

Topic No. 4

Cards

Taxonomy

How to classify viruses?



بكل عنوان

In the past viruses were named **haphazardly**, based on the diseases they caused or on the place of their isolation.

They were grouped according to affinity to different systems or organs of the body (tropism). So, human viruses were classified as:

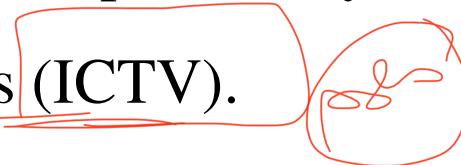
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Dermotropic: Producing skin lesions (smallpox, chickenpox, measles)

Neurotropic: Affecting the nervous system (poliomyelitis, rabies)

Pneumotropic: Affecting the respiratory tract (influenza, common cold)

Viscerotropic: Affecting visceral organs (hepatitis).

From the early 1950s, viruses began to be classified into groups based on their physiochemical and structural features. Nomenclature and classification are now the official responsibility of the International Committee on Taxonomy of Viruses (ICTV). 

Viruses are classified into two main divisions based on the type of nucleic acid they possess:

- Riboviruses:** Contain RNA
- Deoxyriboviruses:** Contain DNA.

Further classification is based on other properties like strandedness of nucleic acid, symmetry of nucleic acid, presence of envelope, size and shape of virion and number of capsomeres.

The Baltimore Classification

Is a virus classification system developed by David Baltimore, in this system viruses grouped into families, depending on their type of genome (DNA, RNA), single-stranded (ss), double-stranded (ds), etc.) and their method of replication.

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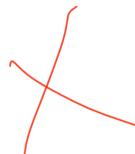
ATGC DNA
AUGC RNA

Class I

ds DNA (Small pox, Herpes, Papilloma)

Class II

ss DNA (Parvo)



Class III

ds RNA (Rotavirus)

Class IV

ss RNA -positive- (Polio, Rhino, Corona)

Class V

ss RNA -negative- (Measles, mumps, Rabies, Influenza)

Class VI

ss RNA -positive-(Retroviruses)

(replication intermediate DNA)

Class VII

ds DNA (Hepadnaviruses)

(replication intermediate RNA)

CCUSij

Before **replication** of viral nucleic acid can occur,
messenger RNA molecules **transcribed** from the virus genome encode new virus proteins.

In some RNA viruses, the viral RNA itself is the mRNA; in others, the virus genome is a template for the formation of viral mRNA. In certain cases, essential transcriptional enzymes are contained in the virion

By convention, mRNA is said to be in the plus (+) configuration. Its complement is said to be in the minus (-) configuration. This nomenclature is also used to describe the configuration of the genome of a single-stranded virus, whether its genome contains RNA or DNA.



For example, a virus that has a single-stranded RNA genome with the same orientation as its mRNA is said to be a **positive-strand RNA virus**.

A virus whose single-stranded RNA genome is complementary to its mRNA is said to be a **negative-strand RNA virus**.

The Baltimore classification



- All viruses must produce mRNA, or (+) sense RNA
- A complementary strand of nucleic acid is (-) sense
- The Baltimore classification has + RNA as its central point
- Its principles are fundamental to an understanding of virus classification and genome replication, but it is rarely used as a classification system in its own right

1- ssDNA Viruses:

- Small genome, 2-7 Kb
- Possibly due to unstable nature of ssDNA compared to dsDNA
- Circular genomes with the exception of Parvoviridae
(hairpin)
- No envelope
- Predominantly icosahedral capsids

2- dsDNA Viruses:

X

- Genome size varies from 5 to 1180 Kb
- Among the largest known viruses
- Large genome size attributed to stability of dsDNA
- Both linear and circular
- Low error rate during replication
- No dsDNA virus is known to infect plants
- Phages are dsDNA viruses (95%)

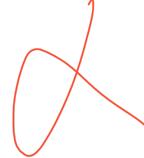
dsDNA viruses that infect humans (HSV, HPV and adenoviruses)

3- dsRNA Viruses:

- They utilize RNA dependent polymerase
- Icosahedral capsids
- Capsids stays intact inside cell. Why? Genome protection.
- Transcription occurs via viral RNA polymerases
- Reoviruses (dsRNA) are capable of infecting multiple species (plants, vertebrates, fungi). Not a common phenomenon.
- Rhabdoviridae infect multiple species as well
- The fact that they carry their own RNA replication/transcription proteins makes them more adept

4- (+) strand RNA:

Very common of plant viruses to be + ssRNA



Only one phage family is + ssRNA

RNA viruses have linear genomes

Similar to ssDNA viruses they are susceptible to nucleases and divalent cation degradation

Coronavirus has the largest genome of + ssRNA virus
(16-30 Kb)

5- (-) ssRNA Viruses:

- This group includes some of the deadliest viruses
Ebola, rabies, influenza, measles
- Only helical nucleocapsids
- Nucleocapsid seems to provide stability for RNA dependent RNA polymerase to generate + ssRNA
+ ssRNA=mRNA

6- Viruses With Reverse Transcription:

3 families belong to this group

Retroviridae, Ex. HIV \rightarrow infl

Hepadnaviridae, Ex. Hep B

Caulimoviridae, Ex. Cauliflower Mosaic Virus

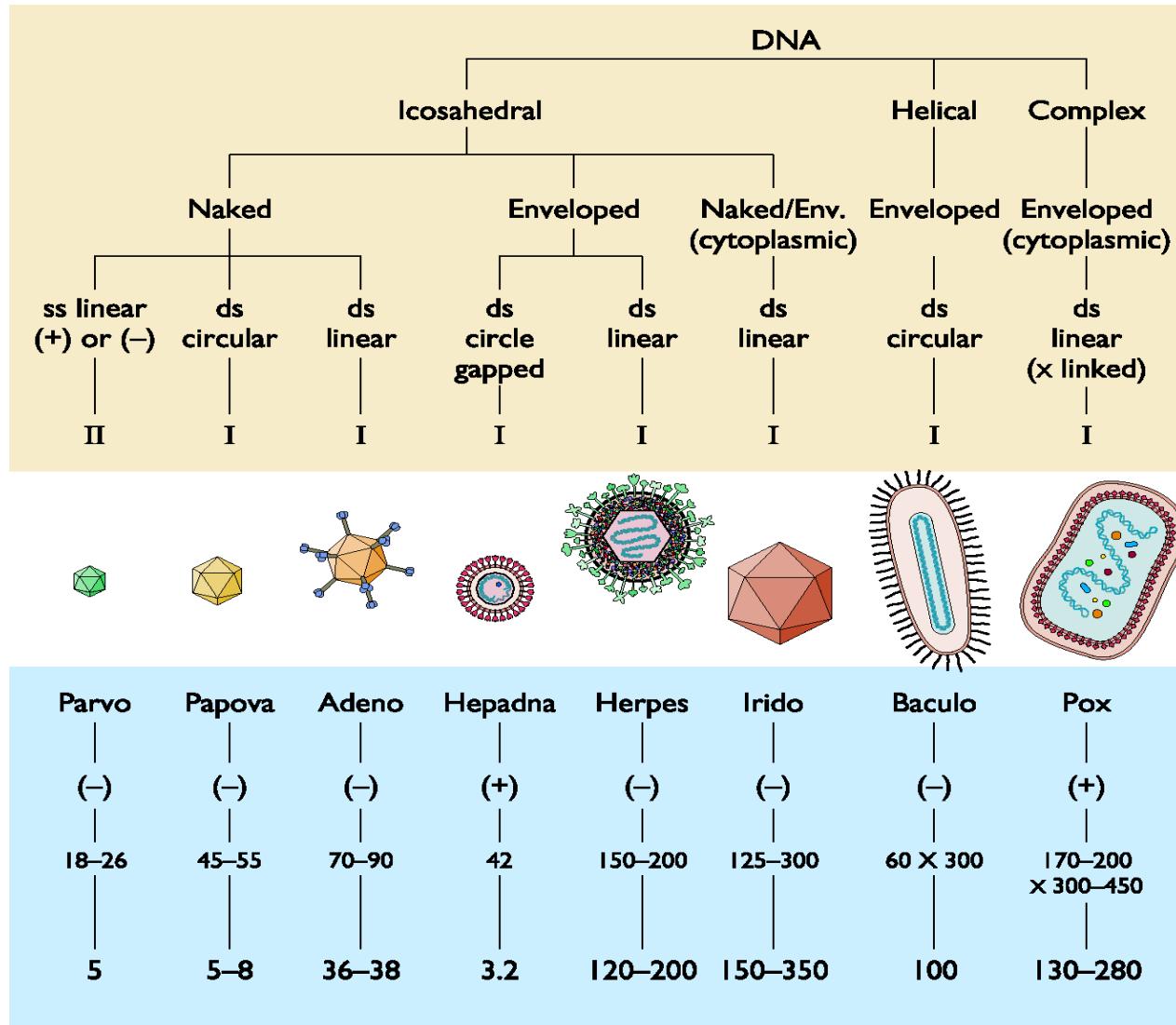
These families utilize enzyme that uses an RNA template to make DNA template

