MICROBIOLOGY

بسم الله الرحمن الرحيم

MID – Lecture 2
1) Viral Classification 2
2) Replication and Pathogenesis 1

﴿ وَإِن تَتَوَلَّوْا يَسْتَبْدِلْ قَوْمًا غَيْرَكُمْ ثُمَّ لَا يَكُونُوا أَمْثَالَكُم ﴾

اللهم استعملنا ولا تستبدلنا

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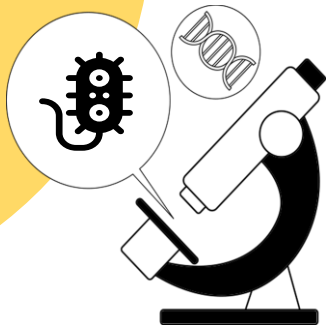


Short Quiz for Viro 1

- https://docs.google.com/forms/d/e/1FAIpQLScl0G55W7ZF6XvAv5cyhOFJZpsQFtQg0HPg8xAu9Ih4WRkzyQ/viewform?usp=sf_link

Virus Classification

- Historically based on:
  - Host preference: Plant, insect, animal, human
  - Target organ: respiratory, hepatic, enteric, etc.
  - Vector: arboviruses

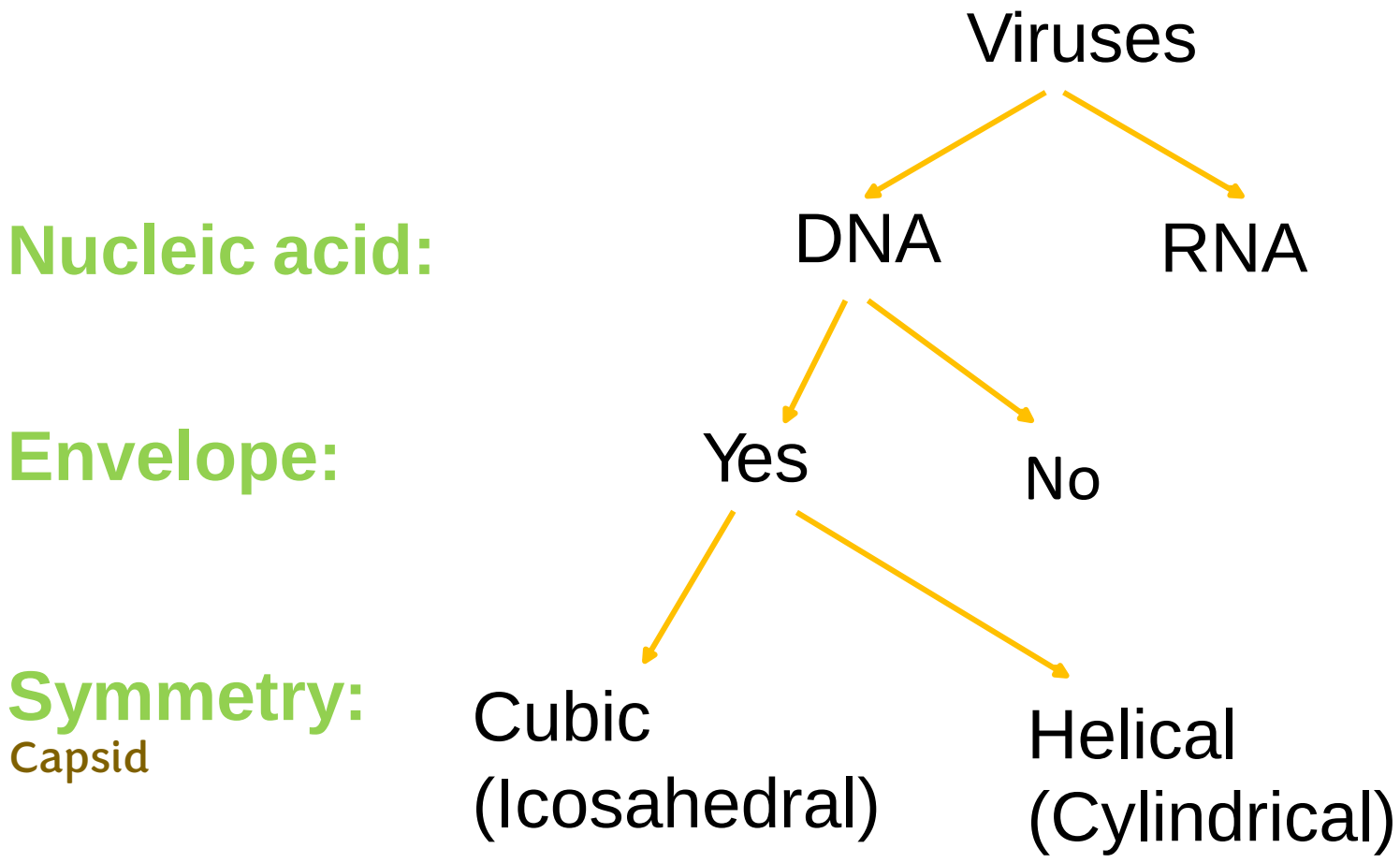
Certain viruses need an intermediary "middle man" or vector, such as an insect, to transmit them instead of spreading directly between humans. These viruses are referred to as arboviruses.

- Overlapping, inconsistent
- Classification is Currently based on molecular biology of genome and biophysical structure

No DNA virus shares the same sequence of another virus

Viruses can infect both plants and animals, and also can target multiple systems (respiratory for ex.) thus making this classification overlapping which makes the previous historical classification invalid

Virus Classification



A virus's characteristics never change; for example, the shape of the capsid remains constant for the same virus, DNA does not turn into RNA (Retrovirus is an exception, which will be explained later), and if a virus has no envelope, it cannot acquire one later.

