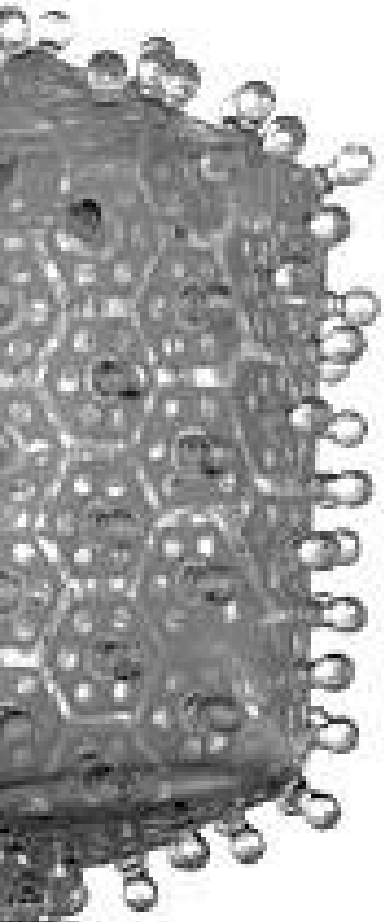


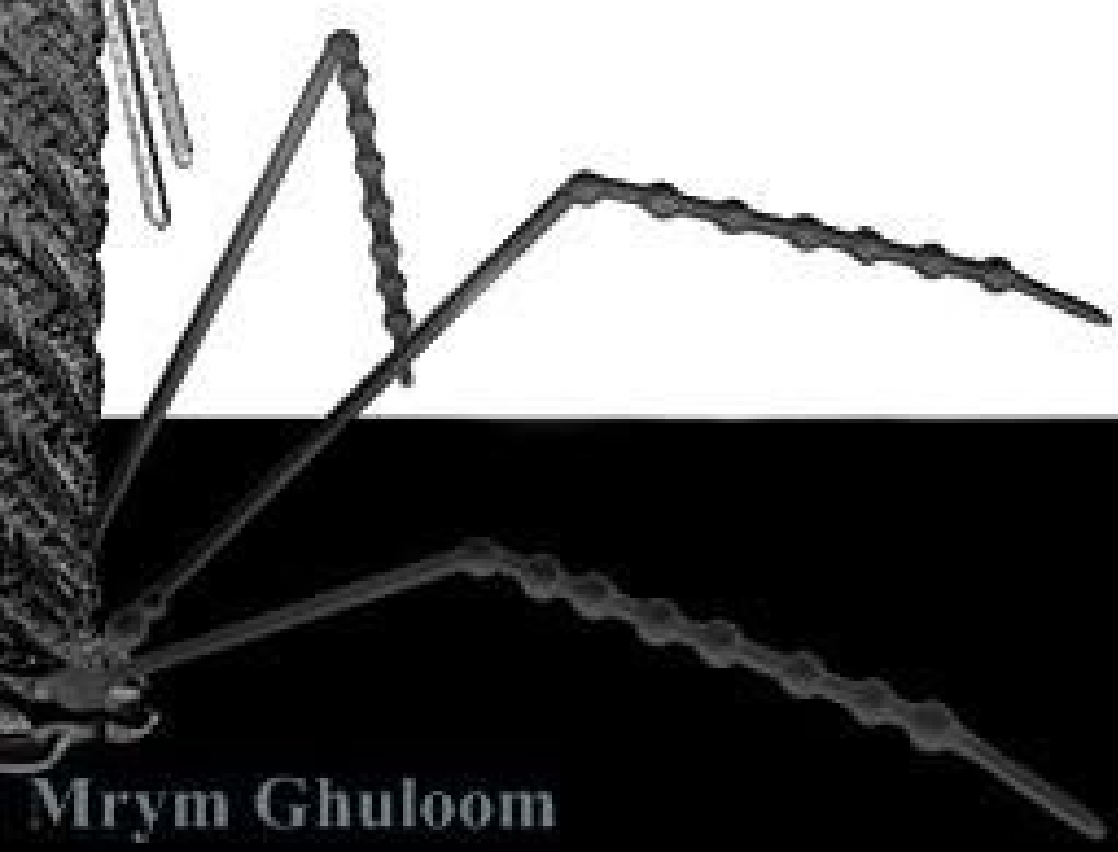
Microbiology

Lecture No:.....9-(3 viro).....

