Microbiology

Subject :

Lec no : 28

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وقل رب زدني علما

Pathogenesis of viral infection

Virology Lecture 3

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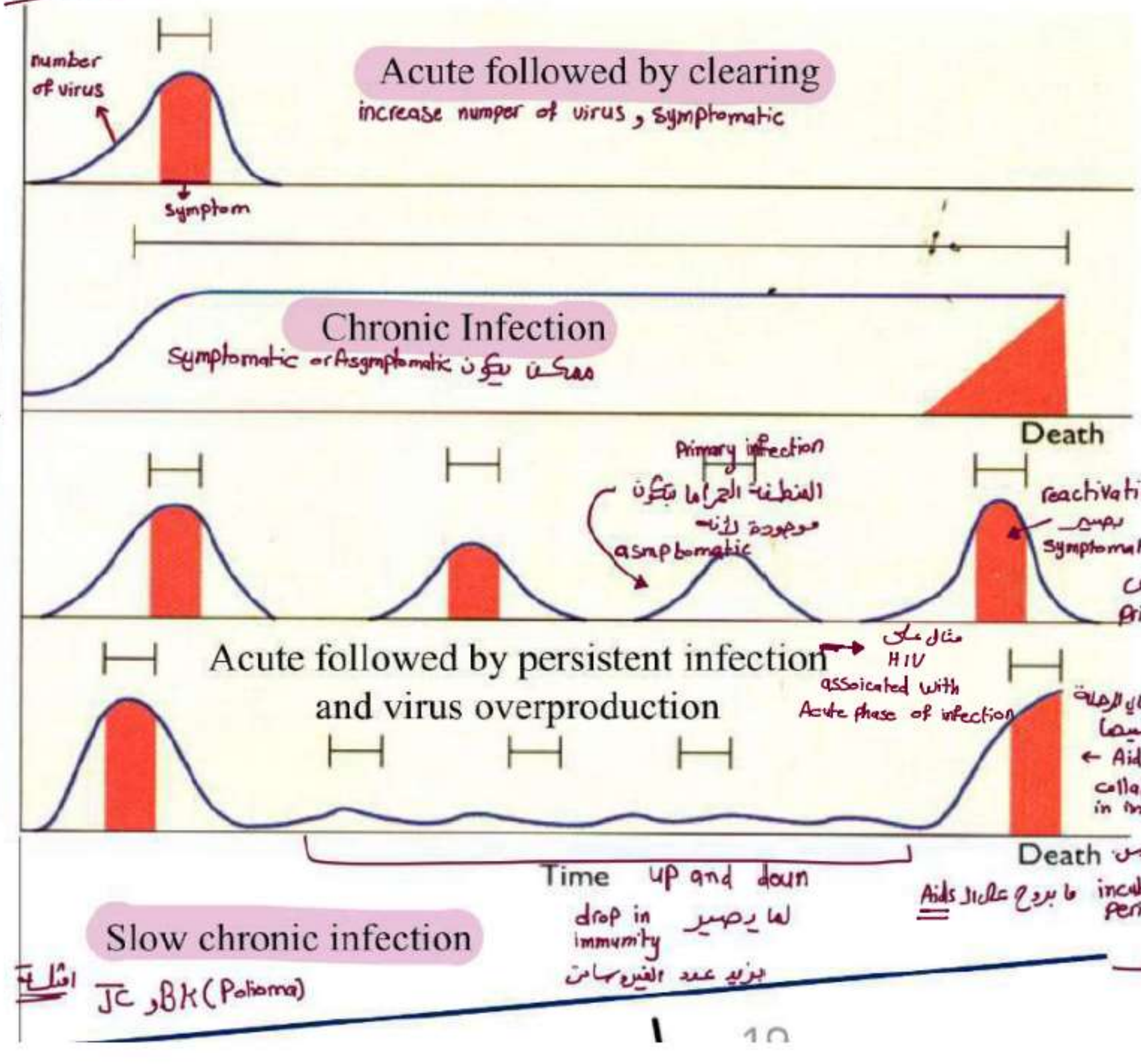
الدكتور بالبدايت رجع عاد
هاي المعلومات

