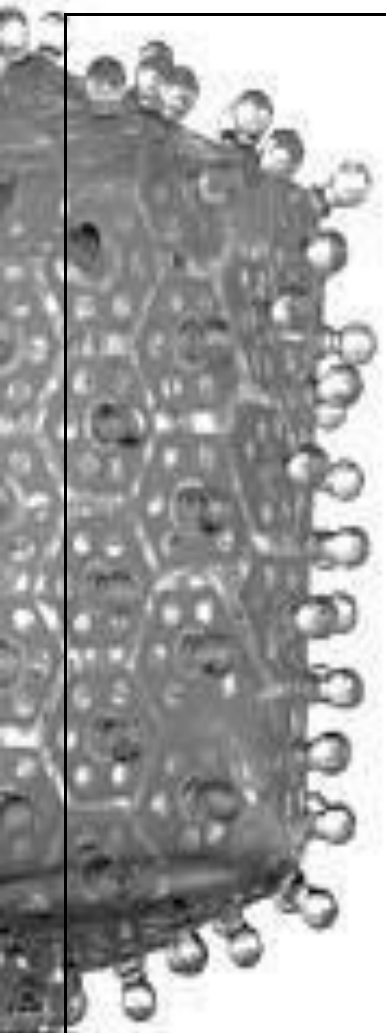

Microbiology

Lecture No: 12 #4 Viro

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Done by: Ibtehal Al-Hasanat

Sheet ■ Slide □

Mrym Ghuloom

Virology – genetics and life cycle

Please refer to the slides; the sheet does not cover everything in the slides.

This lecture is the complementary of the life cycle, today we are going to talk about:

-Genetics

-Life cycles for some viruses; We took it, and it divided as what you remember between (attachment; penetration, uncoating) we took it step by step, so we are going to study some examples to see the steps together in order to understand the whole life cycle in its different stages, we will talk about Influenza virus, Polio virus (شلل الأطفال), Rabies virus(السّعار), Adenovirus and HIV (Human Immune Deficiency Virus - which we will talk about in simple way -; the doctor put simple figure in the slides about the HIV and with the paragraph written in our book about it, hopefully you will get a solid knowledge about the life cycle and this will enable you to understand later on easily management in the modules the and very simply the diagnosis).

Genetics:

1.Low fidelity of reverse transcriptases and RNA replicases compared to DNA polymerase (proof reading).

Mutations:

If you remember we said that we might face some mutations during the life cycle and the RNA polymerase job because it has no proof-reading mechanism (the error-correcting processes), so these mutations are very common in RNA viruses, but they are less common in DNA viruses; because their polymerase has the proof-reading mechanism.

-The mutations will result from a mistake carried out by the enzyme

Quasi – species:

It is a term that you will face in the text book, it believes that all viruses of the same species are actually different under the base , 2 bases; 3 bases whatever. And one virus of a special sequence will dominate such populatio; this is calle Quasi – species.

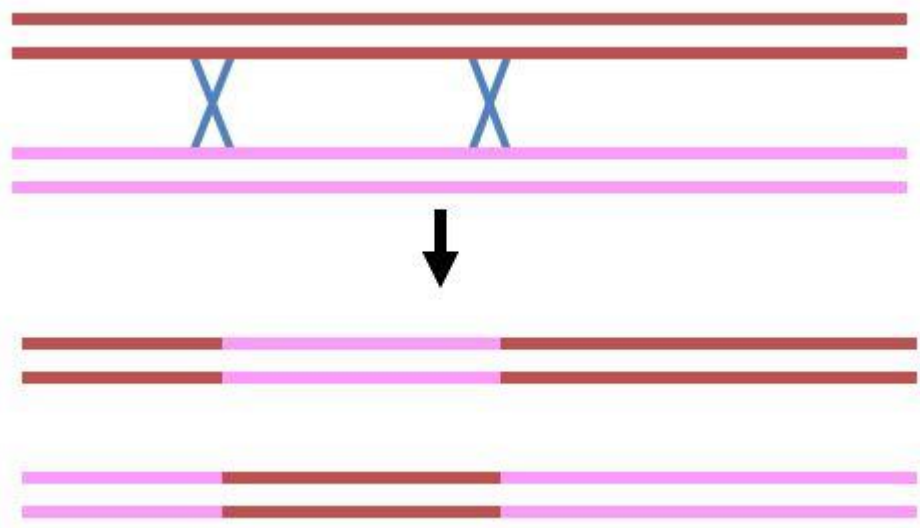
Quasi – species: collection of population with mutations and different sequences; however there is one sequence that might dominate the population.