Dr Name:.....Hamed Al Zoubi.....

Done by:.....Mohammad Akkawi.....

Sheet ■ Slide □



Mrym Ghuloom

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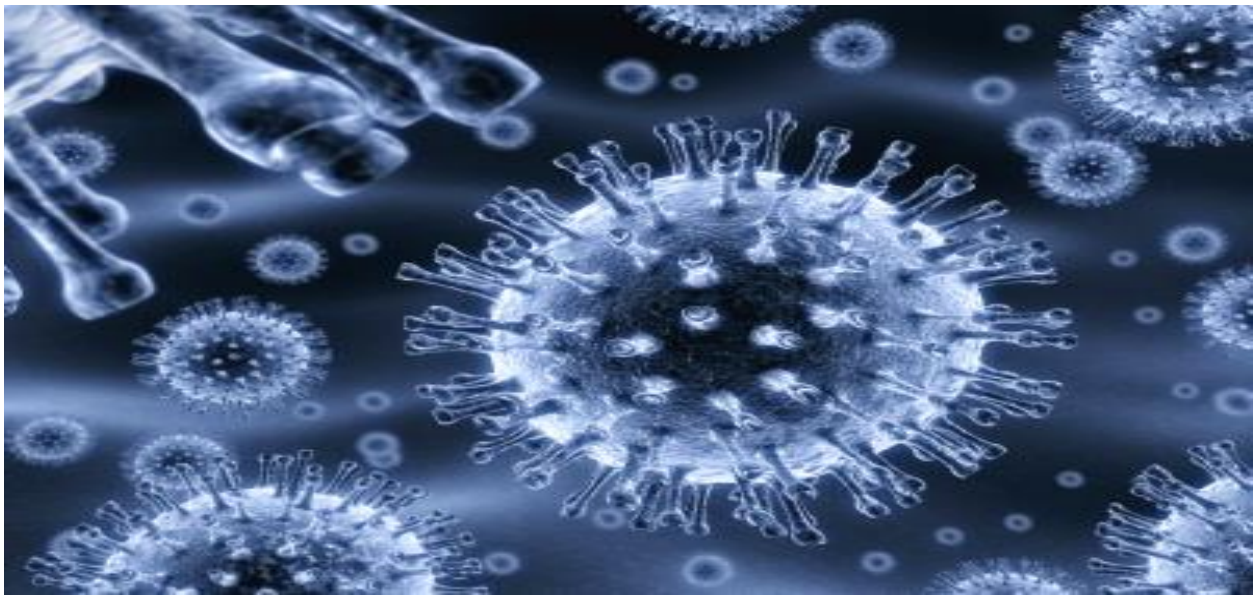


Today we are going to continue what we started to talk about viral replication and life cycle.

1-formation of viral mRNA

2-replication

3-control of viral replication

4-synthsis of viral proteins (talk a little bit about mutations)

5-post-translation modifications of viral proteins

6-assembly,release and maturation

Written by Mohammad Akkawi

Formation of viral mRNA & replication :

