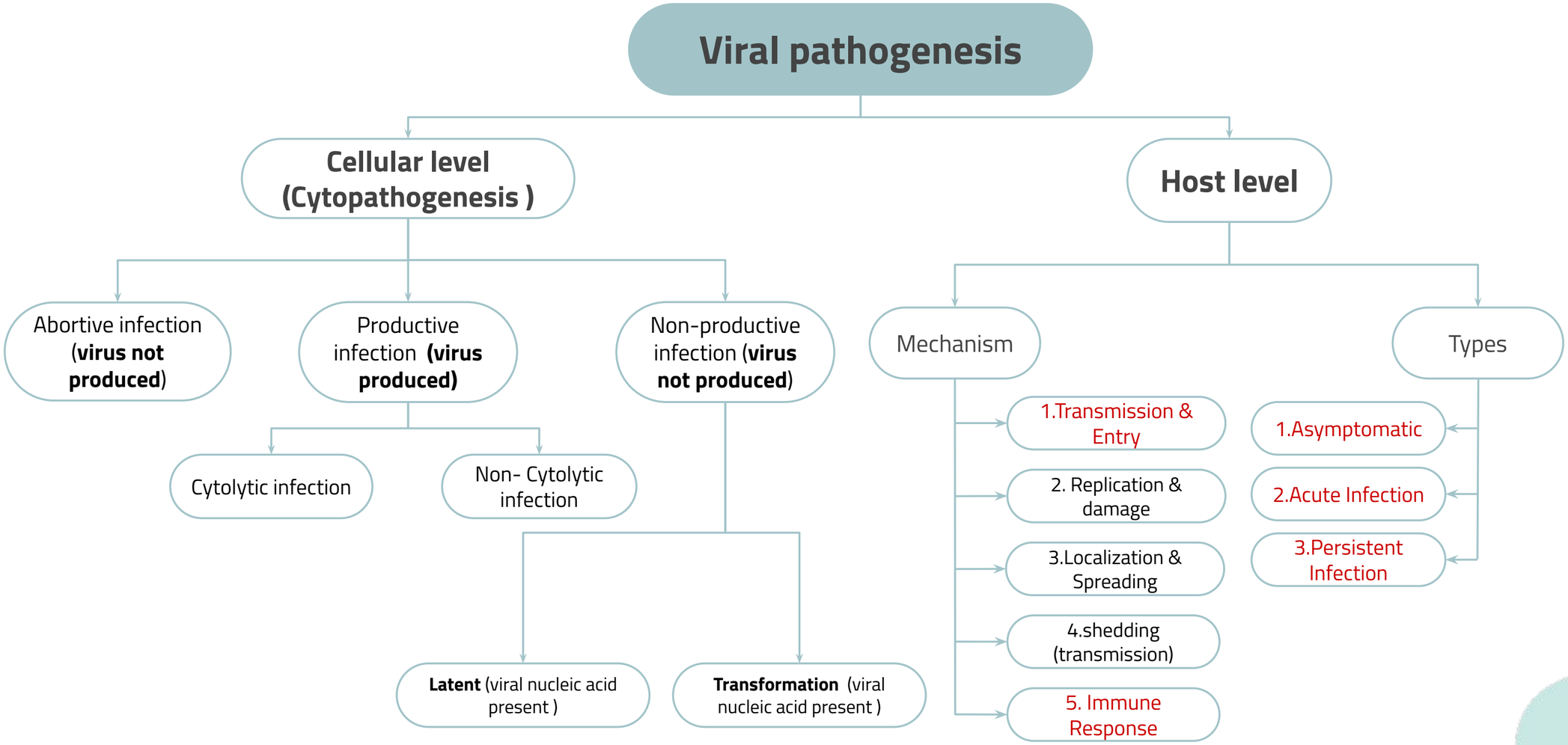
Viral diseases at host level.