Patterns of viral infection



Acute infection
- Rhinovirus
- Rotavirus
- Influenza virus

Persistent infection
- Hepatitis B & C

Latent, reactivating infection
- Herpes simplex virus

لما يظهر ال Fever blister بتكون شي Primary infection

Slow virus infection
- Measles virus SSPE
- Human immunodeficiency virus

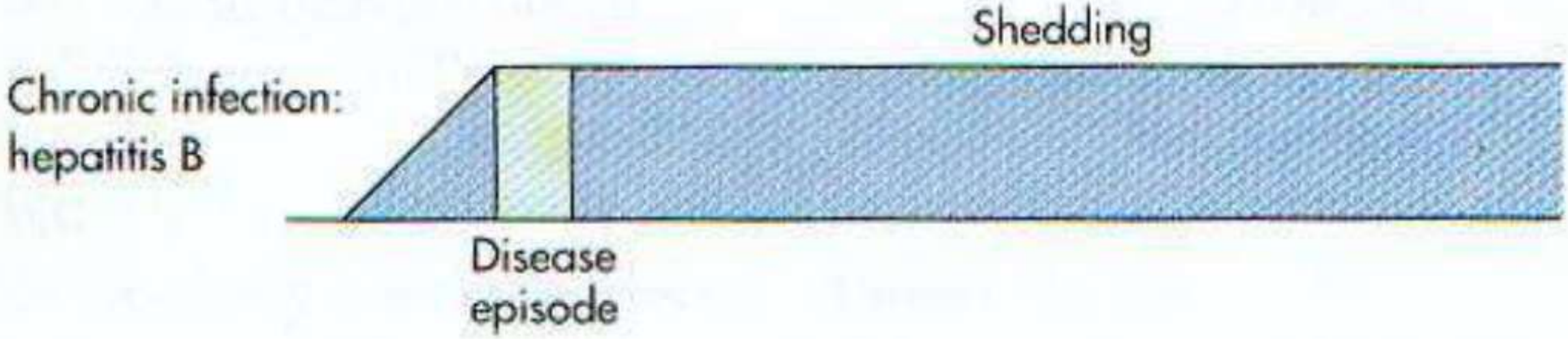
← Aids
هاي المرحلة بسيطة
collabes in immunity

جزء كبير من الناس بضلهم بال incubation period ما يروح على ال Aids

هدول اعادة للحي الحي فوق

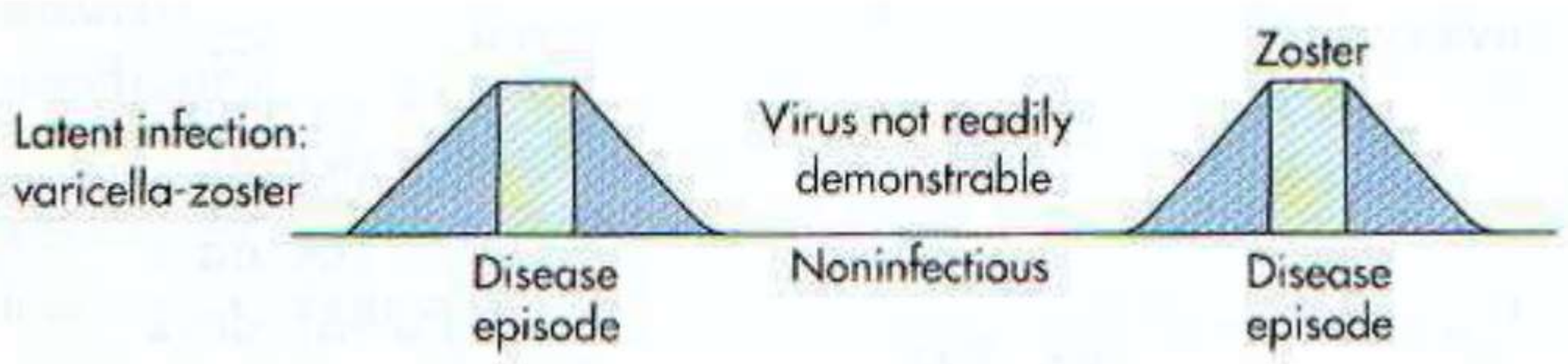
Chronic Infection

- Virus can be continuously detected ; mild or no clinical symptoms may be evident.



Latent infection

The Virus persists in an occult, or cryptic, from most of the time. There will be intermittent flare-ups of clinical disease , Infectious virus can be recovered during flare-ups . Latent virus infections typically persist for the entire life of the host



Slow virus infection

- A prolonged incubation period, lasting months or years, during which virus continues to multiply. Clinical symptoms are usually not evident during the long incubation period .