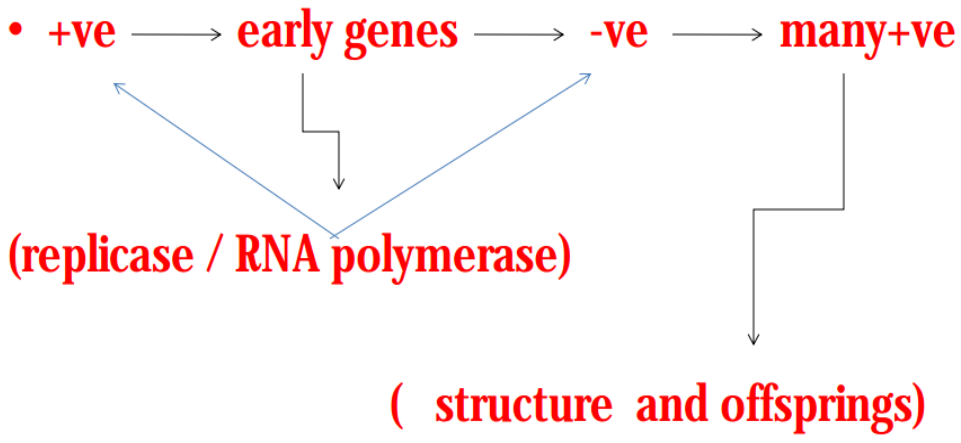
-

DNA viruses

- in the last lecture we said that these viruses **use cellular DNA-dependent RNA polymerase (synthesized in the host cell)**
- **EXCEPTION: POX virus>>>** uses it`s **own RNA polymerase (packed inside the virus)**

+ve ssRNA viruses

- they have a **homologous structure** mRNA
- its considered as mRNA and will be used to synthesize **proteins**
- the first proteins to be synthesized are **the early protein (of which is the RNA polymerase** -a non structural enzyme**-)**
- this RNA polymerase will be used to create a **-ve copy** of the RNA
- this -ve copy will be used to copy this strand **into +ve RNA**
- the **+veRNA :** _ part of it will be used to **express structural proteins**
- _the other part is packed into the offspring (ذرية)



This picture here is a clarification to **(Mechanism of replication of +ve ssRNA):**

1. **+ve ssRNA** enter the cell and become translated into **early proteins (the early genes will be translated into early proteins)**
2. one of the early proteins is **RNA polymerase**
3. the **RNA POLYMERASE** will act on the **+ve ssRNA** and convert it into **–ve**
4. **the -ve** will act as a template to create many **+ve copies**

one –ve copy —**RNA polymerase**→ **many +ve copies**

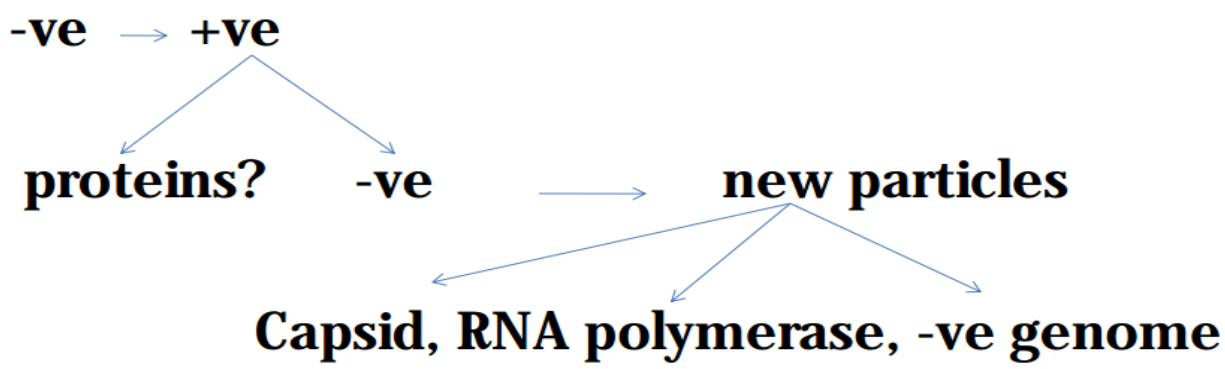
5. **+ve copies** are used to:

a- synthesize **structural proteins (ex: the capsid)**

b- synthesize the **genetic material of the offspring**

***** NOTE:** we have an **intermediate stage** (in which the +ve will become a –ve)

WHY?!! This –ve copy will act as a **template to copy more +ve**, because originally we only have 1 +ve copy and this 1 copy will not be able to make a lot of copies from itself .



