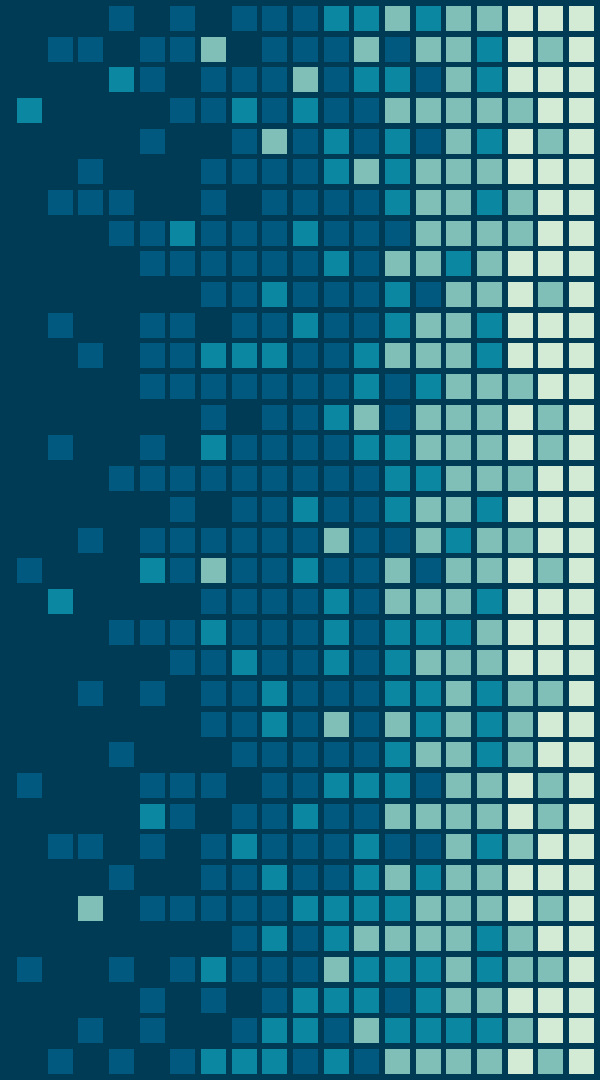
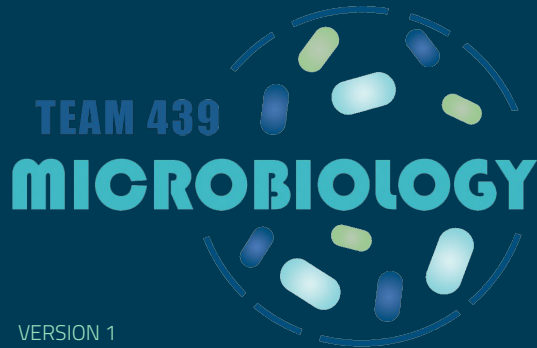


Viral Pathogenesis



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.

Colour index:

- **Red: Important.**
- Grey: Extra info & explanation.
- **Purple: Only in girl's slides.**
- **Green: Only in boy's slides.**
-

Any future corrections
will be in the editing
file, so please check it
frequently.

Scan the code
Or click [here](#)



Definitions

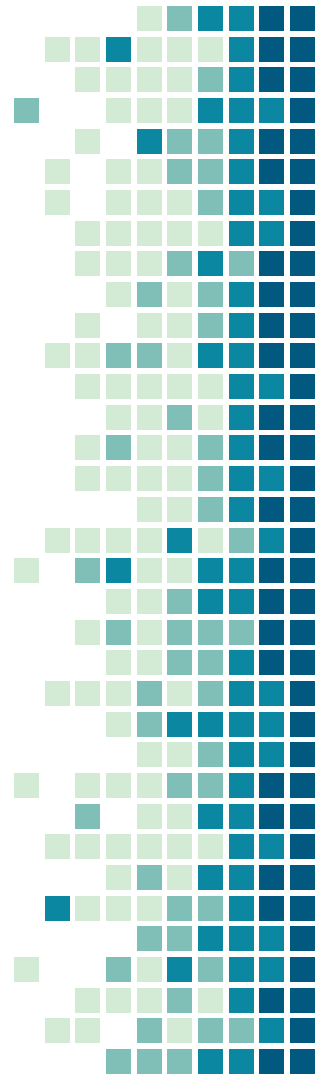
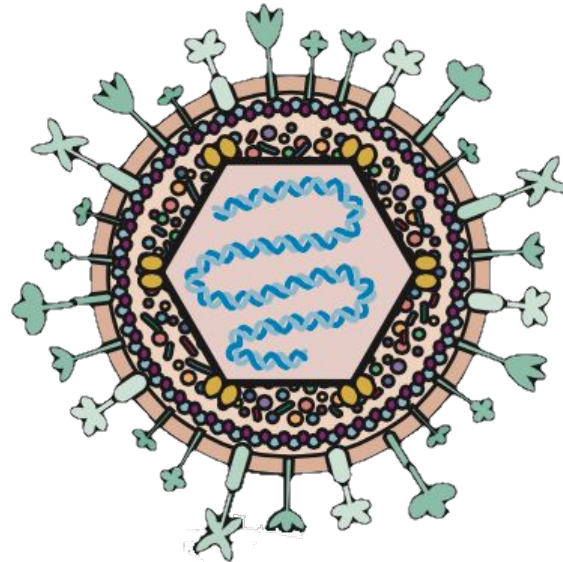
Cytopathogenicity: viral disease at a cellular level (cause cell damage or death)

Cytopathic/Cytopathogenic effect (CPE): changes in host cells that are caused by viral invasion.