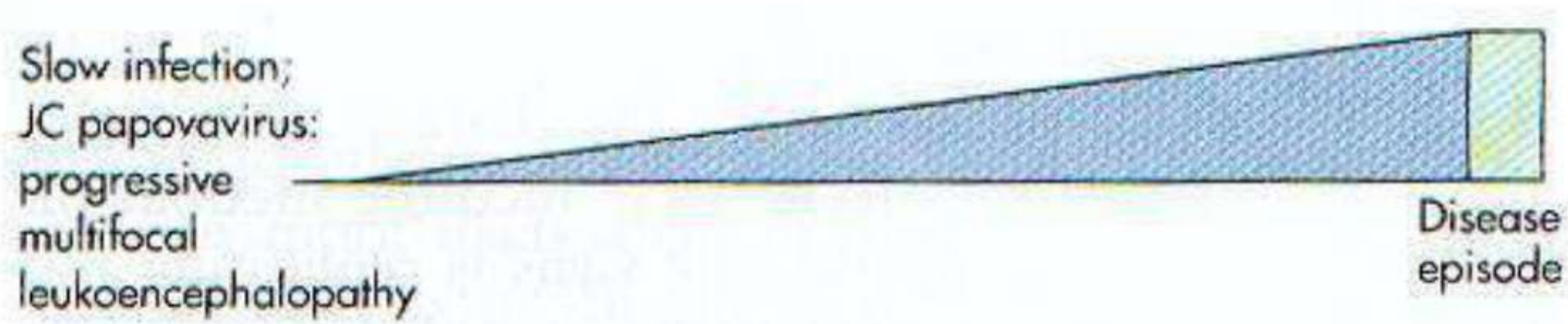
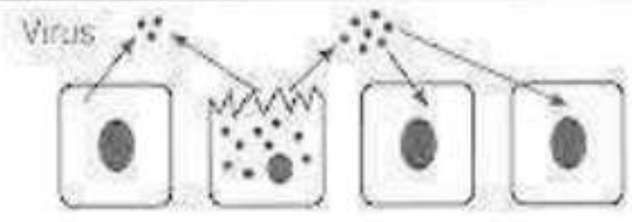
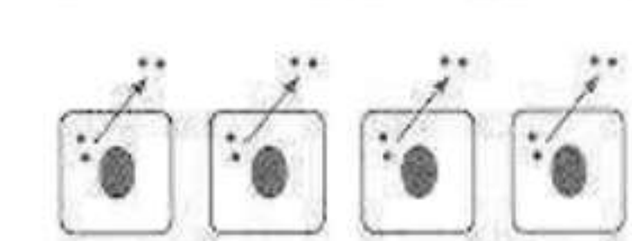
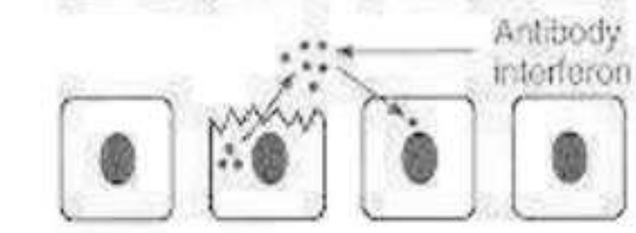
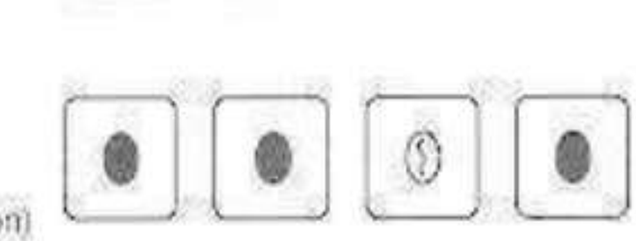


TABLE 46-1 Virus-Cell Interactions *In Vivo*

Types of Infection	Fraction Cells Infected	Cell Death	Infectious Virus	Schematized Mechanism	Disease Examples	Controlling Mechanism
Acute Cytocidal	All	+	+		Influenza Poliomyelitis Togavirus encephalitis	None
Persistent Chronic diffuse	All	O	+		Rubella Lymphocytic Choriomeningitis	Noncytocidal viruses
Chronic focal	Few	+	+		Adenovirus infections	Antiviral substances (e.g., antibody, interferon)
Latent	Few	O (during latency)	+ (with reactivation)		Varicella-zoster Herpes simplex	Not known

Overall fate of the cell

- The cell dies in **cytocidal** infections
  this may be **acute** (when infection is brief and self-limiting) or **chronic** (drawn out, only a few cells infected while the rest proliferate)-Cytocidal effect
- The cell lives in **persistent** infections
  this may be **productive** or **nonproductive** (refers to whether or not virions are produced) or it may alternate between the two by way of **latency** and **reactivation** - Steady state infection

as the result of viral infection normal cell become Cancer cell

- **Transformation**-Integrated infection (Viruses and Tumor)
  - RNA tumor viruses usually transform cells to a malignant phenotype by integrating their own genetic material into the cellular genome and may also produce infectious progeny. [HIV] بحكي هون عن ال
  - Retroviruses: integration of viral genome into the cellular genome this advice the both (RNA و DNA virus)

viral genome is integration of cellular genome has not developed source of cancer ⇒ high risk بكون بس

اذا اجينا بمرحلة من المراحل كشفنا عن المريض ولقينا انه

توضيحها بالصور تحت

    - Acute transforming viruses: *v-src* oncogene mimic cellular genes (proto-oncogene)
    - Insertional mutagenesis: inappropriate expression of a proto-oncogene adjacent to integrated viral genome
    - Transactivating factors: *tax gene in HTLV-1; turns on cellular genes causing uncontrolled cellular proliferation*

HIV من عيلة ال

  - DNA tumor virus infections are often cytocidal; thus, transformation is associated with abortive or restrictive infections in which few viral genes are expressed. The persistence of at least part of the viral genome within the cell is required for cell transformation. This is accompanied by the continual expression from a number of viral genes.
  - P53: regulates the cell cycle; functions as a tumor suppressor that is involved in preventing cancer. HPV
  - pRb: prevent excessive cell growth by inhibiting cell cycle progression until a cell is ready to divide. HPV

- **Apoptosis**
  - P53: initiate apoptosis, programmed cell death, if DNA damage proves to be irreparable

