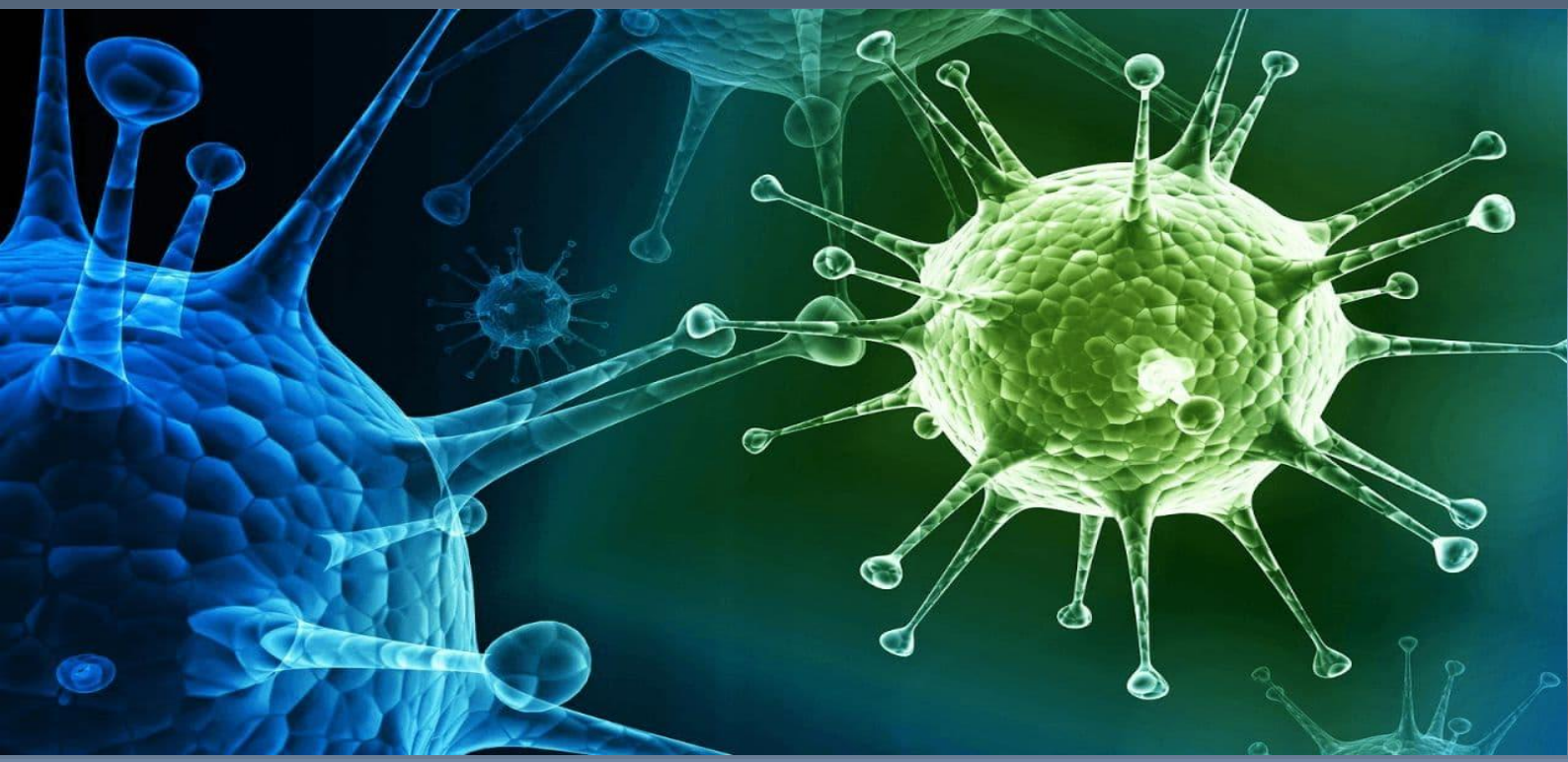
Athar Batch



Microbiology

Lecture: 19

Done By : Mariam Almahrooq

النادي الطبي

Microbiology lecture 19

Viral life cycle

Done By : Mariam AlMahrooq

Viral replication terminology

- Multiplicity of infection (MOI): ratio of infectious agents (e.g. phage or virus) to infection targets
- Eclipse phase: period during which the input virus becomes uncoated; 10-12h
- Synthetic phase: time during which new virus particles are assembled; 4-6h
- Latent period: no extracellular virus can be detected
- Burst size: amount of infectious virus produced, per infected cell ; 10-10,000

very important terms in viral life cycle you should to memorize & understand them :

^ MOI : ratio of virus / phage toinfection target .

_ If number of viruses = number of infection target -→ ratio =1.

_ High MOI -→ viruses > infection target .

_ Low MOI-→ viruses < infection target .

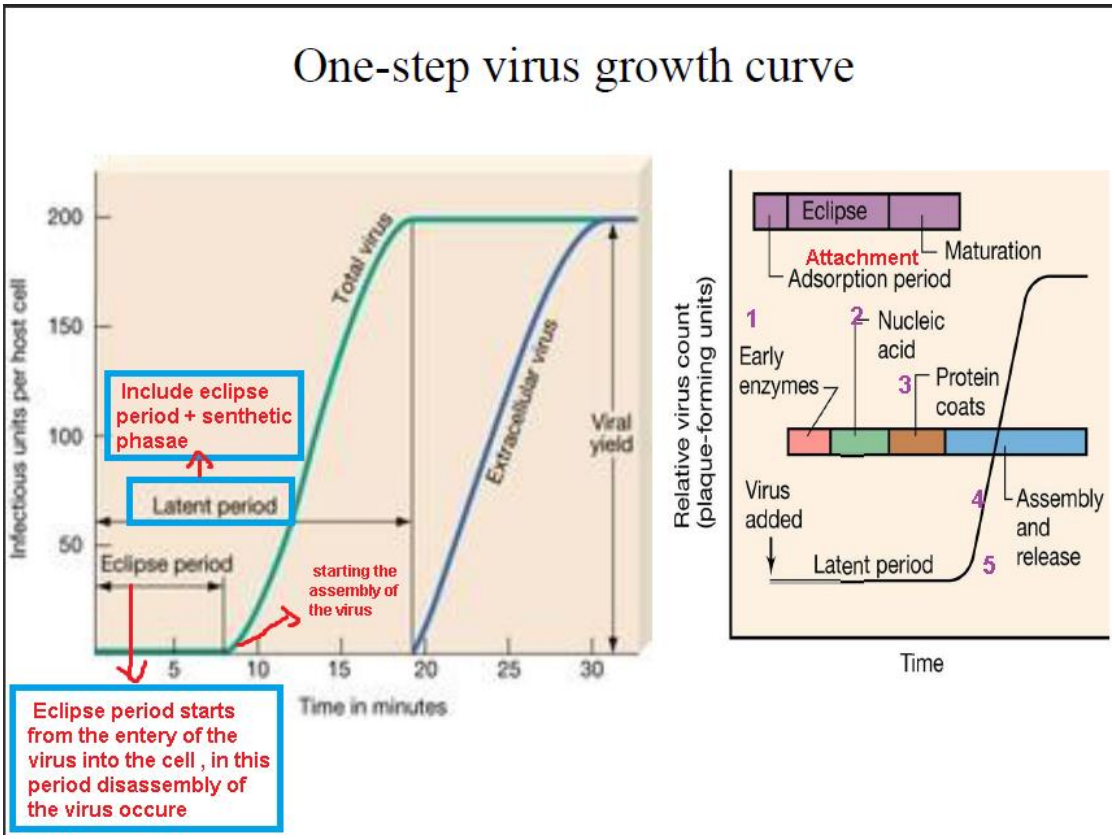
^ Eclipse phase : period during which the input virus becomes uncoated (disassembly of virus) .

في فيروس بس ما نلاقيه كله قطعة وحدة .

^ synthetic phase : time during which new virus particles are assembled .

^ latent period : no extra celluler virus can be detected .

^ **Burst size :** **amount of infectious virus produced , per infected cell .**



Pecture 1:

_ This curve represent the one step virus growth curve .

_ In eclipse period , the disassembly of the virus occure .

وبالتالي اذا اجينا ندور على فيروس كامل بهالمرحلة ما رح نلاقيه . (هو موجود بس مو قطعة وحدة) .

Pecture2 :

_ تبدأ بال **attachment** بعدين عنا ال **eclipse** وبعد هيك يدخل الفيروس في مرحلة التصنيع (الأرقام يلي بالبنفسجي عالصورة) .

_ أول ما يحتاجه الفيروس هو ال **viral enzymes** يلي تعتبر

. non structural proteins

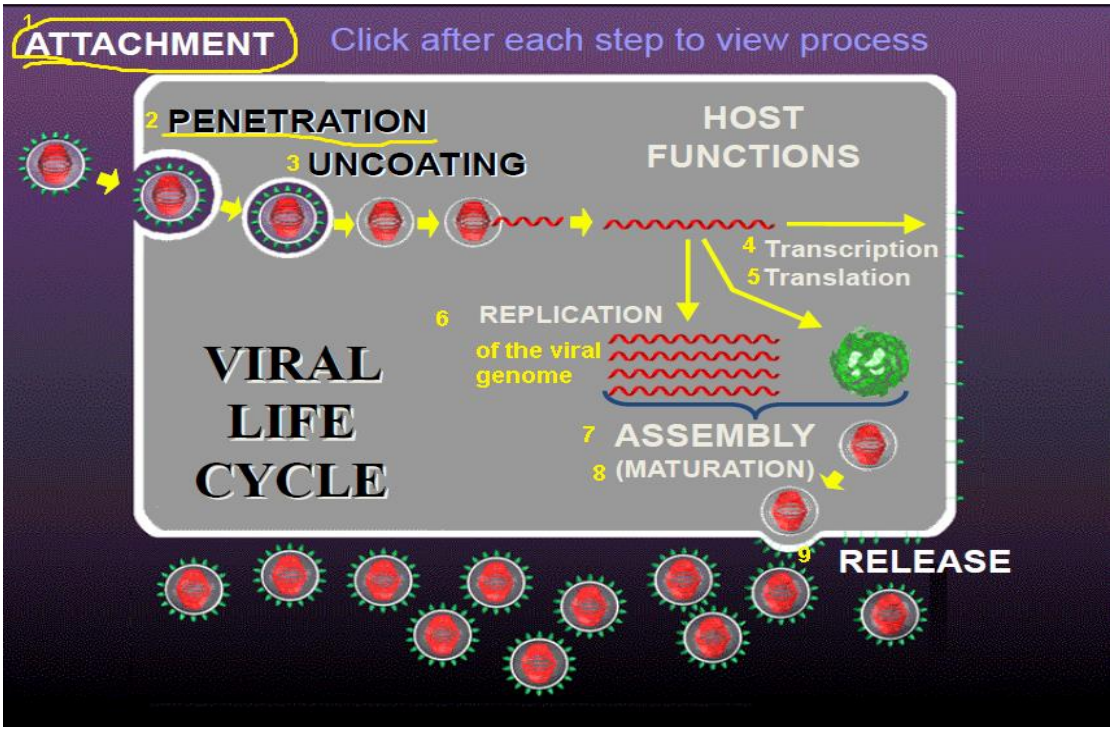
_ Non structural enzyme/ proteins : enzymes that are required for virus replication .

