النادي الطبي MC راعي

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لا تنسونا من دعائكم بالتوفيق

Localized Infections:

Virus:	Primary Replication:
Rhinoviruses	U.R.T.
Rotaviruses	Intestinal epithelium
Papillomaviruses	Epidermis

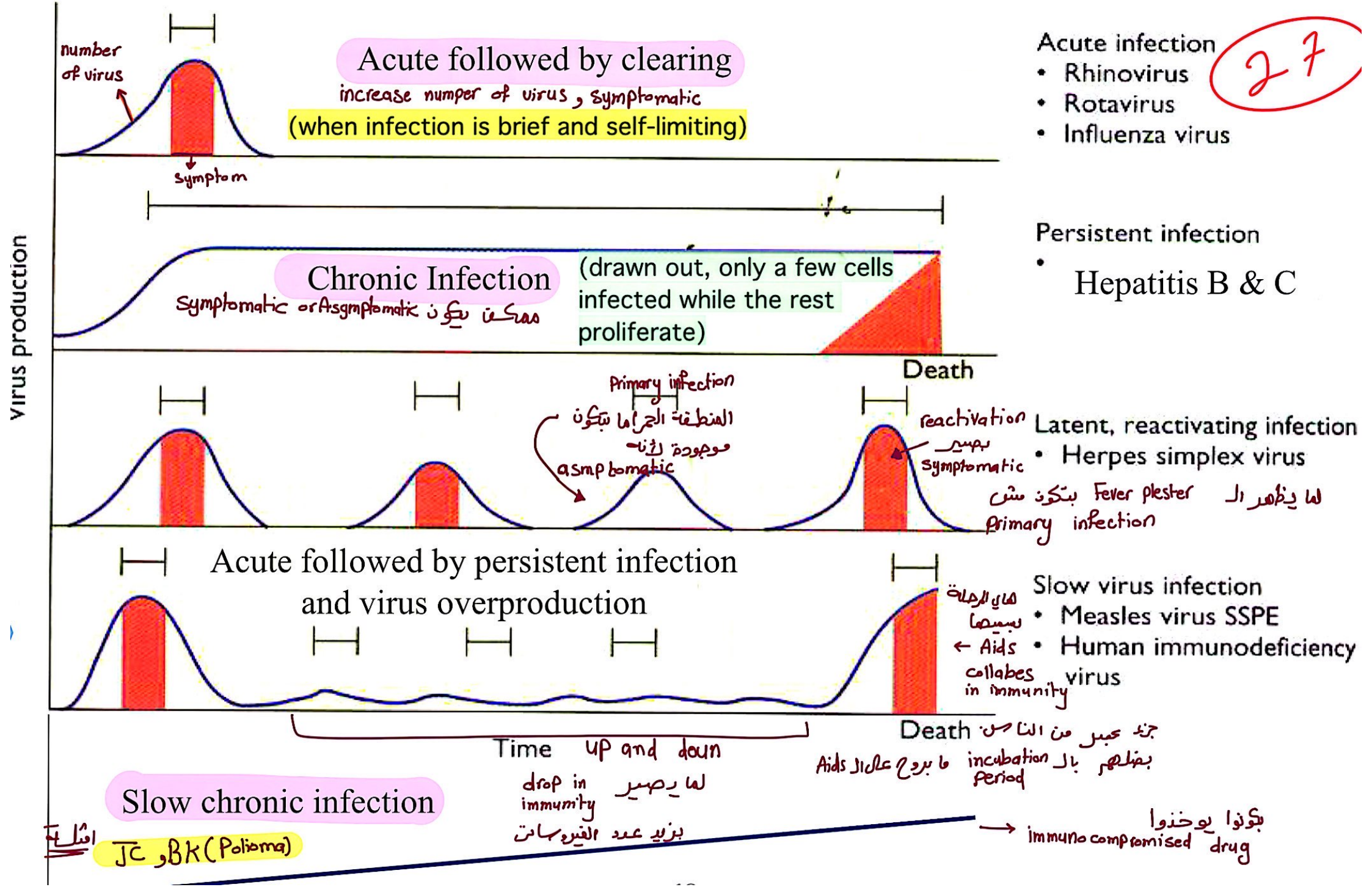
Systemic Infections:

Virus:	Primary Replication:	Secondary Replication:
Enteroviruses (Polio viruses)	Intestinal epithelium	Lymphoid tissues, C.N.S.
Herpesviruses	Oropharynx or G.U.tract	Lymphoid cells, C.N.S.