You don't have to memorize it

Abbreviations for viruses names :

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 = Human T-lymphotropic virus
YFV = Yellow Fever Virus
VZV = Varicella zoster virus
EBV = Epstein-Barr virus
CMV = Cytomegalovirus

Introduction:



Types of Viral infection at cellular level (Abortive Infection)

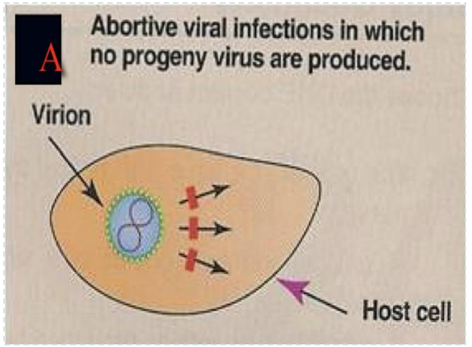
Viruses don’t complete the replication cycle, **so there is no production of new viruses**

EXPLANATION of Defective Interfering Particles: They are virus like particles. (It's not mutation in the viral genome) but the majority of genetic material is lost. What happens is that these defective particles compete with the virus (for the replication) resulting non-completed replication cycle. #med439

Interferons (IFNs) are a group of signaling proteins made and released by host cells in response to the presence of several pathogens, such as viruses, bacteria, parasites, and tumor cells #MED439

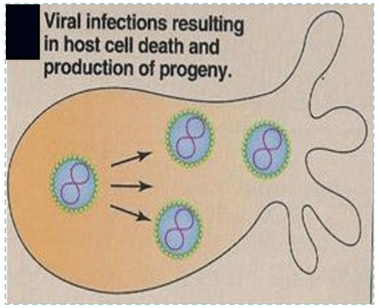
Why does it occur?

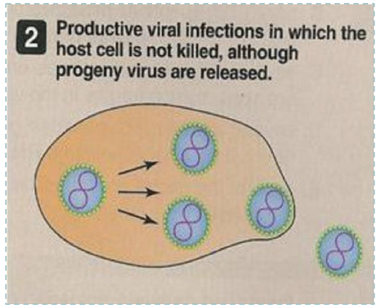
1. Due to mutation of viral genome
2. Defective interfering particles
   -Like a deletion in the viral genome or incorrect enzymes produced
3. The action of Interferons (IFNs)
   Interferons are cytokines produced by infected cells to protect other healthy cells.
   (Causing nearby cells to heighten their antiviral defenses)



Types of Viral infection at cellular level (Productive Infection)

Productive Infection: It has two types	
Cytolytic infection **Kill cell by cell lysis**	**Non-Cytolytic infection** **Doesn't Kill cell by cell lysis**
- Viruses replicate and produce progeny MED439 : reproduction cycle is completed, so there are new viruses produced in both types	
Results cell death & cytopathic effects (morphologic changes) The cell is destructed due to rupture of its member وشكلها بيتغير بعد For non-enveloped viruses	Virus released by cell budding & Little or no cytopathic effects Usually, the cell is not destructed. For enveloped viruses
Inhibition of cellular protein & nucleic acid synthesis In this type of infection the virus stops the synthesis of proteins & DNA for the cell	Identified by: hemadsorption (adherence of RBCs to the surface of virus or cell) & direct immunofluorescence

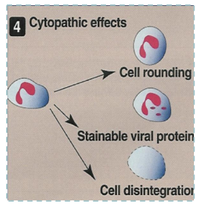




Cytopathic Effects (CPE):

The morphological/structure changes that occur in the host cell

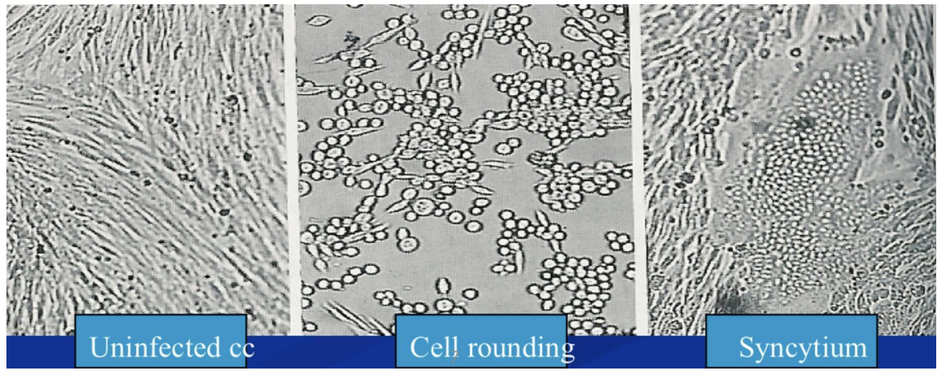
تختلف الCPE على حسب نوع الفايروس



CPE Can take several forms:

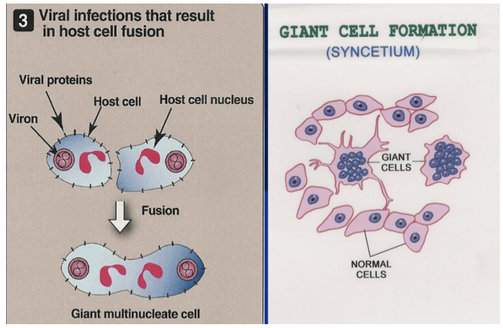
- 1- Cell lysis (Disintegration)
- 2- Cell rounding
- 3-Syncytium formation (cell fusion)
- 4-Inclusion bodies formation

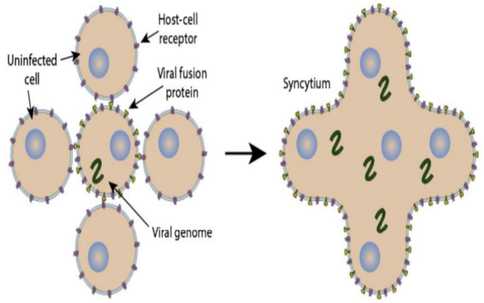
443 Dr. Note:
It converters from spindle shape to round (circle) shape.



Syncytium Formation

It's mean (single cell that contains multiple nuclei)





Giant cell : Two cells joined together

(Multinucleated cell)

- Formed by fusion of an infected cells with neighboring cells, resulting in a giant multinucleated cell

الخلية المصابة تتحد مع الخلايا السليمة وتصير خلية وحدة متعددة الأنوية

- This is due to expression of viral surface proteins on the membrane

الخلية المصابة بتطلع فايرل بروتينز والي راح تتشابك مع ريسيبتور الخلايا السليمة:

- common when cells are infected by either Herpes Paramyxovirus or respiratory syncytial virus(RSV)

Inclusion Bodies Formation

Inclusion bodies are a collection of viral proteins or particles inside the cells (cytoplasm or nucleus).

It takes several forms

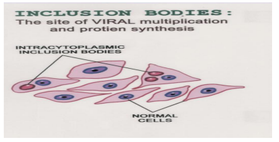
- Single or multiple
- Small or large
- Round or irregular

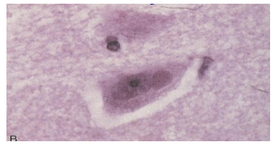
Med439 Note:

Because rabies is RNA virus, its inclusion bodies will be in the cytoplasm. However, herpes is a DNA virus, SO its its inclusion bodies will be in the nucleus.

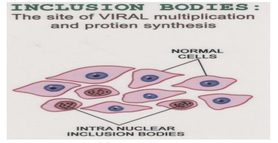
Location (sites)

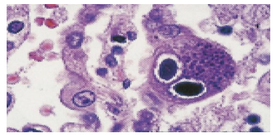
Cytoplasm (Intracytoplasmic) e.g. Rabies (causes Negri bodies)





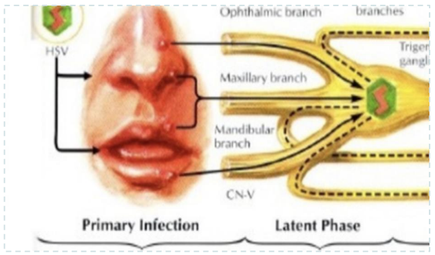
Nucleus (Internuclear) e.g. Herpes





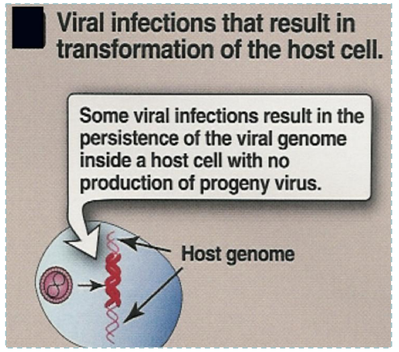
Types of Viral infection at cellular level (non- productive Infection)

Viruses infect cells that restrict or lack the machinery for transcribing viral genes (the virus cannot complete its replication) thus, no virus progeny produced.