بينما ال **structural proteins** هي التي تدخل في التكوين الفعلي للفيروس .

The Replication Cycle

- Virus replication can be divided into eight arbitrary stages. مو كثير مهم الرقم لأنه يختلف من مصدر لآخر
- Regardless of their hosts, all viruses must undergo each of these stages in some form to complete their replication cycle. all viruses either it DNA or RNA viruses should undergo these stages in order to replicate
- Not all the steps described here are detectable as distinct stages for all viruses.

المراحل يلي حكيناهم قبل شوي عالصورة أكيد رح يمر فيها كل الفيروسات بس مو شرط نفس الترتيب يلي حكيناه وحدة وحدة ، ممكن يكونوا يحصلوا كلهم
at the same time



NOTES :

_ **Attachment :** entery of the viruse inside the host cell .

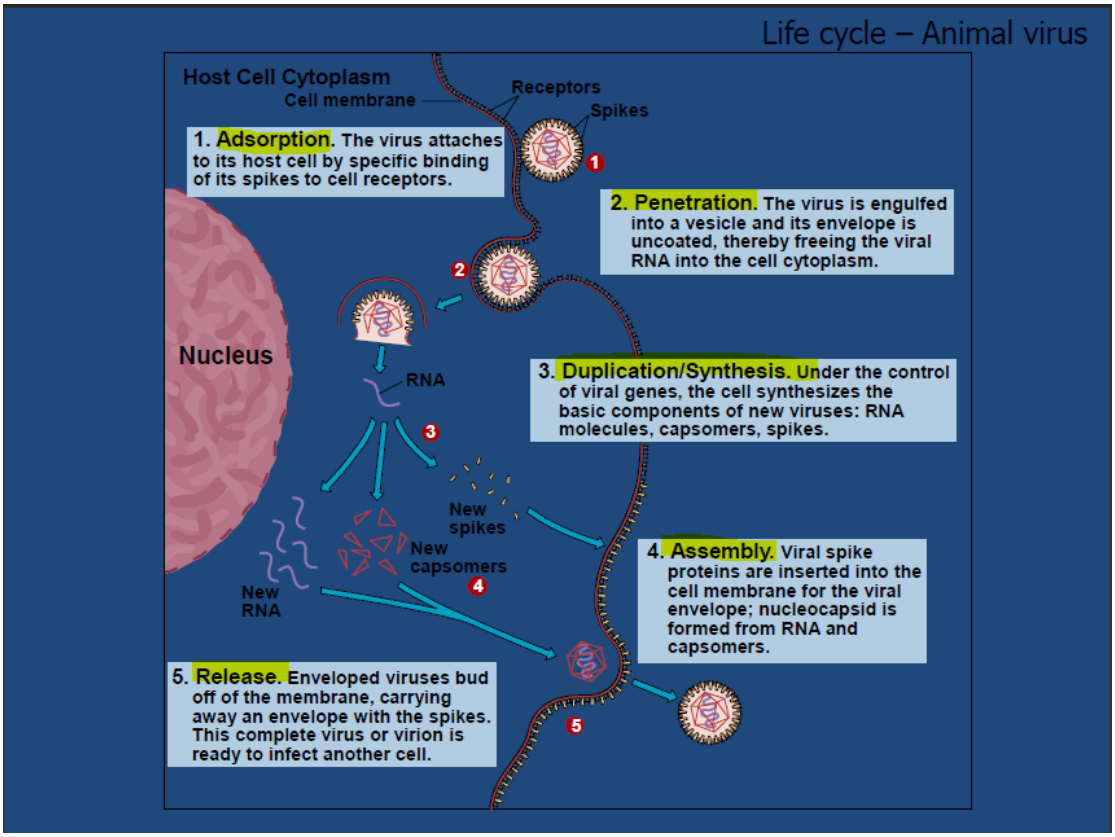
هي خطوة ضرورية ومهمة لحتى يصير عنا **infection** .

_ **uncoating :** **disassembly of the virus.**

ترقيم الخطوات موجود عالسلايد

_ **Maturation :** **mature virus can cause infection & its protein in its correct site .**

_ **Maturation could occure inside or outside the cell .**



نفس الخطوات يلي حكيناهم بالسلايد السابق بس بتوضيح أكثر .

Attachment

- Virus attachment consists of specific binding of a virus-attachment protein (or 'antireceptor') to a cellular receptor molecule.
- Target receptor molecules on cell surfaces may be proteins (usually glycoproteins), or the carbohydrate residues present on glycoproteins or glycolipids.
- Some complex viruses (e.g. poxviruses, herpesviruses) use more than one receptor and have alternative routes of uptake into cells.

Notes:

_ Attachment must occure .

_ in enveloped virus : interaction between spikes (glycprotein)& celluler receptor .

_ In naked virus : interaction between capsid grooves & celluler receptor .

_ More than one type of spikes on the surface of the virus

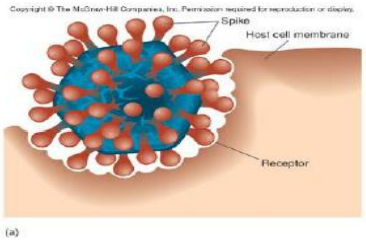
Is it enough one glycoprotein to interact with celluler receptor on the target cell ?

Usually yes , but for some viruses muliple interaction occure . what is that mean ??

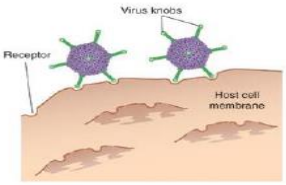
Different type of spikes either attach to the same receptor to initiate the virus entery or they might bind to multiple or different receptors on the target cell in order to initiate virus entery .

Adsorption Attachment

Enveloped
With prominent spikes



Naked; with capsid spikes



- Host range: the collection of hosts that an organism can utilize as a partner
- Cellular (tissue) tropism: the cells and tissues of a host which support growth of a particular virus

Notes:

_ In enveloped virus :

تبدأ عملية ال **attachment** من خلال ارتباط ال **spikes** مع ال **receptor**
بعدين يصير عنا عملية شد بحيث يصير **approximation between cell membrane & viral envelope** ويصير عنا بالمحصلة **fussion** و الفيروس لما يدخل عالخلية يدخل **as a nucleocapsid** فقط وبالتالي عشان يصير ال **fussion** هل يكفي **one spike _receptor complex** ؟

The answer is No , most of the viruses need more than one spike_ receptor complex to achive fussion .

For example , HIV virus need 3_5 spike _ receptor complexin order to approximate cell membrane & viral envelope & achive fussion .

_ In naked viruses:

بنفس الطريقة يلي حكيناها لل **enveloped** بس بدل ال **spikes** ال **grooves** هم يلي يرتبطوا مع ال **receptors** .

_ Host range :

المقصود فيها عدد ال **species** يلي يقدر الفيروس يعمللها **infection** مثلاً عنا فيروسات تكون قادرة تعمل عدوى للانسن والحيوانات والنباتات مثلاً ،

Influenza virus can infect human , birds , catteles

_ celluler torpism :

عدد الخلايا او الأنسجة يلي ممكن يسببلها عدوى بس بنفس ال **species** .

For example :

^ influenza virus infect then respiratory tract cells .

^ hepatitis infect the hepatocytes .

^ SARS cov _2 infect the lower respiratory tract . (alvioli)

^ SARS cov _ 2 omecron has high affinity for upper respiratory tract.

omecron : it is 8_10 time more contagious but infection is more confine to the upper respiratory tract (not alvioli we take about bronchi)

TABLE 6–6. Examples of Viral Receptors

Virus	Target Cell	Receptor*
Epstein-Barr virus	B cell	C3d complement receptor CR2 (CD21)
Human immunodeficiency virus	Helper T cell	CD4 molecule and chemokine co-receptor
Rhinovirus	Epithelial cells	ICAM-1 (immunoglobulin superfamily protein)
Poliovirus	Epithelial cells	Immunoglobulin superfamily protein
Herpes simplex virus	Many cells	Immunoglobulin superfamily protein
Rabies virus	Neuron	Acetylcholine receptor
Influenza A virus	Epithelial cells	Sialic acid
B19 parvovirus	Erythroid precursors	Erythrocyte P antigen (globoside)

*Other receptors for these viruses may also exist.
ICAM-1 = Intercellular adhesion molecule.

Coreceptor: CCR5
CXCR4 ~~CROX4~~

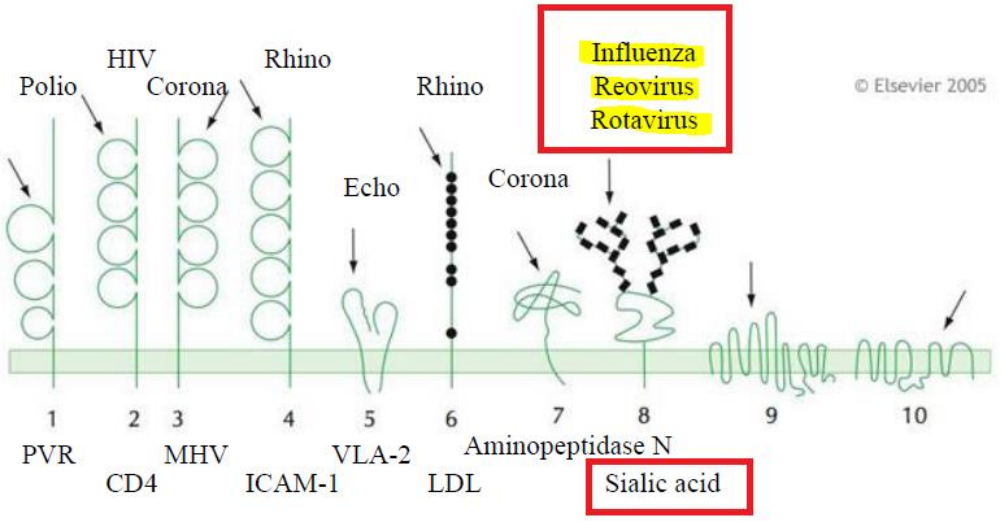
هون عم نحكي عن خلايا الدم الحمراء بالتالي ال receptor هو erethrocyte antigen

هاي خطأ الصح هو

هاي السلايد مهمة كثير ومهم نميز عن شو بيسأل عن **target cell** أو **receptor** _ ممكن يكون في عنا **more than receptor for one virus** و عنا **receptors shared with more than one viruses such as sialic acid** .