* النقطة الاولى من الـ Retrovirus ←

C-Src (cellular) و V-Src (Viral)

Similarity between the gene which present inside the cell and the gene of virus → control الفيروس اذا على الخلية بقل

viral gene going to be Produce in excess if this gene in the cell has the role of controlled the replication Life cycle this Viral protain going to interfer with intercellular singling

* النقطة الثانية

لازم يكون قدامه فيه Promotore حتى يقل expression

responsible of gene expression

IF the viral promotore integrated befor the cellular gene

going to tern on cellular gene

over production بحيث يصير
of the cellular gene

going to effect the intracellular singling

Other the RNA Viruses that might need to transformation !!

hepatitis C → mechanism (death 3 generation)

* واحد Certein viral protein in hepatities C they are oncogenic by themself !! شيء لحالها

* DNA virus → AdenoVirus is it an oncogenic !!
↓
احد الفيروسات اللي ممكن تضل لـ ١٨ شهر بلاقيها بـ Adenois

* it is Associated with cance transformation in human !!

No, human are the natural host of Adeno virus

P53, PRb كيف بيشتغلوا !! (الدكتور حكا شوفوها لحالكم) ← بيشتغل على retinoblastoma

Papiloma virus, Peshtan Poliovirus !! DNA virus that are Capble of transforming * شو عنا

hepatitis B,

herpes من عيلة الـ

Basophringial Cance, Cancerome بتعمل

Types of Viral infections at the cellular level

Type	Virus production	Fate of cell
Abortive	-	No effect
Cytolytic	+	Death
Persistent		
Productive	+	Senescence
Latent	-	No effect
Transforming		
DNA viruses	-	Immortalization
RNA viruses	+	Immortalization

Mechanisms of viral cytopathogenesis

Inhibition of cellular protein synthesis	**Polioviruses, HSV, poxviruses, togaviruses**
Inhibition and degradation of cellular DNA	**herpesviruses**
Alteration of cell membrane structure **Glycoprotein insertion** **Syncytia formation** **Disruption of cytoskeleton permeability**	**All enveloped viruses** **HSV, VZ virus, HIV** **HSV, HIV, RSV** **Togaviruses, herpesviruses**
Inclusion bodies	**Rabies**
Toxicity of Virion components	**Adenovirus fibers**

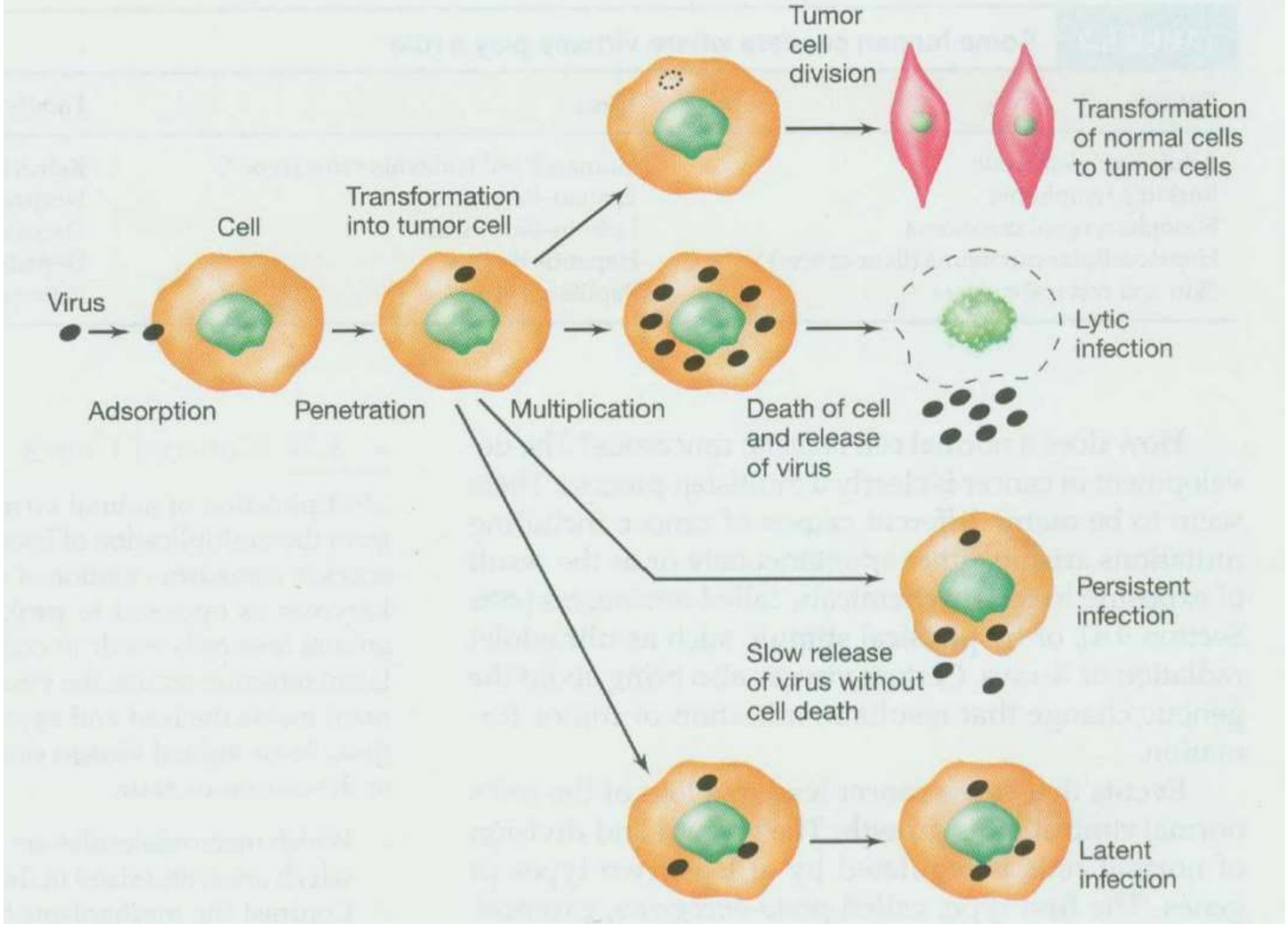
Possible consequences to a cell that is infected by a virus