Viral genome is found either

- integrated into cell DNA
- As circular episome (Stays in the cytoplasm)
- Both



Latent infection

Persistent infection because there is limited expression of viral genes,

The cell retains its normal properties

- الفايروس موجود في الخلية لكن صامت بدون اعراض ممكن يصير له تنشيط بعد فترة قد تستمر لسنوات، او ان الفايروس مايصير له تنشيط ويموت الانسان وهو ما يدري عنه

- It is difficult to detect in tests

E.g.: HSV (herpes virus):

الهربس يحمله الانسان بدون اعراض او أعراض خفيفة ومجرد ما يضعف جهازه المناعي مثلا يصاب بالايدز وقتها راح يتفعل وتبين اعراضه

Transformation (Oncogenic viruses)

Dr. Note: you should understand it very well.

- Viruses can stimulate uncontrolled cell growth causing Tf by alternating the balance between growth activators & growth suppressors gene products
- Can transform cell culture
- Causes tumors in animals & human :

المادة الوراثية للفايروس بتتحد مع المادة الوراثية للخلية وتسبب اختلال بالتوازن مما راح يخليها تتكاثر بطريقة غير صحيحة وبسرعة ويصير Cancer

E.g. EBV, HPV and HTLV.

Summary

Cytopathogenesis (Team 436)			
Infection	**Types**	**Causes**	**Outcomes**
Abortive Infection	-	-Mutation -Defective interfering particles -The action of INs (Interferons)	Viruses **don't complete** the replication cycle
Productive Infection	Cytolytic infection	-Viruses replicate & produce progeny (nonenveloped viruses) -Inhibition of cellular protein & NA synthesis	**Cell death & Cytopathic effects [CPE]** which cause morphologic changes
	Non-cytolytic infection	-Viruses replicate & produce progeny -Identified by hemadsorption & direct IF	Viruses released by cell **budding & little or no CPE.**
Non-productive infection	Latent infection	-Viruses 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.
	Transmission	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.

Pathogenesis at Host level:

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

2-Replication of the virus & damage to cells

3-Virus remains **localized** or spread to other organs

4-Viral shedding:
expulsion and release of virus progeny following successful reproduction during a host-cell infection

5-**The immune response** as :
- Host defense
-Immunopathogenesis

Transmission

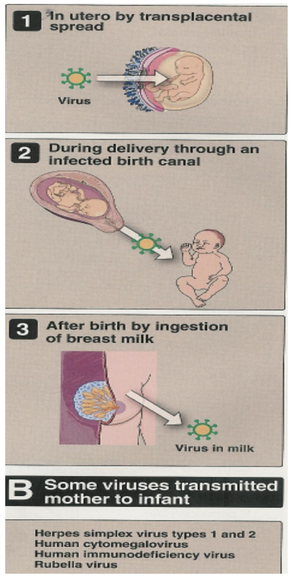
Transmission

Person to person

Vertical

Mother to fetus

1-In utero by transplacental
2-During delivery through
Skin contact, blood
an infected birth canal
3- After birth by ingestion of
breast milk



Horizontal

- Skin contact , Blood
- Respiratory route
- Fecal - oral route
- Genital contact

Animal to person

Reservoir -> human **e.g. Rabies virus**

مثل داء الكلب ينتقل للإنسان بشكل مباشر عند العض

Reservoir -> vector -> human **e.g. Yellow fever virus**

ينتقل بشكل غير مباشر عن طريق بعوضة مثلاً

Common routes of human infection by viruses :
- Skin
- GIT
- Genital tract
- Respiratory tract:

(Viruses are usually localized at portal of entry unless if arrived to the bloodstream, it will be generalized and spread to the rest of the body)

Types of viral infections at host level:

Asymptomatic infection

(most common).

