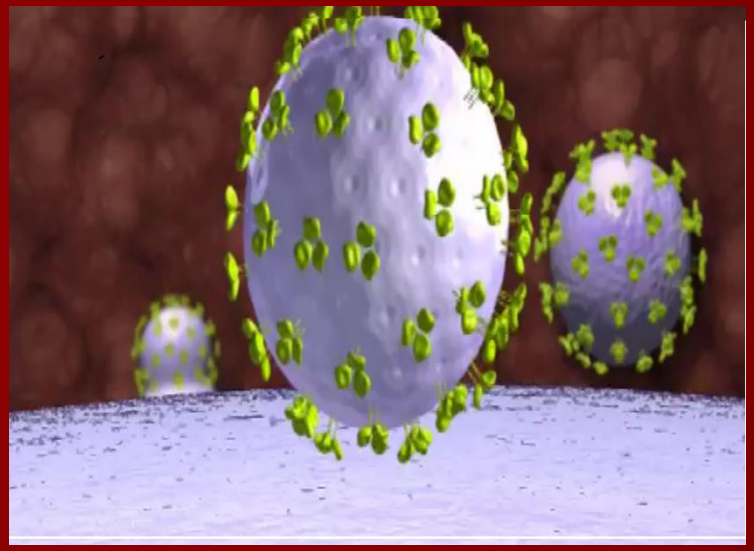
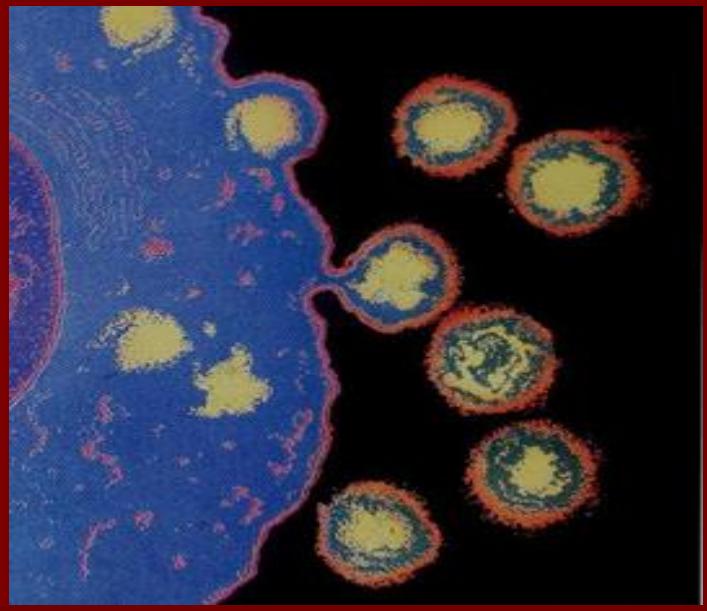