Exceptions in Virology مهم (من النادي)

عمر و صنادي

1. Viruses are very small to be seen under light microscope Except Poxvirus.
2. All Hepatitis viruses are RNA Except Hepatitis B
3. All DNA Viruses has an icosahedral capsid Except Poxvirus [Complex]
4. All viruses are invading Except Parvovirus.
   S phase لي بجيبوا الخلية تدخل
5. All enveloped viruses has a helical capsid Except DNA viruses + Retrovirus
6. All RNA viruses has a helical capsid Except Nacked viruses + Retovirus + Togavirus + Flavivirus
7. All DNA viruses replicates in nucleous Except Poxvirus
8. All RNA viruses replicates in cytoplasm Except HIV + influenza
9. All enveloped viruses obtain their budding through the cellular membrane of the host cell Except Poxvirus.
10. All DNA viruses are double stranded Except Parvovirus.
11. All RNA viruses are single stranded Except Rotavirus [Reovirus]
12. All nacked Virus cause GIT infection Except B19
13. All RNA (+) sence translate it's mRNA virus directly in ribosomes Except HIV.
14. All viruses contain 1 copy of genetic material Except HIV (2)



"أنواع الـ (HSV)"

واجب مهم

-(HHV-1) human herpes virus 1 = Herpes Simplex 1

-(HHV-2) human herpes virus 2 = Herpes Simplex 2

-(HHV-3) human herpes virus 3 = Vericella zuster (responsible for chickenpox , shingles)

-(HHV-4) human herpes virus 4 = Epstein-Barr virus (causes infectious mononucleosis or kissing disease .

-(HHV-5) human herpes virus 5 = Cytomegalovirus(mostly seen in immunocompromised or those with chronic illnesses) .

-(HHV-6 and 7) human herpes virus 6 and7 cause roseola infantum, exanthem subitum in children mostly in HHV-6 / HHV-7 associated also with respiratory tract illnesses fever diarrhea vomiting .

- HHV-8 = Kaposi sarcoma cause blackish discoloration lesion of the skin in AIDS patient.

هذا الحكي اللي حكاه الدكتور عن انواع ال HSV
كمان نقطة انه ال 1 , 2 و ال Vericella zuster هدول الثلاثة ع خلاف باقي الانواع ما بطلعوا من الجسم
اللي بعملوه انه بروحوا بنخبوا جوا ال ganglia لحد ما يصيرلهم reactivation
و بعدها برجعوا بنتقلوا عن طريق ال axonal transport

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

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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	**All enveloped viruses**
Glycoprotein insertion	**HSV, VZ virus, HIV**
Syncytia formation	**HSV, HIV, RSV**
Disruption of cytoskeleton permeability	**Togaviruses, herpesviruses**
Inclusion bodies	**Rabies**
Toxicity of Virion components	**Adenovirus fibers**

Specific

شوفوا اللي عليه خط أخضر

Immunity to microbes: general principles

B cell → بتعطي → Plasma cell → بتعطي → Antibody

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

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

- **Extracellular microbes: antibodies, phagocytes; TH1** (cellular response) **(stimulate B cell to produce IgM and IgG), TH2** (T helper 1) **(Stimulate humoral immune response, B cell proliferation and IL-4 production)** (T helper 2. (humoral response))

لول ما بيدخل الفيروس intra cellular وقبل ما يصير is going to be engulfment macrophages → Antigen بصير Presentation

break down the macrophages and dendritic cell

كل خلاياه من هذول بس!! لـ all cell they have this system

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

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 intra cellular phase.

Cytotoxic T-cells

(رشاش) perforin - تثقيب الخلية

granzymes - destraction of the cell.

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

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)

targeting بعمل 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.