- **Lytic infections: Result in the destruction of the host cell; are caused by virulent viruses, which inherently bring about the death of the cells that they infect.**

- **persistent infections: Infections that occur over relatively long periods of time, Where the release of the viral particles may be slow and the host cell may not be lysed.**

- **latent infections: Delay between the infection by the virus and the appearance of symptoms.**

- **Transformation: Some animal viruses have the potential to change a cell from a normal cell into a tumor cell which grows without restraint.**


Tumor cell division
Transformation of normal cells to tumor cells
Transformation into tumor cell
Cell
Virus
Lytic infection
Adsorption
Penetration
Multiplication
Death of cell and release of virus
Persistent infection
Slow release of virus without cell death
Latent infection

Immunology of viral infections

التقزيغ من فيديو
دفعة اثر كونه
اوضح وتم توقيته
من ريكوردانتا

Virology Lecture 4

Ashraf Khasawneh

Faculty of Medicine

The Hashemite University

Hematopoietic stem cell differentiation

* Hematopoiesis: formation of WBC and RBC

Multipotential hematopoietic stem cell (Hemocytoblast)

Common myeloid progenitor

innate

Common lymphoid progenitor

Adaptive

Megakaryocyte

Thrombocytes

Erythrocyte

RBC

Mast cell

Myeloblast

Basophil

Neutrophil

Eosinophil

Monocyte

Macrophage

Small lymphocyte

B lymphocyte

Plasma cell

antibody

T lymphocyte

Natural killer cell

(Large granular lymphocyte)

innate

* all of which ar a part of the innate immune response can be found in Blood and tissue

Immunity to microbes: general principles

Host response to virus infection:

The body's defense mechanisms to virus infection are of two types:

1) Nonspecific ← another name (innate immunity)
Basophils, Neutrophils, Macrophages

2) Specific ← another name (adaptive immunity) قتل B cell - T cell

- **Defense against infections is mediated by the early reactions of innate immunity and the later responses of adaptive immunity**
  call of the innate immunity ← which cell are going to take care! ← وجدوا دخل عندي فيروس على الجسم
  - **The innate immune response controls infection long enough for adaptive responses to kick in, and can often eradicate the infection**
  - **Many pathogenic microbes resist innate immunity**
  - **Adaptive immunity is able to combat (مكافحة) these microbes -- the lymphocyte expansion that is characteristic of adaptive immunity helps to keep pace with rapidly dividing microbes; specialized immune responses are better able to deal with diverse microbes**

* primary infection is the first infection with a certain virus or microorganism so when the body first encounters this foreign pathogen

* What is the difference between nonspecific and specific ?

[1] non specific or innitate → its act the same every time, once the body encounters a foreign antigen or a foreign pathogen and doesnt have specfic immunity, so if a virus attacks for the first time, fifth time, tenth time, the non specific immune response is almost the same every time

[2] Specific → the first encounter is different, once the virus or the pathogen has been firstly detected by the immune system, then the immune system is going to have a memory and the second or third response is going to be more quick than the first encounter. and is going to be able to combat fight this virus and control it faster than the previors time.

Immunity to microbes: general principles

B cell → بتعطي → Plasma cell → بتعطي → Antibody

- **The immune system is specialized to generate different effector mechanisms for different types of microbes**

  - **Extracellular microbes: antibodies, phagocytes; TH1** (stimulate B cell to produce IgM and IgG), **TH2** (Stimulate humoral immune response, B cell proliferation and IL-4 production)

  - **Intracellular microbes: phagocytes + TH1 (Stimulate cellular response); CTLs**

once the virus enters the body with infection at the early stages → B lymphocytes.