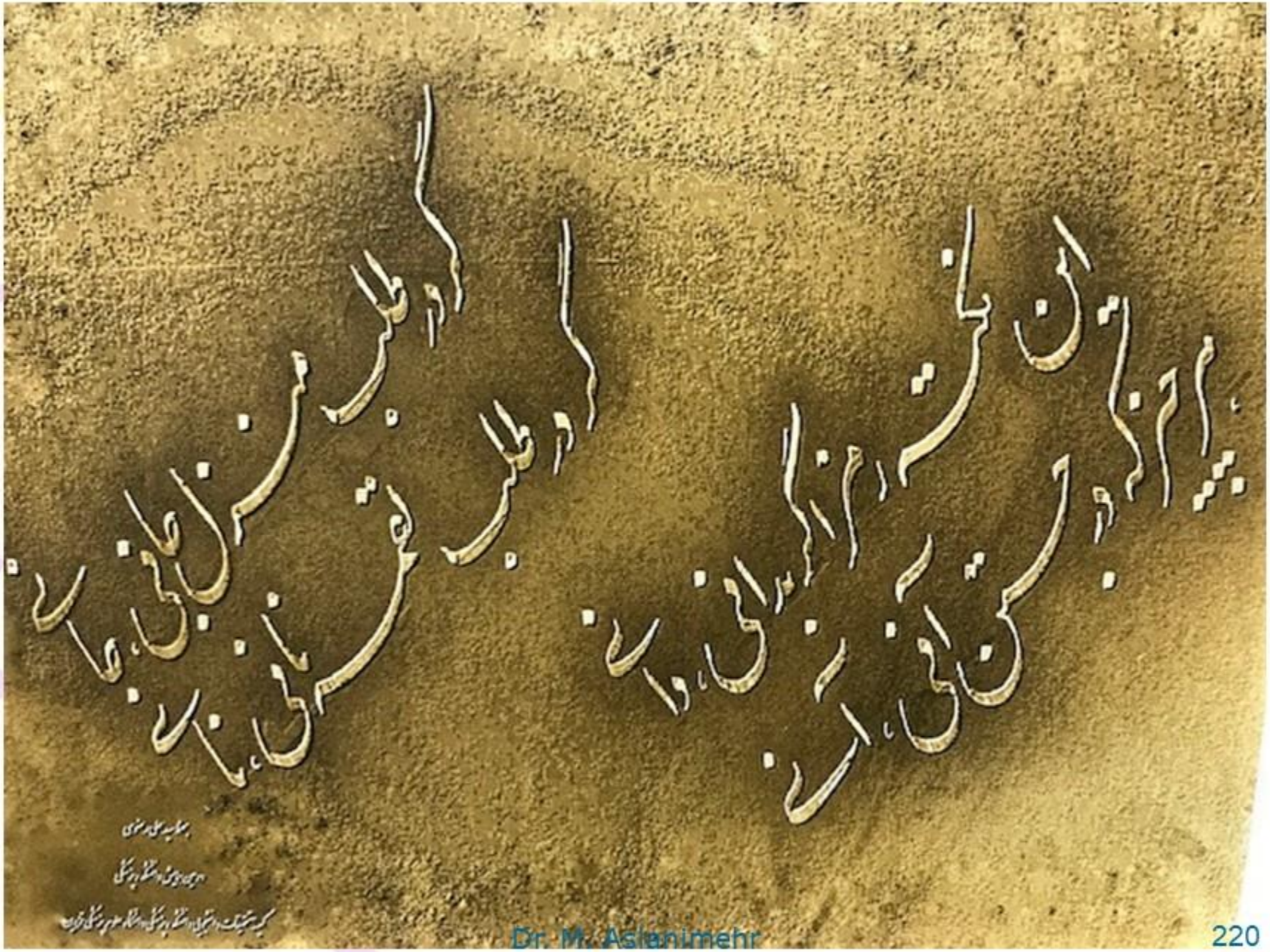
Qazvin University of Medical Sciences