Mechanism of the disease: viral disease at host level

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



Viral Pathogenesis

Cellular Level (Cytopathogenesis)

1. Abortive Infections

Virus not produced

2. Productive Infections

Virus produced

Cytolytic Infection

Non-Cytolytic Infection

3. Non-productive Infections

Virus not produced

Latent

Viral nucleic acid remains

Transformation

Viral nucleic acid remains

Host Level

Types

1. Asymptomatic

2. Acute Infection

3. Persistent Infection

Mechanism

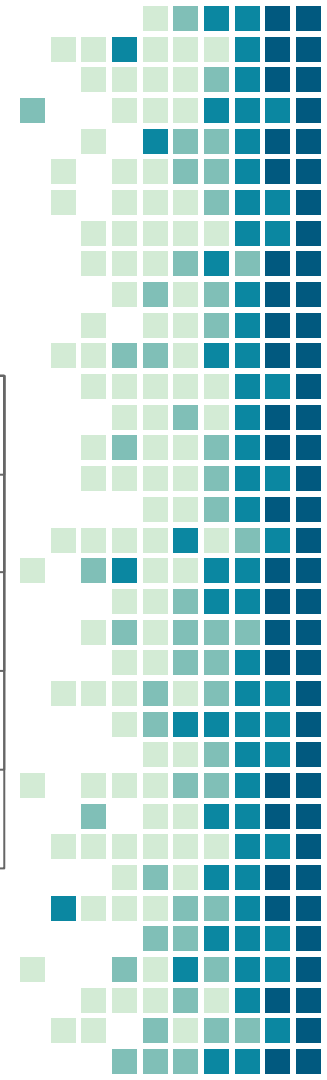
1. Transmission & Entry

2. Replication & Damage

3. Localizing or Spreading

4. Shedding (transmission)

5. Immune Response



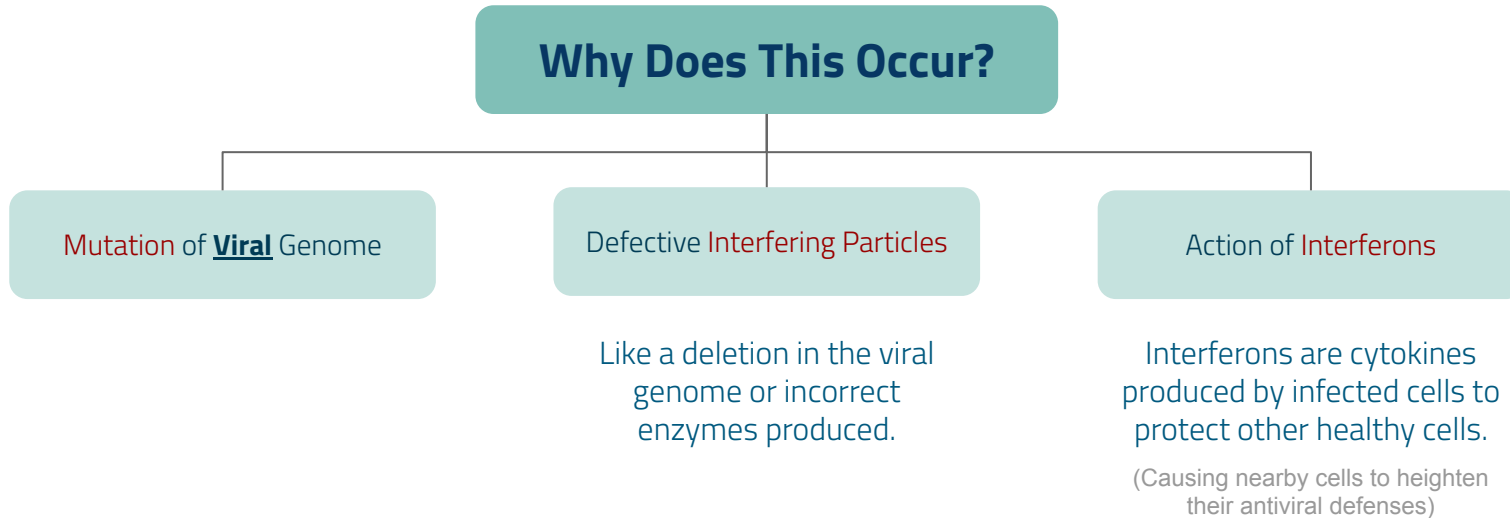
Types Of Viral Infections at cellular level (**Abortive**)

Progeny = Offspring

1-Abortive Infections:

The virus infects the cell but it cannot continue it's replication cycle. Thus, **no virus progeny is produced**.

Replication cycle is not completed, 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.