Virus Receptors

Many examples of virus receptors are now known.
Schematic representation of some virus receptors
- arrows indicate virus attachment site:



NOTES :

_ some viruses can share the same receptor .

بس لما نحكي share receptors هل هو تماماً نفسه ، لأ ال structure هو لكن sialic acid it have a distingtive shape of different viruses .

هلأ الفيروسات هدول مو للحفظ بس الدكتور اهتم بالفيروسات يلي تشترك بال sialic acid

TABLE 6–5. Examples of Viral Attachment Proteins — glycoprotein or spikes

Virus Family	Virus	VAP
Picornaviridae	Rhinovirus	VP1-VP2-VP3 complex
Adenoviridae	Adenovirus	Fiber protein
Reoviridae	Reovirus	σ-1
	Rotavirus	VP7
Togaviridae	Semliki Forest virus	E1-E2-E3 complex
Rhabdoviridae	Rabies virus	G Protein
Orthomyxoviridae	Influenza A virus	HA
Paramyxoviridae	Measles virus	~~HA~~ NA
Herpesviridae	Epstein-Barr virus	gp350 and gp220
Retroviridae	Murine leukemia virus	gp70
	Human immunodeficiency virus	gp120 (gp 160 which have 2 component)

gp = glycoprotein; VAP = viral attachment proteins. HA: Hemagglutinine

_ **HIV VAP is gp160 which have 2 component (the transmembrane & the subunit empeded with the enveloped of the virus , gp41 &gp120).**

When we take about HIV virus : once the gp 120 attach to the CD4 receptor on the T cells . it falls of

approximation & ، interaction ليعمل gp41 يوقع ويفتح المجال لل . fussion

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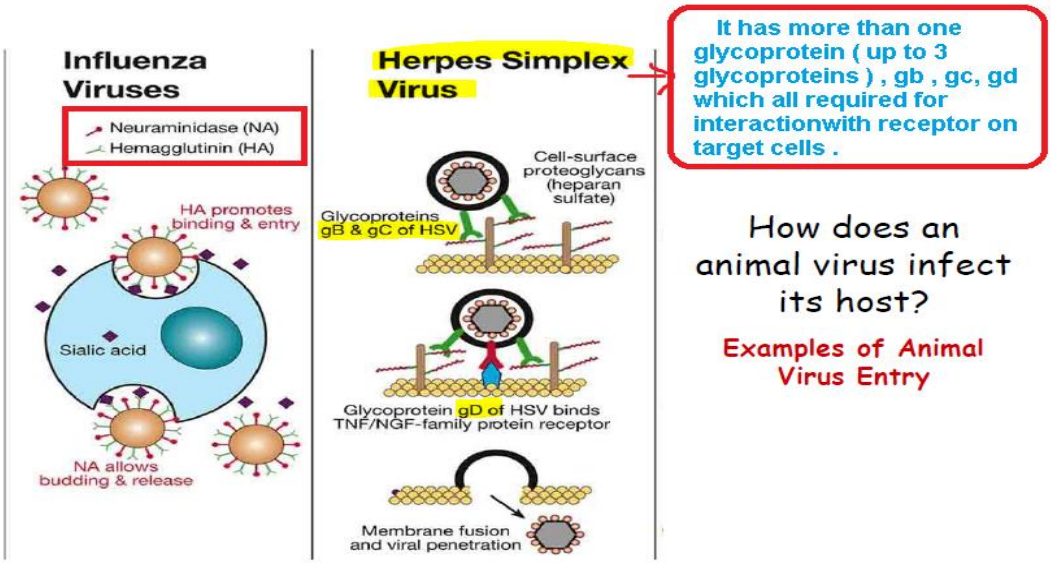


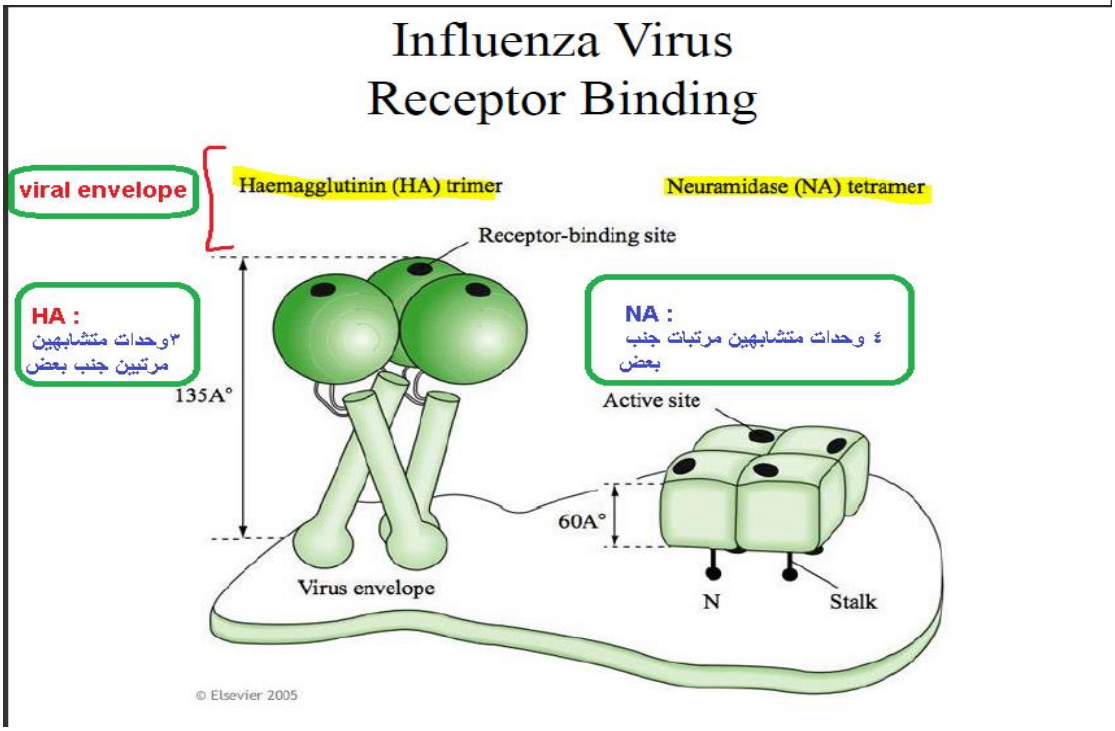
influenza virus : it has 2 VAP (HA & NA) .

_ **HA** : it response for the interaction with receptor on the target cell & initiation of the virus entery .

_ **NA** has a role but the major role s for the **HA** .

Influenza Virus Receptor Binding

- The influenza haemagglutinin protein is one of two types of glycoprotein spike on the surface of influenza virus particles, the other type being the neuraminidase protein.
- Each haemagglutinin spike is composed of a trimer of three molecules, while the neuraminidase spike consists of a tetramer. 4 molecules
- The haemagglutinin spikes are responsible for binding the influenza virus receptor, which is sialic acid (N-acetyl neuraminic acid).
- As a result, there is little cell-type specificity imposed by this receptor interaction and therefore influenza viruses bind to a wide variety of different cell types.



Multiple Receptors

such as herpis virus , HIV

- In some cases, interactions with more than one protein are required for virus entry - neither protein alone is a functional receptor.
- Adenovirus receptor-binding is a two stage process involving an initial interaction of the virion fibre protein with a range of cellular receptors, including MHC class I molecule and the coxsackievirus-adenovirus receptor (CAR).

الدكتور حكى هاي الفقرة مو مهمة بس المهم نعرف أنهم مرحلتين

- Another virion protein, the penton base, then binds to the integrin family of cell surface heterodimers allowing internalization of the particle via receptor-mediated endocytosis.

- The primary receptor for HIV is the T cell antigen, CD4.
- These are Several members of a family of proteins known as b-chemokine receptors play a role in the entry of HIV into cells, and their distribution may be the primary control for the tropism of HIV for different cell types (lymphocytes, macrophages, etc).

هون نفس الحكي يلي حكيناه على الجدول

example of target cells

Penetration

- Penetration of the target cell normally occurs a very short time after attachment of the virus to its receptor in the cell membrane.
- Unlike attachment, cell penetration is generally an energy-dependent process, i.e. the cell must be metabolically active for this to occur.
- Three main mechanisms are involved.

two mechanism because translocation is no longer considered as one of them .

قبل شوي حكينا عن وحدة منهم وهي ال fussion

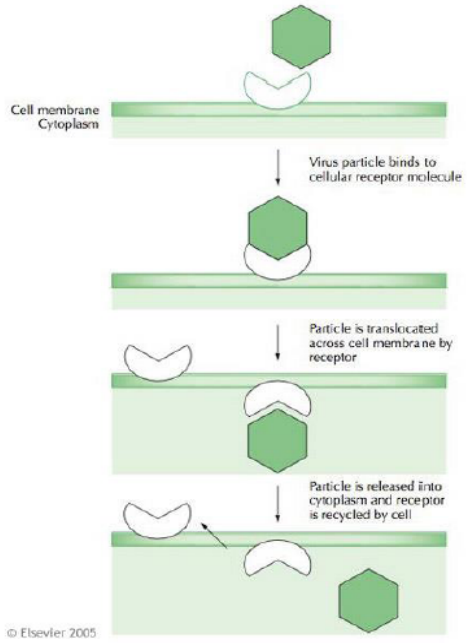
ورح نحكي عنها بالتفصيل كمان شوي

Translocation

rarely seen in viruses , but it occure in the case of nutreint or other things .

1) Translocation of the entire virus particle across the cytoplasmic membrane of the cell.

- This process is relatively rare among viruses and is poorly understood.
- It is mediated by proteins in the virus capsid and specific membrane receptors.



_ Translocation :

then it flips inside the cell يعني أنه الفيروس يرتبط مع جزء خارج الخلية

(يقلب قلب يعني) و مثل ما حكينا هي **very rare in virus** لذلك صرنا نحكي

There are 2 mechanisms of entery of the virus inside the cell :

1 _ Receptor mediated endocytosis .

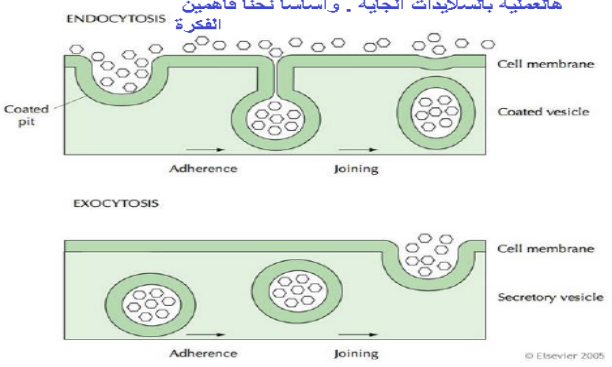
2 _ fussion .