Reverse transcriptase is packaged in capsid

Similar to + ssRNA and - ssRNA that package the RNA dependent polymerase

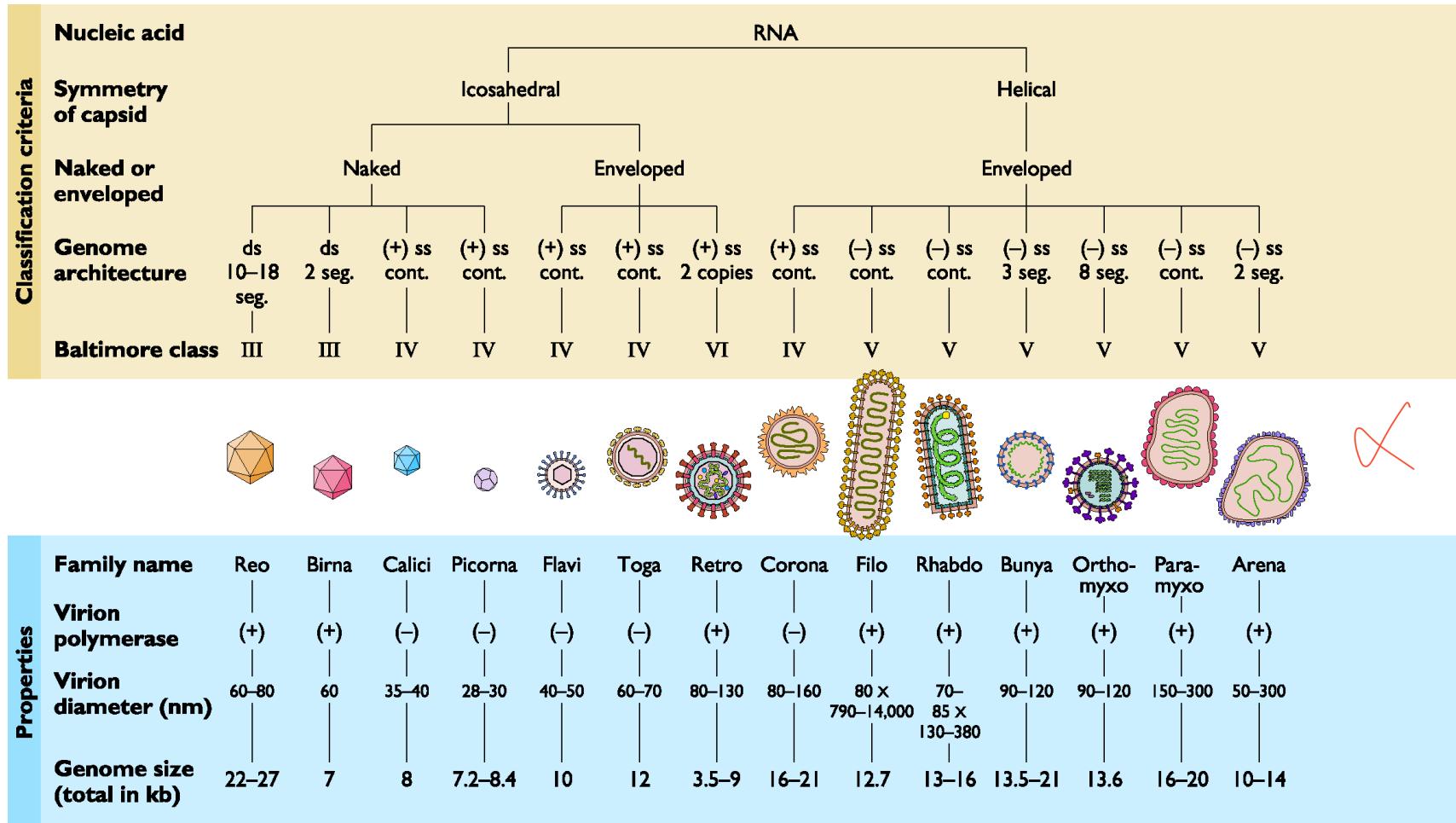
Retroviruses package 2 copies of their RNA genome in the capsid

DNA viruses



From Principles of
Virology Flint et al
ASM Press

RNA viruses



From Principles of Virology Flint et al ASM Press

الجنة الدولية لتصنيف الفيروسات

ICTV Classification

CB*

✓

The International Committee on Taxonomy of Viruses began to devise and implement rules for the naming and classification of viruses early in the 1970s, an effort that continues to the present. It is the only body charged by the International Union of Microbiological Societies with the task of developing, refining, and maintaining a universal virus taxonomy. The system shares many features with the classification system of cellular organisms. However, this system of nomenclature differs from other taxonomic codes on several points. A minor point is that names of orders and families are italicized unlike in the International Code of Nomenclature for algae, fungi, and plants and International Code of Zoological Nomenclature.

Viral classification starts at the level of order and continues as follows, with the taxon suffixes given in italics:

Order (-*virales*)

Family (-*viridae*)

Subfamily (-*virinae*)

Genus (-*virus*)

Species

Species names generally take the form of [Disease] virus

eg. Sin Ch

The establishment of an order is based on the inference that the virus families it contains have most likely evolved from a common ancestor. The majority of virus families remain unplaced. Currently (2012), seven orders, 96 families , 22 subfamilies, 420 genera, and 2,618 species of viruses have been defined by the ICTV.

X

ج ١٥ | Ligamenvirales | Caudovirales | Herpesvirales | Mononegavirales | Nidovirales | Picornavirales | Tymovirales

1- Ligamenvirales, infecting Archaea, are the most recent addition to the classification system.

2- Caudovirales are tailed dsDNA (group I) Bacteriophages. 

3- Herpesvirales contain large eukaryotic dsDNA viruses.

4- Mononegavirales include non segmented (-) strand ssRNA (Group V) plant and animal viruses.

5- Nidovirales are composed of (+) strand ssRNA (Group IV) viruses with vertebrate hosts.

6- Picornavirales contains small (+) strand ssRNA viruses that infect a variety of plant, insects and animal hosts.