2.Recombination:

It is another genetic term that you need to know. It is the process by which two DNA molecules exchange genetic information.

Recombination-DNA :

In the DNA viruses we might face recombination. When we talk about virus recombination during the DNA replication there will be a fragmentation and breakage of the DNA viruses and malrecombination as you see in the figure below.



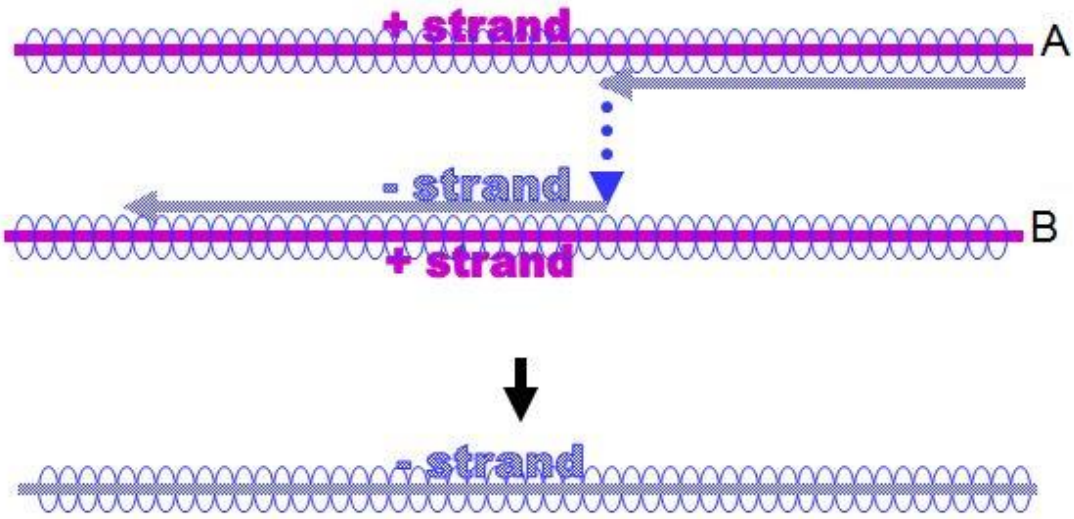
- As you see in the figure: This is for the DNA viruses some of the pieces at the DNA may jump into other DNA pieces and we will end with a new double stranded DNA that has recombination part of another DNA genetic materials (common in DNA viruses).

Recombination-RNA:

- For the RNA viruses there is a mechanism in which the RNA polymerase might follow which is **Switch mechanism**.

-Some of the RNA polymerase will jump from one strand into another

For example : if you imagine the purple colored strand (A) is the strand that currently been copied, so the RNA polymerase will copy the strand from A, then it will jump into another strand B , so it will come out with a new strand that has 2 parts (one from strand A and another part of it from strand B), so it is a new strand and it is resulted from jumping mechanism of the RNA polymerase during copying.



3.Reassortment :

- Usually you will face Such a genetic mechanism in the segmented viruses (example on the segmented viruses is influenza which is a member of orthomyxoviruses family).

- Can extend the gene pools of the virus and allow the emergence of new and successful variants and result in pandemics.

-If you imagine that influenza virus can affect human being (at the left side) and a bird (avian)(at the right side), and we have a host for the influenza virus that can accommodate the virus which is the porker or the pig.