Endocytosis Receptor mediated endocytosis

الدكتور ما قرأ هاد السلايد أبداً لأنه رح نحكي عن هالعملية بالسلايدات الجاية . وأساساً نحنا فاهمين الفكرة

2) Endocytosis of the virus into intracellular vacuoles is probably the most common mechanism.

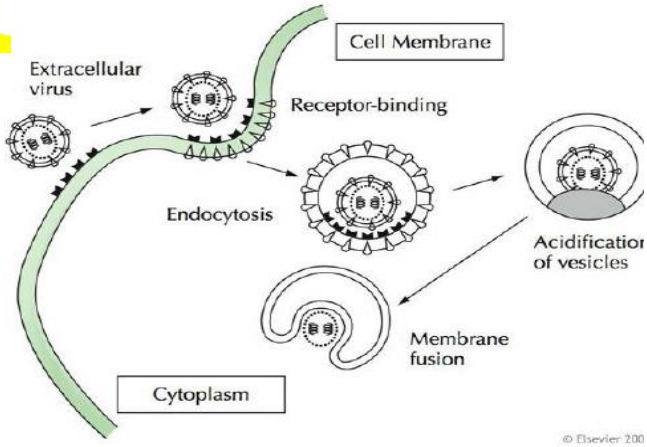
- Does not require any specific virus proteins (other than those utilized for receptor binding) but relies on the formation and internalization of coated pits at the cell membrane.
- Receptor-mediated endocytosis is an efficient process for taking up and concentrating extracellular macromolecules.



Fusion

3) Fusion of the virus envelope with the cell membrane, either directly at the cell surface or in a cytoplasmic vesicle.

- Fusion requires the presence of a fusion protein in the virus envelope which promotes joining of the cell and virus membranes, resulting in the nucleocapsid being deposited directly in the cytoplasm.
- There are two types of virus-driven membrane fusion: pH-dependent and pH-independent.



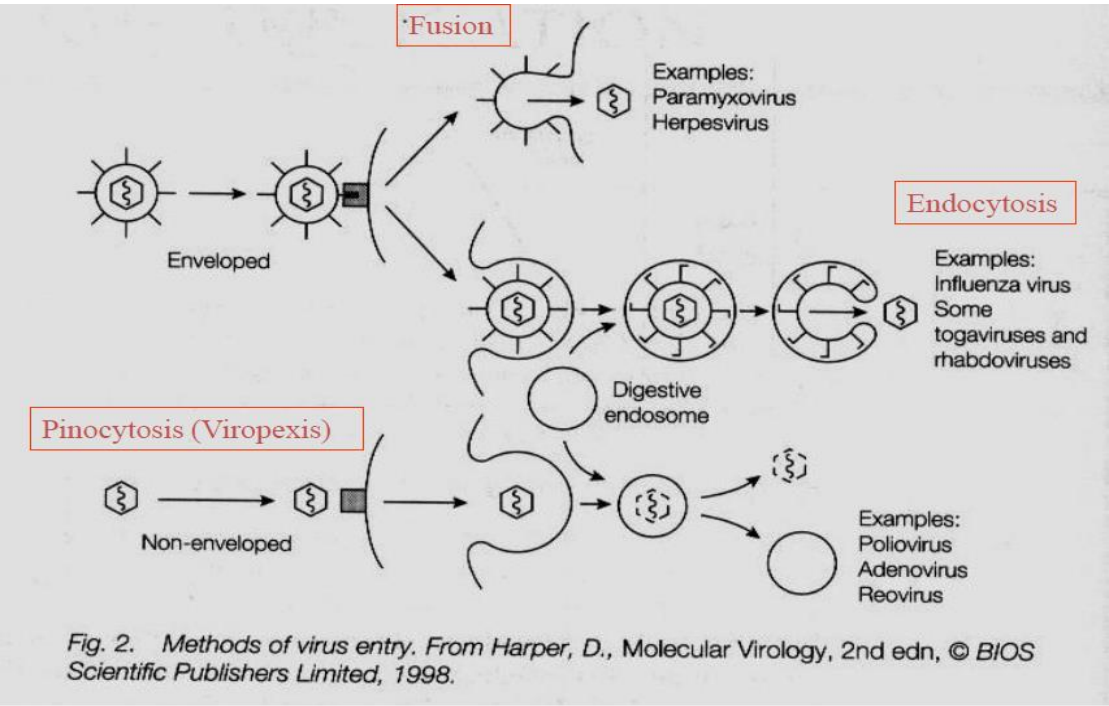


Fig. 2. Methods of virus entry. From Harper, D., Molecular Virology, 2nd edn, © BIOS Scientific Publishers Limited, 1998.

_ enveloped viruses :

هاد ال **enveloped virus** ارتبطت ال **glycoproteins** تبعونه مع ال **receptors** الموجودين على ال **host cell** بعد هيك عنده احتمالين :

1 _ it might enter via receptor mediated endocytosis .

يدخل عن طريق **endostatic vesicle** (يعني الفيروس كله يدخل) ، طيب وبعدين مش لازم يصير **trigger** لحتى يطلع الفيروس من ال **vesicle** ؟ أكيد وال **triger** هو ال **acidification or drop in the PH vesicle** .

2 _ fussion :

اندماج ال **viral envelope** مع ال **cell membrane** بحيث يصير جزء منه ، وفقط يلي يدخل عالخلية هو ال **nucleocapsid** . مو كل ال **virus** مثل ال **endostatic vesicle** .

_ Naked virus :

لأن ال **naked virus** ما عنده **envelope** بالتالي ما يقدر يلتحم مع ال **cell membrane** ، لهيك بيقدر يدخل الخلية بطريقة وحدة وهي **receptor mediated endocytosis**

Note : in certain naked viruses the genom only leave the endostatic vesicle & in another the nucleocapsid leave the vesicle .

يعني ممكن ال **capsid + genome** يطلعوا من الحويصلة أو بس ال **genome** حسب الفيروس .

ملاحظة : ال **enveloped viruses** دائماً يغادروا الحويصلة **as a nucleocapsid** .

ال **trigger** لحتى يطلع الفيروس من ال **vesicle** هو ال **acidification** سواء كان الفيروس **naked** او **enveloped** .

_ Acidificaton might lead to :

1 _ conformational changes in the viral envelope to attach & fuse with endostatic vesicle membrane -→ release of the virus .

2 _ virus (naked / enveloped) may release certain substances that leads to the lysis to the endostatic vesicle & release virus .

يلي يعمل ال **fussion** مع ال **endostatic vesicle membrane** بال **naked virus**.

_ acidification is a limited step in the entery of the virus inside the cell .

Paramyxovirus -→ parainfluenza virus

Orthomyxovirus -→ influenza virus

Uncoating

Disassembly of the virus

- Uncoating is a general term for the events which occur after penetration.
- Uncoating is one of the stages of virus replication that has been least studied and is relatively poorly understood.
- The product of uncoating depends on the structure of the virus nucleocapsid.
- The structure and chemistry of the nucleocapsid determines the subsequent steps in replication.

_ **Un coating : disassembly of the virus .**

بالمختصر يتفكك ال capsid ويصير عنا release of the genetic material in the cytoplasm of the target cell

BOX 6–6. Steps in Viral Replication

1. Recognition of the target cell
2. Attachment
3. Penetration
4. Uncoating
5. Macromolecular synthesis
   a. Early mRNA and nonstructural protein synthesis: genes for enzymes and nucleic acid–binding proteins
   b. Replication of genome
   c. Late mRNA and structural protein synthesis
   d. Post-translational modification of protein
6. Assembly of virus
7. Budding of enveloped viruses
8. Release of virus

NOTES :

_ recognition of the target cell : is arandom process ,depend on the number of virus & availability of receptors .

كلما زاد عدد الفيروسات تزداد فرصة ارتباطها بال receptor on the target cells .

وهاي الخطوات حكيناهم أول المحاضرة بالسلايد الثاني ، حكينا لو مشينا فيهم بالترتيب

_ attachment.

_ penetration.

_ uncoating .

_ earlyenzyme synthesis (non structural protein).

_ genetic material replication .

_ structural protein synthesis .

*** Is this order apply on the DNA & RNA viruses ?**

The answer is No , DNA Viruses depend on celluler machinary in its replication , so it can not pack their own enzymes .

بالتالي ال DNA viruses ما عندها خطوة ال early enzyme synthesis وهاي الخطوات بهالترتيب تنطبق على ال RNA Viruses بشكل أكبر .

_ Post translational modification may occur in step number 5 or maybe occure after assembly of the virus.

ال modification مهمة عشان موضوع ال maturation .

Genome Replication and Gene Expression

- All viruses can be divided into seven groups - a scheme was first proposed by David Baltimore in 1971.
- Originally, this classification included only six groups, but it has since been extended to include the hepadnaviruses.
- For viruses with RNA genomes in particular, genome replication and the expression of genetic information are inextricably linked, so both are taken into account.

Last lecture we mentioned the 7 Balitmore for viruses replication . (ssDNA , ds DNA , ss RNA + sense , ssRNA – sense , dsRNA , ss RNA (+) sense reverse transcriptase , DNA reverse transcriptase).

حكينا عن 4 special وهم :

_ ssDNA-→ Parvovirus

_ dsRNA -→Reoviridea (Rotavirus)

تذكروا هاد الفيروس يعمل gastrointritis بالأطفال يلي عمرهم أقل من سنتين ، وممكن يعمل نفس الشي لغاية عمر ٦ سنين عادي بس شائع أكثر عند الصغار .

_ RNA reverse transcriptase -→ HIV virus

_ DNA reverse transcriptase -→ Hepatitis B

The genomes

- **I: Double-stranded DNA. Examples: Adenoviruses, Herpesviruses, Papillomaviruses, Poxiviruses, T4 bacteriophage** parvoال ما عدا .DNAviruseكل
  Some replicate in the nucleus e.g adenoviruses using cellular proteins. Poxviruses replicate in the cytoplasm حكينا لأنه حجمه كبير ما يدخل عالنواة
- **II: Single-stranded (+)sense DNA. Examples: phage M13, chicken anaemia virus, maize streak virus** parvoviruse is the most important example because it infects human
  Replication occurs in the nucleus, involving the formation of a (-)sense strand, which serves as a template for (+)strand RNA and DNA synthesis.
- **III: Double-stranded RNA. Examples: Reoviruses, Rotavirues** هو نفسه يا جماعة
  These viruses have segmented genomes. Each genome segment is transcribed separately to produce monocistronic mRNAs.
- **IV: Single-stranded (+)sense RNA Examples: Hepatitis A and C, Small RNA phages, common cold viruses, SARS** these viruses have segmanted genome
  a) Polycistronic mRNA e.g. Picornaviruses; Hepatitis A. Genome RNA = mRNA. Means naked RNA is infectious, no virion particle associated polymerase. Translation results in the formation of a polyprotein product, which is subsequently cleaved to form the mature proteins.
  b) Complex Transcription e.g. Togaviruses. Two or more rounds of translation are necessary to produce the genomic RNA.