Most Virus. Classification (Common) Classification

DNA

- Hepatitis **B** → Primarily affects the liver (can sense pain there clinically) and causes hepatitis (inflammation of the liver) which may lead to jaundice
- Human Papilloma Virus → Causes Warts + Cervical cancer risk factor
- Parvovirus B19
- Adenovirus
- Herpesviridae → Mouth rash + common cold ulcer
- Polyomaviruses → Cancer risk virus
- Papovaviruses
- Poxviruses

RNA

Are mostly respiratory effectors

- Influenza
- RSV
- Parainfluenza

(Respiratory)

- Hepatitis **A, C, D, E**
- Enteroviruses → Goes to GI
- Encephalitis viruses
- Measles, Mumps, Rubella — MMR vaccine used for them
- Norwalk, Rotavirus
- Virtually all others

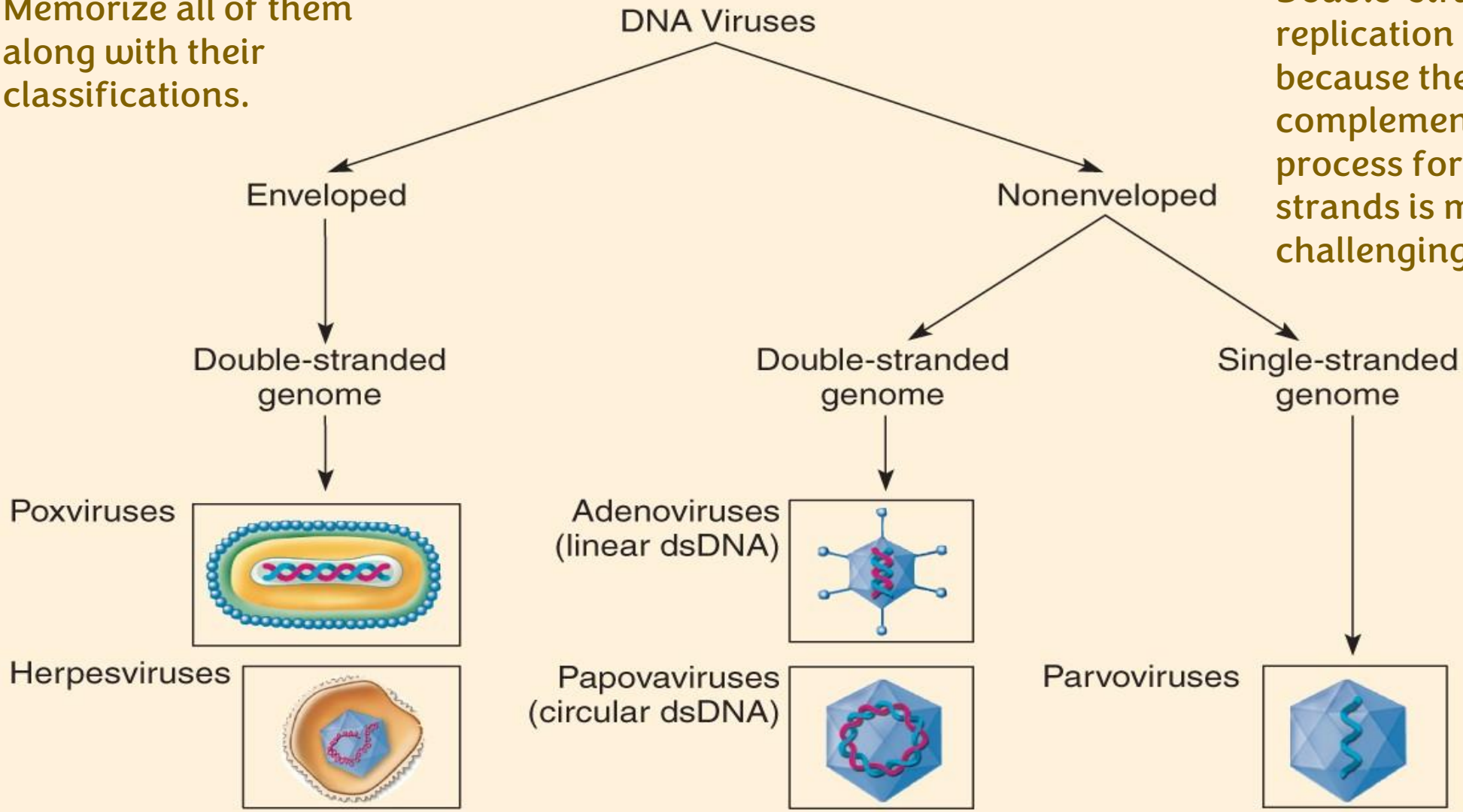
If a virus is being questioned about and it isn't mentioned here or in the images, it is an RNA virus

Memorize everything.
Will be elaborated on later

TABLE 6.2 Medically Relevant DNA Virus Groups

Memorize all of them along with their classifications.