-The virus will affect the pig from the human being and from the bird, so it will replicate in the pig as a new host.

Imagine the left virus came from the human being and the right one came from the bird, during replication there will be uncoating so the genetic materials will be exposed (the 8 segments of the influenza virus will be exposed). During assembly, if you remember acid encapsidation of genetic material, the new virus might take some genetic material from the human virus and other 2 pieces or 3 whatever from the bird virus.

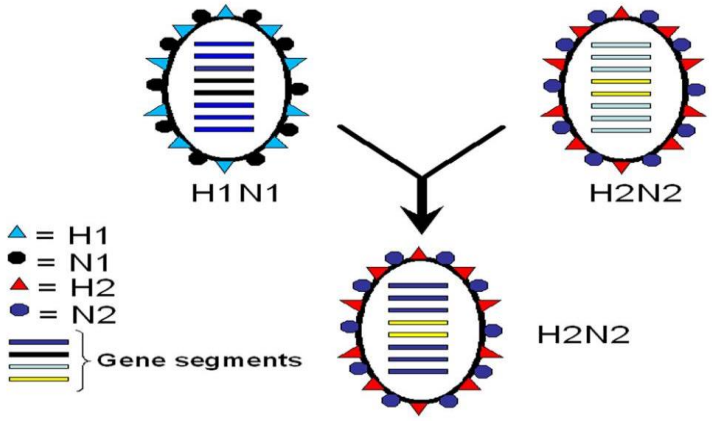


Figure 4. Mechanism of reassortment of RNA segments of influenza virus

For human we have 8 segments, 2 in black and 6 in blue. At the right hand side we have 6 in light blue and 2 in the yellow, and the new virus has 2 yellow segments from the bird virus and 6 blue segments from human virus and this is what we call **Reassortment .**

Now the pig has a new virus (a new components), it might break the barrier of being transmitted between pigs into transmitting itself to the humans ,whether like some people treating such animals (like: home animals), if they are farmers or something like that; the virus might jump to

the human being so the human being will be now exposed to a new virus that is reassorted. It is important to understand this point.

Life cycles

Life cycle of the **influenza virus**:

- Influenza virus → (-ve) virus

Before talking about the life cycle we need to talk about the structure of the Hemagglutinin (HA) and Neuraminaidase which are two important structures on the surface of this virus.

Hemagglutinin (HA):

Each spike is made up of 3 parts, in the top we have the receptor binding site which is like saucer (زبدية)-shaped depression near the HA tip. We have also the antigenic part (which is located in the hydrophilic part) by which the immune system will recognize this virus and produce antibodies.

If you remember also in the endosomal vesicles when we said that there are acidity changes (pH changes) that will enable the virus to release itself from the endosomal vesicles, How does this happen? actually it happens by a remodification of the shape of HA.

HA is made basically of 2 polypeptide chains, they are bound together by disulfide bond in the middle. The pH changes will force the HA polypeptides to reshape itself specially at pH = 5, when the pH of the endosomal vesicle will be 5 there will be a modification of HA polypeptide, and one of the proteins that is contained in the HA is called a fusion mutave, this fusion mutave will come in contact with the endosomal vesicles leading to interaction between the envelop of the virus and the endosomal vesicles fusion then virus will be released.

Nenraminaidase:

It is the second part of the influenza virus that we need to know.

It has an enzyme active site to start with and an antigenic site .

When the virus is released from the cell it will stuck with sialic-acid, so the Nenraminaidase will cut it and release it , NA is essential for the release of the virus from the infected cells, so if we have Nenraminaidase inhibitors and you inhibit the Nenraminaidase then you will inhibit the release and spread of the virus from cell to cell.

You might use such Inhibitors as a treatment. We have 2 medications - 2 antivirus - that we use in influenza treatment which are:

1) Oseltamivir or Tamiflu
2) Zanamivir.

The general policy of the replication of influenza virus :-

-It's a negative stranded so it follow this way during replication:
-ve → +ve → -ve
"for more details please refer to the previous lec."