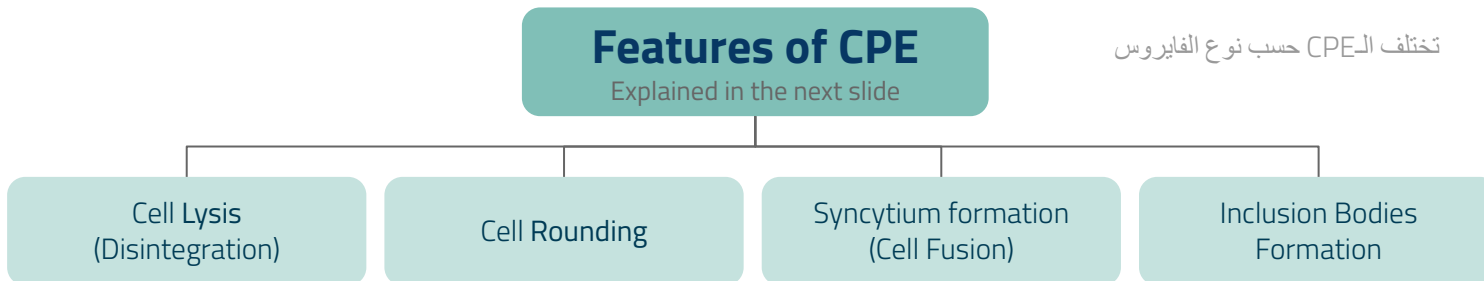


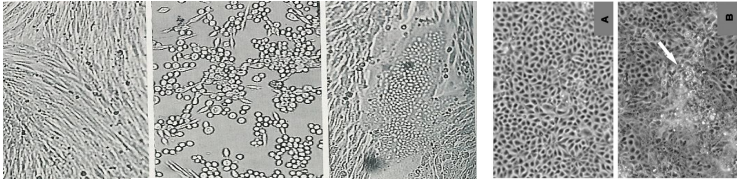
Types Of Viral Infections at cellular level (**Productive**) because it produces new viruses

2-Productive Infections: has two types..

Cytolytic infection AFFECTS (KILLS) THE CELL BY CELL LYSIS	Non-cytolytic infection DOES <u>NOT</u> AFFECT THE CELL BY CELL LYSIS
★ Viruses replicate & produce progeny Reproduction cycle is completed, so there are new viruses produced in both types.	
Results cell death & cytopathic effects (morphologic changes) The cell is destroyed due to rupture of its membrane <i>وشكلها يتغير بعد</i> For non-enveloped viruses	Virus released by cell budding & Little or no cytopathic effects Usually, the cell is not destroyed . For enveloped viruses
<u>Inhibition</u> of cellular protein & nucleic acid synthesis. <i>في هذا النوع من الانكسار الفيروسي يوقف انتاج البروتين و ال DNA حق الخلية</i>	Identified by: hemadsorption (adherence of RBCs to the surface of virus or cell) & direct immunofluorescence

Cytopathic Effects (CPE): The morphological/structural changes that occur in the host cell.

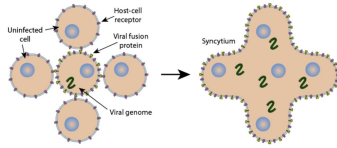




Uninfected (normal) Cell Rounding Syncytium (of RSV) Uninfected (normal) Cell lysis
تتحلل الخلايا المصابة

◆ Syncytium formation

(single cell that contains multiple nuclei)



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

الخلية المصابة تندمج مع الخلايا السليمة حولها وتصبح عندي خلية كبيرة متعددة الأنوية

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

الخلية المصابة بتطلع فايبرل بروتينز (e.g. spikes) والتي راح تشبك مع receptors الخلايا السليمة

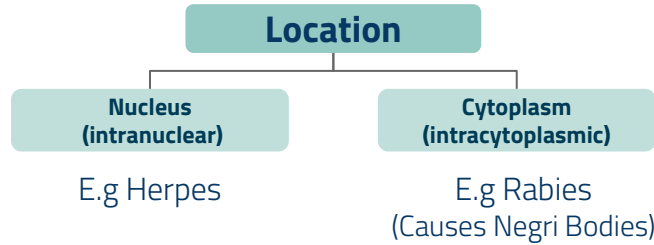
- ◆ Common when cells are infected by either Herpes Paramyxovirus or respiratory syncytial virus (RSV)

◆ Inclusion Bodies Formation

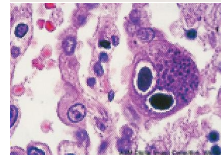
It is a collection of viral proteins or particles inside the cells (cytoplasm or nucleus).

It takes several forms:

- Single or Multiple
- Small or Large
- Round or Irregular

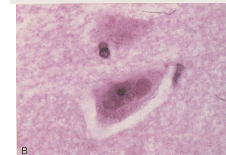
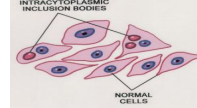


INCLUSION BODIES :
The site of VIRAL multiplication and protien synthesis



Owl's eye inclusions
caused by CMV

INCLUSION BODIES :
The site of VIRAL multiplication and protien synthesis



Negri bodies



Scan or Click

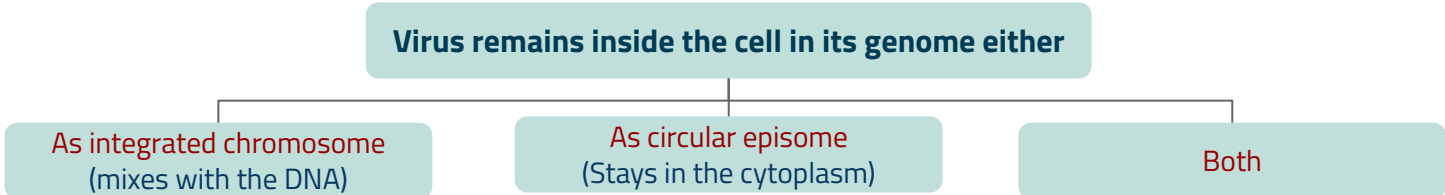
NOTE:

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.