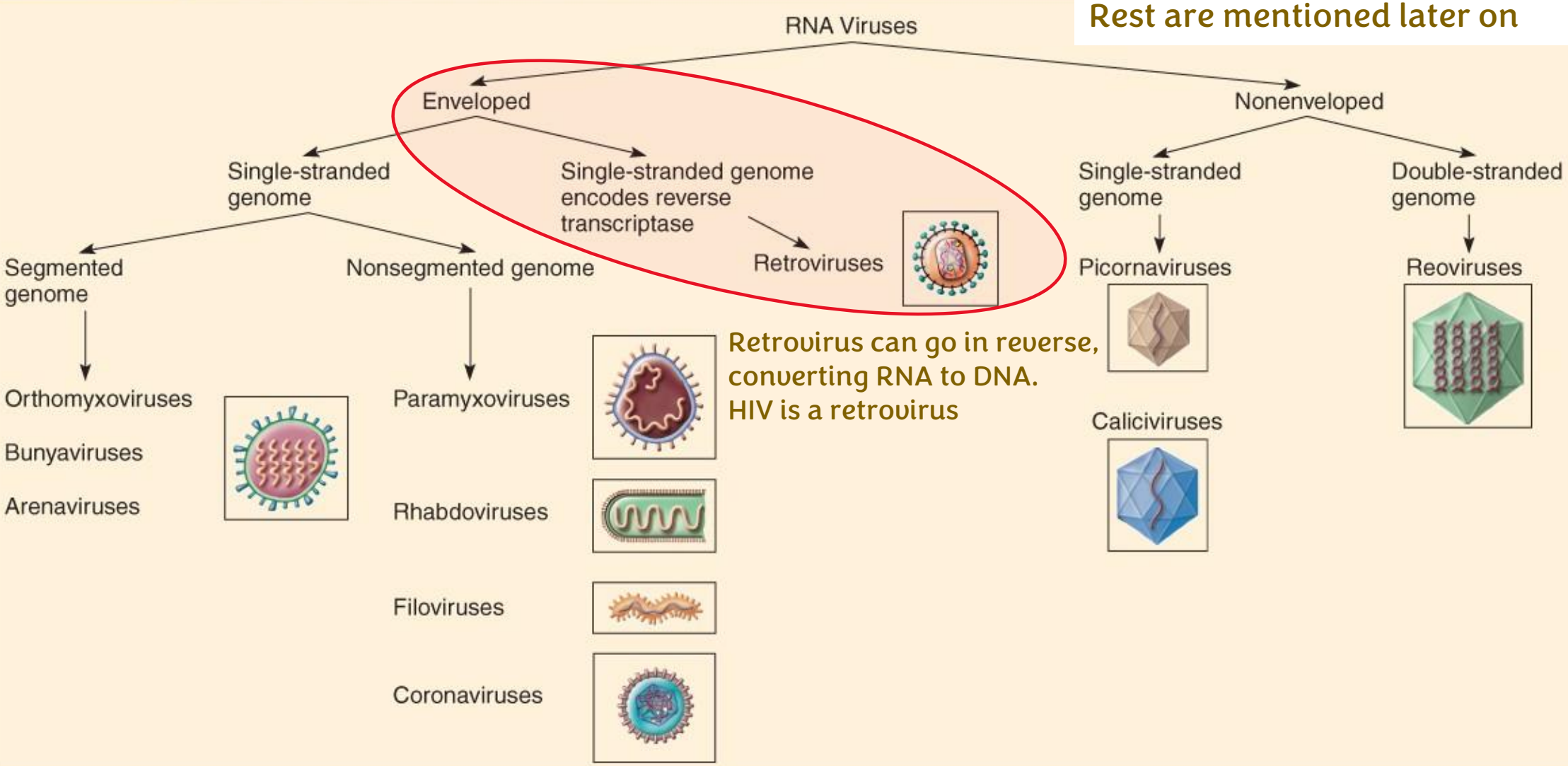
Double-strand replication is easier, because the complementary process for single strands is more challenging.



Source: Adapted from: *Poxviridae* from Buller et al., National Institute of Allergy & Infectious Disease, Department of Health & Human Services.

TABLE 6.3 Medically Relevant RNA Viruses

Just memorize Retrovirus here
Rest are mentioned later on



Retrovirus can go in reverse, converting RNA to DNA.
HIV is a retrovirus

Regarding Retroviruses

- Recall that
- DNA → RNA → mRNA → tRNA
- While going backwards isn't typically the norm, Retroviruses can reverse their RNA into DNA because of reverse transcriptase.
- HIV virus is a Retrovirus

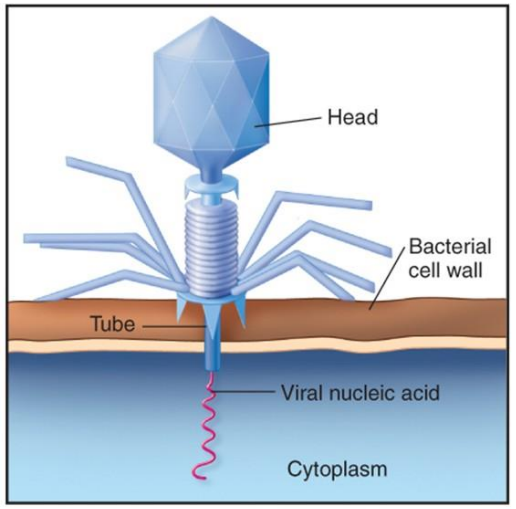
Viruses that Infect Bacteria

Only infects bacteria

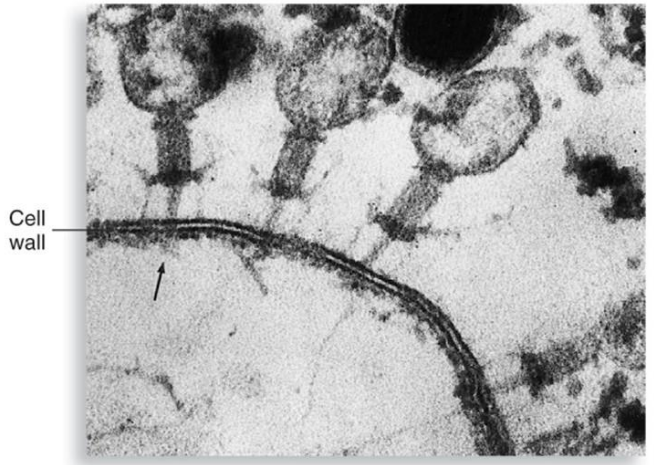
- Bacteriophage
- Most contain dsDNA
- Often make the bacteria they infect more pathogenic for humans

(Not always DNA)
DNA in bacteriophages is the key to infecting bacteria, the reasoning for that is as mentioned before, dsDNA are easier to replicate and since bacteria has a nucleoid (so no membrane, no cover) so even easier for it to replicate

Even if the Bacteria is initially non pathogenic it will turn pathogenic



(a)



(b)

Quiz?