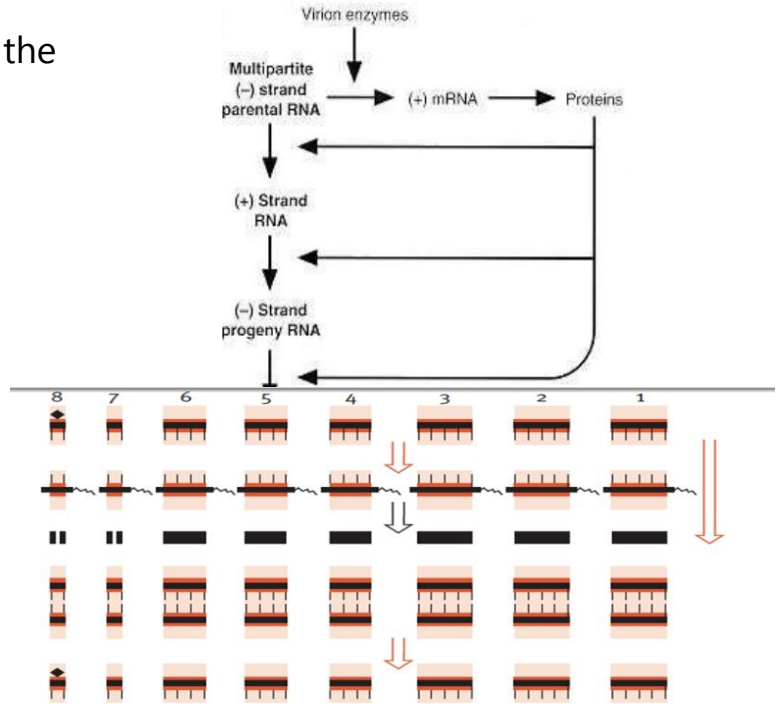


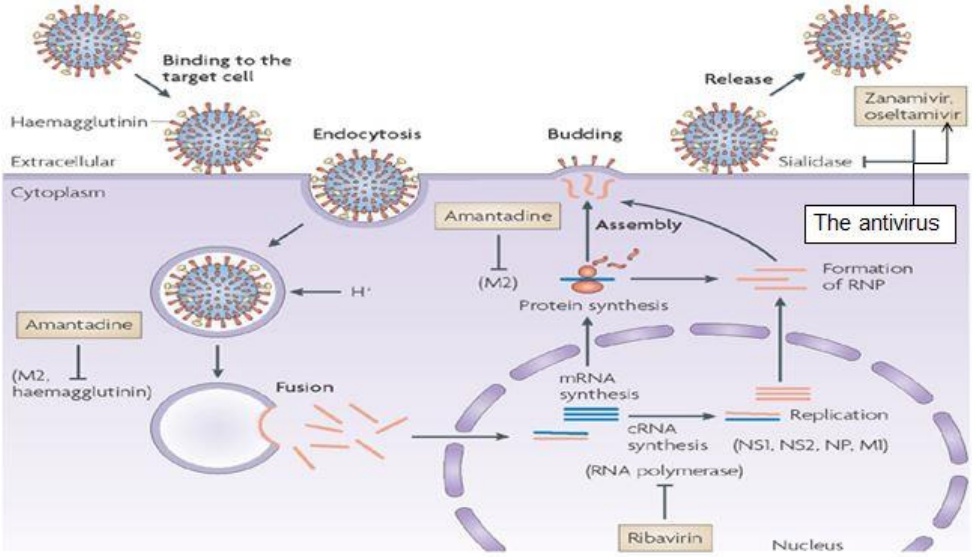
Fig. 3.6 Replication strategy of influenza, a negative-stranded RNA virus. The viral genome is in the form of eight loosely linked single-stranded RNA segments. Most transcribed mRNAs are monocistronic, i.e. they code for a single protein. However, the mRNAs of genes 7 and 8 have undergone splicing and each now codes for two viral proteins. The mode of transcription and replication of influenza virus is unique as it requires co-operation with cellular RNA polymerase II ('cap snatching'). ∿, poly(A) tail; ◆, RNA-dependent RNA polymerase.