Replication Cycle of Viruses

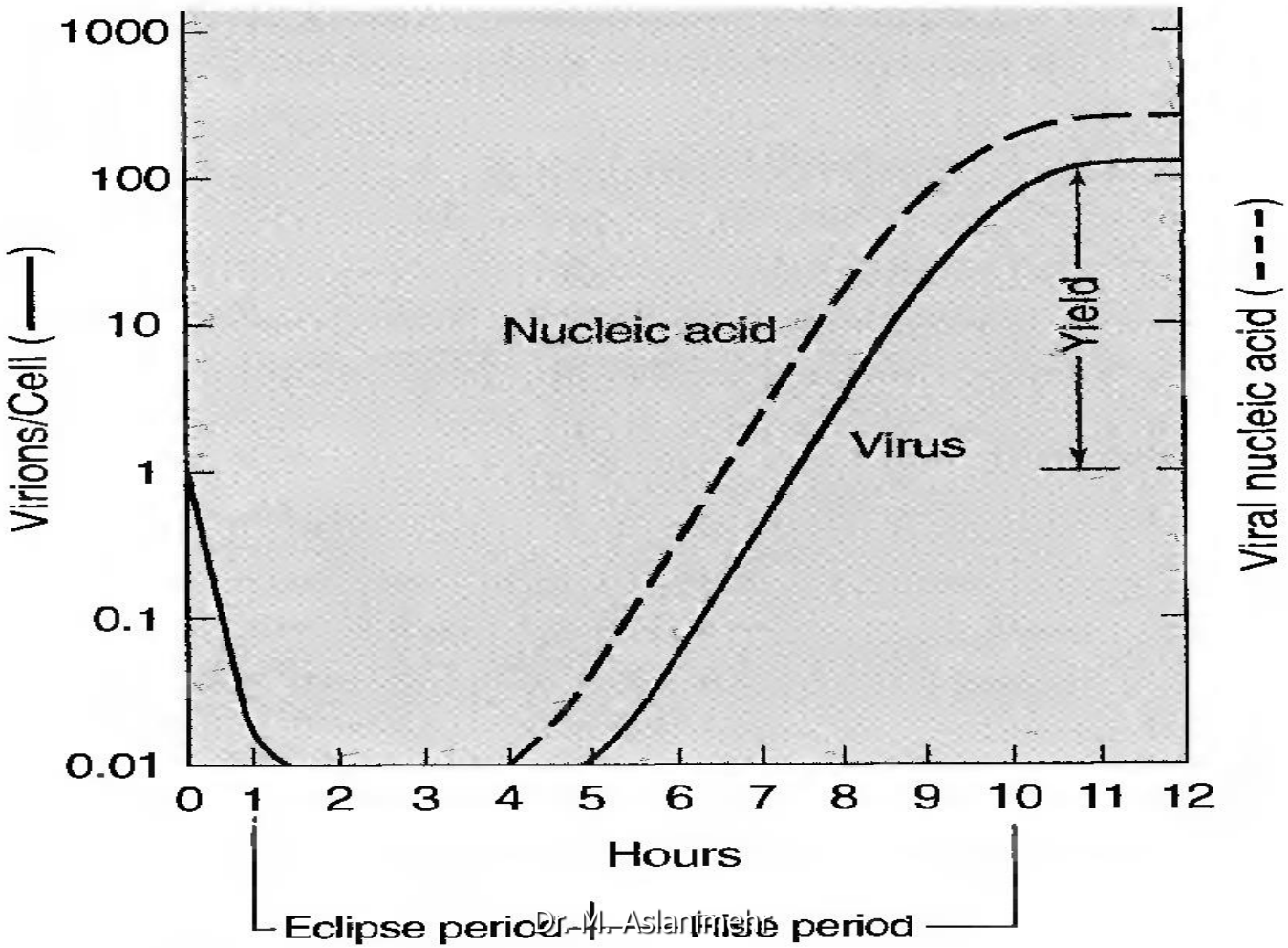