بحفز وا حلا يا ألكترمن جهاز المناعة انهم يجو للمنطقة

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

جهاز المناعة فيو جزيئات صغيرة

Interferon as Body Defense Mechanism

Non-specific

- Small protein produced by certain cells *3 type of interferon
  - 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 → interferon (Q)

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**

Body Defense Mechanisms

* اذا بدي اشوف resist infection ولاقل !! بدور بالاول على IgM

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Humoral (antibody) response:

Three immunoglobulins are mainly responsible for humoral immunity in virus infections:

Pentomer 5 Y

←**1) IgM-** the earliest antibody produced: appears at a variable interval after exposure, depending on the virus, incubation period, dose and route of transmission; persists for about 4-6 weeks, sometimes longer; a pentamer of five IgG molecules.

mono

←**2) IgG-** formed later than IgM but persists long term, often for years: responsible for immunity to reinfection.

dimer or mono

←**3) IgA-** a dimeric molecule, found in body secretions (as well as blood), i.e., saliva, respiratory secretions, tears and intestinal contents; the main antibody involved in immunity to respiratory viruses and in gut immunity associated with enteric virus infection; secretory IgA acquires a carbohydrate 'transport piece" in extracellular fluids that is absent from serum IgA.

* ليش في مصطلح !! أزكي وطعوم فايزر اللي اعطوه بكورونا اكثر من مرة (poster doeses

Protective level لتوصل لـ increase in IgG

←

Antigen processing and presentation

Epitope

ال antigen بتكون من protein او glycoprotein
هسه ال antigen بتكون من multiple arms كل arm منهم الها شكل اما دائرة او مثلث
كل هذول الarms او ال shapes بعلموا ال antigen
لكن ال shape الواحد منهم بعمل epitope

MHC Distinguish between self and nonself

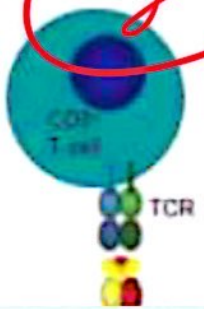
MHC I all cells

ال Major histocompatibility complex بكون موجود ع ال surface تاع الخلية
بفرق بين ال antigen تبع خلايا الجسم و ال antigen تبع الاجسام الغريبة
عندك نوعين منه MHC I الموجود بكل الخلايا ما عدا ال RBCs

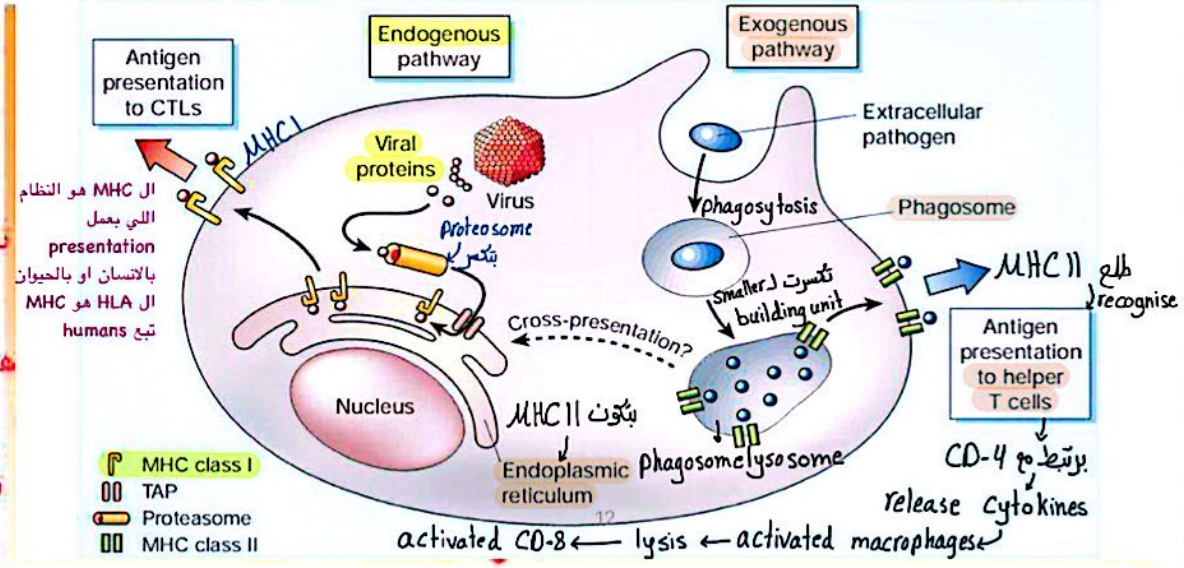
MHCII Macrophages, dendritic cells, some T and B cells

Macrophages, dendritic cells, some T and B cells و اللي بكون موجود بال و ال MHC II