Types Of Viral Infections at cellular level (Non-Productive), because there is no production of new viruses

3-Non-productive Infections (Persistent):

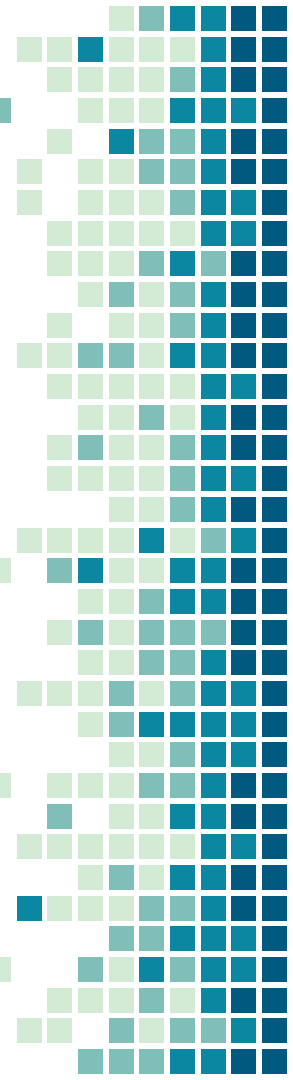
When the virus infects the cell, the virus cannot complete its replication cycle (because the cell lacks machinery to transcribe viral genes). Thus, **no virus progeny produced.**



Latent Infection	Transformation (oncogenic viruses)
<p>Persistent infection because there is limited expression of viral genes.</p> <ul style="list-style-type: none"> - The cell retains its normal properties <p>الفايروس يكون موجود بالخلية عالصامت (خامل) بدون ما يسبب اذى واعراض لفترة طويلة، قد تستمر لسنوات لحد مايصير له reactivation (وأصلا ممكن مايحصل reactivation ابد ويموت الانسان وهو ماحس فيه)</p> <p>- It is difficult to detect in tests</p>	<ul style="list-style-type: none"> -Causes tumors in animals & humans -Can transform cell culture. -Viruses can stimulate uncontrolled cell growth causing transformation by alternating the balance between growth activators & growth suppressors gene products. <p>الفايروس ما يتكاثر لكنه بالمقابل بيندمج الـDNA حقه مع حق الخلية وراح يحوس الـbalance او التوازن بين محفزات و مثبطات النمو عندها، واللخبطه ذي راح تسبب انقسامات غير منتهية للخلية وبيصير tumor.</p>
<p>E.g.: HSV (herpes virus)</p> <p>مثال: الهريس يحمله الإنسان بدون اعراض أو اعراض خفيفة، ومجرد ما يضعف جهازه المناعي مثلا يصاب بالايديز HIV وقتها راح يتفعل وتبين أعراضه</p>	<p>E.g. EBV, HPV and HTLV.</p> <p>NO NEED TO MEMORIZE</p>

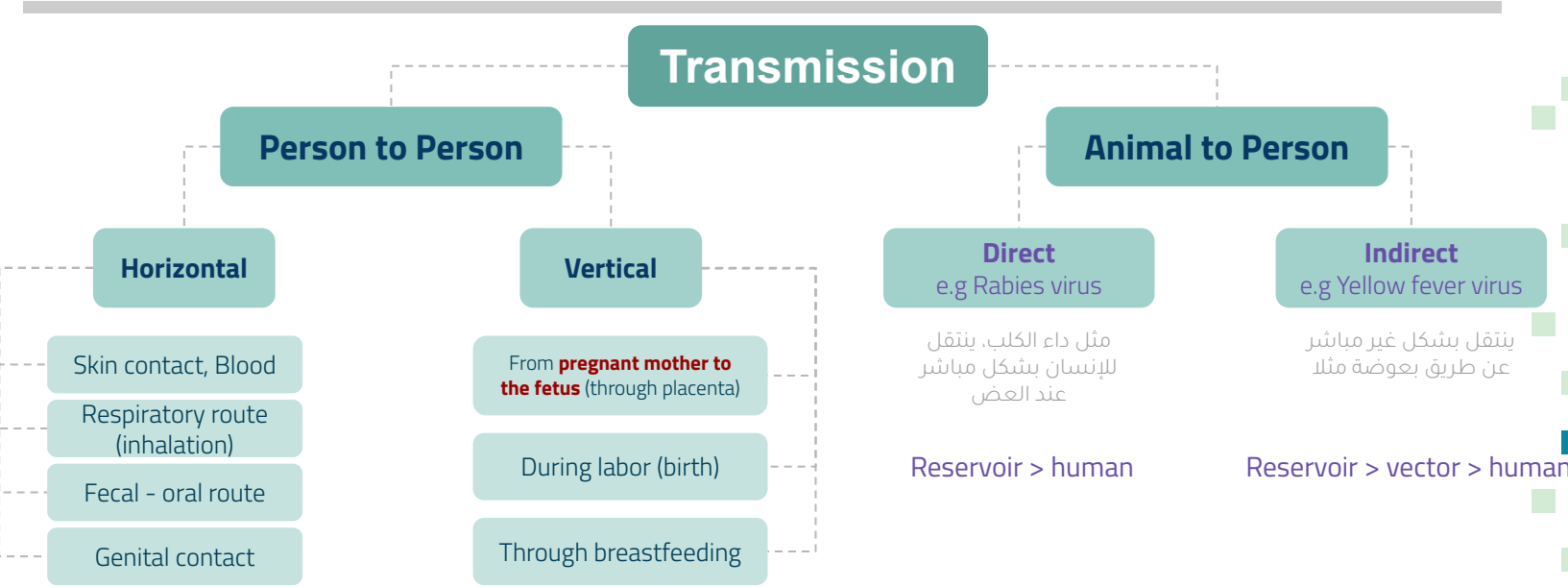
Cytopathogenesis (Team 436)