Dr Masoumeh Aslanimehr



Viral growth curve



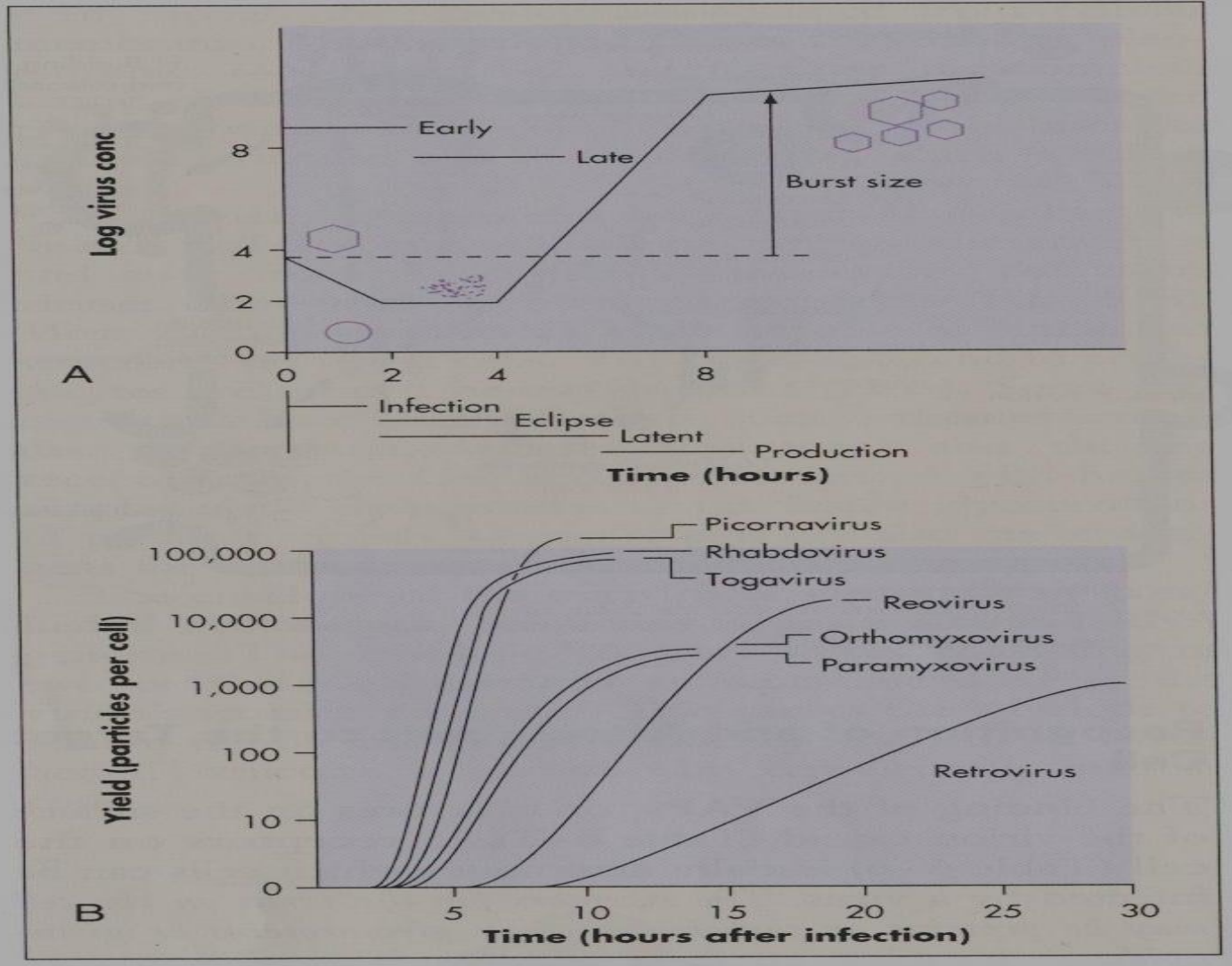