هاد السلايد الملاحظات مكتوبة عليه .... بس ركزوا على المستطيلات الحمر يلي حطيتهم على آخر فقرة رح نعرف معناهم كمان شوي مع الشرح ان شاء الله .

- **V: Single-stranded (-)sense RNA. Examples: Influenza viruses, Hantaviruses**
  Must have a virion particle, containing RNA directed RNA polymerase.
  a) Segmented e.g. Orthomyxoviruses. First step in replication is transcription of the (-)sense RNA genome by the virion RNA-dependent RNA polymerase to produce monocistronic mRNAs, which also serve as the template for genome replication.
  b) Non-segmented e.g. Rhabdoviruses. Replication occurs as above and monocistronic mRNAs are produced. رح أشرحها تحت السلايد
- **VI: Single-stranded (+)sense RNA with DNA intermediate in life-cycle (Retroviruses). Examples: HIV, Avian leukosis virus** RNA reverse transcriptase
  Genome is (+)sense but unique among viruses in that it is **DIPLOID**, and does not serve as mRNA, but as a template for reverse transcription. it mean it contain 2 copies of ss (+)sense RNA
- **VII: Partial double-stranded (gapped) DNA with RNA intermediate (Hepadnaviruses) Example: Hepatitis B** DNA reverse transcriptase This group of viruses also relies on reverse transcription, but unlike the Retroviruses, this occurs inside the virus particle on maturation. On infection of a new cell, the first event to occur is repair of the gapped genome, followed by transcription.

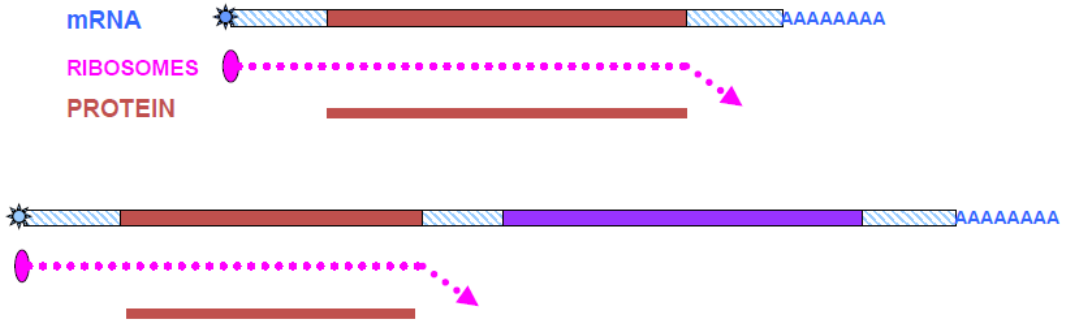
ss(-)sense RNA :

حكينا المرة الماضية لأنه **sense** – ما يقدر يروح عالرايبوسوم مباشرة ، يرتبط مع **RNA dependent RNA polymemarase** يصنع **complementary + sense strand** لهدفين :

_ تروح عالرايبوسوم وتعمل **viral protein synthesis** .

_ تشتغل **as a template** لتصنيع **sense strand** – يلي هي ال **genetic materials** لهاد النوع من الفيروسات.

The monocistronic mRNA problem



- Make one monocistronic mRNA per protein
- Make a primary transcript and use alternative splicing
- Make a large protein and then cut it into smaller proteins
- Include special features in the mRNA which enable ribosomes to bind internally

_ Monocistronc mRNA : each gene encoded into separate mRNA molecules ,which encode into separate proteins .

_ Do our cells do monocistronic mRNA ?

Yes

_ Do viruses do monocistronic mRNA ?

Usually yes , but not always .

طيب كيف يعمل ال **monocistronic mRNA** ؟؟ بوحدة من الطرق ال ٤ يلي موجودة بالسلايد والتفاصيل مو مطلوبة الهم .

Class I: Double-stranded DNA

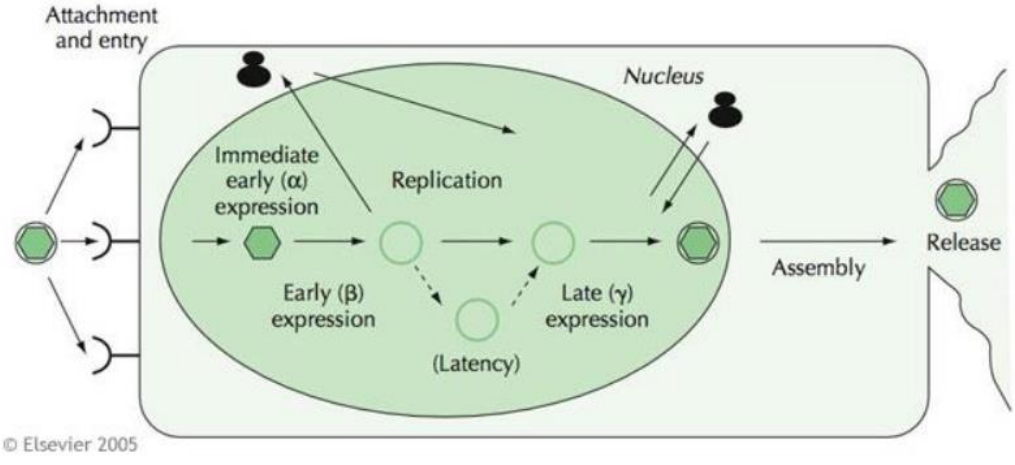
This class can be subdivided into two further groups:

A) Replication is exclusively nuclear. The replication of these viruses is relatively dependent on cellular factors.

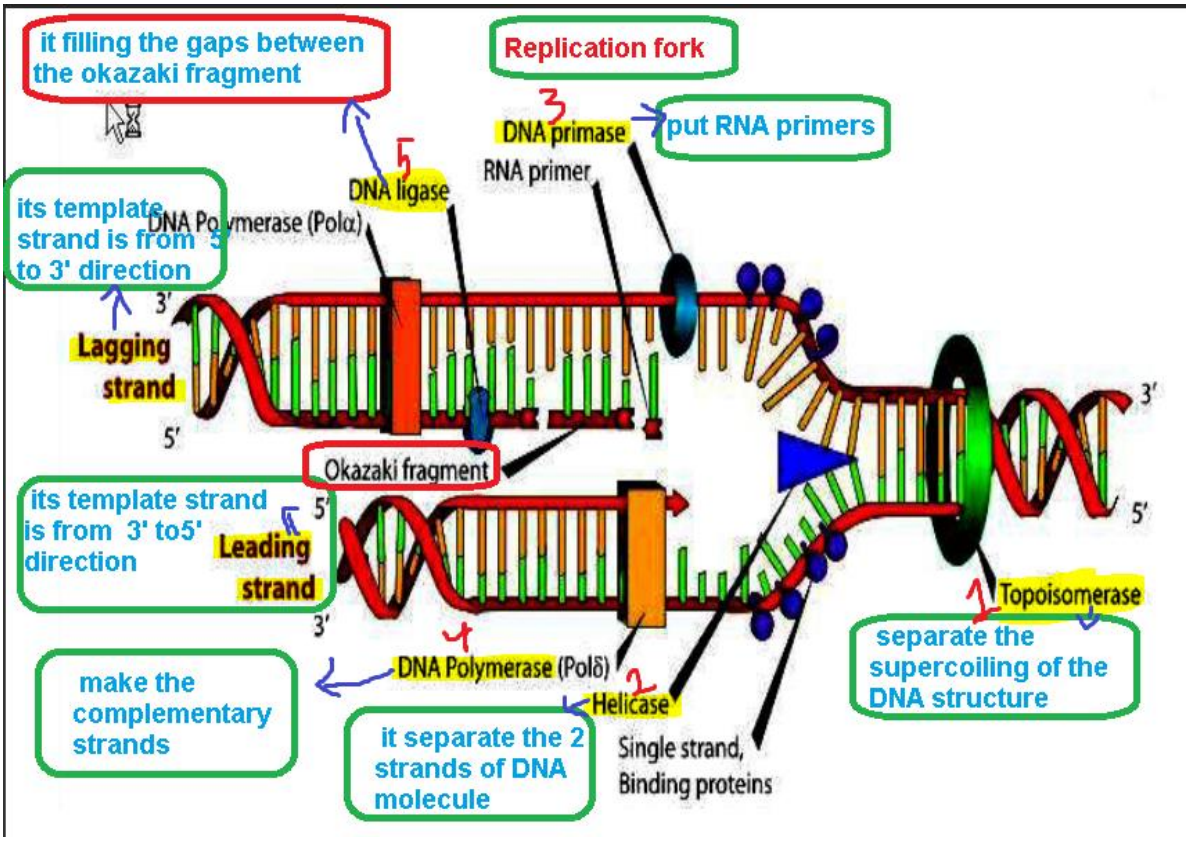
B) Replication occurs in cytoplasm (*Poxviridae*). These viruses have evolved (or acquired) all the necessary factors for transcription and replication of their genomes and are therefore largely independent of the cellular machinery.

so it has its own enzymes

Class I: Double-stranded DNA



بشكل مختصر وسهل يدخل الفيروس عالخلية ، يصيرله **uncoating** تروح ال **dsDNA** على النواة وهناك يصيرلها **replication** تماماً مثل ما أخذنا بالجينيتكس ، يعمل بروتينات بعدين **assembly** و **release** .

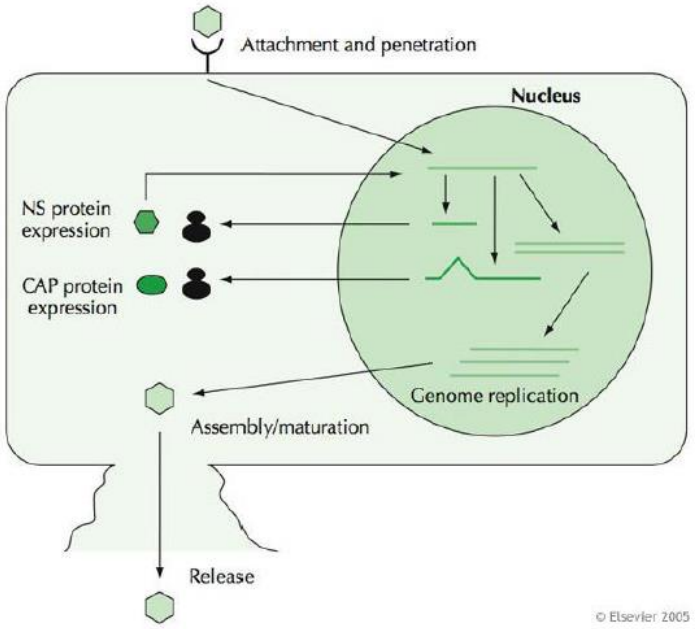


كل مرة يصير فيها **replication** رح يقصر ال **DNA** شوي ، مين يحل هالمشكلة؟؟

أكيد عرفتوه هو ال **telomerase** ، هاد الانزيم **use its own RNA as a template to build DNA**

Class II: Single-stranded DNA

- Replication occurs in the nucleus, involving the formation of a double-stranded intermediate which serves as a template for the synthesis of single-stranded progeny DNA.