What are the proteins that will be expressed from the positive copy ? (there is a question mark on it)

1-structural proteins

2- early proteins : like RNA polymerase and it will be packed with the virus

-ve ssRNA viruses

- has it`s own **RNA polymerase**
- **-ve ssRNA** will be copied into **+ve (intermediate state)**
- **+ve** will be **translated into proteins** (eg: **early - their might be RNA polymerase- and structural proteins)**
- **note :**the **newly synthesized RNA polymerase,the -ve genome and structural proteins** will all be **packed into the new cell**

DNA viruses

- we have already mentioned that DNA viruses use **cellular RNA polymerase** *except* ***the Pox virus***
- **ssDNA viruses:** there will be a **transient state (DNA intermediate is synthesiazed)**
- **plz read the rest of the slide**

dsRNA (Reoviruses only)

- they are **-ve RNA viruses**
- they carry their own **dsRNA-dependent RNA polymerase**

+ve ss RNA viruses (retrovirus)

- retrovirus has a special mechanism we will talk about it in details in the next lecture

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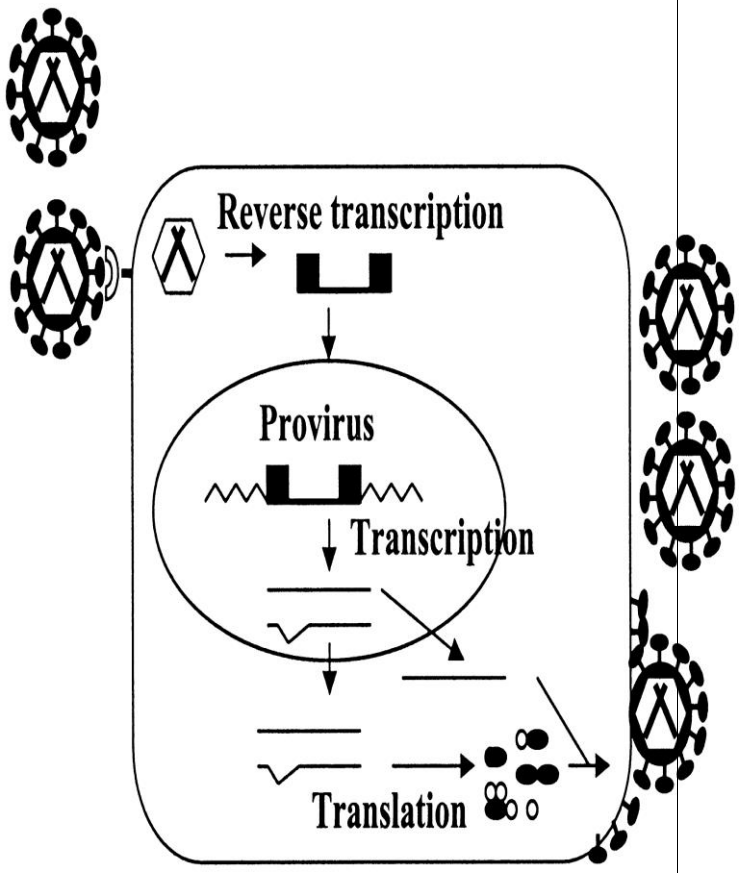
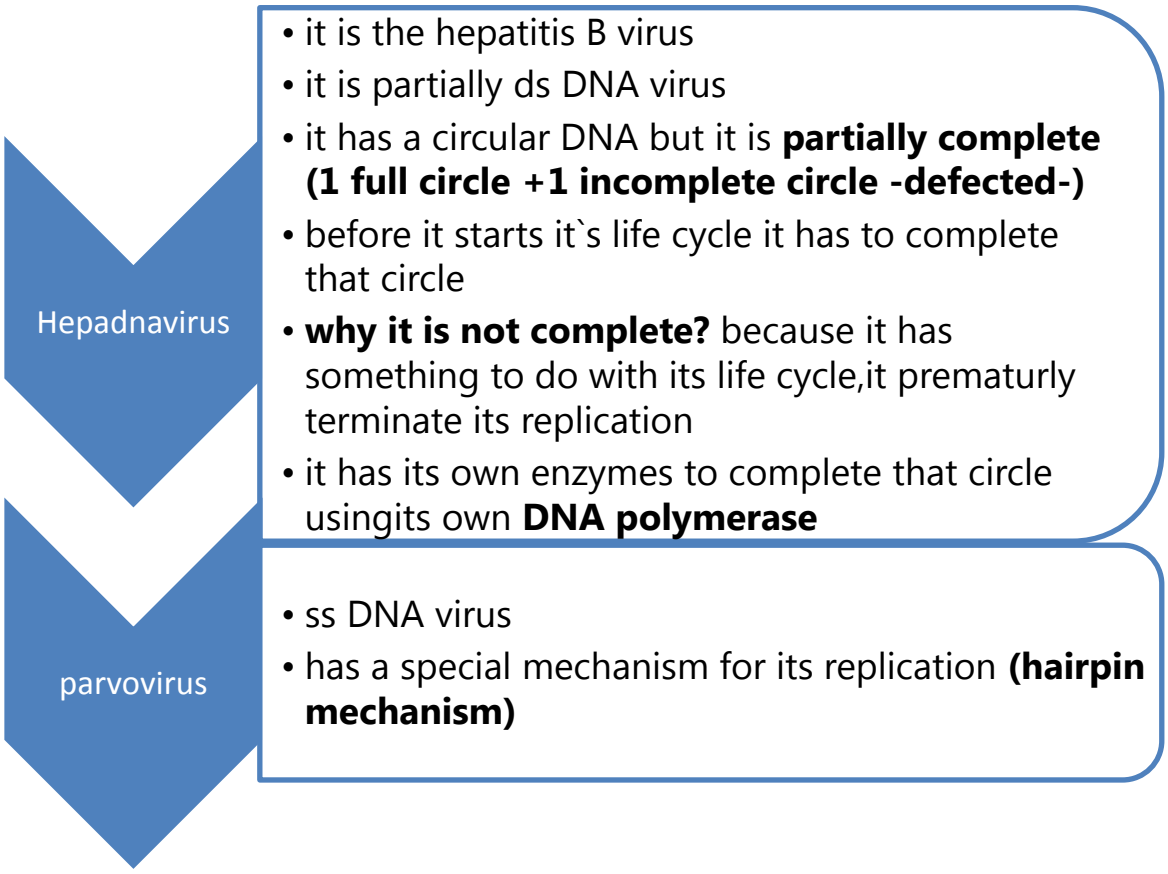
Retrovirus replication mechanism-in brief-:

retrovirus replication mechanism:



1. The ssRNA will replicate itself into dsRNA
2. The dsRNA will be **reverse transcribed** into a DNA molecule by (**reverse transcriptase)**
   dsRNA REVERSE TRANSCRIPTASE DNA
3. The DNA molecule will be **integrated** into the human DNA (cut a part of the cellular DNA and ligate itself) by **integrase enzyme**
4. The viral DNA molecule will be translated and transcribed just like the human DNA



control of viral replication:-

1-transcription:

-might be blocked by **M PROTEINS**

- might be enhanced by **some viral or signal structure** such as:

1-overlapping reading frame

2 – primary RNA transcript splicing

2-translation:

-Usually happens at the ribosome

-Some viruses bind directly to the human ribosomes and compete with our mRNA **(competition mechanism) eg:poliovirus,hepatitis A+C (they bind using special structures)**

#synthesis of viral proteins:

Starts at the start codon (ATG,AUG) and stops at the stop codon (UAA , UAG,UGA)

#mutations:

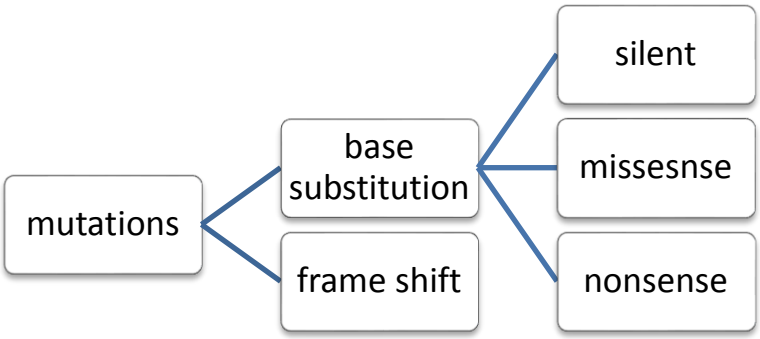
Some mutations take place during the amplification of the virus due to many reasons some of them are:

RNA polymerase:

- it has some mistake /some error rate

- It does not have **proof reading (checking the last nucleotide if it`s In the right place)**

One of these errors is mismatch



- **Base substitution:**
  1. **Silent mutation: eg**

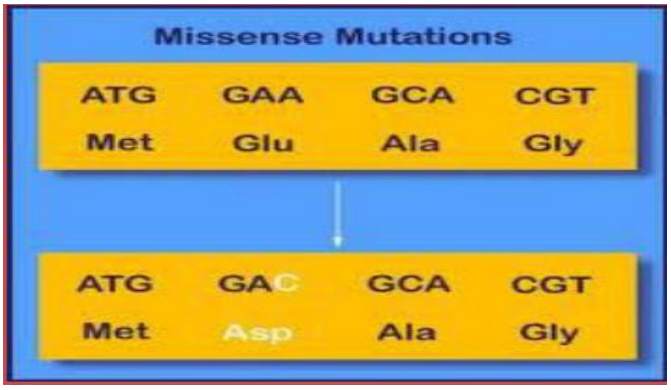
     UCU ⟶ UCC

     SER ⟶ SER

So nothing has changed before and after

2. **Missense mutations: it's a point mutation at which a single nucleotide change results in a codon that codes for a different amino acid**

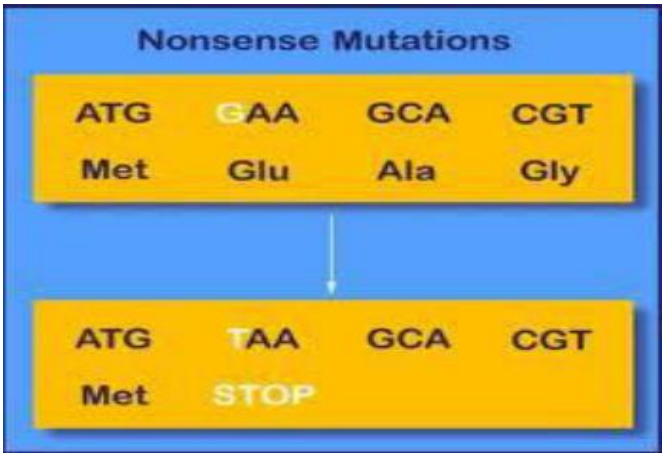
Ex : GAA give rise to glutamic acid which is a different amino acid from aspartic acid which arise from GAC



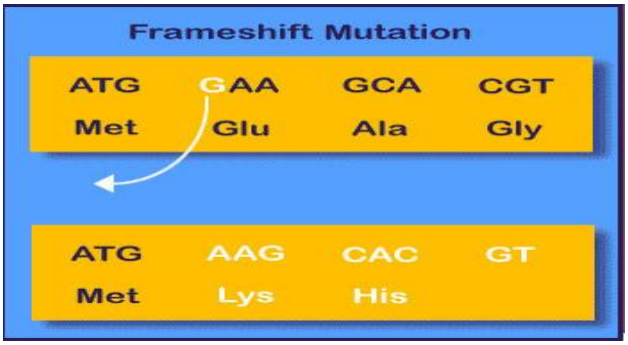
3. **Nonsense: it's a point mutation in the sequence of nucleotides that results in a premature stop codon in the transcribed mRNA so there is incomplete translation**

   ex :**GAA**(glu)⟶ TAA(stop codon)

   ***NOTE:stop codons are (TGA,TAG,TAA) in the DNA and (UGA,UAG,UAA) in the RNA**



4.frame shift: it's a genetic mutation caused by insertion and deletion of a nucleotide which will result in a complete different proteins



#post translation modification:

-**biochemical modifications**

-some of it are important for the 3D structure of protein

You know that the protein has a primary,secondary and tertiary structures

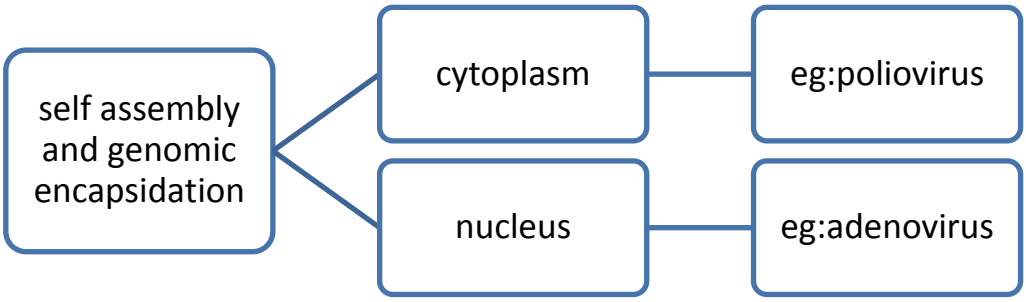
Some changes in these structures are important for the folding and the 3D structure to produce a functional viral protein

Modifications:

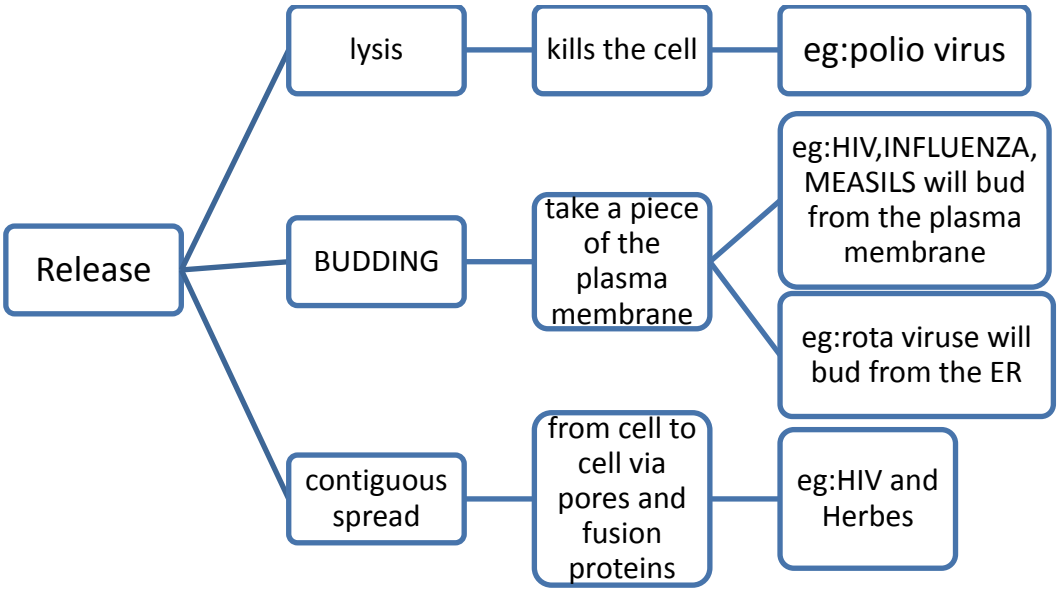
1- glcosylation
2- addition of a sulfate or phosphate
3- acylation-addition of acyl group

-Some of the viruses such as **adenovirus** synthesize a **polyprotein** than needs to be spliced by **proteases(could be from the cell or the virus itself)**

#Assembly, release and maturation:



*__genomic encapsidation:__ the process in which the genetic material of the virus will be entered to the capsid



**__NOTE__:a lot of budding might cause the cell to kill itself

But the general outcome of killing the cell is a characteristic of naked (nonenveloped) viruses .

After release there might be some changes(modifications) for the virus to complete its life cycle

Some of these modifications:-**HIV: will cut a part of its capsid so it will change the morphology using proteases coded by the virus**

-INFLUENZA: when it comes out it will stick to syalic acid by the Hemaglutinnin it is necessary to set the virus free so this binding (hemagluttinin----syalic acid)and this will be achieved by the help of proteases and <u>neuraminidase</u>

انا اعتذر عن اي خطا سقط سهوا

كل عام و انتم بخير

Done by : Mohammad Akkawi