Infection	Types	Cause	Outcome
Abortive Infections	-	<ul style="list-style-type: none"> -Mutation -Defective interfering particles -The action of IFNs (Interferons) 	Viruses don't complete the replication cycle
Productive infection	Cytolytic Infections:	<ul style="list-style-type: none"> -Viruses replicate & produce progeny (enveloped viruses) -Inhibition of cellular protein & NA synthesis 	Cell death & Cytopathic effects [CPE] which cause morphologic changes
	Non- Cytolytic infection	<ul style="list-style-type: none"> -Viruses replicate & produce progeny -Identified by hemadsorption & direct IF 	Viruses released by cell budding & little or no CPE.
Nonproductive infection	Latent infection	<ul style="list-style-type: none"> -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.
	Transformation	<ul style="list-style-type: none"> -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. Viruses remain **localized (on the surface)** or **systemic (entered the bloodstream and 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 or Immunopathogenesis

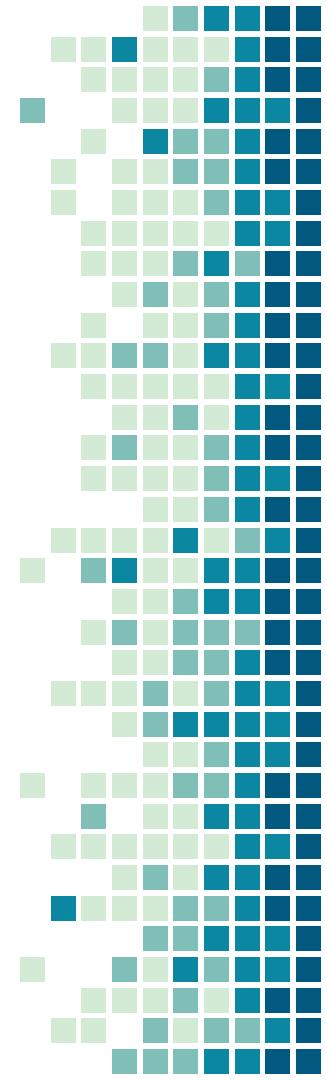


Types of Viral Infections on the Host Level:

- 1) **Asymptomatic Infection** (most common). Patient is a carrier but with no symptom.
- 2) **Acute Infection** (like the common cold).
- 3) **Persistent Infection**: where the infected cells survive viral replication
 - a) It is a late complication of acute infection
 - b) Can be either Latent or Chronic

Important features of acute viral disease

	Localized Infection Surface	Generalized (systemic) infections Entered the bloodstream
Example of disease	Rhinovirus يسبب الزكام	Measles (الحصبة)
Site of pathology	Portal of entry Ex: entered through nose (inhalation, nasal breathing), so the infected place will be the nose too!	Distant site Ex: : entered through respiratory tract, but it will enter the bloodstream and infect distant places e.g. skin.
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 antibodies IgA in resistance	Usually important	Usually not important



Team 435: Common Routes of Human Infection by Viruses (Only Found in Boy's Slides)

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	<ul style="list-style-type: none"> ▪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)

Note:
L = (Local) Virus
doesn't reach blood

G = (General) Virus
reaches the blood

Don't like the
table? Check out
the mind map!



Scan or Click

The Stages of a Typical Viral Infection

1

Incubation Period (IP)

When the person is infected but **symptoms are not shown**.

هنا يصير حامل للمرض بس ما تبين عليه الأعراض، يعني ممكن ينقل المرض بدون ما يدري عن نفسه

2

Prodromal Period

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

3

The Specific-illness period

More severe symptoms begin to appear, these symptoms are due to cell killing by:

- 1) Inhibition of cellular macromolecular synthesis مثال: البروتينات
- 2) Immunologic attack (immunopathogenesis) - Cytotoxic T cells e.g Hepatitis (type A,B, or C)
التهاب الكبد أعراضه تشدد متى؟ لما الجهاز المناعي يشتغل والـ Cytotoxic T cell تبدأ تهاجم الخلية المصابة بالفايروس وتقتلها

4

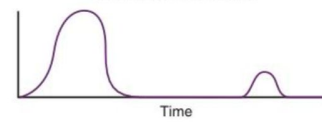
The Recovery Period

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

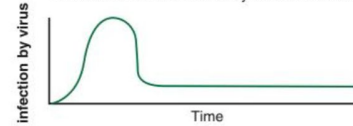
A. Acute infection followed by viral clearance by the immune response