ANSWERS ARE IN THE NEXT SLIDE

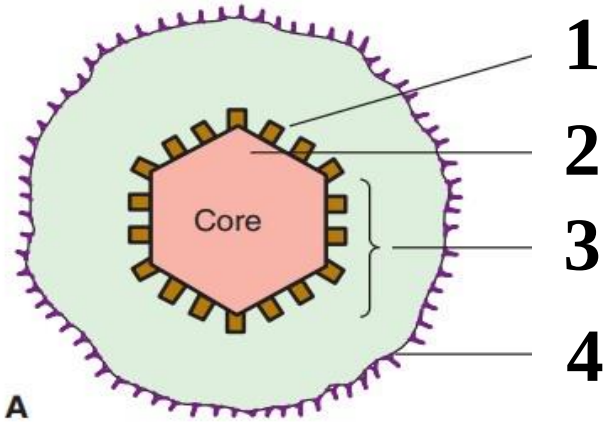
Q1. Identify the following structure/units in the attached diagram:

1……..

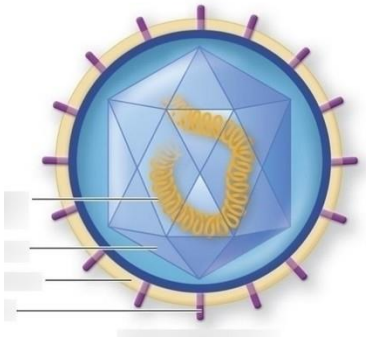
2……..

3……..

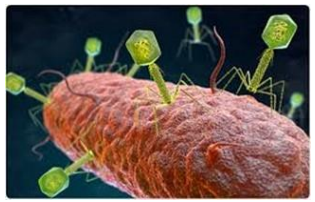
4……..



Q2. Describe the following viral structure:



Q3. Why does bacteriophage make bacterial infection more pathogenic to humans?



Remember that viruses can cause us cancer (sarcoma) via onceogensis

Answers

- Q1
- 1: Capsomere (since the arrow is on a single unit rather than the whole thing)
- 2: Genome (DNA or RNA)
- 3: Nucleocapsid
- 4: (Spike) (since the arrow is on a single unit rather than the whole thing which is an envelope)
- Q2
- Linear intact Single stranded (Can't specify if DNA or RNA), Icosahedral capsid, has an envelope, has spikes.
- Q3
- Viruses genetically mutate bacteria and add some drug resistant effects to them (Remember that Bacterial DNA isn't as preserved as ours)

2- Viral Replication and Pathogenesis

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صلّوا على الحبيب

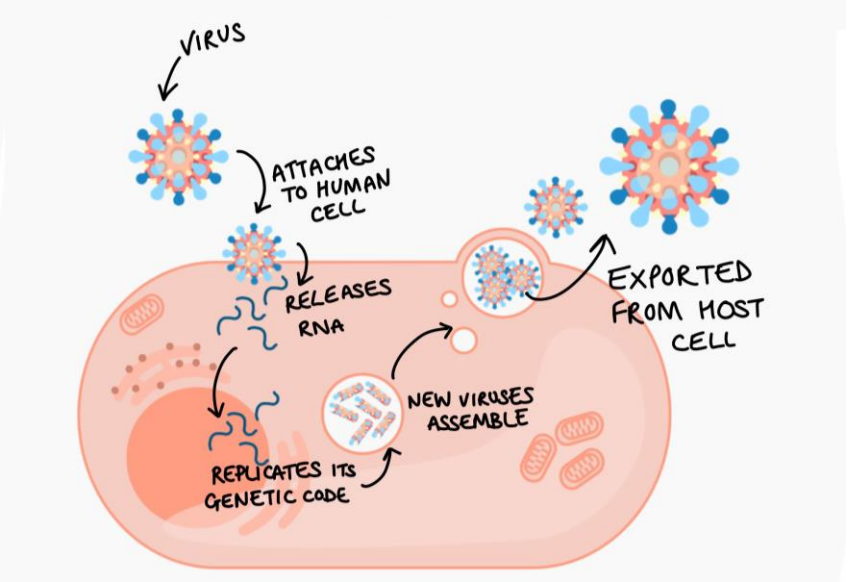
Objectives

1. Understand the steps of viral replication
2. Differentiate DNA and RNA viral replication
3. Understand steps of viral pathogenesis
4. Factors affecting viral pathogenesis
5. Outcomes of viral infections
6. Host Responses to Viral Infections