7- Tymovirales contain mono partite (+) ssRNA viruses that infect plants

الطرق التي تتفاعل بها الفيروسات مع خلاياها المضيفة وتتهرب من
الكشف المناعي

Topic No. 5

Ways in which viruses interact with their host cells and evade immune detection

The infection process at the level of cells and organisms (Basic life cycle of relevant viruses)

VIRAL REPRODUCTION

Topic

- Viruses cannot reproduce outside a living cell.
- Viruses are host specific e.g. bacteriophages infect only bacteria, HIV virus infects certain blood cells, hepatitis virus infects only liver cells etc.
- A virus relies on the host's metabolic machinery for its own reproduction.
- Once inside the host the bacteriophage or virus will either go into Lytic cycle: Destroying the host cell during reproduction.

Lysogenic cycle: A parasitic type of partnership with the cell

LYTIC CYCLE

دورة الحياة

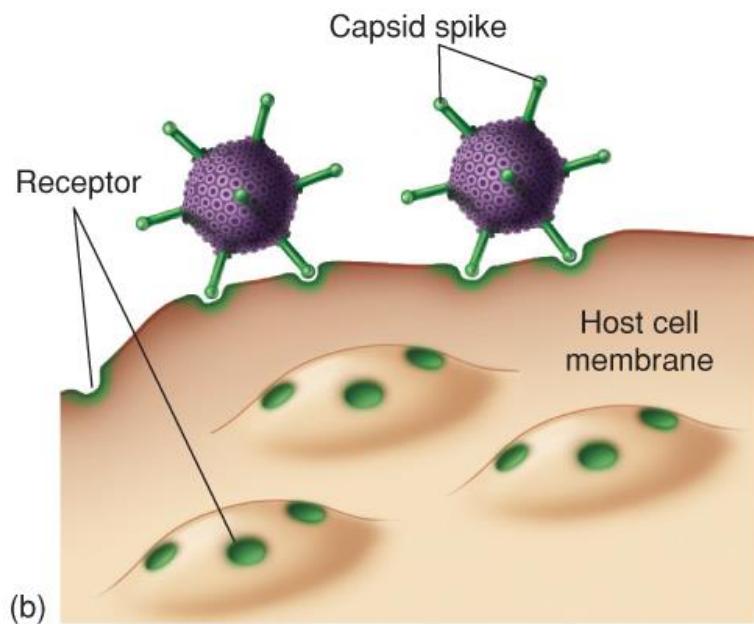
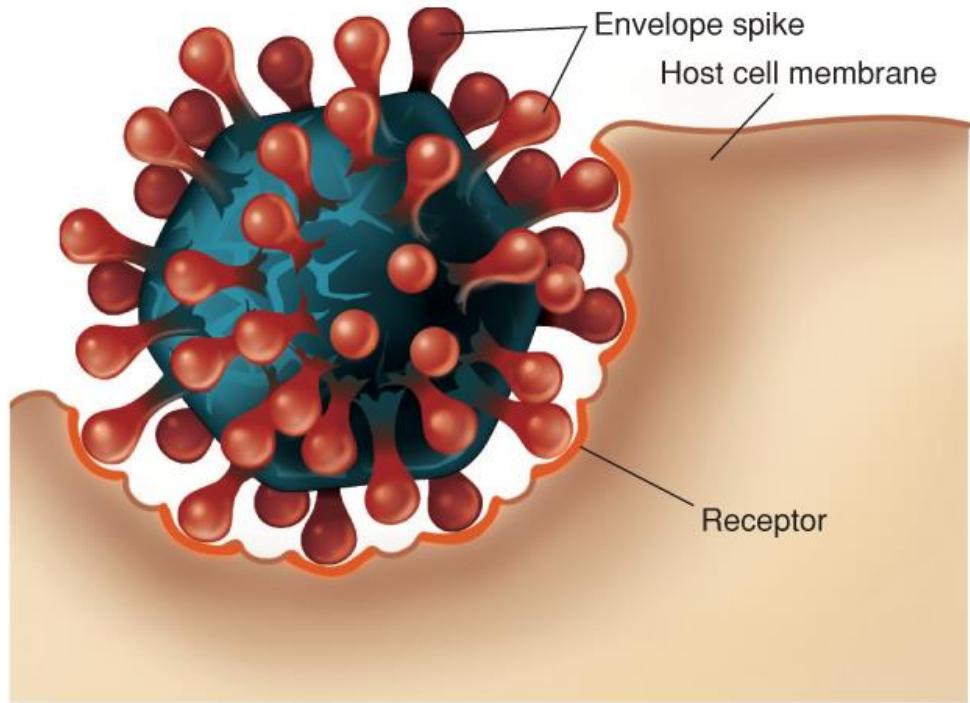
The lytic cycle may be divided into 5-6 stages:

1. Attachment: a protein on the surface of the virus

has a shape that matches a molecule in the plasma membrane of its host (receptor), allowing the virus to lock onto the host cell. (lock and key).

Because of the exact fit required, viruses have a limited host range

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اختراق

2. Penetration: Flexible cell membrane of the host is penetrated

يتم اختراق غشاء الخلية المرن للمضييف بواسطة الفيروس بأكمله أو حمضه النووي.

by the whole virus or its nucleic acid.

The virus is able to get into the cell in one of three ways.

A. Endocytosis: The virus is engulfed by the cell membrane and

الخلايا الداخلية: يغمر الفيروس غشاء الخلية و
enclosed in a vacuole or vesicle.

محاط بفراغ أو حويصلة.

الزلاق

B. Fusion: The viral envelope and cell membrane fuse, allowing

الانصهار: يندمج الغلاف الفيروسي وغشاء الخلية، مما يسمح للفيروس
the virus to enter the cell.
بدخول الخلية.

C. Injection: The virus injects its genome into the cytoplasm

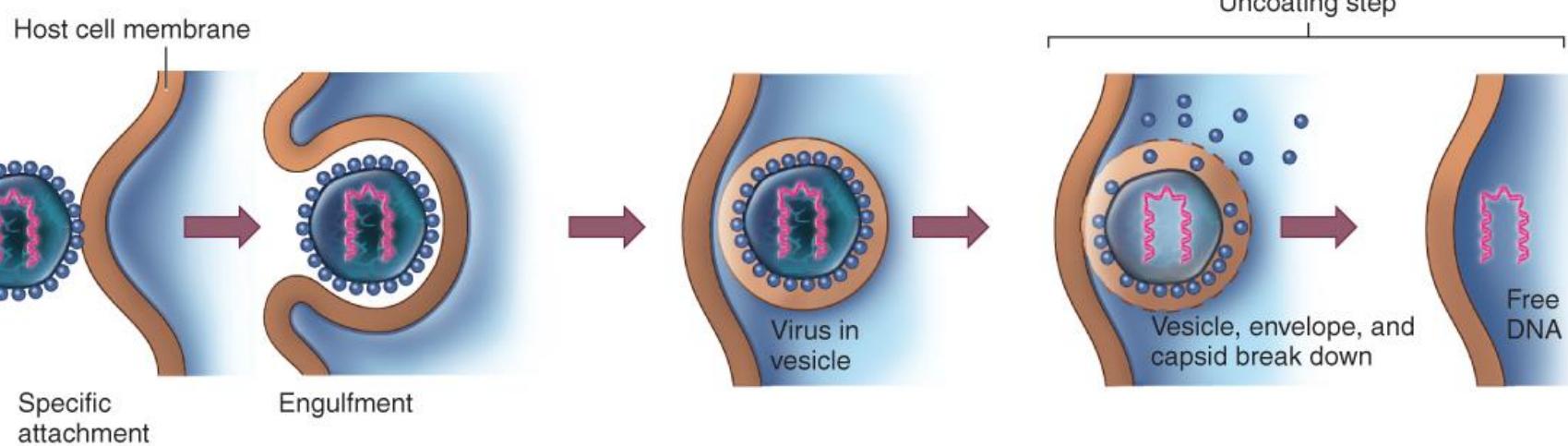
الحقن: يحقن الفيروس جينومه في السيتوبلازم في