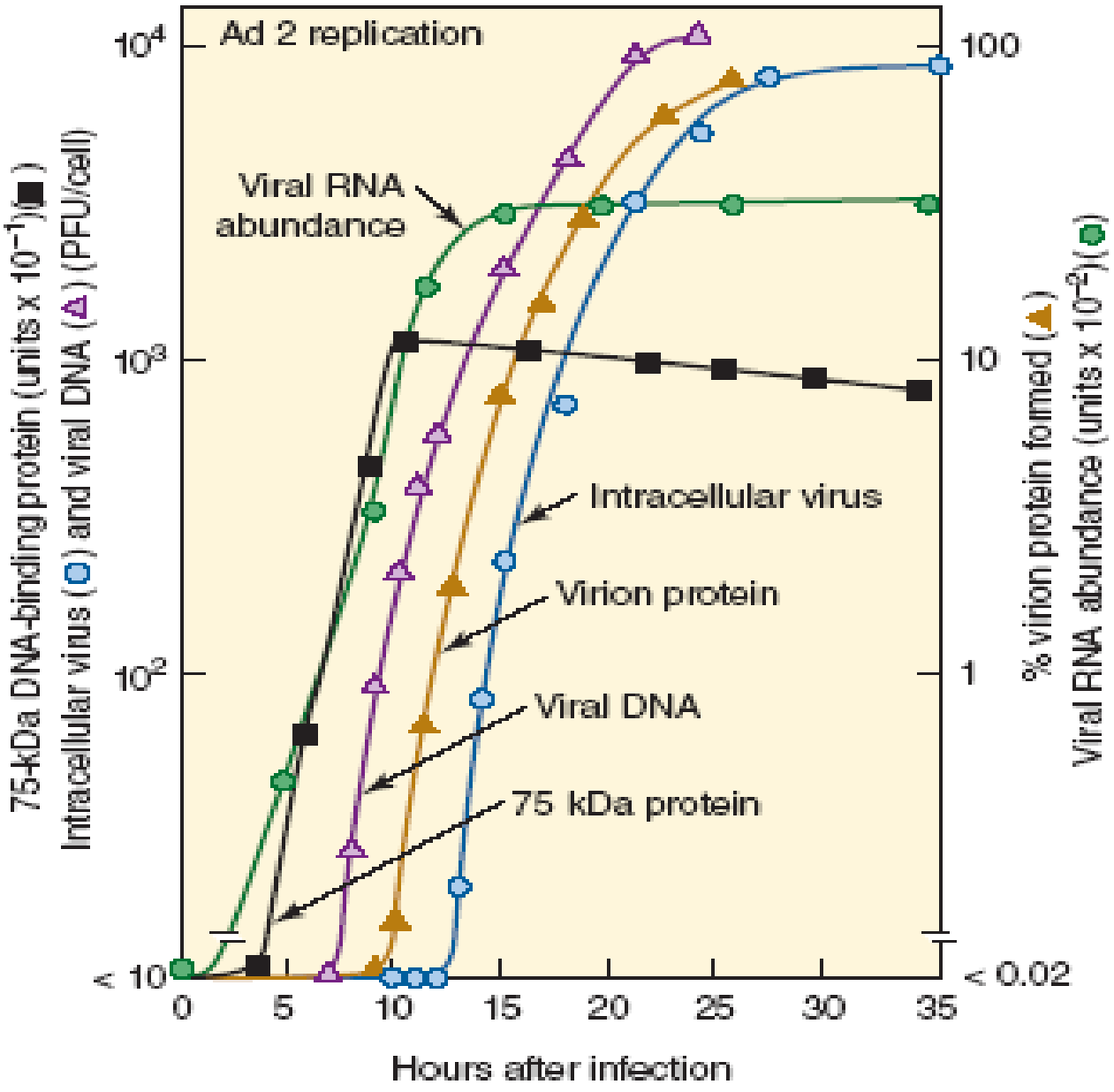
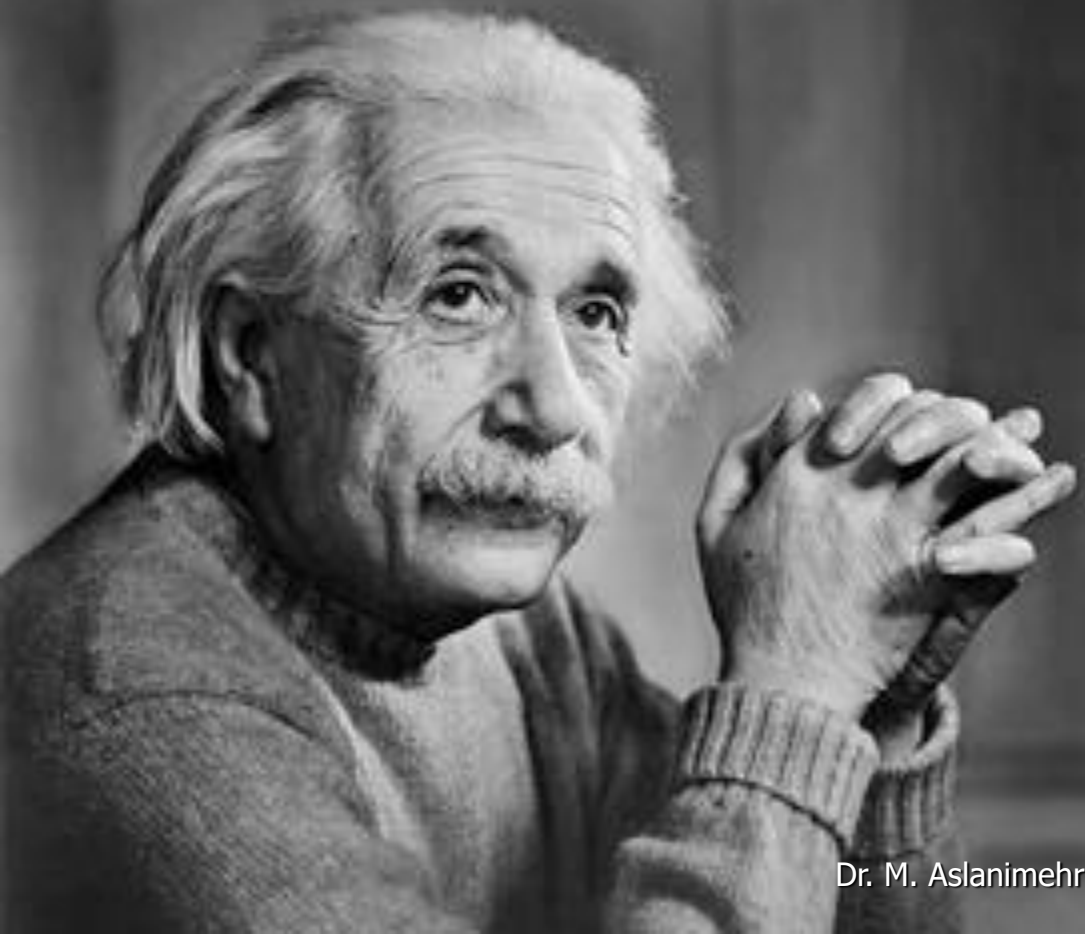