Viral Replication

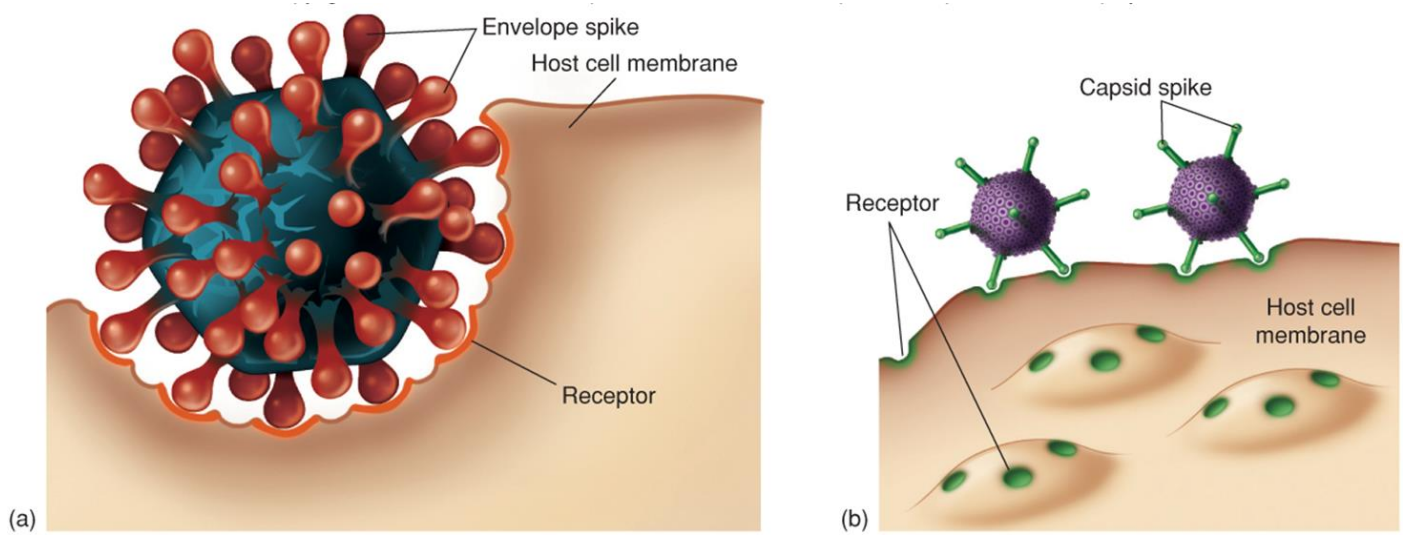
- The host cell is absolutely necessary for viral multiplication

1. adsorption (attachment)
2. entry
3. uncoating
4. transcription
5. synthesis of virus components
6. assembly
7. release



1. Adsorption (attachment):

- random collision
- interaction between specific proteins on viral surface and specific receptors on target cell membrane name of this process is called (tropism)
- some viruses may use more than one host cell receptor
- able to infect a limited spectrum of cell types



Spikes on the virus are important for this step, they attach to the envelope. If there isn't and envelope they attach to the capsule.
If spikes (receptor mediated which can either be specifically linked or commonly linked if it links with any plasma membrane of any cell type)

If no spikes, virus links via random collusion

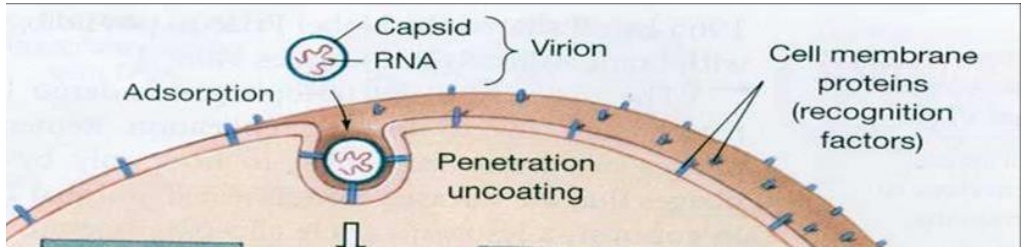
2. Entry (penetration):

- Flexible cell membrane of the host is penetrated by the whole virus or its nucleic acid

Most of the time

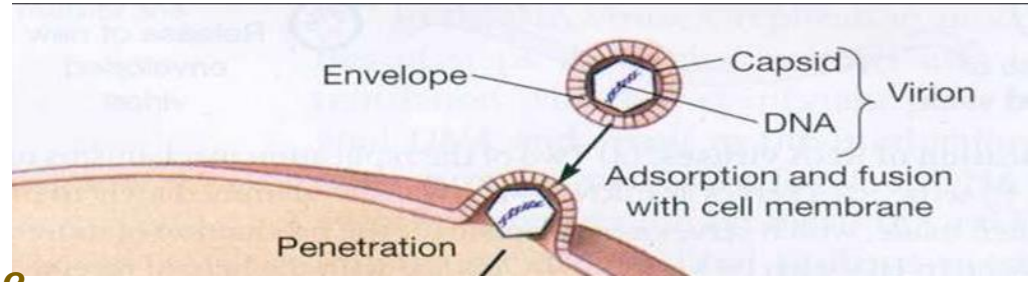
- 2 mechanisms
- Endocytosis: entire virus engulfed by the cell and enclosed in a vacuole or vesicle

((Primarily) for non-enveloped viruses only)



- The viral envelope can also directly fuse with the host cell membrane(for enveloped viruses only)