جميع أنحاء غشاء البلازما

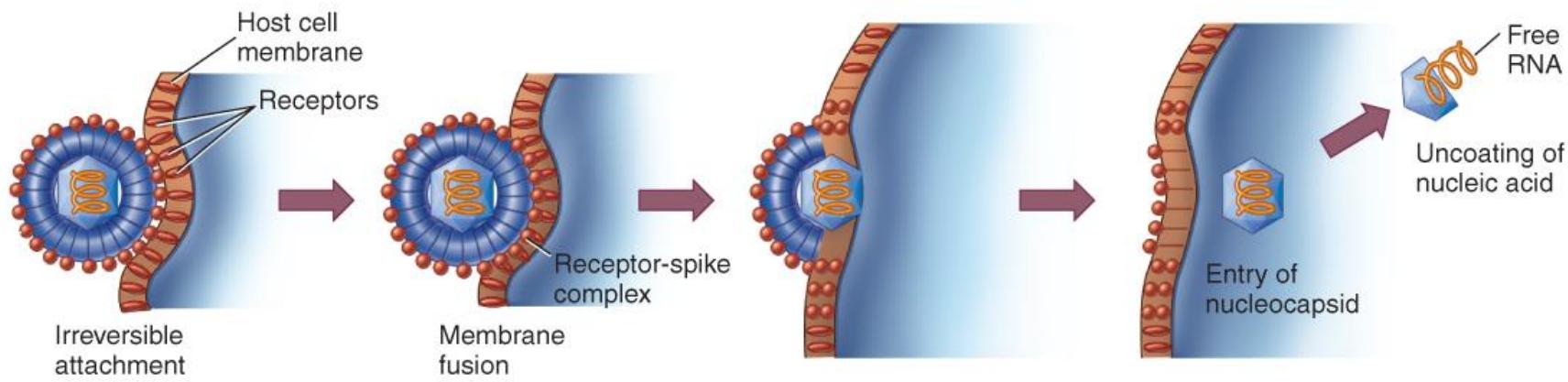
(a) Endocytosis

(b) Fusion

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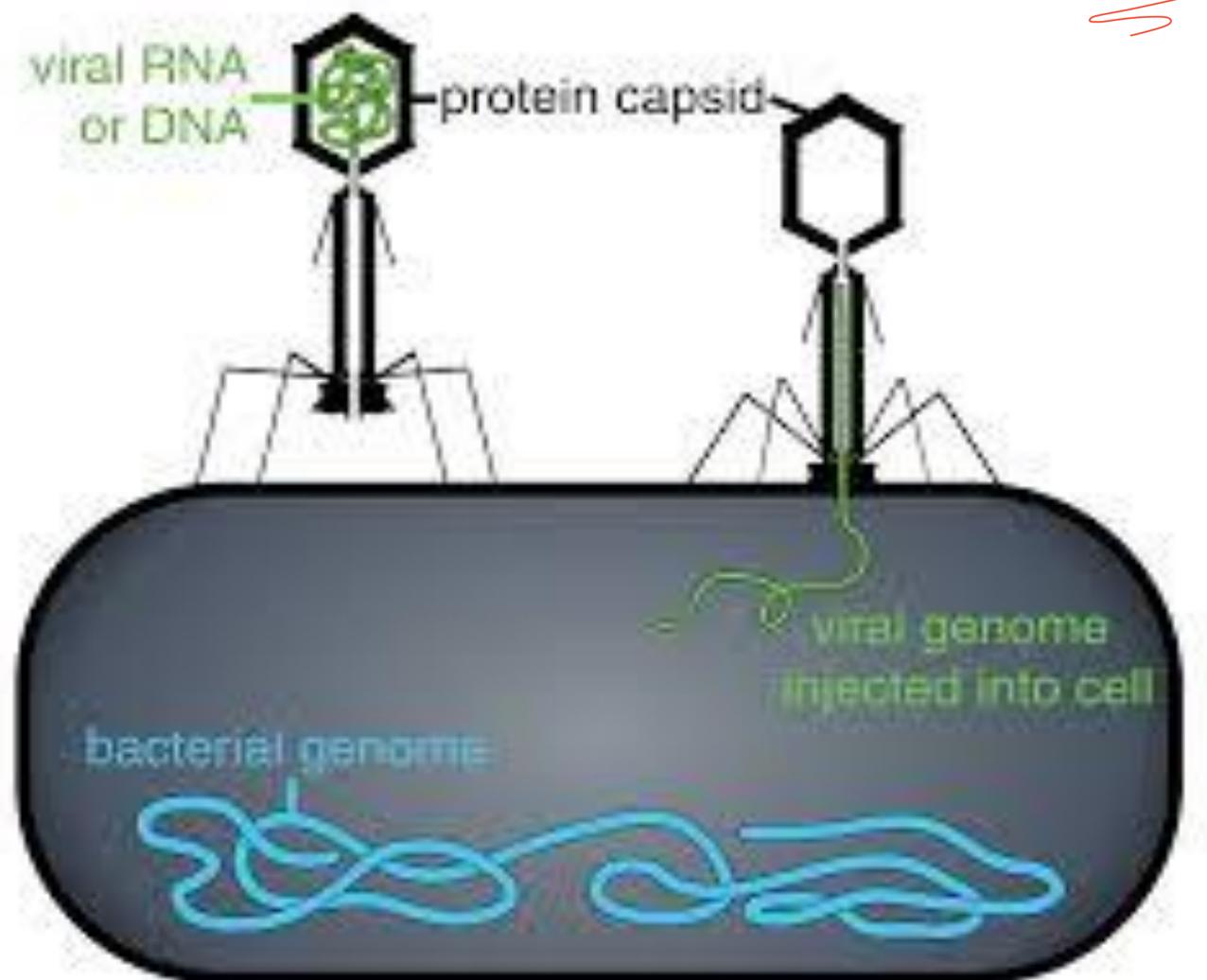


(a)



(b)

(c) Injection



3. Uncoating: Enzymes in the vacuole dissolve the envelope and capsid

The virus is now uncoated.

الإنزيمات في الفراغ تذوب الغلاف والغطاء أصبح الفيروس الآن غير مطلي

4. Synthesis: Free viral nucleic acid exerts control over the host's

synthetic and metabolic machinery

يمارس الحمض النووي الفيروسي الحر السيطرة على الآلات الاصطناعية والتتمثل الغذائي للمضيف

➤DNA viruses- enter host cell's nucleus where they are replicated and assembled

DNA enters the nucleus and is transcribed into RNA

The RNA becomes a message for synthesizing viral proteins
(translation)

New DNA is synthesized using host nucleotides

➤RNA viruses- replicated and assembled in the cytoplasm

5. Assembly or Maturation: Mature virus particles are constructed from the growing pool of parts (viral genome and capsids are assembled to produce several hundred virions).

يتم إنشاء جزيئات الفيروس الناضجة من مجموعة متنامية من الأجزاء (يتم تجميع الجينوم الفيروسي والقفيصة لإنتاج عدة مئات من الفيروسات).