FIGURE 6–10. *A,* Single-cycle growth curve of a virus that is released on cell lysis. The different stages are defined by the presence or absence of visible viral components (eclipse period), infectious virus in the media (latent period), or macromolecular synthesis (early/late phases). *B,* Growth curve and burst size of representative viruses. (*A* modified from Davis BD et al: *Microbiology,* ed 4, Philadelphia, 1990, JB Lippincott; *B* modified from White DO, Fenner F: *Medical virology,* ed 3, New York, 1986, Academic Press.)


Ad 2 replication
Viral RNA abundance
Intracellular virus
Virion protein
Viral DNA
75 kDa protein
75-kDa DNA-binding protein (units x 10^{-1})(■)
Intracellular virus (○) and viral DNA (△) (PFU/cell)
% virion protein formed (▲)
Viral RNA abundance (units x 10^{-2})(●)
10^4
10^3
10^2
< 10
100
10
1
< 0.02
0
5
10
15
20
25
30
35
Hours after infection

- If you can't explain it **simply**, you don't understand it well enough.

– Albert Einstein



Replication cycle of Bacteriophage

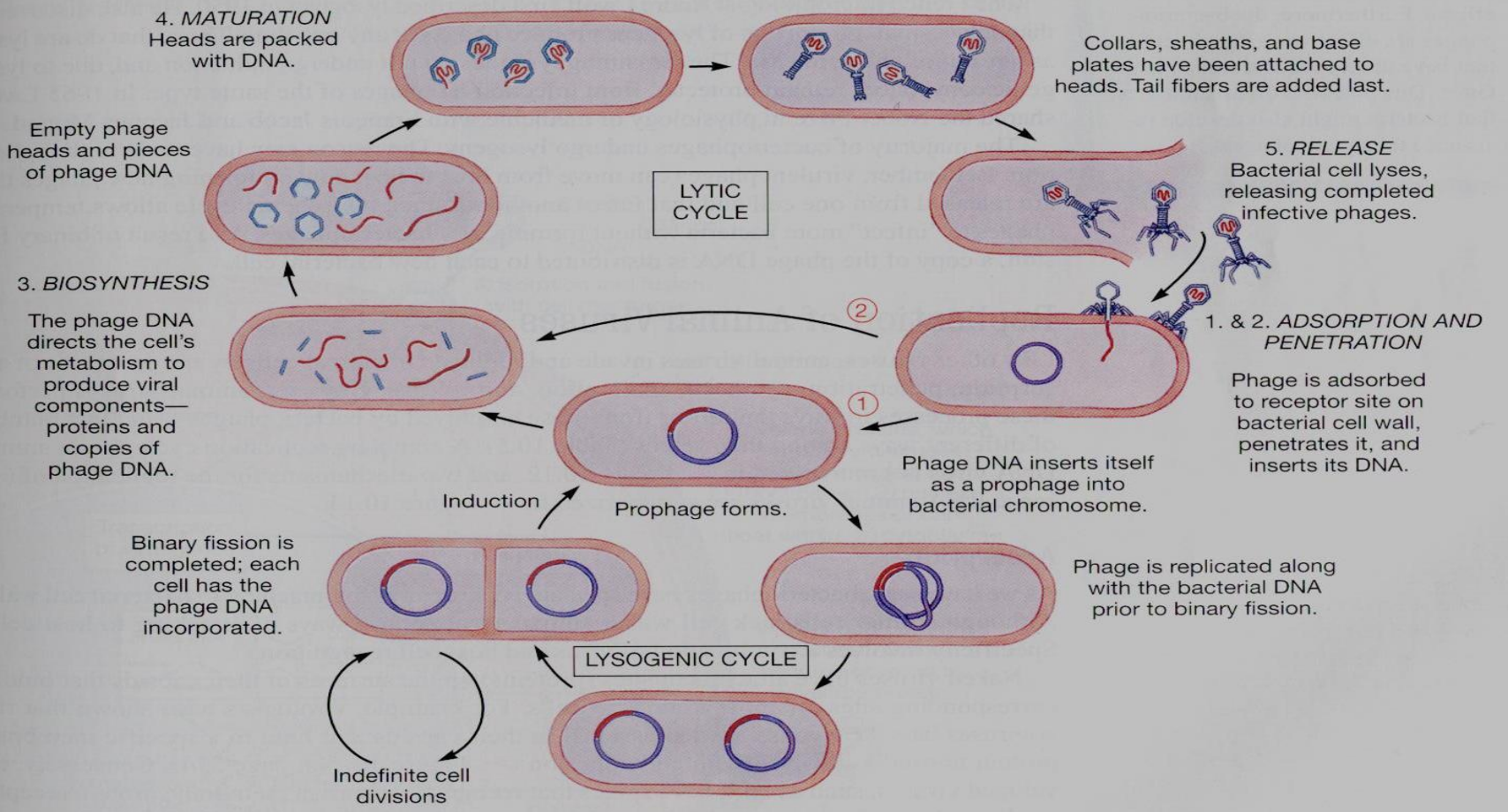


Figure 10.11 **Replication of a temperate bacteriophage.** Following adsorption and penetration, the virus undergoes prophage formation. ① In the lysogenic cycle, temperate phages can exist harmlessly as a prophage within the host cell for long periods of time. Each time the bacterial chromosome is replicated, the prophage also is replicated; all daughter bacterial cells are "infected" with the prophage. Induction involves either a spontaneous or environmentally induced excision of the prophage from the bacterial chromosome. ② A typical lytic cycle, involving biosynthesis and maturation, occurs, and new temperate phages are released

Stages of the viral Replication cycle.

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

mRNA = messenger RNA.