Easier since it has already a part of the plasma membrane

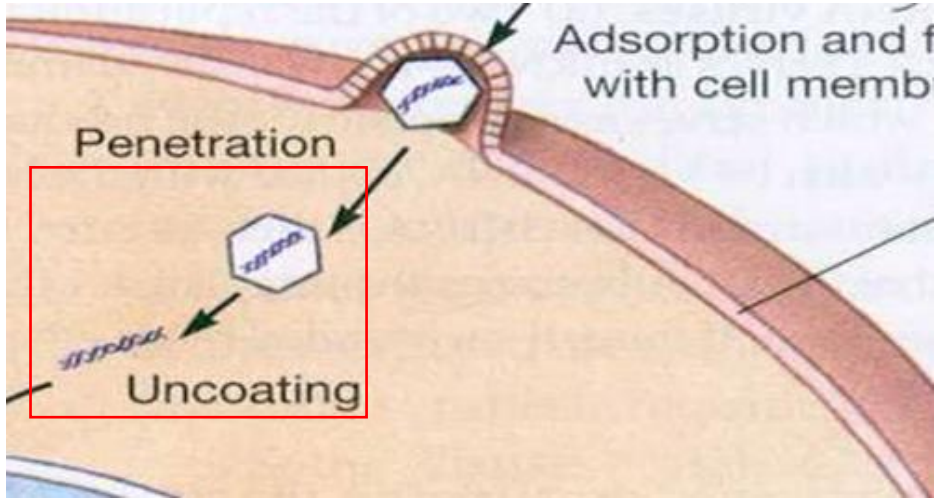


3. Uncoating

Naked

- release of viral genome
- cell enzymes (lysosomes) strip off the virus protein coat (capsid)
- virion can no longer be detected; known as the “eclipse period”

for enveloped viruses, the envelope is lost in the cell membrane



During the eclipse period, the virus is temporarily non-infectious (can’t enter and penetrate another cell) due to uncoating.

4. Transcription/Translation

a) DNA viruses:

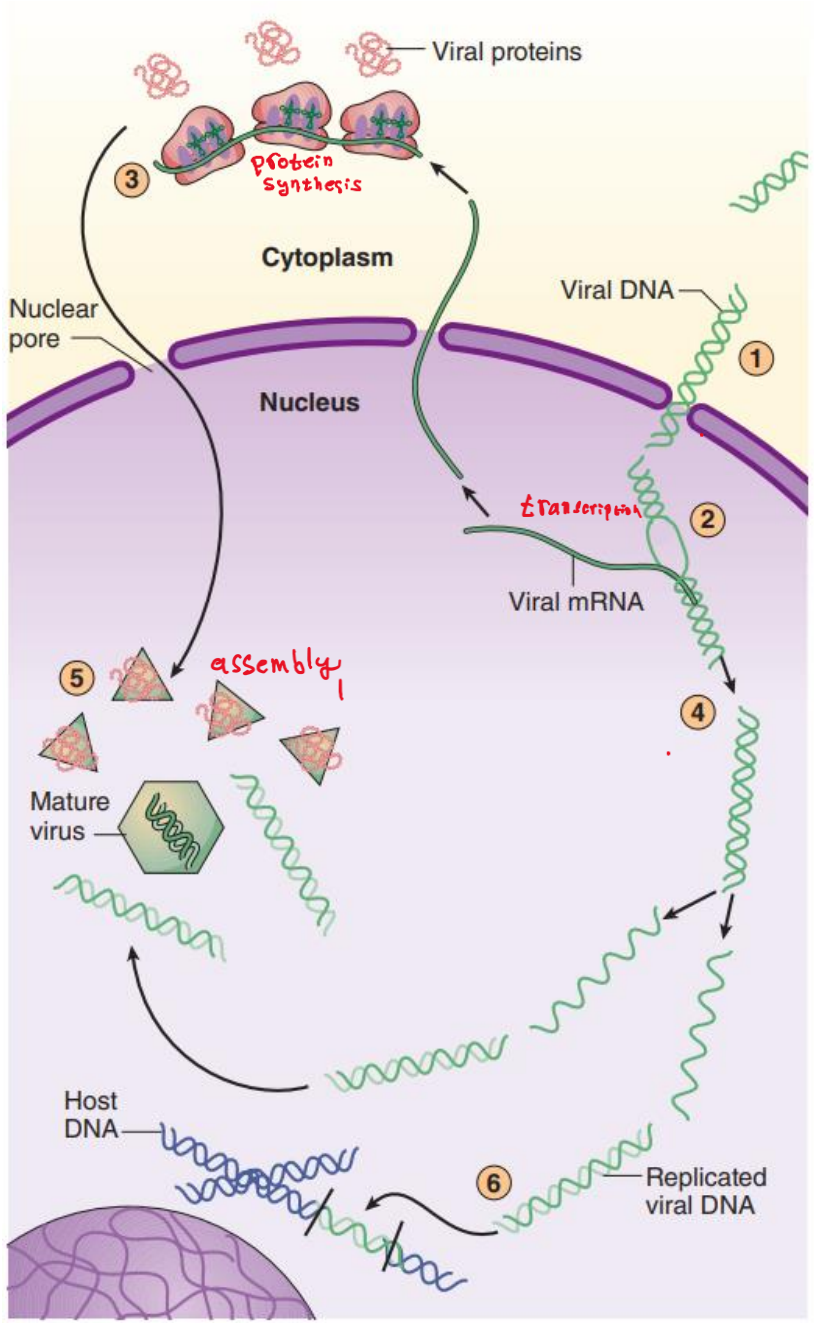
- replicate their DNA in host cell nucleus mediated by viral enzymes
- synthesize capsid and other proteins in cytoplasm using host cell enzymes
- new viral proteins move to nucleus where they combine with new DNA to form new viruses