-These are the proteins that will be expressed from the virus.

-You can notice that the genes 7 and 8 will result in a protein that will be cleaved later into 2 proteins , but basically each segment will code for one protein.

-At the end we will have 10 proteins. (this was mentioned in sec.1)

Life cycle of the influenza virus:



NOTE: this figure is not from the text book , but the doctor find it the simplest figure that might represent in the lec. Which represents the life cycle. It is not for the sake of the exam, it is just to understand the life cycle.

The steps of the life cycle of the influenza virus:

1. Attachment .
2. Endocytosis.
3. pH changes.
4. Fusion of the viral membrane with the endosomal vesicle membrane.
5. Release of the genetic segment of the virus into the nucleus through the pores.
6. Replication mechanism will take place inside the nucleus.
7. Formation of the new genetic material, ribonucleic proteins and the capsid proteins then assembly and body.

So this is the life cycle as simple as that.

The other virus that we need to talk about is:

Poliovirus

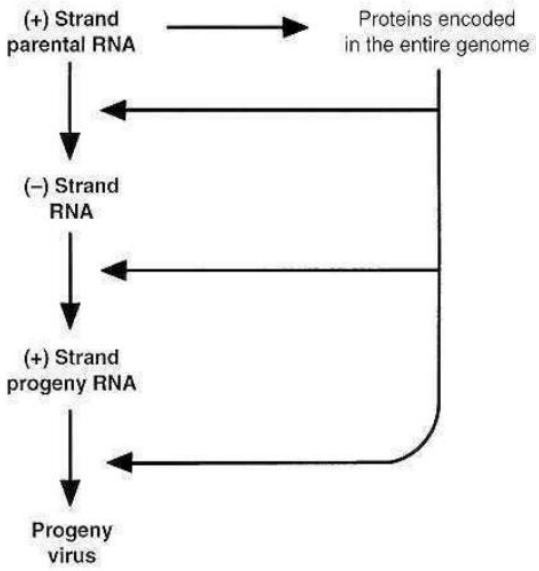
- Member of the family of Picornaviridae.
- +ve virus
- At the at the 3'-end we have a protein that called polyadenylated glycoprotein that is glycosylated.
- We have 4 proteins that will be translated that we call viral particles or viral proteins from 1 to 4 (VP1,VP2, VP3, and VP4), the RNA polymerase, two proteases, and some minor products
- Some regions are not translated.

The mechanism of replication:

Poliovirus is (+ve) RNA.

In this figure we have +ve → -ve → +ve, plus early proteins and genetic materials

"for more details please refer to the previous lec."



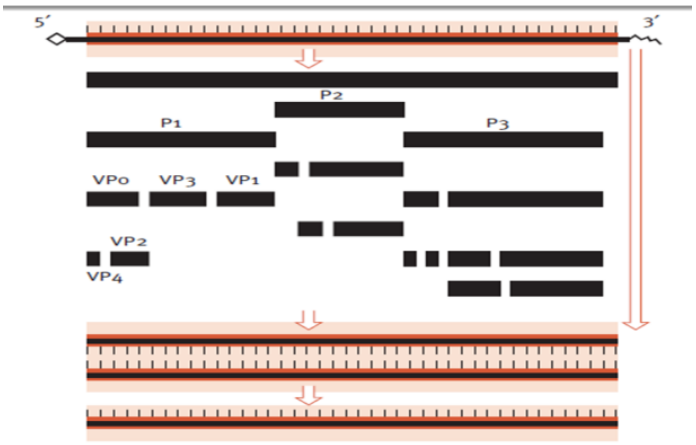
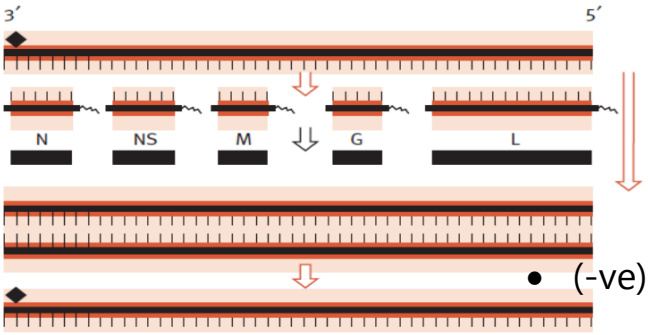