TH1 → cellular response → T helper 1

TH2 → T helper 2. (humoral response)

اول ما بيدخل الفيروس

intra cellular وقبل ما يصير

is going to be engulfment macrophages

Antigen Presentation يصير

break down the macrophages and dendritic cell

كل خلايا من هذول بس!! لا

all cell they have this system

there is no great role for phagocytosis once inside the cell

once it attaches to receptors and enter into the cell it becomes into the intracellular phase.

Phagocytosis occur via the components of the monocytes which is macrophages and dendritic cells and these are going to recognize the foreign viru they are going to phagocytose the virus and inside the phagocytic vesicle its going to destroy the virus into parts and another name for phagocytic cells such as macrophages dendritic cell is antigen presenting cells

Cytotoxic T-cells

(رشاش) perforin - تثقيب الخلية

granzymes - destraction of the cell.

The virus opligate intracellular Parasite ← مجرد ما يدخل الفيروس على الجسم

Not going to replicate (إلا) inside the host cell

befor that does the immune recognize the virus befor intering the target cell !! yes.

* هضم الـ phagocytosis ← Kiling and distruction

* innete immunity ← نفعل Activation ← كيف !! ← عن طريق Antibodies

Action of innet immunity يعني انه Non specific ← innete to Adaptive immunity

exposure first time , second time , 3,4,5 time is going to be the same

adaptive immunity → exposure the first time is going to take aperiod of time in order to take actio

دخل Forign Antigen (X) ← حتى يكون Antibody aganist the X ← is going to take some time

بالكورونا كان يحكي انه ليش دول العالم الثالث نسبة كورونا فيها اقل حكو بسبب استخدام PCG Vaccine بالتالي اعطاء الطعوم بفعل training of the immun system exposur the Antigen

* This system present in the all cell

Antigen presenting cell → profitinal Antigen cell → major ↑ complex number 2

all Neucliated cell → Major hestocomplity number 1

hesto complimity → System displaced the Forigen Antigin from the intracellular to surface the infect cell

* how does the immune system respond to the viruses when they are extracellular? via activation of the lymphocytes specific B lymphocyte which going to produce plasma cell → antibiodes aganist the invading virus → these will go to neutralize the virus which means (we know that the spike or glycoprotein of the virus is the outermost part of the virus and its the most immunogenic part of the virus (most immunogenic: this is a part of virus that is recognize by the immune system) the antibodies are going to produced against the spikes or glycoproteins and are going to be neutralizing means these antibodies are going to bind to the spike or protein and is going to prevent the virus from attaching its spike or glycoprotein into the receptor of target cell and this is going to prevent the virus to entry into the target cell

Body Defense Mechanisms

Nonspecific defense mechanisms (Innate immunity):

The body has defenses which are not specifically directed at particular infectious agents, but which serve as non-immunological barriers to infection:

1) Skin- an effective and impermeable barrier unless breached by injury, disease, etc…

2) Respiratory tract- upwards flow of mucus by ciliated epithelium removes virus particles, to prevent invasion of the lower respiratory tract.

IgA + Cilia + macrophages

also we have Iga antibodies which can neutralize any invading microorganism before reaching the lower respiratory tract

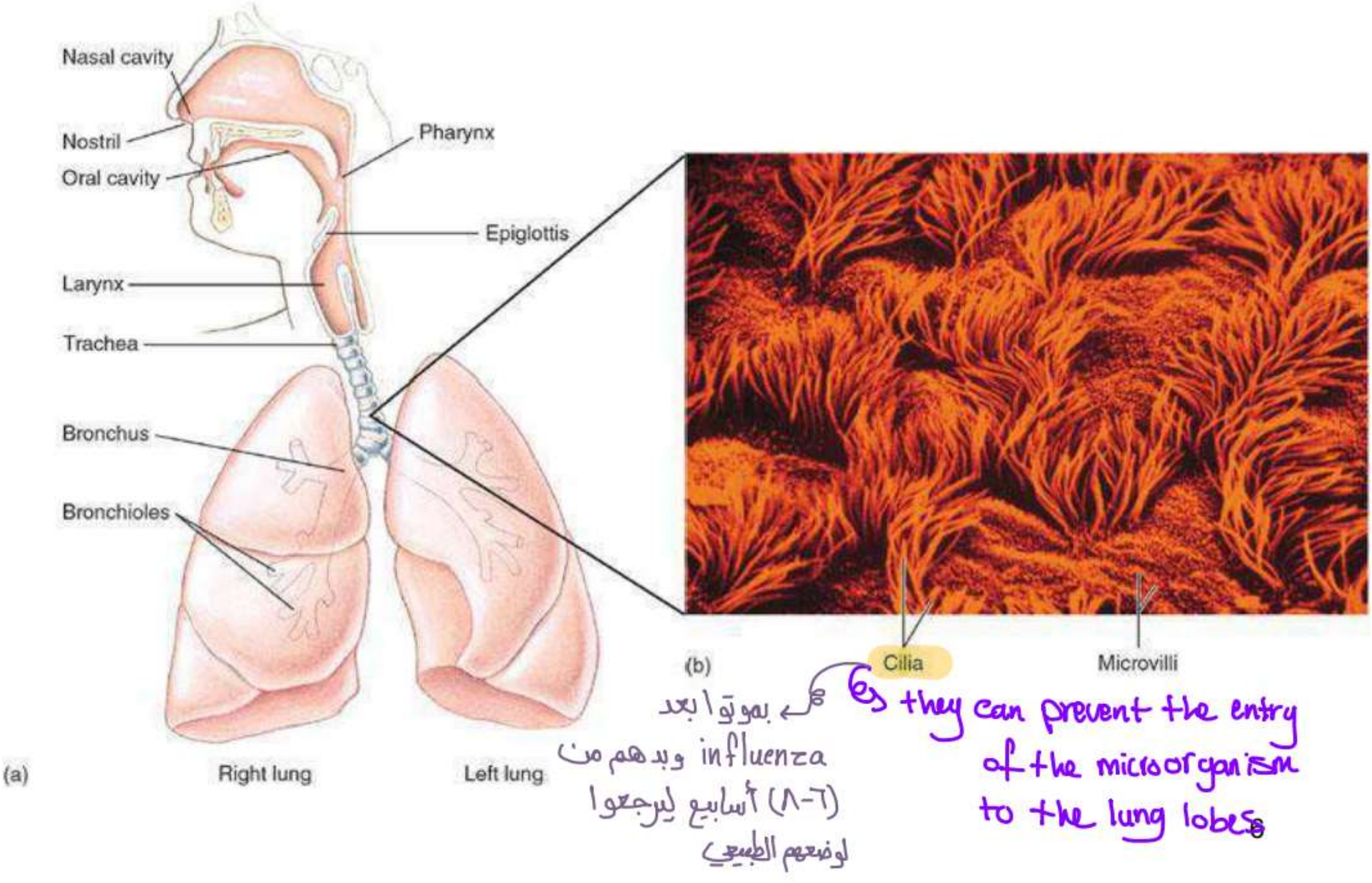
3) Gastrointestinal tract- stomach acid inactivates acid-labile viruses. Bile (lyses enveloped viruses), movement of intestinal contents and uptake of virus by lymphoid tissue all aid elimination of ingested viruses.