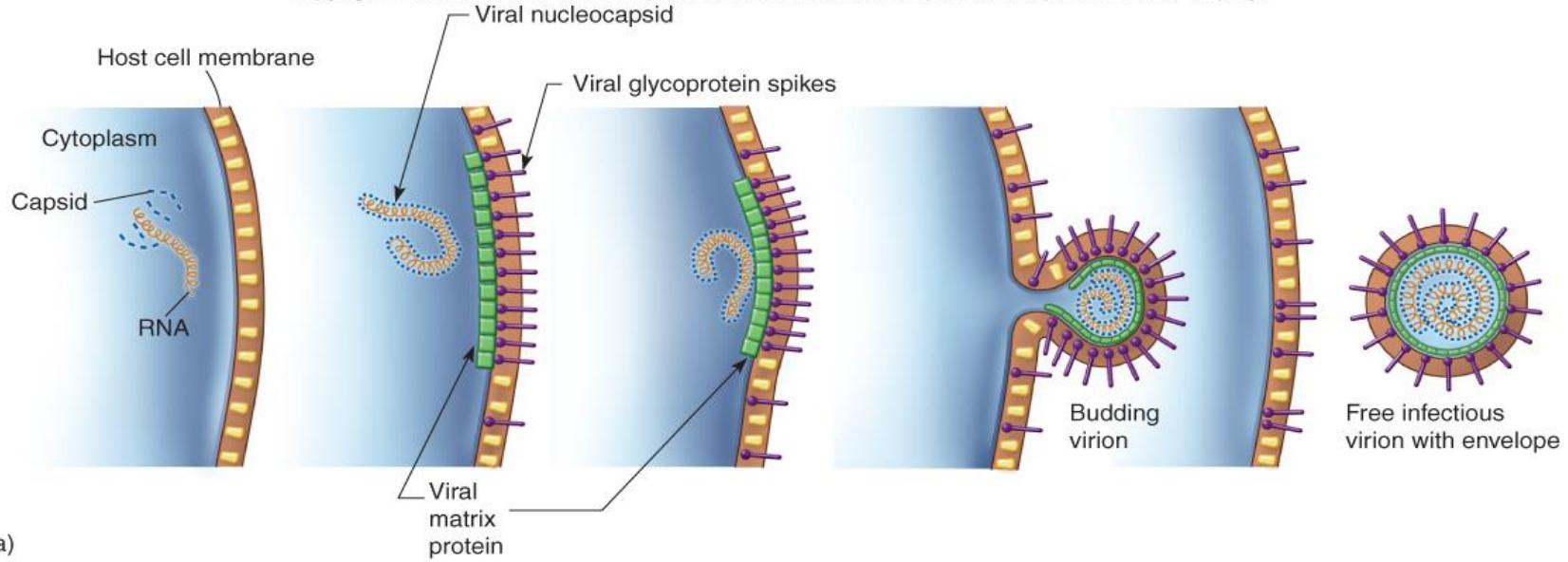
6. Release:

- Nonenveloped and complex viruses are released when the cell lyses or ruptures
- Enveloped viruses are liberated by budding or exocytosis
- 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

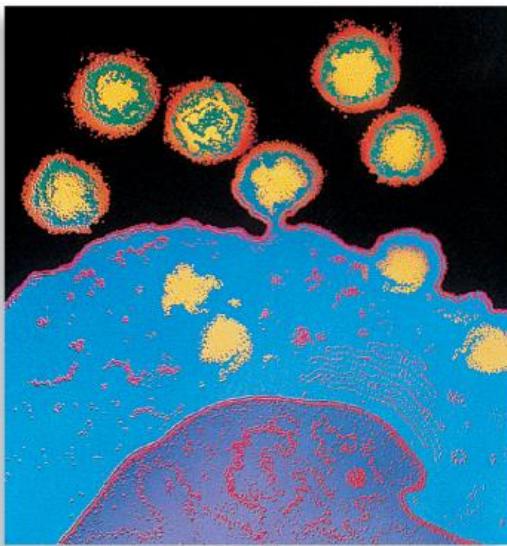
(Viruses that are in a lytic cycle are described as Virulent)

توصف الفيروسات الموجودة في دورة تحاليلية بأنها خبيثة

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(a)

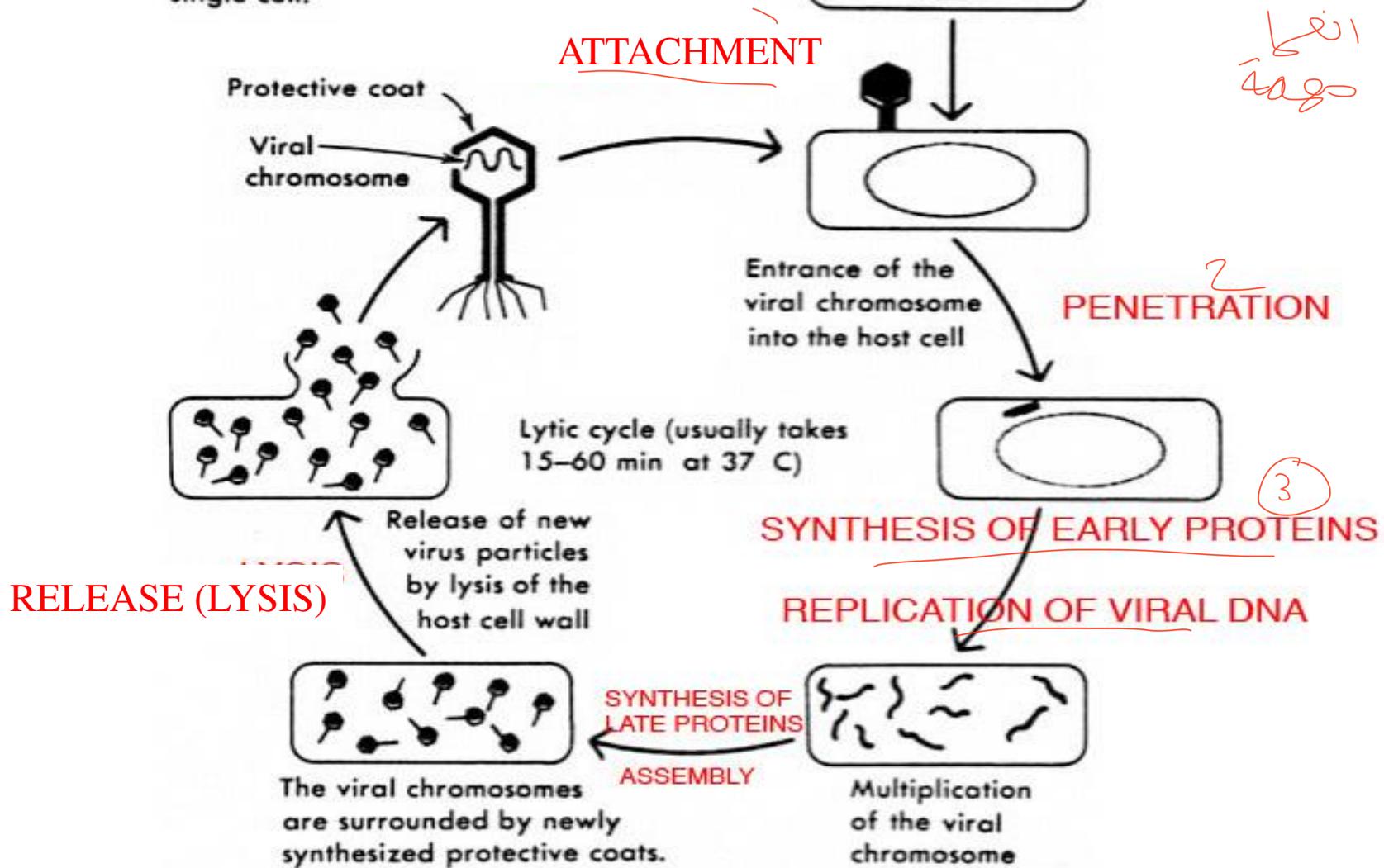


(b)

© Chris Bjornberg/Photo Researchers, Inc.