Fig. 3.5 Replication strategy of polio, a positive-stranded RNA virus. The genomic RNA acts directly as mRNA and is translated to give a polyprotein, which is rapidly cleaved by virus-coded proteases into 12 or more smaller proteins (not all illustrated). At a later stage during replication the number of positive RNA strands increases and these are used either as mRNAs or are packaged into virions. ∿ poly(A) tail; ◇ 5′ cap.

These are the proteins that will be produced from the poliovirus, we have 3 proteins p1,p2 and p3, some of these proteins will be cleaved into 2 proteins by the viral protease.

At the end we will end up with 12 proteins.



Rabies :

- (-ve) RNA

Fig. 3.7 Replication strategy of rabies, a negative-stranded RNA virus. The viral genome is in the form of a single complete strand of RNA. The five genes are positioned in a linear manner. There is an intergenic sequence, a translation start signal and a poly(A) signal at the end of each gene. Five mRNAs are transcribed by a start-and-stop mechanism and each is translated into a viral protein. ∿, poly(A) tail; ◆, RNA-dependent RNA polymerase.

- Member of Rhabdo viridae family.
- We have 5' methylated and polyaenylated messenger RNA
- The 3' end which will result in the expression of proteins like the (P) phosphoprotein, (M) matrix, (G) glycosylated membrane spike, polymerase (L)polypeptides.

Adenovirus:

- We have 30 genes that will expressed of this virus.
- In slide 27 there are the proteins that will be expressed.

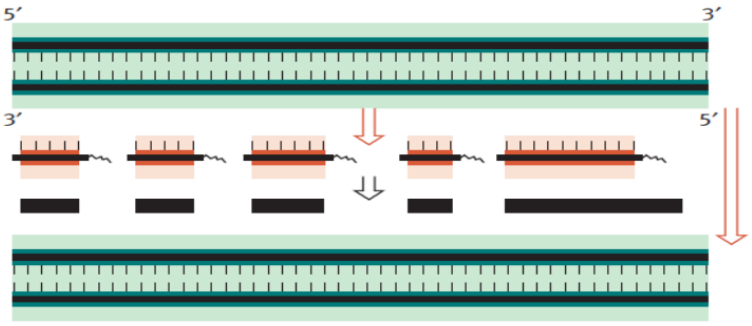
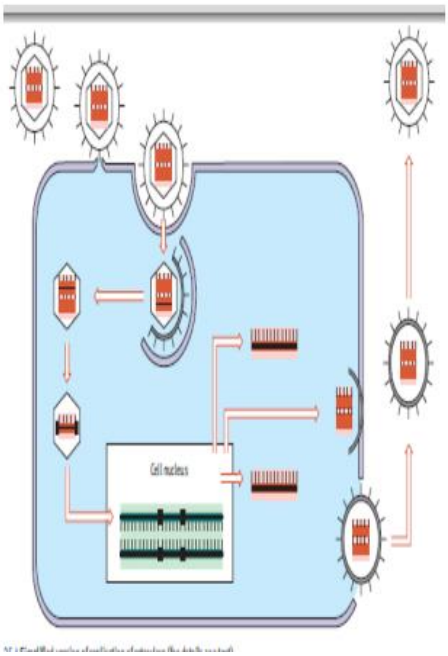


Fig. 3.8 Replication strategy of adenovirus, a DNA virus. The adenovirus genome is transcribed and replicated in the cell nucleus. Replication is mediated by a protein (P) at the 5′ end of each DNA strand. Multiple mRNAs (not all shown) are transcribed from both DNA strands. Early mRNAs are encoded by input parental DNA. Later mRNAs are encoded on both DNA strands. Splicing is extensively utilized and can provide control of different regions of the genome, as well as a means of changing the reading frame. ~, poly(A) tail.