Notes :

_ ال ssDNA يُعامل معاملة ال leading strand ، يرتبط فيه ال DNA dependent DNA polymerase يعمل لها complementery strand بعدين يرجعوا ينفصلوا السلسلتين عن بعض بال 2ed round of replication ويرجع يرتبط فيهم DNA polymerase وهيك .

_ What about of protein synthesis in ssDNA & dsDNA , How does it occure ?

Replication is occure in nucleus ,

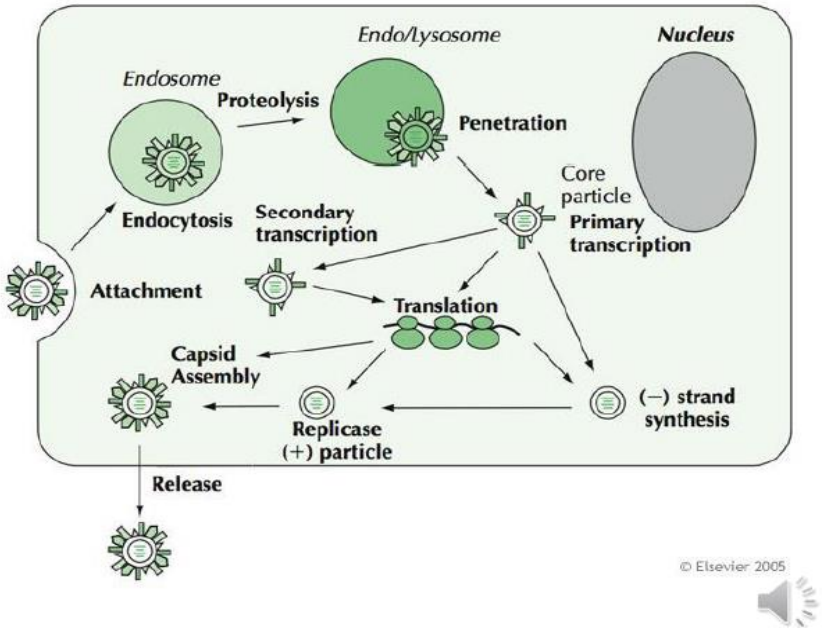
ولما يصير عنا host transcription ينتج ال mRNA بعد هيك

It exit the nucleus & go to the ribosome to make protein synthesis .

_ في ال DNA viruses مومهم اذا كانت ال strands + او - .

Class III: Double-stranded RNA

- These viruses have segmented genomes.
- Each segment is transcribed separately to produce individual monocistronic mRNAs.



_ ds RNA viruses : it contain 2 strand one of them is (+) sense & another one is (-) sense .

لما تصير عملية ال **replcation** ينفصلوا السلسلتين عن بعض بعد هيك عن طريق انزيم **RNA dependent RNA polymerase** ال **(+)sense** رح تكون ال **complementery** الها **(-) sense** ، وال **(-)sense** تكون المكملة الها **(+) sense** . هيك تكون خلصت عملية ال **replication** شو بالنسبة لل **protein synthesis** ؟؟

ال **(-) sense** رح ينفصل وماله علاقة أبداً بتصنيع البروتين .

ال **(+) sense** يروح عالرايبوسوم ويصنع ال **viral proteins** .

Class IV: Single-stranded (+)sense RNA

- These can be subdivided into two groups:
  - Viruses with polycistronic mRNA. As with all the viruses in this class, the genome RNA forms the mRNA. This is translated to form a polyprotein product, which is subsequently cleaved to form the mature proteins.
  - Viruses with complex transcription. Two rounds of translation (e.g. *Togavirus*) or subgenomic RNAs (e.g. *Tobamovirus*) are necessary to produce the genomic RNA.

_ ss(+) sense RNA :

هي strand وحدة صح ؟ ، يصيرلها replicaton عن طريق ال RNA dependent RNA pol وتنتج سلسلة مكملة الها تكون (-) sense شو نستفيد منها بما انها ما تقدر تروح عالرايبوسوم وتعمل بروتينات ؟؟

تضل تشتغل as a template لتصنيع ال (+) sense لأنه (+) sense وحدة ما تكفي لتصنيع البروتينات كلها وباقي ال + الناتجين يضلوا as aviral genom لل new viruses .

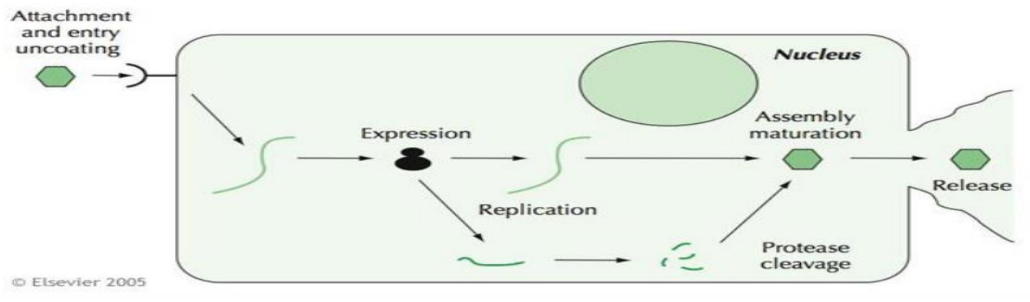
ملاحظة صغيرة مو مهمة حالياً :

ال RNA dependendent RNA pol يلي يعمل سلاسل مكملة تروح عالرايبوسوم وتصنع البروتينات يختلف عن ال RNA dependent RNA pol يلي يعمل السلاسل المكملة الخاصة بعملية ال replication .

Polycistronic mRNA :

لما يروح على الرايبوسوم ويصيرله translation يطلع البروتين قطعة وحدة ، يصيرلها cleavage عن طريق انزيم اسمه protease .

Class IV: Single-stranded (+)sense RNA



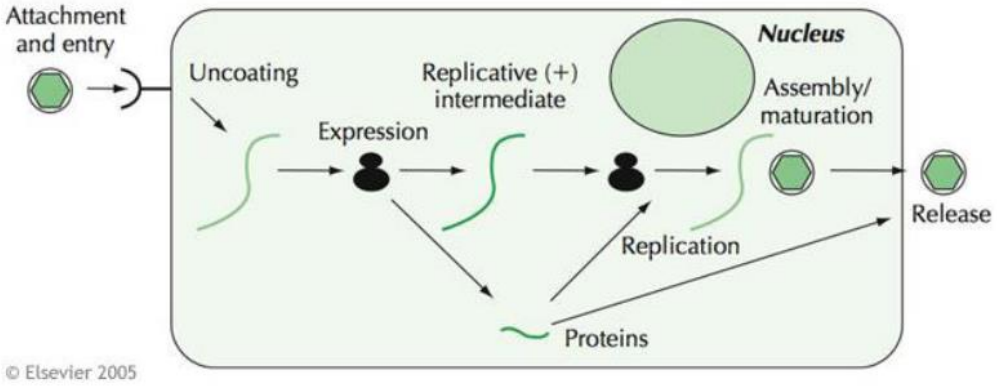
Class V: Single-stranded (–)sense RNA

- The genomes of these viruses can be divided into two types:
  - Segmented genomes
    - First step in replication is transcription of the (-)sense RNA genome by the virion RNA-dependent RNA polymerase to produce monocistronic mRNAs, which also serve as the template for genome replication.
  - Non-segmented genomes

_ ss(-)sense RNA :

هو (-) يجي ال RNA pol يعمل له سلاسل مكملة تكون (+) sense منها تروح عالرايبوسوم وتصنع ال viral proteins والباقيات تشتغل as a template لنطلع (-) sense من جديد .

Class V: Single-stranded (–)sense RNA

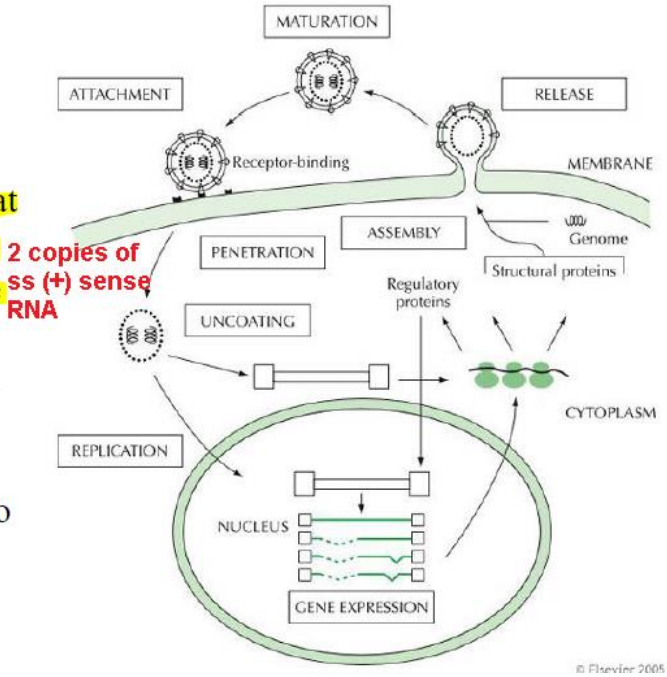


Class VI: Single-stranded (+)sense RNA with a DNA Intermediate

such as HIV virus

- Retrovirus genomes are (+)sense RNA but unique in that they are diploid, and do not serve directly as mRNA, but as a template for reverse transcription into DNA.

2 copies of ss (+) sense RNA



lecture 19 viral life cycle Tuesday 21. Dec. 2021

* HIV ~~life cycle~~ replication cycle:-

- HIV:- enveloped single strand (+) sense RNA.

[1] يرتبط مع ال cD4 receptor على ال T-cells ، ويحتاج كمان لـ coreceptors يلي هي:- (CXCR4 + CCR5) وهاي الخطوة نسميها Attachment.

[2] fussion between cell membrane & viral envelop.

[3] يدخل فقط ال nucleocapsid على ال host cell بينما ال envelop يبقى جزء من جدار الخلية (مهمة هاي المعلومة) بالرغم من أنه ال envelop يحتوي على ال viral glycoprotein إلا أنه الجسم ما يعتبرها كأنها nonself & يطلعها خارج الخلية، وهاي الخطوة كلها هي ال penetration

[٤] تحصل عملية ال uncoating لـ ال HIV يحتوي على 2 copies of ssRNA ، وبالتالي يتفكك ال RNA وال capsid.

[٥] رح يشتغل لي اسمه (Reverse transcriptase complex) عليه إنزيمات رح نحكي عنهم واحد واحد.