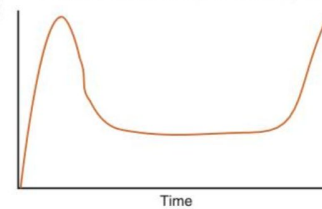
B. Acute infection followed by latent infection and periodic reactivation



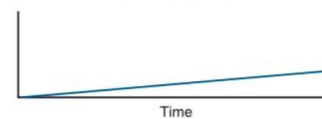
C. Acute infection followed by chronic infection



D. Acute infection followed by persistent infection (set point) and virus overproduction (eg, HIV)

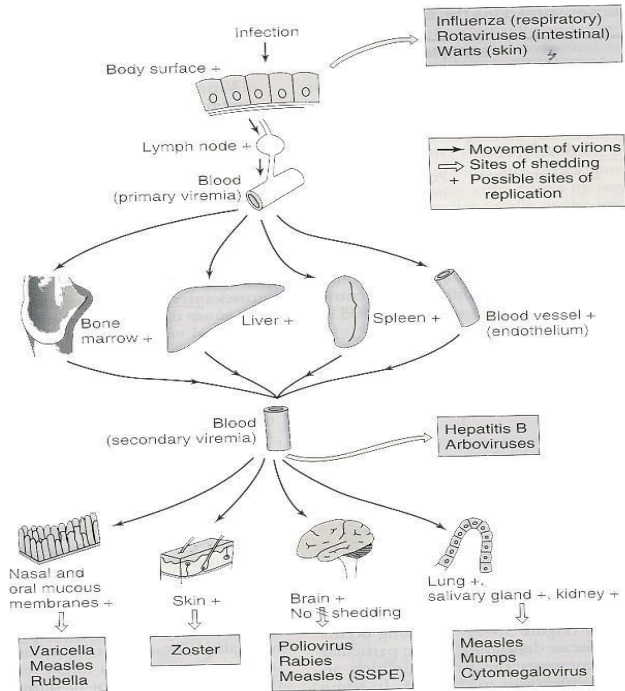


E. Slow chronic infection



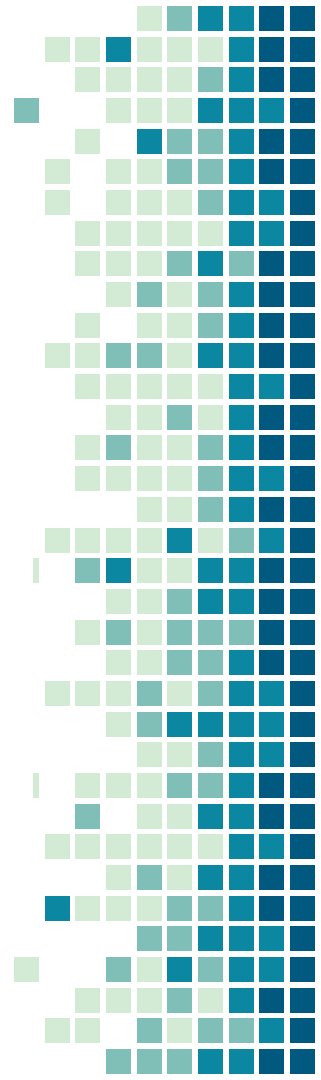
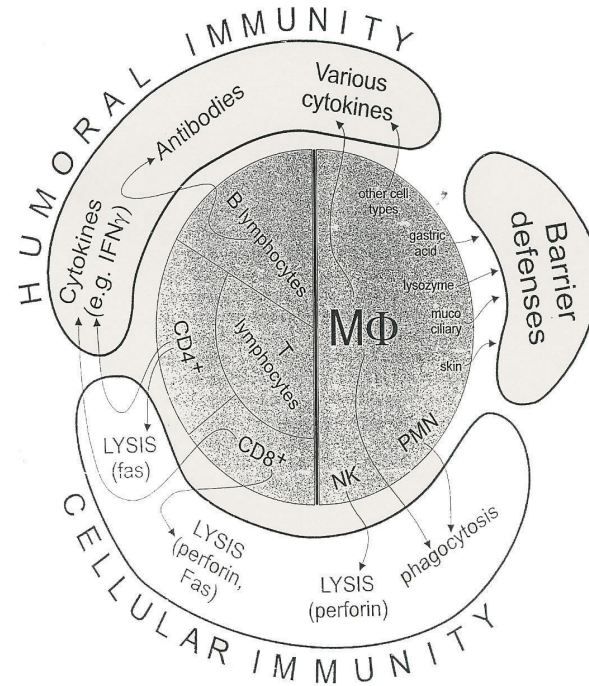
Mechanisms of spread of virus through the body

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 to virus

Check the next slide



The immune response to virus

For this section it is recommended to understand it from immunology team 439

1-Macrophages:

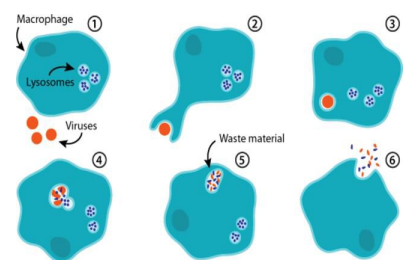
- 1) It is an Antigen Presenting Cell (APCs)
- 2) Function in phagocytosis
- 3) It Produce cytokines

2- Natural killer (NK) cells:

Function in lysis of infected cells

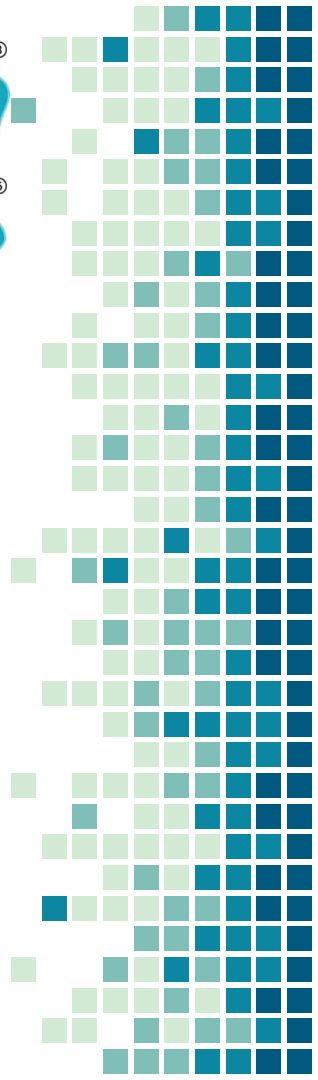
3- Cytokines:

(e.g. Interferons/interleukins) released from virus infected cell

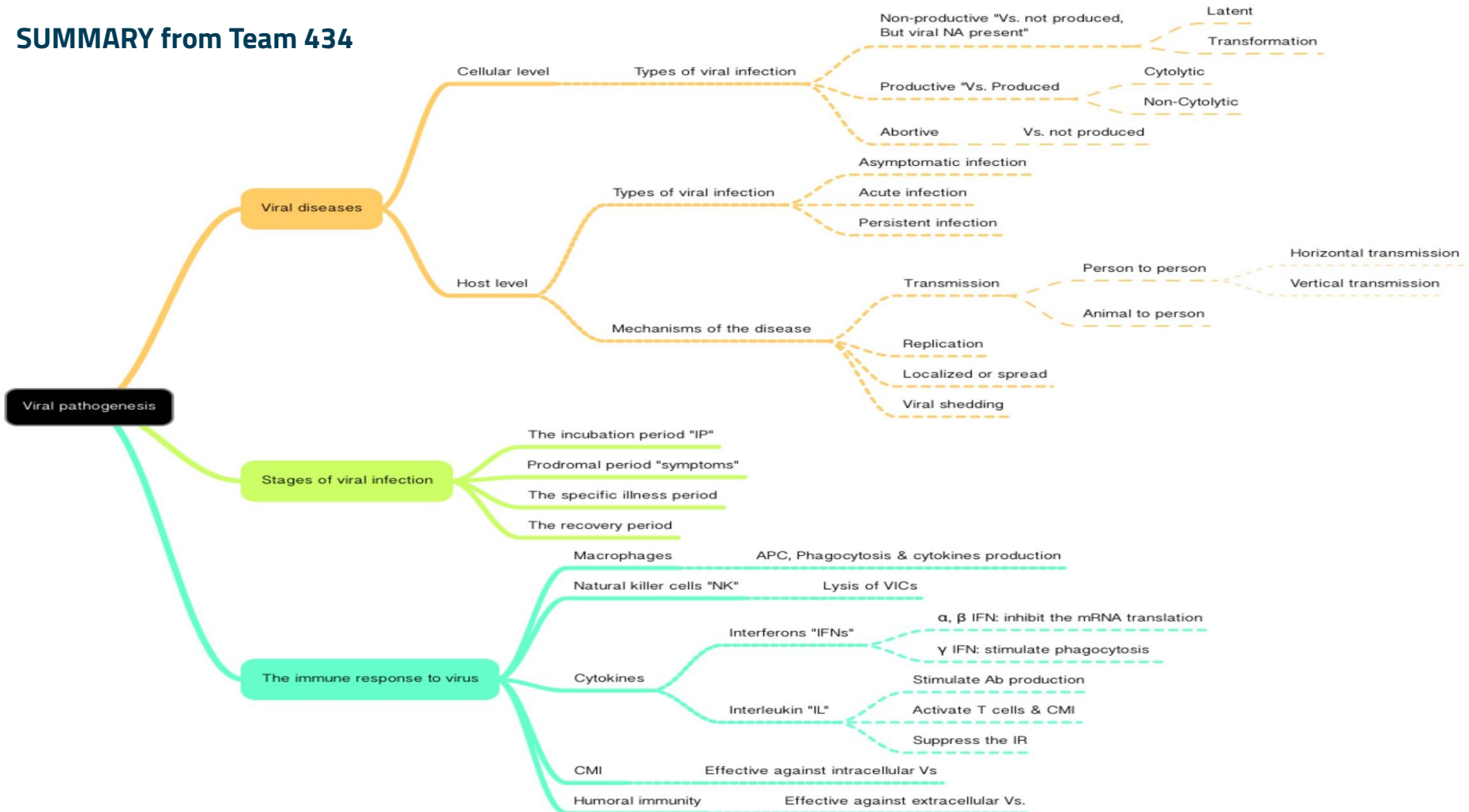


Adaptive Immunity	
Cell Mediated immunity (CMI)	Humoral Immunity
Effective against intracellular viruses	Effective against extracellular viruses (i.e viremia -viruses in blood)
Lysis of <u>virally infected cells</u> by Cytotoxic T Cells [CD8]	Usually act by neutralization Involves cytokines, antibodies, 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

Interferons (INF):	Interleukin (IL) : Only in boy's slide
تفرزه الخلية المصابة عشان تحذر الخلية اللي جنبها انها توقف تصنيع البروتين عشان مايصير transcription/translation للفايرس إذا دخلها	
A- α and β Interferons (INF): inhibit the viral and the host cell mRNA translation.	A- Stimulate antibody production بداية الانفكشن B- Activate T cells & cell mediated immunity C- Suppress the immune cells بعد ماينتهي الانفكشن
B- γ Interferons (INF): stimulates phagocytosis and killing by macrophages and NK cells.	