Patient is a carrier but with no symptoms

Acute infection

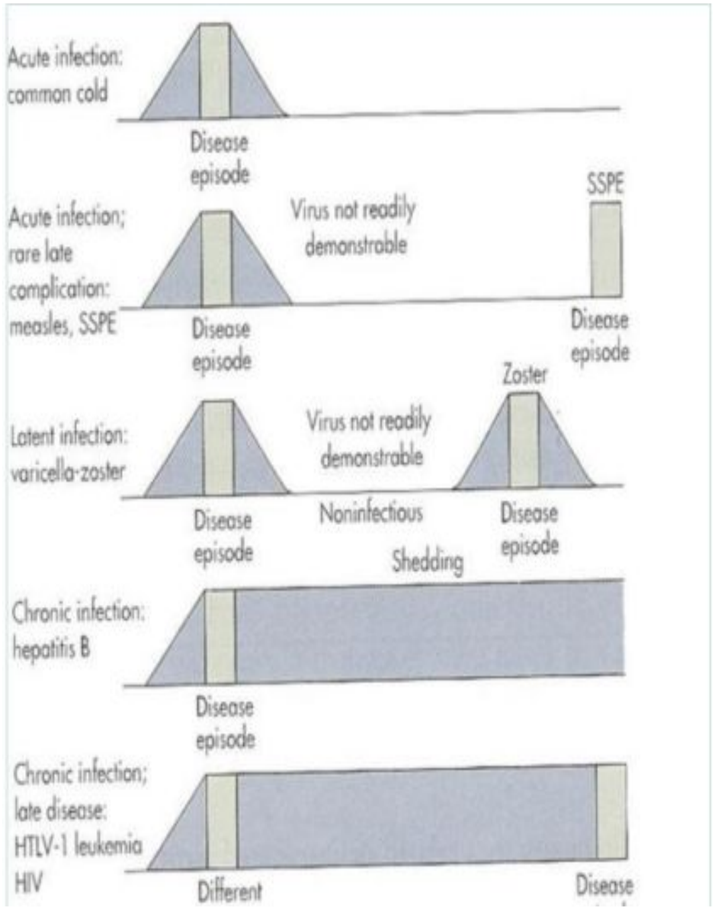
Like common cold

Persistent infection:

Where the infected cells survive viral replication

a) It is late complication of acute infection

b) Can be either Latent or Chronic infection



Important Features of Acute Viral Disease :

	Local infection Surface	Systemic infection Entered the bloodstream
Ex . of specific disease	Rhinovirus بسبب الزكام	Measles الحصبة
Site of Pathology	Portal of entry	Distant site يؤثر على اكثر من جهاز
Incubation period	Relatively short	Relatively long
Viremia (presence in blood)	Absent	Present
Duration of immunity	Variable-may be short	Usually life long
Role of secretory Ab (IgA) in resistance	Usually important	Usually not important

Common Routes of Human infection by virus :

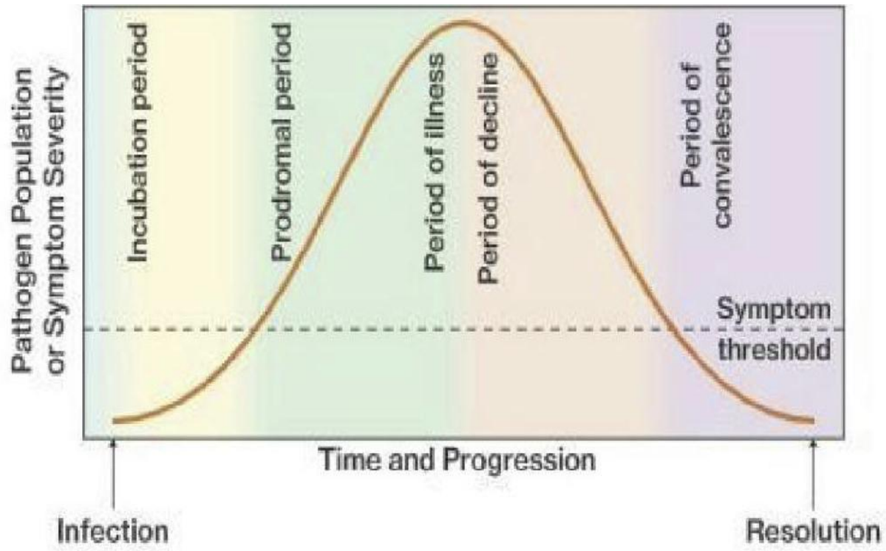
	Routes of entry	Viruses	Disease (L/G)
Skin	Mild Trauma	HPV	Warts (L)
	Injection (Blood)	HBV, HCV, HIV	Hepatitis B, Hepatitis C, AIDS (G)
	Bite of insect/animal	Yellow fever virus Rabies	Yellow fever (G) Rabies (G)
Respiratory Tract		HSV-1 Rhinovirus RSV Respiratory tract Adenovirus VZV Measles virus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