4) Urinary tract- flow of urine exerts a protective flushing effect.

So any stagnation of urine in the bladder might lead to a infection.

5) Conjunctiva- tears flush viruses from the eye.

Lysosomal enzymes



بموتوا بعد ما يصابوا بـ influenza وبدهم من (٦-٨) أسابيع ليرجعوا لوضعهم الطبيعي

Cilia ← they can prevent the entry of the microorganism to the lung lobes

Body Defense Mechanisms

6) **Phagocytosis-** an important defense mechanism in bacterial infection and in virus infections also: invading viruses- like bacteria- are ingested by two types of scavenger cell:

a) neutrophil polymorphonuclear leukocytes (PMN).

B) macrophages (or mononuclear cells of the reticuloendothelial system)- of two types:

1) free macrophages in lung alveoli, peritoneum.

2)fixed macrophages in lymph nodes, spleen, liver (Kupffer cells), connective tissue (histiocytes) and CNS (microglia).

Phagocytosis is enhanced by antibody (a specific immune mechanism) and complement: this effect is known as *opsonization.* labeling of the foreign antigen by a bound antibody (IgG)

بعمل targeting للفايروس او البكتيريا ويؤدي ل lysis

Macrophages 'activated' by cytokines released by T lymphocytes a specific immune mechanism) have increased phagocytic activity and are attracted by chemotaxis to the site of infection.

بحفزوا خلايا الكترص جهاز المناعة انهم يجو للمنطقة

جهاز المناعة فيو جزيئات صغيرة(cytokines) بتطلع من immune cells حتى يعرف باقي الخلايا انو في microorganisms مثل IL-1, IL-6

Body Defense Mechanisms

Cytokines

Cytokines are small protein molecules released by many cells, including lymphocytes and macrophages: they function as signals or mediators to activate, modulate and control the immune responses (and other activities) of cells.

If / IL / TNF

There are numerous cytokines, e.g., interferons, interleukins and tumor necrosis factor: many act sequentially and interact with other cytokines.

بمشوا بالترتيب

In addition to their role in the immune response, some have physiological functions such as tissue repair, differentiation and signaling activity in the CNS.

① ② ③

Interferon as Body Defense Mechanism

- Small protein produced by certain cells *#3 type of interferons
  - Alpha interferon- lymphocytes & macrophages
  - Beta interferon – fibroblasts & epithelial cells
  - [Gamma interferon – T cells (specific immunity)]
- Produced in response to viruses, RNA, immune products, and various antigens
- Bind to cell surfaces and induce expression of antiviral proteins
- Inhibit expression of cancer genes

Mechanism of action of Interferons :

- **Induction** of the following enzymes:

1) a protein kinase which inhibits protein synthesis

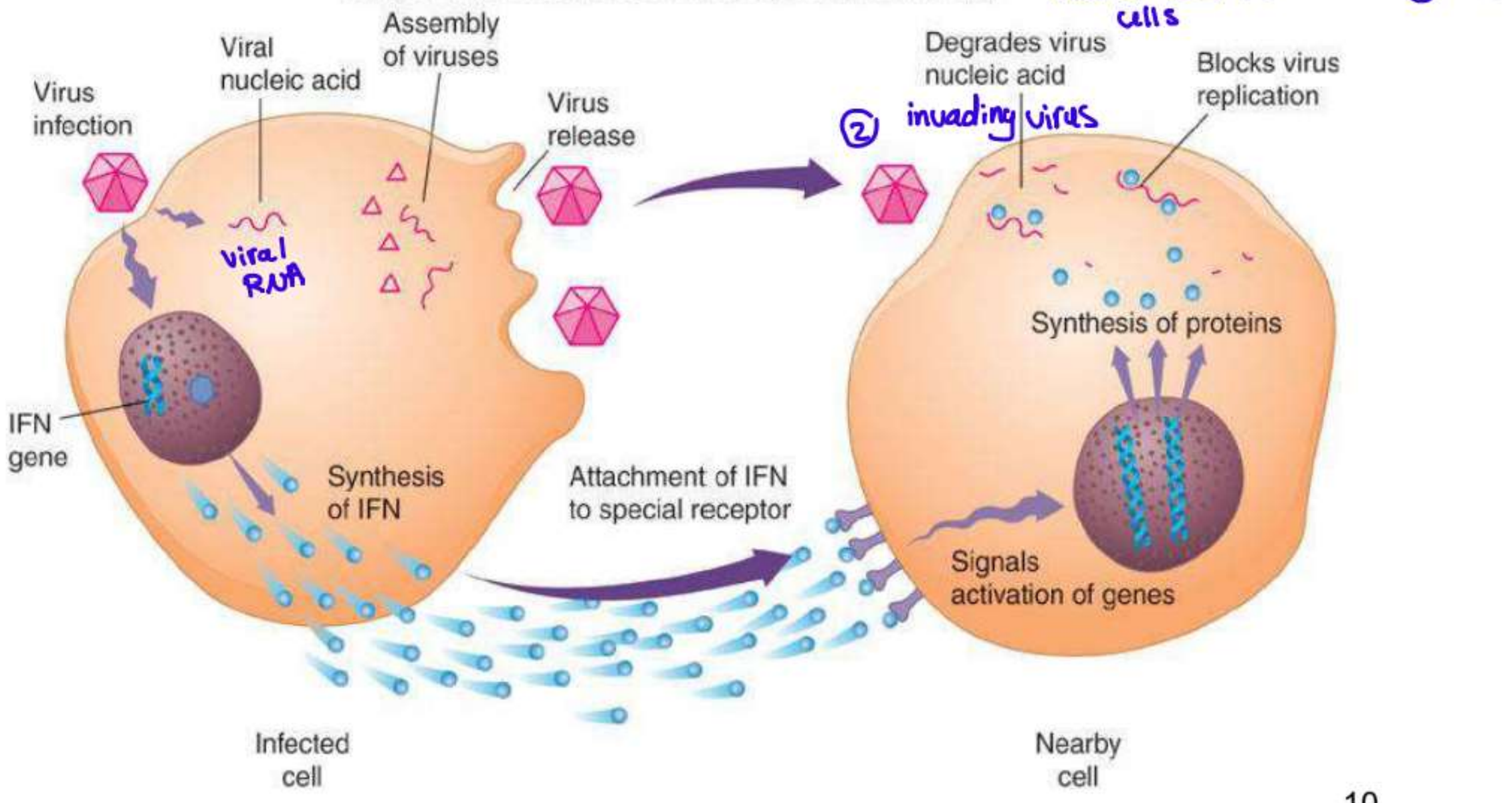
2) an oligo-adenylate synthase which leads to degradation of viral mRNA → So viral proteins are not going to be synthesized ⇒ كلهم هيك بشتغلوا

3) a phosphodiesterase which inhibit t-RNA

The action of these enzymes leads to an **inhibition of translation**

Interferon

① once the viral rna is inside the cell this is going to activate the interferon gene and the interferon gene is going to synthesize the interferon → will released by this entirely infected cell to warn neighboring cells



Attendance 21.12.2023

activation of B cell → plasma cell → antibodys

Body Defense Mechanisms

have receptor that differentiate one pathogen from another by their unique parts called antigens.

Specific (Adaptive immunity) defense mechanisms: we have two type of adaptive immunity

Immunological responses are of two types:

1) Humoral- main effect is neutralization of viruses: responsible for protective immunity. outside

2) cellular- main effect is localization of lesions: kills virus-infected cells. inside

Innate → antigens يتعرف ع مثلات
وبتعرف ع البكتيريا دون تحديد نوعها

Specific → antigens بتعرف ع ملايين
وبقدر يتعرف ع البكتيريا ويحدد اذا هي
... مثلا staph/strep

ال **T cell deficiency is more important** لانو **B** شو ما كانت **efficient**
الفايروس رح تدخل لل **target cell** وبما انو مافي عندي **cellular immunity**
عشان اقتل ال **cell** ف انا ما بقدر اني امنعه ...