1
2
3

The first step in the multiplication of a virus is its attachment to a host cell; more than one virus particle can simultaneously adsorb to a single cell.



LYSOGENIC CYCLE

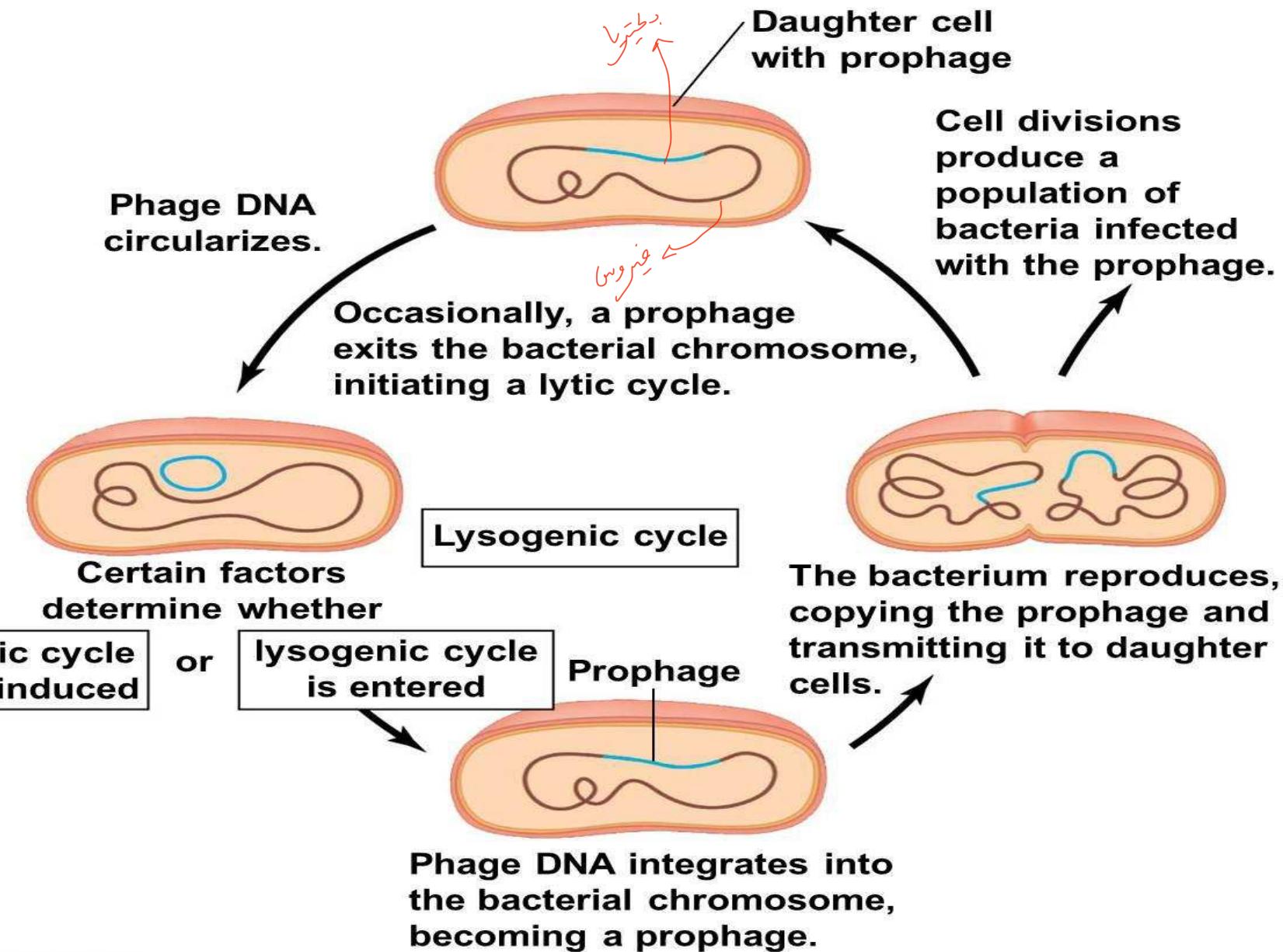
Steps **1** and **2** are identical to the first two steps in the lytic cycle

3. Integration: viral DNA integrates into host DNA. At that time, the viral genome is called **prophage**.

4. Replication: The prophage is replicated along with the host DNA, and all produced cells carry a copy of the prophage.

(Viruses that enter into a lysogenic cycle are known as Temperate viruses)

Lysogenic cycle



THANK YOU

Topic No. 6

**Virus uptake, replication of the genome,
gene regulation, protein synthesis,
production of virions, and viral egress**

الخروج الفيروسي

Viral egress

الخروج الفيروسي هو عملية الهروب الفيروسي من الخلية التي تقترب في كثير من الأحيان بالتكوين الحيواني الفيروسي.

Viral egress is the process of viral escape from the cell that is frequently coupled with viral biogenesis.

تعتمد الفيروسات على الخلايا الحية للتكاثر ويجب أن تهرب من الخلايا لإصابة خلية أخرى.

Viruses rely on living cells to multiply and they must escape from the cells to infect another cell.

الخروج الفيروسي هو الخطوة الأخيرة من دورات النسخ المتماثل الخاصة بهم. بصرف النظر عن تحلل غشاء الخلية، فإن البراعم على سطح الخلية أو الأغشية داخل الخلية هي طرق خروج فيروسية شائعة جداً.

Viral egress is a final step of their replication cycles. Apart from lysis of the cell membrane, budding at the cell surface or intracellular membranes are very common viral egress methods.

Viruses of many families hijack the host endosomal sorting complexes required for transport (ESCRT) machinery to remodel membranes at the budding site.

تحتفظ مواقعها الناشئة واعتمادها على مكونات ESCRT الدقيقة اعتماداً على كل فيروس. كيف تنشأ هذه التنوعات غير واضحة.

Their budding sites and dependence on the precise ESCRT components are different depending on each virus. How these diversities arise is unclear.

ومن المثير للاهتمام أن الخصائص الفيزيائية ومسارات التكوين الحيوي لبعض الفيروسات تشبه خصائص الحويصلات خارج الخلية التي تتجهها الخلايا، على الرغم من أن العلاقة أو الاختلاف بينهما لم يتم توضيحها.