① reverse transcriptase enzyme ←

use RNA strand as a template to synthesis ~~DNA~~ complementary DNA strand, in other word it is RNA Dependent DNA polymerase

ال RNA strand كان (+ sense) لـ ال DNA رح تكون -sense

ينتج عنا (RNA-DNA intermediate) (فيه سلسلتين و وحدة DNA والثانية RNA)

② RNase enzyme:

it distroye the RNA strand.

اما ال DNA strand رح ترتبط مع DNA polymerase تعمللها replication و تحولها لـ (Ds DNA) ، يدخل للنواة.

③ integrase enzyme ←

هاد الإنزيم داخل النواة يعمل sticky ends على ال DNA يلي اما من الفيروس و ال DNA تاع ال our cells.

لأنه طويل تركته بخط ايدي بعتذر على سوء الخط

اذا في شي مو مفهوم ارجعولي يا حلوين

بعد ين يعملوا integration 6 يعني it is integrate viral genom with celluler genome تاع ال host cell. بعد هيك يستخدم ال celluler machinery ليعمل ~~replication~~ transcription . ال HIV 6 هو موضوع it dominate on the cell & use all the celluler resorces for it's own benifit.

وبالتالي يجبرها انها تظل بال replicative phase.

و بهاد المرحلة يصير عنا transcription لل celluler & viral genome at the same time.

- الناتج الوحيد هو mRNA .

(كان ال viral DNA ← - sense و بالتالي ال mRNA هو +sense) . هاي موجودة بالمحاضرة .

- يغادر ال mRNA النواة و يروح عالرايبوسوم ليعمل translation .

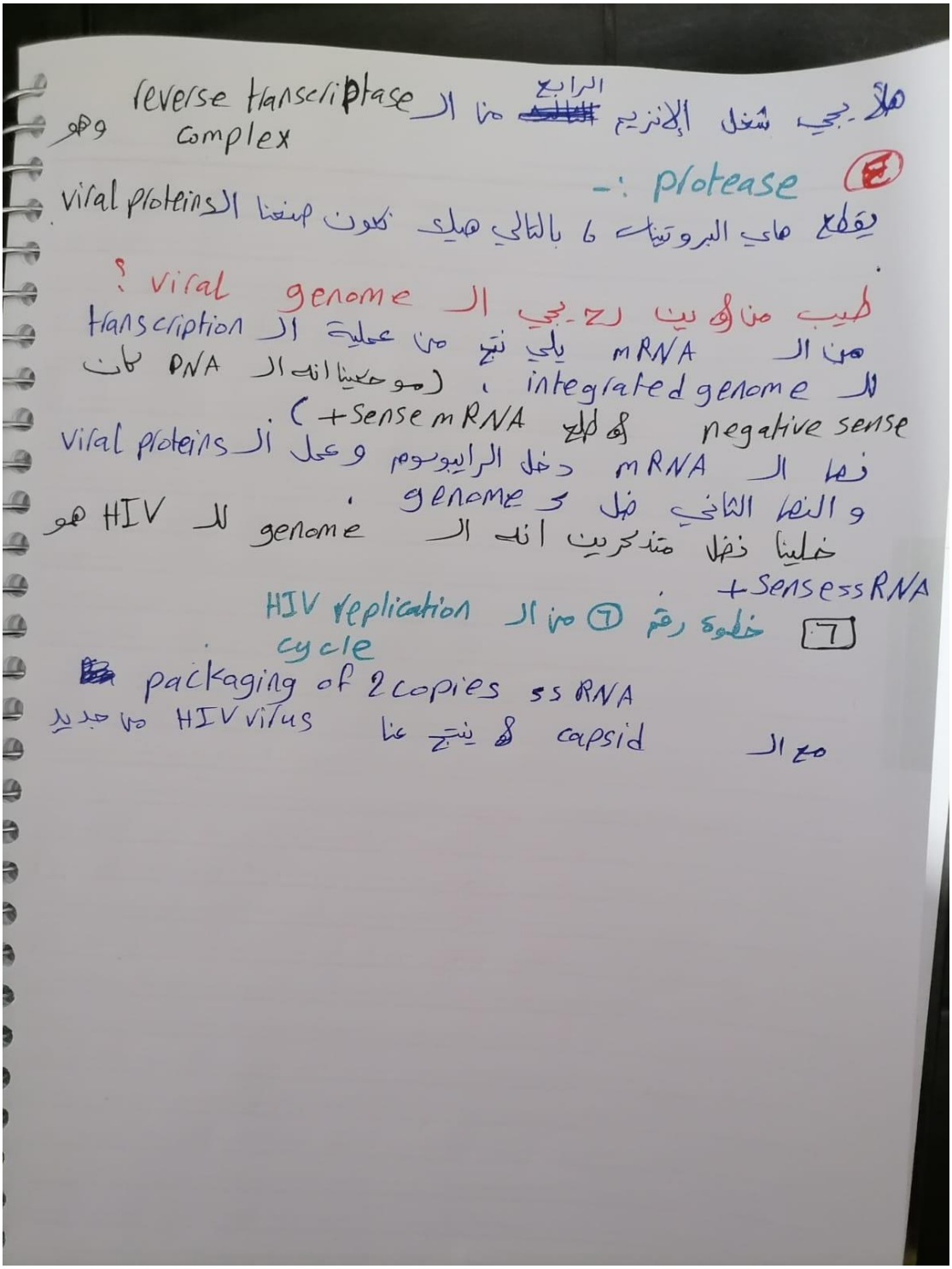
شكل ال translation تكون ← poly proteins .

شو يعني ؟؟

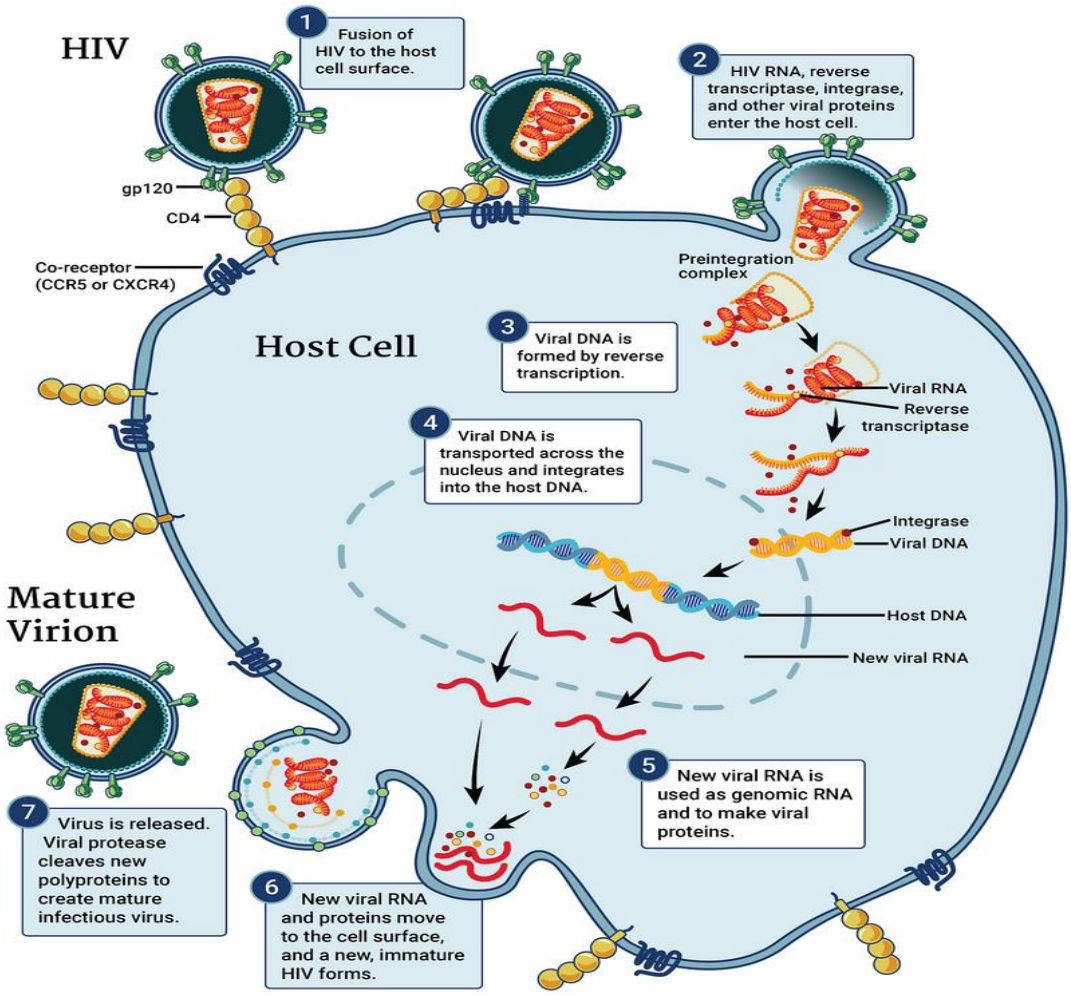
هلأ قبل شوي حكينا انه في عنا فيروسات تعمل mono cistrones صح ، ومعناها :-

Mono cistronic mRNA:- each gene is encoded into a separate protein.

لكن بال HIV يدخل ال mRNA ~~كامل~~ عالرايبوسوم و يطلع poly proteins مقطعة و مبدئ يعني سلسلة من البروتينات المتصلة .



هاي الصورة مو من السلايدات بس حلوة وبتلخص الخطوات : وفي فيديو رح أحطه بالبوست ان شاء الله



Note :

_ all RNA viruses replicate in the cytoplasme except 2 , HIV & Influenza virus they are replicate in nucleus

_ All DNA viruses replicate in the nucleus except poxvirus , it replecate in the cytoplasme .

Class VII: Double-stranded DNA with RNA Intermediate Hepatitis B virus

- This group of viruses also relies on reverse transcription.
- Unlike the retroviruses (class VI), this occurs inside the virus particle during maturation.
- On infection of a new cell, the first event to occur is repair of the gapped genome, followed by transcription.