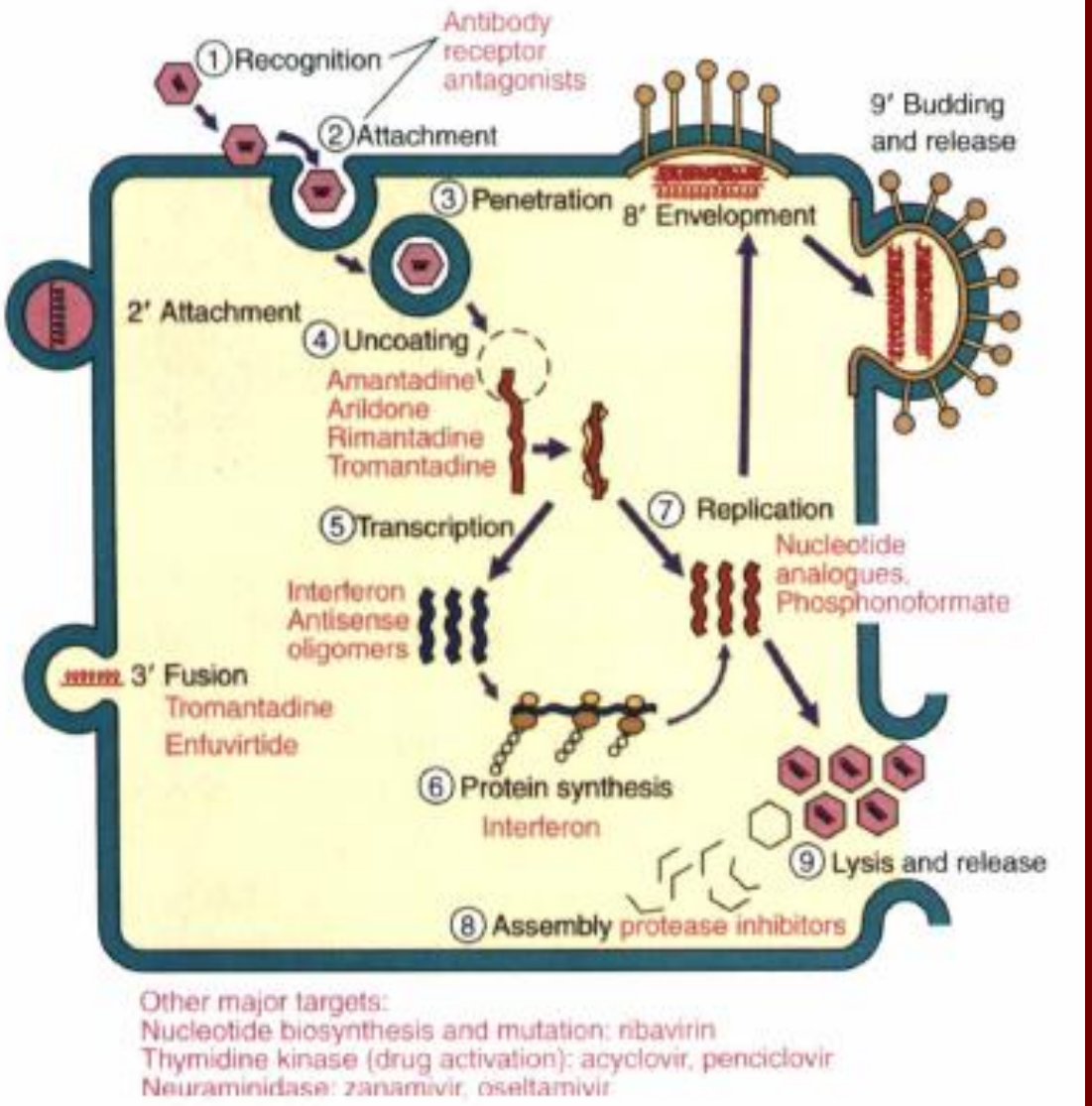


Figure 4–9. A general scheme of viral replication. Enveloped viruses have alternative means of entry (3) assembly, and exit from the cell (8′ and 9′). The antiviral drugs for susceptible steps in viral replication are listed in magenta.

Example of Viral Attachment Proteins (VAP)

TABLE 36.5 Examples of Viral Attachment Proteins

Virus Family	Virus	Viral Attachment Protein
Picornaviridae	Rhinovirus	VP1-VP2-VP3 complex
Adenoviridae	Adenovirus	Fiber protein
Reoviridae	Reovirus	σ-1
	Rotavirus	VP7
Togaviridae	Semliki Forest virus	E1-E2-E3 complex gp
Rhabdoviridae	Rabies virus	G-protein gp
Orthomyxoviridae	Influenza A virus	HA gp
Paramyxoviridae	Measles virus	H gp
Herpesviridae	Epstein-Barr virus	gp350 and gp220
Retroviridae	Murine leukemia virus	gp70
	Human immunodeficiency virus	gp120

gp, Glycoprotein; *H* or *HA*, hemagglutinin.

Examples of Viral Receptors

TABLE 36.6 Examples of Viral Receptors

Virus	Target Cell	Receptor[a]
Epstein–Barr virus	B cell	C3d complement receptor (CR2, CD21)
HIV	Helper T cell	CD4 molecule and chemokine coreceptor
Rhinovirus	Epithelial cells	ICAM-1 (immunoglobulin superfamily protein)
Poliovirus	Epithelial cells	Immunoglobulin superfamily protein
Herpes simplex virus	Many cells	Herpesvirus entry mediator (HveA), nectin-1
Rabies virus	Neuron	Acetylcholine receptor, NCAM
Influenza A virus	Epithelial cells	Sialic acid
B19 parvovirus	Erythroid precursors	Erythrocyte P antigen (globoside)

[a]Other receptors for these viruses may also exist.
CD, Cluster of differentiation; *ICAM-1*, intercellular adhesion molecule; *NCAM*, neural cell adhesion molecule.

able to bind to receptors expressed on cells of many animal species, including arthropods, reptiles, amphibians, birds, and mammals. This allows them to infect animals, mosquitoes, and other insects and to be spread by them.