Stages of typical viral infection :

1 Incubation Period (IP)

When the person is infected but symptoms are not shown

هذا يصير حامل للمرض ما تبين عليه الأعراض يعني ممكن ينقل المرض بدون ما يدري



2 Prodromal Period

General (non-specific) symptoms appear (e.g headache, fever, loss of appetite)

3 The Specific Illness period

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

1) Inhibition of cellular macromolecular synthesis
2) Immunologic attack (immunopathogenesis)-Cytotoxic T cells e.g Hepatitis(A,B or C)

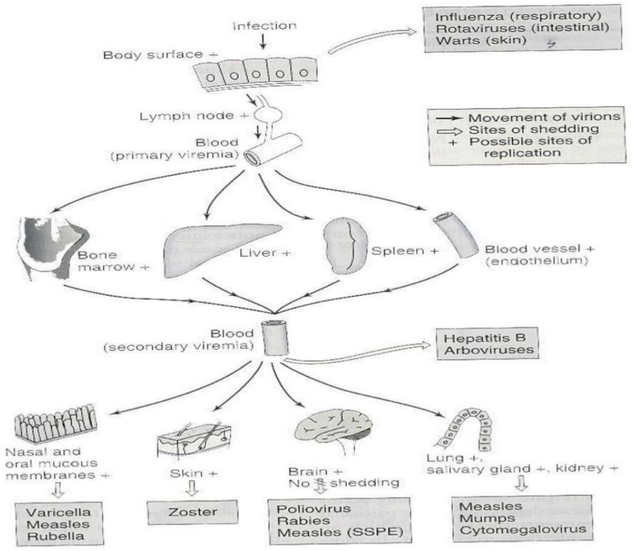
التهاب الكبد أعراضه تشتد متى؟ لما الجهاز المناعي يشتغل و الـ Cytotoxic T cell تبدأ تهاجم الخليه المصابة بالفايروس و تقتلها

4 The recovery period

Symptoms begin to fade until the time patient recovers from the disease

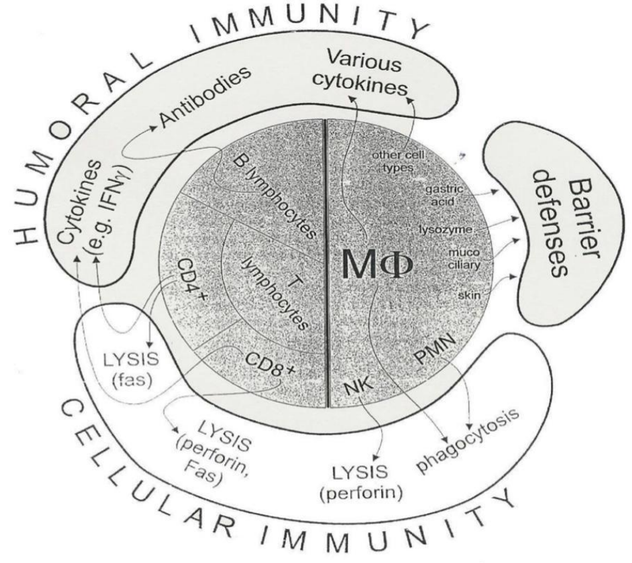
Mechanism of spread virus through the body (Virus Shedding):