Capsid

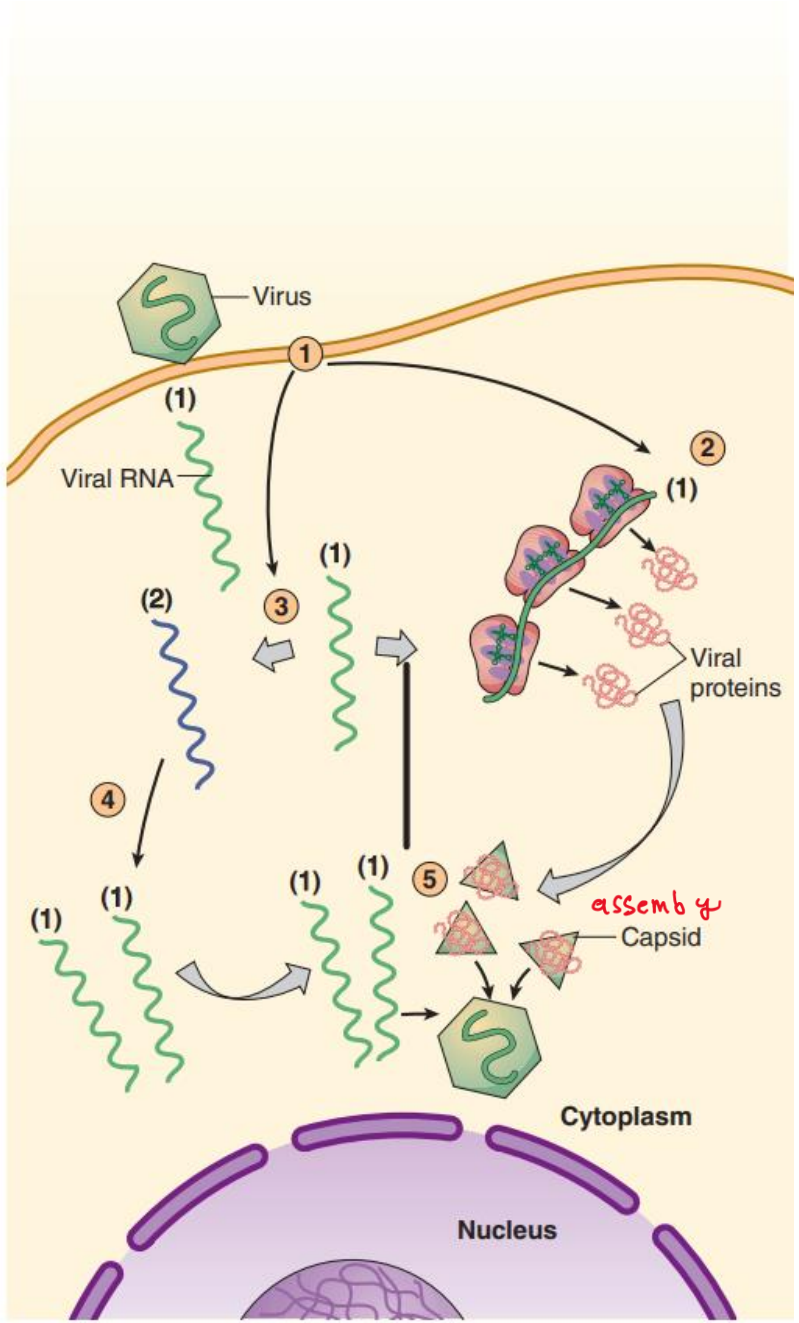
b) RNA viruses:

- “+” sense RNA acts as mRNA - viral proteins are made immediately in cytoplasm mediated by viral enzymes
- “-” sense RNA - 1^{st} makes a “+” sense RNA copy via viral enzyme

DNA has to get to the nucleus unlike RNA which goes to cytoplasm



DNA virus



RNA virus

DNA Virus is more dangerous and has a higher probability of causing cancer since it interacts DIRECTLY with the host's DNA and enters the nucleus

Image A (DNA Virus Pathway)

1) The DNA virus enters the host cell and transports its viral DNA into the nucleus through the nuclear pore (where mRNA usually exits the nucleus).
2) Once inside the nucleus, the viral DNA makes viral mRNA using the host cell's.
3) The viral mRNA leaves the nucleus and moves to the cytoplasm, where it is translated into viral proteins (especially capsid) by the host cell's ribosomes.
4) Back in the nucleus, the viral DNA is replicated, producing more copies of the viral genome, ((If the viral genome was a single strand, it fuses with the host DNA, so whenever our DNA replicates it replicates too)) this causes our DNA to break and be mutated.
5) Since the DNA can't leave the nucleus the capsid enters the nucleus and assembles with the viral DNA forming a new virus with the same characteristics of the old one

Examples of viruses with DNA genomes that can cause cancer (which are mentioned before):

1) Human Papilloma Virus (HPV). 2) Polyomaviruses

Image B (RNA Virus Pathway)

Occurs in the cytoplasm.

1) The virus enters the cell and the viral RNA genome is uncoated
2) As a positive-sense, single-stranded genome, the RNA is directly translated, producing viral proteins.
3) The newly synthesized positive-sense RNA molecules are assembled with viral structural proteins to produce new viruses.

Viruses do not have the metabolic enzymes as well as the ability to produce proteins. However, many viruses do carry specific enzymes that are essential for their replication such as polymerase.

During the COVID-19 pandemic, mRNA vaccines were widely used as a key tool in combating the virus. RNA alone doesn't infect our genome , since it isn't in the nucleus, so it is safe. Traditional vaccines often involve introducing whole pathogens or parts of them to provoke an immune response. In contrast, mRNA vaccines deliver genetic instructions to cells, which then produce the target protein (like the spike protein) and elicit an immune response.