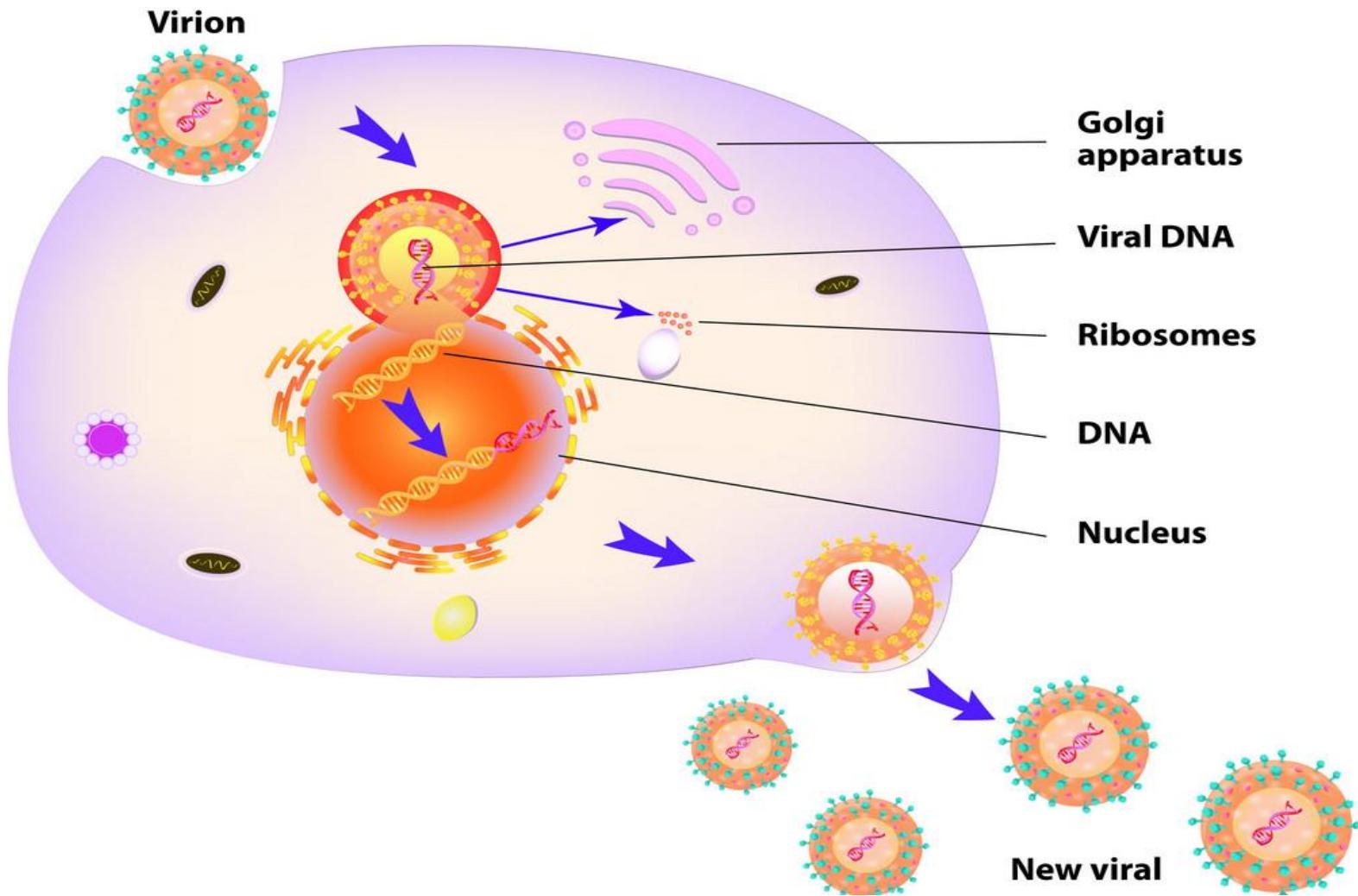
Interestingly, the physical characteristics and the biogenesis pathways of some viruses resemble those of extracellular vesicles produced by cells, although the relation or difference between them has not been elucidated.

نظراً لأن الخروج الفيروسي هو خطوة أساسية للتکاثر الفيروسي ويعتمد على الآلات الخلوية، فإن تحديد عوامل المضيف المسؤولة عن هذه الخطوة

قد يؤدي أيضاً إلى اكتشاف أهداف جديدة للاستراتيجيات العلاجية المضادة للفيروسات واسعة الطيف التي تستهدف المضيف.

As viral egress is an essential step for viral replication and relies on cellular machinery, the identification of host factors responsible for this step may also lead to the discovery of novel targets for broad-spectrum host-targeted antiviral therapeutic strategies.

Virus Replication



Replication Strategy of ss(-)RNA Viruses

استراتيجية النسخ المتماثل لفيروسات الحمض النووي الريبي (ss-)

الخطوات في النسخ المتماثل:

1. النسخ الأولي للفيرون (-) الحمض النووي الريبي الحسي بواسطة الحمض النووي الريبي المعتمد على الحمض النووي الريبي بول في نواة الفيرون في

السيتوبلازم، والإنتاج (بشكل رئيسي) الحمض النووي الريبي (+) الحمض النووي الريبي، تكون مركب تكاري (RC)

Steps in Replication:

1. Primary transcription of virion (-)sense RNA by RNA-Dependent
RNA Pol in virion core in cytoplasm, production (mainly) mRNA and
(+)sense RNA, formation replicative complex (RC)

ترجمة الحمض النووي الريبوزي الرسول، تراكم المنتجات

2. Translation mRNAs, accumulation of products

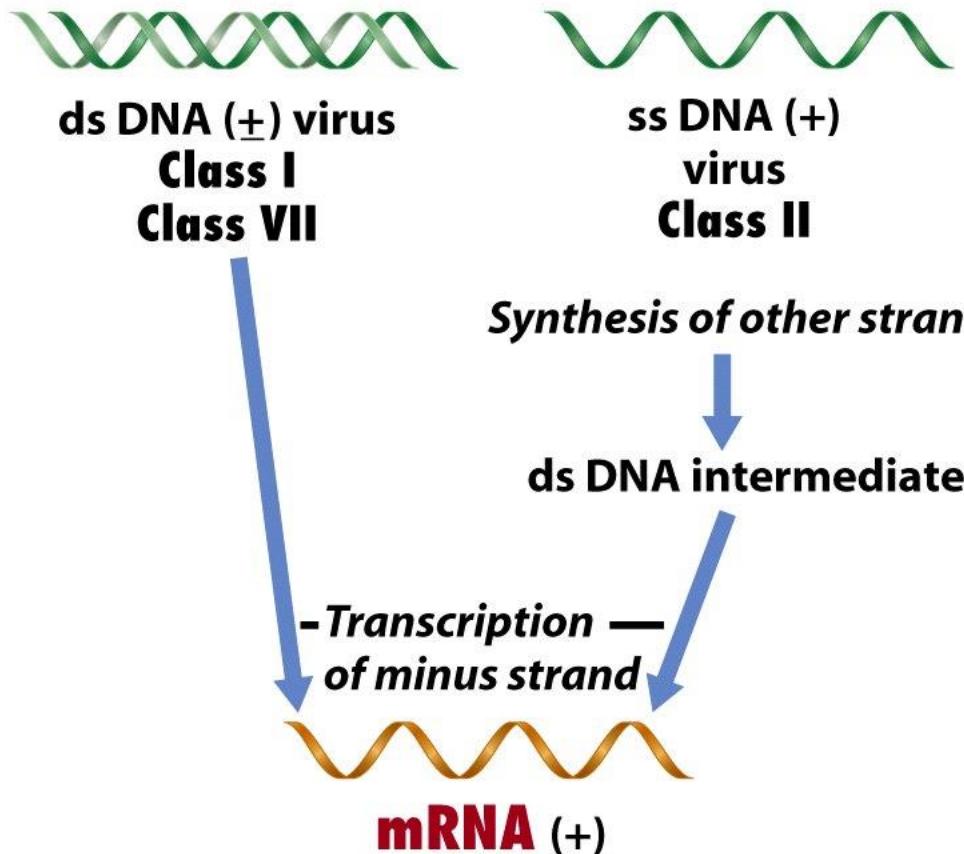
تفاعل بروتينات Virion مع RC، وتحيزها نحو إنتاج كامل-

الطول (+) بمعنى الحمض النووي الريبي وبالتالي من الجين (-) بمعنى الحمض النووي الريبي