Retro virus:

-The figure in the left part of slide no. 28 is from the book, it does not have enough details.



The mechanism of HIV:

1/ HIV (Human Immune Deficiency Virus) it will attach to the receptors (CD4 and CCR5).

2/ It will be internalized into the cytoplasm.

3/ Uncoating of the virus.

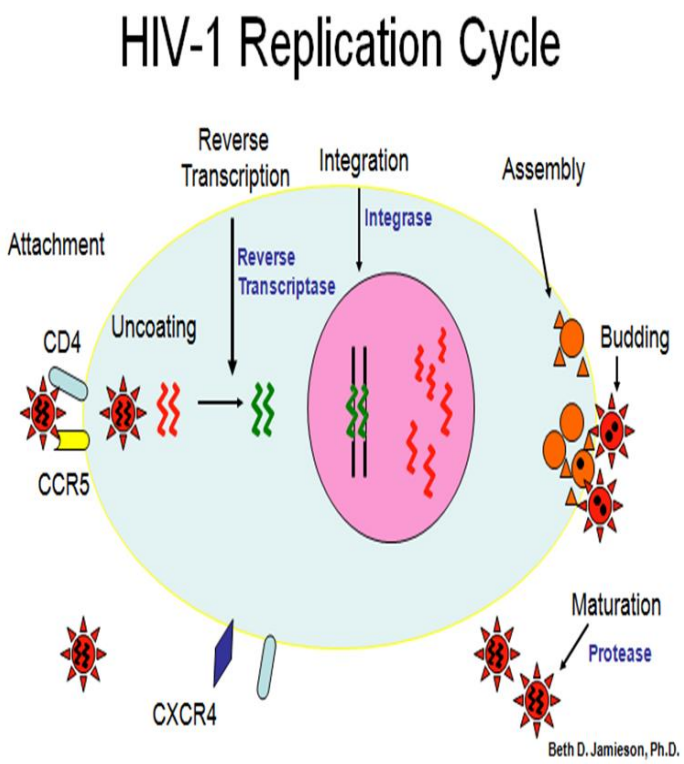
4/ Then the RNA (red crooked line) will be copied into DNA by an enzyme which is called reverse transcriptase (reverse transcriptase carried by the virus itself).

5/ The DNA copied will go into the nucleus and ligate itself into the human DNA by an enzyme called integrase (the virus carries it with itself), now it will be part of human DNA, proviral genome it will be treated just like the human DNA.

6/ New copies of the mRNA will be transcribed then translated into proteins.

7/ The virus will assemble itself.

8/ It will be release by budding from the cell.



This is the end of the life cycle, next week there will be different subject.

A student asks for an explaining for this statement: "DNA replication for early proteins are produced from virus DNA copy , but the late proteins Are newly syntheses copy?!"

we care about producing the functional feature that lately produce the other components
so we need first of all to have functional proteins like enzyme: replicase and polymerase and as a result of that we would be able to copy more of the DNA strands via those enzymes. Consequently,producing the structural one which are needed lately to surround the genetic materials like those used to comple the structure of the capsid.

معليش فقرة زيادة عشان الاقتباس ^_*

"دوزّن حياتك عازفًا عن كل شرٍّ أو شرر
واضبط به قاعِ خطاك على الطريق المنحدر
واشحذ سهام كنانة
واشدد على القوس الوتر
واهززِ بجذعٍ باسقٍ يدنو إلى يدك الثمر
هي أمةٌ كثر الظماء بها وقد حان المطر
الآن تشرق شمسها لتعيد عافية البشر
لا تنتظر
غيّر ففي التغيير للحسن ابتهاجات الظفر"
-لا تنتظر الأشياء فقد يطول انتظارك، اذهب إليها-