5. Synthesis

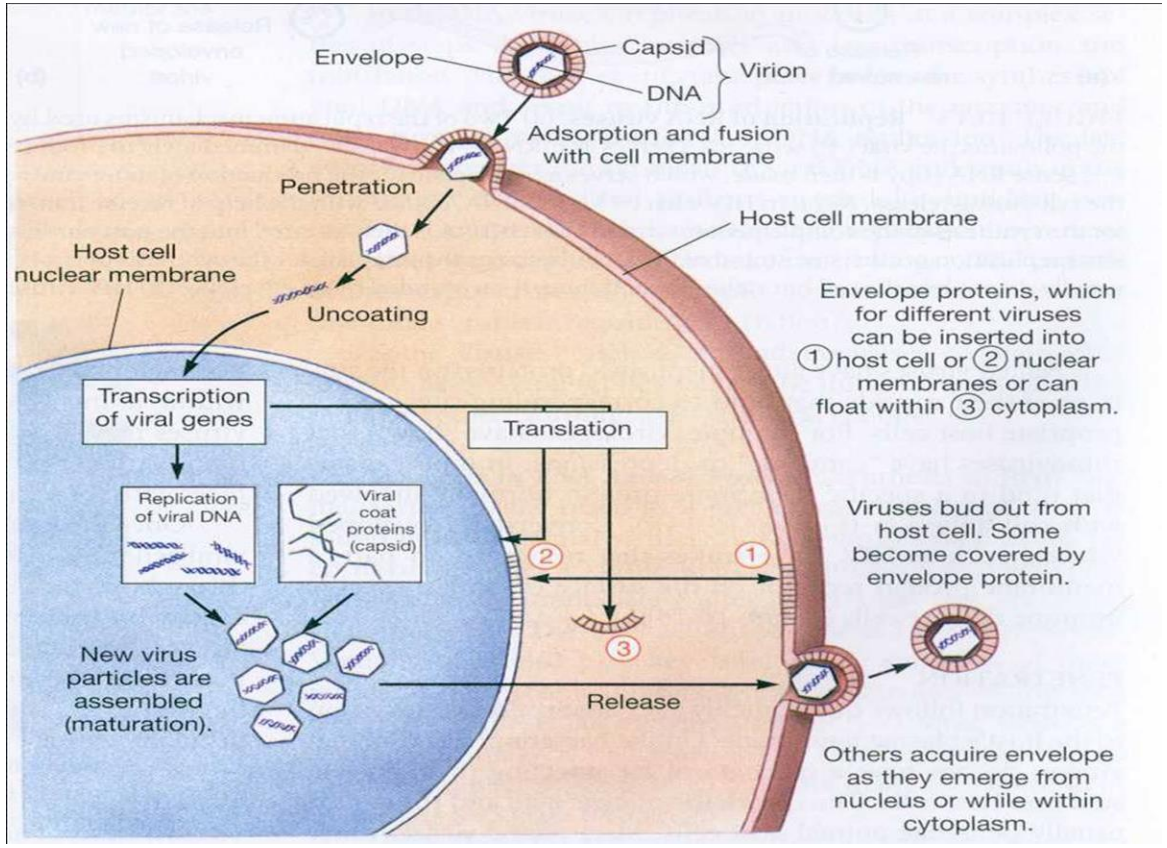
- Protein synthesis - 2 types
  - structural
    1- Capsid
    2- The envelope
  - non-structural (enzymes for replication)
- Nucleic acid synthesis
  - new virus genome
  - most often by a virus - coded polymerase or replicase; with some DNA viruses a cell enzyme carries this out

For Your Information

- Many viruses encode their own polymerases, known as replicases, to facilitate the replication of their genomes. This is particularly common among RNA viruses, which need specific enzymes to copy their RNA genomes. The replicase synthesizes new RNA strands from the viral RNA template. In contrast to RNA viruses, many DNA viruses rely on the host cell's enzymes for replication.

6. Assembly

- Mature virus particles are constructed from the growing pool of parts
- may take place in cell nucleus, cytoplasm or (with most enveloped viruses) at the plasma membrane



The envelope may be taken via 3 ways : when leaving plasma membrane (most likely), from the nuclear membrane or form it by itself)

7. Release

After this cell MAY die:
Non-enveloped: kills it
Enveloped: since it needs the cell's plasma membrane it doesn't damage the cell

- Nonenveloped and complex viruses are released when the cell lyses or ruptures
- Enveloped viruses are liberated by budding or exocytosis (without damaging the cell)
- Anywhere from 3,000 to 100,000 virions may be released, depending on the virus
- Entire length of cycle- anywhere from 8 to 36 hours

Viral Pathogenesis

- The process by which a viral infection leads to disease
- The majority of viral infections are subclinical
- The consequences of viral infections depend on the interplay between a number of viral and host factors

Many viral infections do not produce noticeable symptoms or clinical disease. These subclinical infections can still lead to immune responses, allowing the host to develop immunity without ever experiencing symptoms. Some viruses infect the cell and use 10% of the cell's material to replicate and cause a mild disease "self-limited" then released to infect another host. On the other hand some viruses shut down all the metabolic activities in the host cell and shift to viral metabolism via the usage of 100% of the cell's material and will generate more clinical symptoms.

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1	4 Regarding Hepatitis B	Causes **Junks**	Primarily affects the liver (can sense pain there clinically) and causes hepatitis (inflammation of the liver) which may lead to **jaundice**
V1 → V2	2		Added a quiz

Additional Resources:

رسالة من الفريق العلمي:

Extra References for the Reader to Use:

1. Jawetz Microbiology 27th Ed. Chapter 29

{فَقُلْتُ اسْتَغْفِرُوا رَبَّكُمْ إِنَّهُ كَانَ غَفَّارًا (10) يُرْسِلِ السَّمَاءَ عَلَيْكُم مِّدْرَارًا (11) وَيُمْدِدْكُم بِأَمْوَالٍ وَبَنِينَ وَيَجْعَل لَّكُمْ جَنَّاتٍ وَيَجْعَل لَّكُمْ أَنْهَارًا (12) }
[نوح]

حمى الله الأردن؛ وطنًا و قيادةً و شعبًا.