3. Virion proteins interact with RC, bias it towards production of full-length (+)sense RNA and therefore of genomic (-)sense RNA

4. Secondary transcription from progeny (-)sense RNA, translation,
accumulation structural proteins

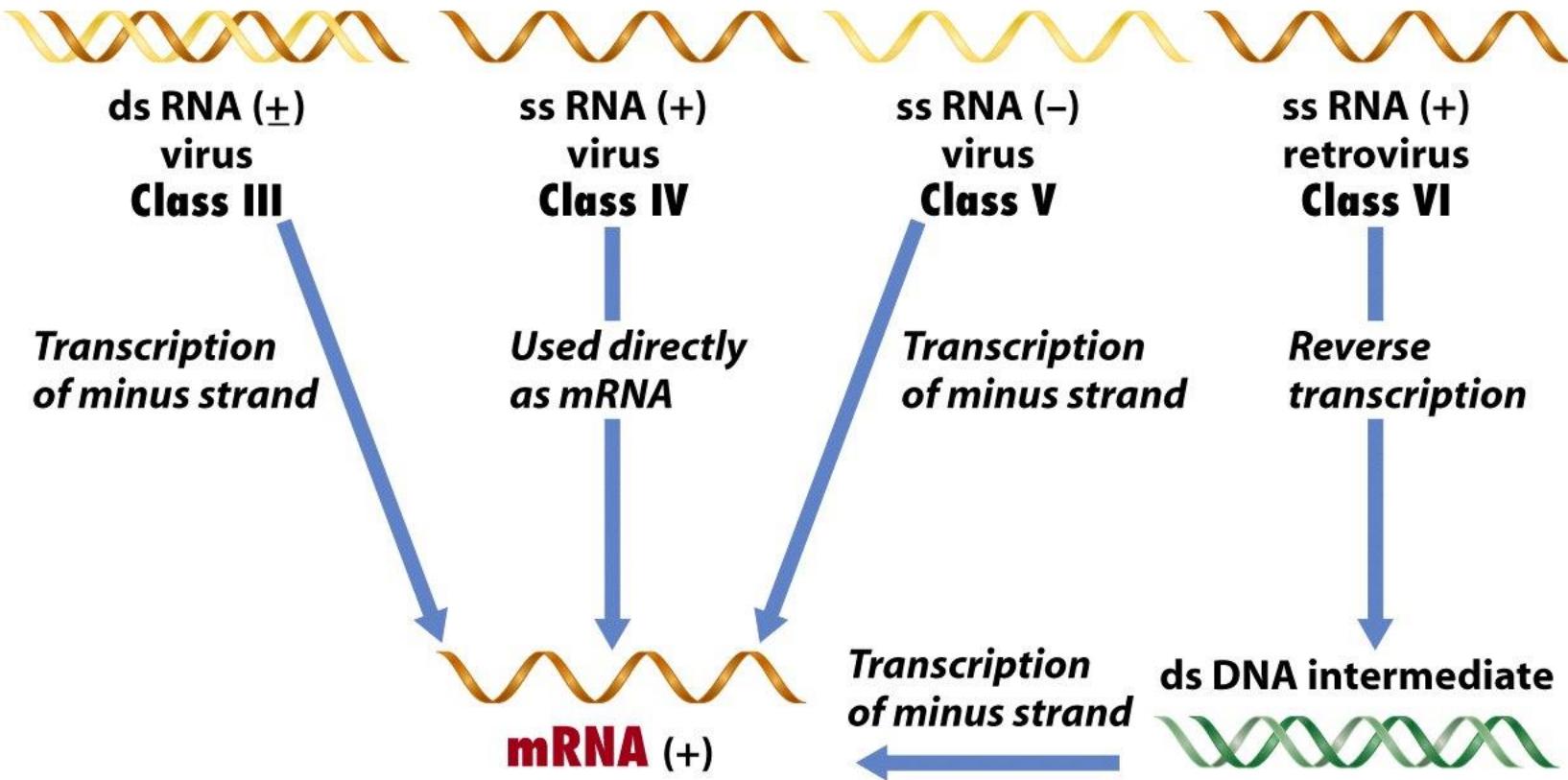
5. Nucleocapsid assembly and maturation, budding of nucleocapsid
through host membrane containing viral envelope proteins



Genome replication: **Class I**, classical semiconservative
Class II, classical semiconservative, discard (-) strand
Class VII, transcription followed by reverse transcription

DNA Viruses

Figure 9-11a Brock Biology of Microorganisms 11/e
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Genome

replication: Class III, classical semiconservative replication, but of RNA not DNA

Class IV, make ss RNA (-) and transcribe from this to give ss RNA (+) genome

Class V, make ss RNA (+) and transcribe from this to give ss RNA (-) genome

Class VI, make ss RNA (+) genome by transcription off of (-) strand of ds DNA

RNA Viruses

Figure 9-11b Brock Biology of Microorganisms 11/e

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Animal RNA viruses are classified into three distinct groups depending on their genome and mode of replication (and the numerical groups based on the older Baltimore classification):

Double-stranded RNA viruses (Group III) contain from **one to a dozen** different RNA molecules, each coding for one or more viral proteins.

Positive-sense ssRNA viruses (Group IV) have their genome directly utilized as if it were mRNA, with host ribosomes translating it into a single protein that is modified by host and viral proteins to form the various proteins needed for replication. One of these includes RNA-dependent RNA polymerase (RNA replicase), which copies the viral RNA to form a double-stranded replicative form. In turn this directs the formation of new virions.

Negative-sense ssRNA viruses (Group V) must have their genome copied by an RNA replicase to form positive-sense RNA. This means that the virus must bring along with it the RNA replicase enzyme. The positive-sense RNA molecule then acts as viral mRNA, which is translated into proteins by the host **ribosomes**. The resultant protein goes on to direct the synthesis of new virions, such as **capsid** proteins and RNA replicase, which is used to produce new negative-sense RNA molecules.

Retroviruses (Group VI) have a single-stranded RNA genome but, in general, are not considered RNA viruses because they use DNA intermediates to replicate. **Reverse transcriptase**, a viral enzyme that comes from the virus itself after it is uncoated, converts the viral RNA into a complementary strand of DNA, which is copied to produce a double-stranded molecule of viral DNA. After this DNA is integrated into the host genome using the viral enzyme **integrase**, expression of the encoded genes may lead to the formation of new virions.

PATTERNS OF VIRAL INFECTION

- Viral infections can be:
 - **Acute** (rapid and self limiting)
 - **Persistent** (long term)
 - **Latent** (extreme versions of persistent infections)
 - **Slow or transforming** (complicated types of persistent infections)



- Cytopathic viruses produce virions and kill host cells rapidly (cytopathology).
- Noncytopathic viruses produce virions but do not cause cytopathology.
- Some viruses do not produce virions or cause cytopathology but still cause infection.

- Incubation periods vary for different viruses.
 - Some are as short as days.
 - Some are as long as years.
 - During the incubation period:
 - The virus is replicating.
 - The host is beginning to respond



Viral Disease	Incubation Period
Influenza	1–2 days
Common cold	1–3 days
Acute respiratory disease (adenoviruses)	5–7 days
Herpes	5–8 days
Enterovirus disease	6–12 days
Poliomyelitis	5–20 days
Measles	9–12 days
Smallpox	12–14 days
Chickenpox	13–17 days
Mumps	17–20 days
Mononucleosis	1–2 months
Hepatitis A	15–40 days
Hepatitis B and C	2–5 months
Rabies	1–3 months
Papilloma (warts)	2–5 months
AIDS	1–10 years

Table 13.1 Microbiology: A Clinical Approach (© Garland Science)