Get the general idea, and remember that the virus first infects locally(e.g. epithelial cells or mucosa) and it might stop there (local infection) or it can move on and cause (systemic/general infection) after it reaches the blood

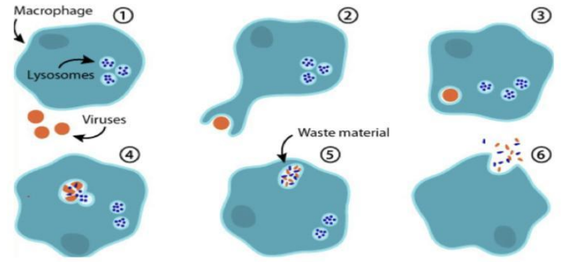


The Immune Response:

IMPORTANT Dr. note: Viruses can be shedding(from primary or target infection), and releasing(from symptomatic or asymptomatic) from clinically normal infected person(people or patients that don't have signs or symptoms of diseases)



The immune response to virus :



1

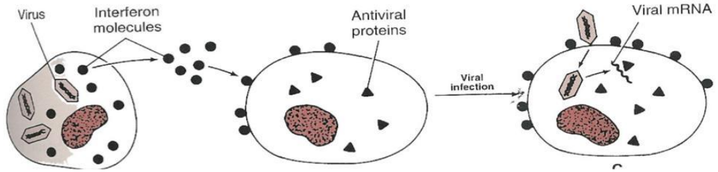
Macrophages:

1) It is an antigen presenting cell(APCs)
2) Function in phagocytosis
3) It produces cytokines

2

Natural killer (NK) cells:

Function in lysis of infected cells



3

Cytokines:

(E.g interferons/interleukins) released from virus infected cell

Interferones (IFN): Excreted by infected cell so that it warns the cells near to it to stop the production of proteins so that translation/transcription don't take place once the virus enters	**Interleukin (IL):**
A-α and β interferons(INF): inhibit the viral and the host cell mRNA translation	A- Stimulates antibody production بداية الانفكشن B-Activates T cells & cell mediated immunity C-Suppress the immune cells بعد ماينتهي الانفكشن
A- γ interferons (INF): stimulates phagocytosis and killing by macrophages and NK cells	

The immune response to virus :

Adaptive immunity	
4- Cell Mediated Immunity (CMI)	**5- Humoral Immunity**
Effective against intracellular viruses	Effective against Extracellular viruses (i.e viremia-viruses in blood)
Lysis of virally infected cells by Cytotoxic T cells {CD8}	Usually act by neutralization Involves cytokines, antibodies, etc.
Faster than humoral	The antibodies will prevent the replication of the free (Extracellular) virus & prevent it from binding to the host's cell receptors

Quiz

Q1: Negri bodies are caused by? Slide 7							
A	Rabies virus	B	Rhinovirus	C	HPV	D	Yellow fever virus
Q2: What type of infection releases viral progeny? Slide 6							
A	Cytolytic	B	Abortive	C	Latent	D	Non-productive
Q3: Viruses infect cells that restrict or lack the machinery for transcribing viral genes. Slide 8							
A	Non-productive infection	B	productive infection	C	Syncytium formation	D	abortive infection
Q4: how many type of viral infection at host level? Slide 12							
A	1	B	3	C	5	D	7
Q5: Choose the correct statement. Slide 18							
A	CMI is effective against extracellular viruses	B	Humoral immunity is effective on intracellular viruses	C	CMI if effective on intracellular viruses.	D	_____

1-A 2-A 3-A 4-B 5-C

MEET THE TEAM

Leaders

- Leena Shagrani
- Abdulaziz Alanazi
- Lujain Darraj

Members

- Huda bassam
- Jenan Al-Sayari
- Nora Alturki
- Bassmah fahad
- Dana Abu Alamah
- Madaen Alarifi
- Rahaf Alaklabi
- Monirah shojaa
- AlJawharah alyahya
- Layal alkhalifah
- Aram alzahrani
- Noor AlTalag
- Norah Albahily
- Ziyad Bukhari
  - Abdulrahman Alnafisah
- Fasial Alamoud
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