2-9



اذا ال antigen دخل عالخلية
ال proteasome راح تكسره لقطع صغيرة بعدها راح تروح القطع على ال MHC الموجود على ال ER
و اللي بغير شكل ال MHC تبع الخلية لواحد جديد و غريب عن الجسم
اللي راح يتعرف عليه هو ال cd8
واللي راح تقتل الخلية
هذا الحكي لو كان ال antigen جوا الخلية
طيب اذا كان برا الخلية
راح تبتلعه ال Macrophage و اللي راح تدمره و تنقله ع ال MCH component اللي في ال ER
و ترتبط ع ال MHC II على ال surface
المهم هون ال cd4 هون هي اللي بتشتغل
و اللي بتعمل ال TH1 , TH2
cellular immunity بعمل TH1
humoral immunity بعمل TH2



MHC1 with cd8
MHC2 with cd4

Immune evasion by viruses

شو الطرق اللي بتخلي الفايروسات يتجاوزوا جهاز المناعة

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- **Antigenic variation**
  - **Influenza, HIV, rhinovirus** RNA virus في ١٠٠ شكل مختلف لل glycoprotein تبعها
- **Inhibition of the class I MHC antigen processing pathway**
  - **Different viruses use different mechanisms**
  - **NK cells are the host adaptation for killing class I MHC-negative infected cells** الفايروس بمنع تصنيع MHC او بمنع ارتباط antigen معه، بنتغلب عليها عن طريق killer cells
- **Production of immune modulators**
  - **Soluble cytokine receptors may act as "decoys" and block actions of cytokines (poxviruses)** بصنع بروتينات بترتبط مع cytokines وبالتالي ما بتعمل لل activation immune system
  - **Immunosuppressive cytokines, e.g. IL-10 (EBV)** Suppression لل immunity
- **Infection of immune cells**
  - **HIV** infected CD-4

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نسبة حدوث الطفرة لدى الفيروسات من نوع (RNA) أعلى منه (DNA)

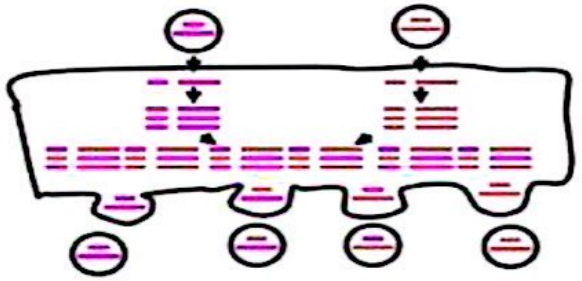
علل: عند الـ (Proofreading) عندها أقل؟ ليش؟ لأنه الـ (RNA) بتحمل انزيماته بينما الـ (DNA)

بتحمل انزيمات الخلية بالتالي بستفيد منه الـ (Proof reading) تاعها

REASSORTMENT

(Antigenic shift)

- form of recombination (non classical)
- very efficient
- segmented viruses only
  - can occur naturally
- used in some newer vaccines
  - eg for influenza and rotaviruses



most human viruses are non-segmented EXCEPT these two viruses

مشان نعرف الفرق بين ال antigenic drift و ال shift تحيلوا معي عنا glycoprotein ع شكل مثلث
بال drift اللي هو mutation عادي راح يتغير شكله بشكل بسيط هذا التغير بسبب العدوى الموسمية و بخلينا نغير المطاعيم
و اللي بيصير سنوات وبتسبب epidemic
اما ال shift لما يتغير هذا ال glycoprotein من مثلث لدائرة هون بكون صار reassortment و اللي بسبب pandemic و
بيصير كل 7ل 10 سنوات

rotavirus vaccine (Rotateq)

- human-bovine reassortants
- live
- oral

as a back bone
segment ال دحاطين فيه ال
human تاعت ال
بجل → development of immunity

rotavirus vaccine (Rotarix)

- attenuated human rotavirus
- live
- oral

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- Defective Viruses lack gene(s) necessary for a complete infectious cycle

proteins على مستوى

- helper viruses provide missing functions

ونتيجة لهذا يتحول الـ(defective) إلى (infectious)

اللهمَّ صلِّ وسلِّم وبارك

على سيِّدنا محمَّدٍ وعلى

آله وصحبه أجمعين ❤️