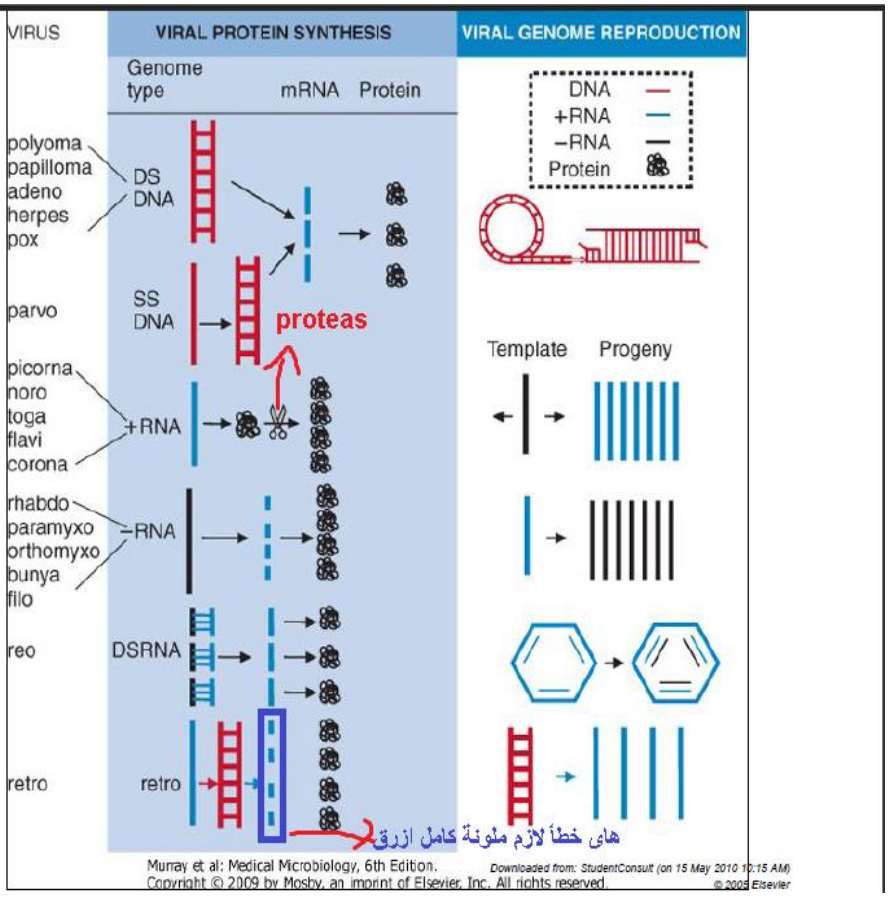
NOTES:

_ Hepatitis B viruse is partial DNA virus .

Bind to the receptor on target cell -→ penetration -→uncoating -→partial dsDNA genome .

ال partial DNA يرتبط مع ال DNA dependent RNA pol يعمل replication بالنواة ، يعمل transcription يعطينا mRNA نصهم يروح عالرايبوسوم ويعملوا viral protein synthesis والباقي بدهم يعملوا ال viral genom ... تمام لهون

ال HBV هو DNA virus ويلي عندي هي mRNA كيف يرجع DNA ؟؟ يلي بيصير أنه يجي ال reverse transcriptase يرتبط مع ال (+)sense mRNA ، يعمل RNA – DNA intermediate (ال DNA المكملة هي (-) sense) يجي ال RNAase يكسر ال RNA وتضل ال DNA ، يرتبط معها DNA like component يعملها ds DNA بس قبل ما يكملها ينفصل ويخليه partial DNA strand .



هاد السلايد تلخيص لكل ال **replication method** بس ناقصها ال **hepatitis B** .

الدرج الأحمر يعني **ds DNA** .

الأزرق المقطع معناها **monocistronic mRNA**

lecture 19 - viral lifecycle (Tuesday) 21/Dec. 2021

* Slide 39:-

- dsDNA —transcription (nucleus)→ monocistronic mRNA.
so it encode into separate proteins after translation.

* + sense RNA (conected blue):-
يروح مباشرة عالرايبوسوم 6 يعطينا polyprotein 6 يجي إنزيم الـ protease و يقطعه لـ different proteins.

* (-) sense RNA (connected Black):-
بعمل complementry +sense RNA 6 تكون as individual (+) sense mRNA
بالتالي هي monocistronic تروح عالرايبوسوم ~~تعطينا~~ يصيرلها ~~تعطينا~~ translation كل واحد منها يعطينا specific protein.

* dsRNA
حكينا هو segmented بالتالي ~~segment~~
each segment encode to one protein.
يعني هو monocistronic

* Retro (HIV):
هو ss (+)sense RNA 6 يصيرله reverse transcription يعطينا polyprotein.
يقطعه الـ protease.

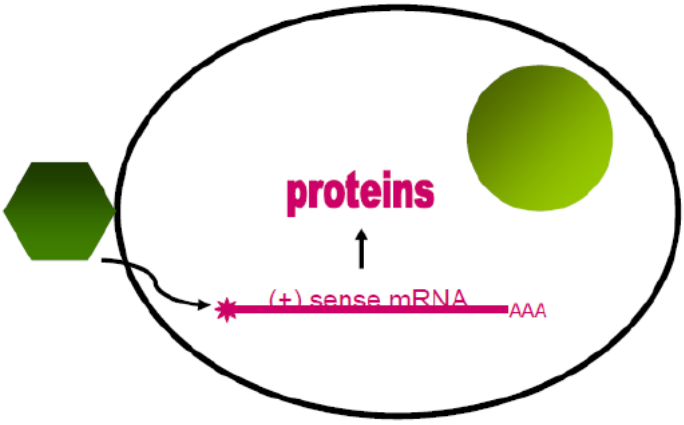
* Hepatitis B:-
يبدأ dsDNA (يعني درج احمر) يدخل النواة يصيرله transcription يتحول لـ mRNA (ازرق) بس إذا هو mono/poly cistronic واجب للمحاضرة الجاي.

All animal RNA viruses code for a Polymerase

- Positive/negative/double-stranded RNA virus genomes all encode a RNA-depend RNA polymerase.
- RNA-depend RNA polymerase is associated with negative RNA viruses.
- Reverse transcriptase is associated with retroviruses.

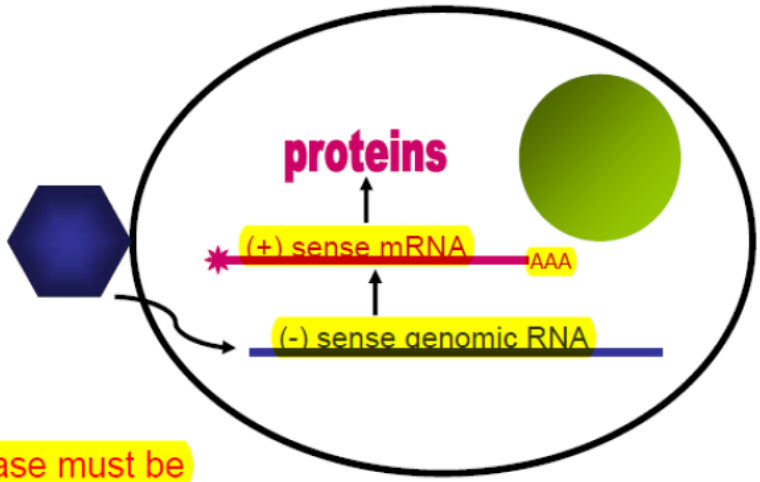
هلأ السلايدات هدول توضح ال **protein synthesis** حكيناهم بنفس الوقت يلي كنا نحكي فيه عن ال **replication** بس شوفوهم .

PLUS (POSITIVE) sense RNA GENOMES (+RNA)



Single-strand positive-sense RNA- the virus genome is the virus mRNA.

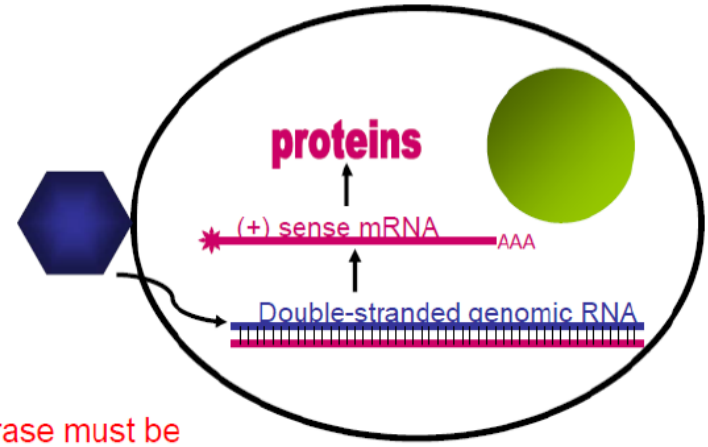
Minus (negative) sense RNA genomes:



RNA polymerase must be packaged in virion.

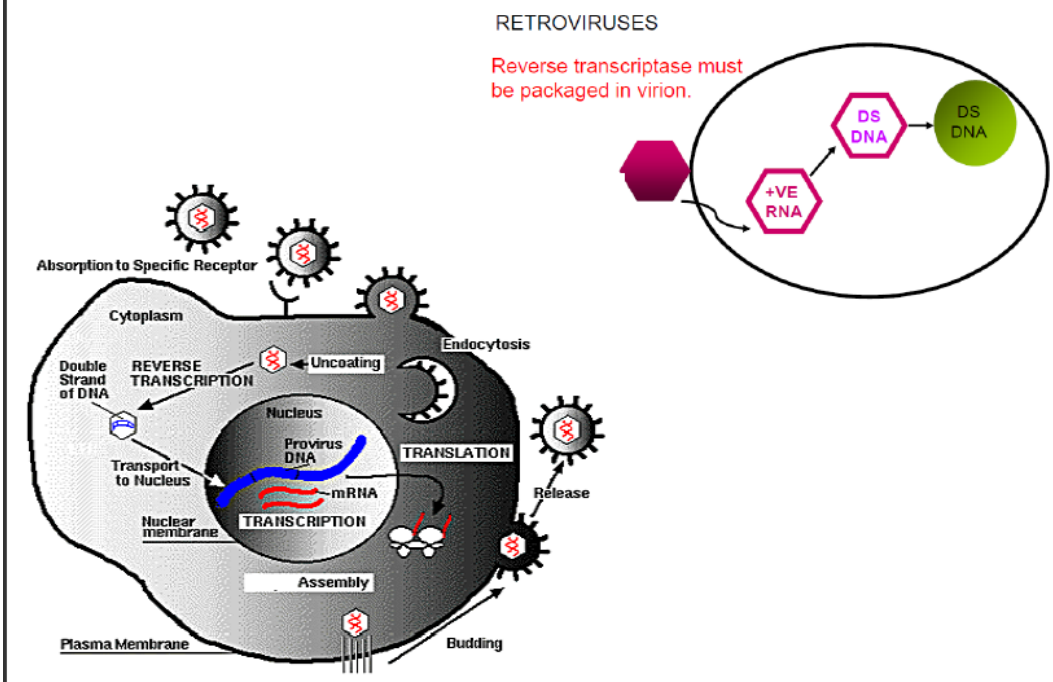
Single-strand negative-sense RNA- virus mRNA is transcribed from the parental genome.

Double-stranded RNA genomes:



RNA polymerase must be packaged in virion.

Double- stranded segmented RNA- individual virus mRNAs are transcribed separately off the parental RNA segments using a transcriptase associated with each segment



Retrovirus replication

"مزاجك أغلى ما تملك فاجعله مرتفعاً،
لتقرأ، لتكتب، لتعمل، لتتفاعل بإيجابية،
لهذا لا تعطي أي مخلوق فرصة لتعكيره."

بالتوفيق إن شاء الله