SUMMARY from Team 434



MCQs

1-Which of the following is a reason that viruses can't continue its replication in abortive infection?

- a) Action of Interleukins
- b) Due to CPE
- c) Deletion in the viral genome
- d) Mutation of host genome

2-All but one of these statements is true, which one?

- a) Cell mediated immunity is effective against intracellular viruses
- b) Cell mediated immunity is faster than humoral
- c) In humoral immunity lysis of virtually infected cell is by CTC
- d) Cell mediated immunity utilizes CD8 cells

3-Negri bodies are caused by

- a) Rabies virus
- b) Rhinovirus
- c) HPV
- d) Yellow fever virus

4-Viruses cannot enter the body by:

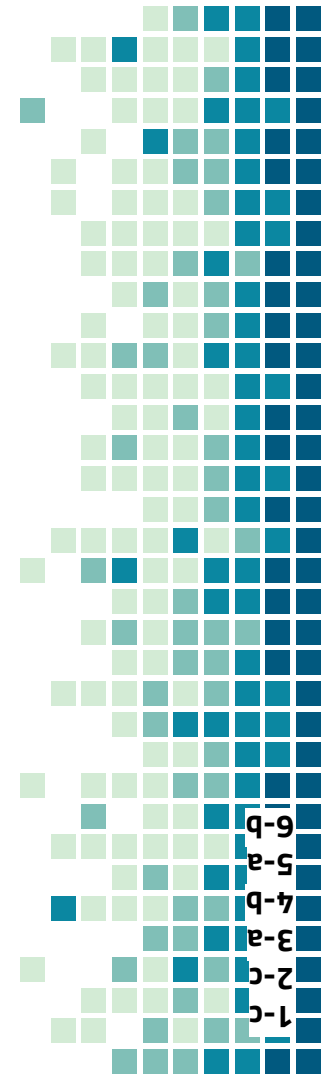
- a) Blood transfusion
- b) Diffusion through skin
- c) Respiratory tract
- d) Insect bite

5-What type of infection releases viral progeny?

- a) Cytolytic
- b) Latent
- c) Non-productive
- d) Abortive

6-At what stage of infection do general symptoms appear?

- a) Incubation Period
- b) Prodromal Period
- c) Specific-illness period
- d) Recovery Period



Q-9
E-5
Q-7
E-3
C-2
C-1

MCQs

7- When are cytopathic effects most prominent?

- A- In Cytolytic Infections
- B- In Non-cytolytic Infections
- C- Abortive infection
- D- None of the above

8- According to host level which of the following is type of viral infection

- A- Abortive
- B- Productive
- C- Non-productive
- D- Asymptomatic infection

9- Inhibition of the viral and the host cell mRNA translation is done by

- A- α Interleukin
- B- β Interleukin
- C- γ Interleukin
- D- None of the above

SAQ

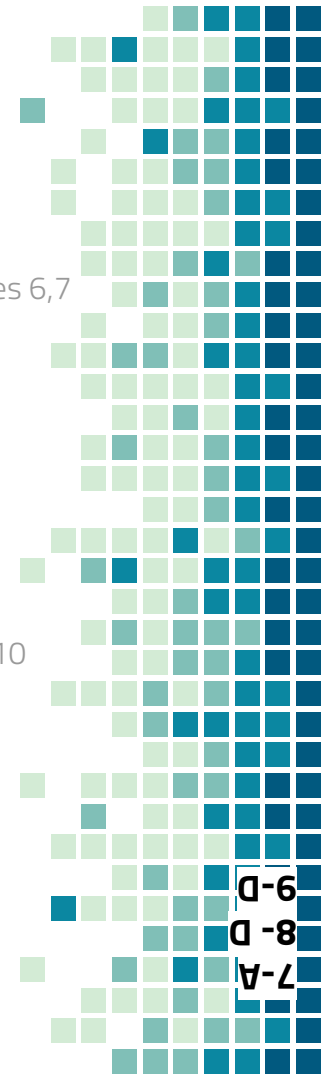
Q1- What are the cytopathic effects?

Slides 6,7

Q2- Give an example of vertical transmission

Slide 10

9-D
8-D
7-A



Team Leaders

- Duaa Alhumoudi
- Manee Alkhalifah

Team Members

- Sarah Alqahtani
- Sadem Alzayed
- Noura Alshathri
- Ghadah Alsuwailem
- Shahad Almezel
- Noura Alsalem
- Sumo Alzeer
- Renad Alhomaidi
- Raghad Albarrak
- Reema Alowerdi
- Abdulaziz Alderaywsh
- Sultan Alqahtani
- Faisal Alomri
- Munib Alkhateeb
- Abdulaziz Alomar
- Muhannad Alomar
- Meshal Alhamed



Contact us through:
Microbiology439@gmail.com