Viral Growth cycle

Jawetez 2019

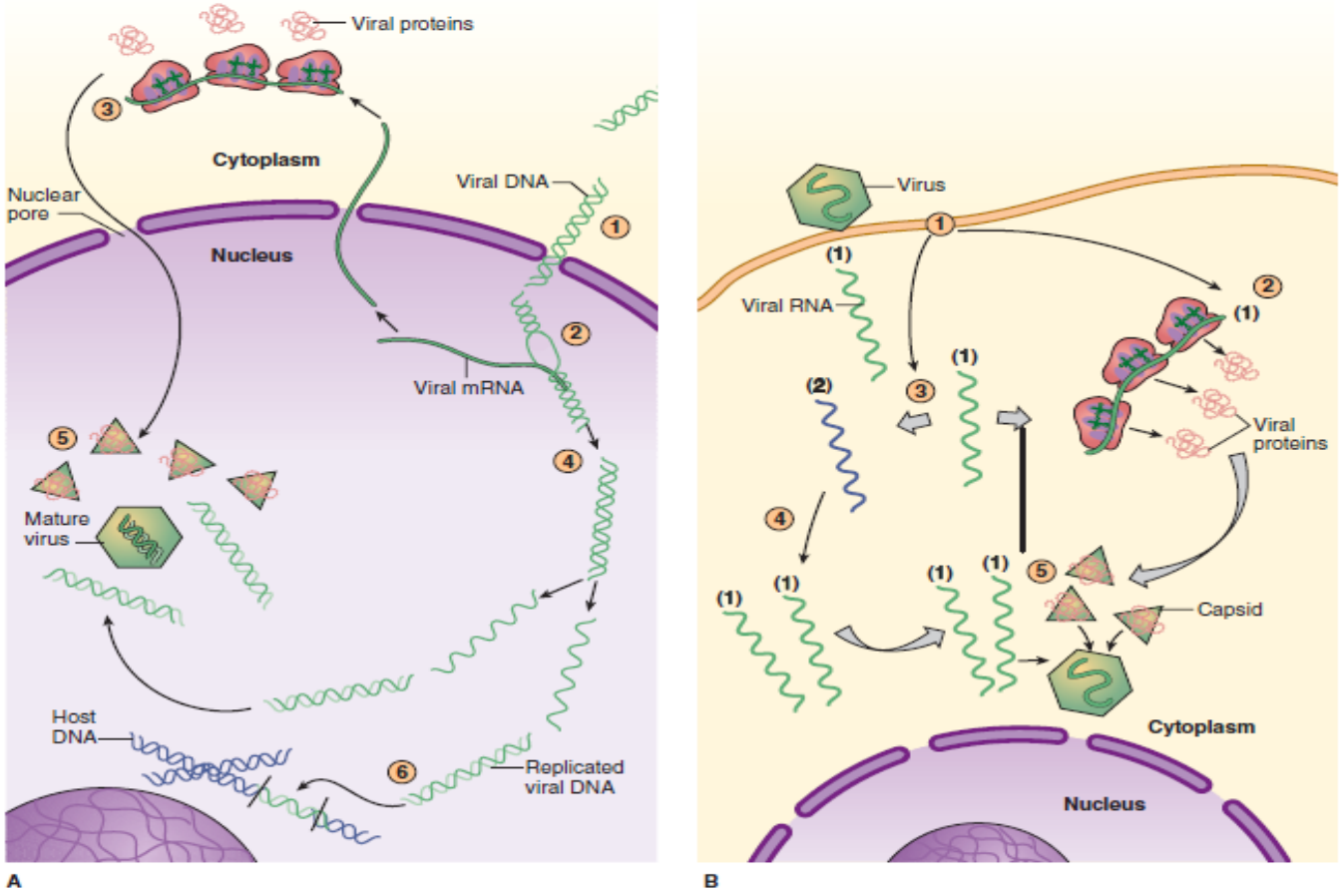


FIGURE 29-5 Example of viral growth cycles. **A:** The growth cycle of a nonenveloped, double-stranded DNA virus. In this example multiple steps in the replication cycle take place in the nucleus. (1) After penetrating the host cell, viral DNA is uncoated and enters the nucleus. (2) Viral genes are transcribed. (3) The mRNAs are translated in the cytoplasm. Newly synthesized proteins enter the nucleus. (4) Viral DNA is replicated in the nucleus, sometimes with the help of newly synthesized viral replication proteins. (5) Viral DNA and viral structural proteins assemble in the nucleus to produce new progeny virions. (6) On rare occasions, viral DNA may be incorporated into cellular DNA as a side effect of infection. **B:** The growth cycle of a positive-sense, single-stranded RNA virus. In this example, the replication cycle 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) A negative-sense RNA copy of the positive template is synthesized. (4) It is used to produce many positive-sense copies. (5) The newly synthesized positive-sense RNA molecules are assembled with viral structural proteins to produce new progeny virions. (Reproduced with permission from Talaro KP: *Foundations in Microbiology: Basic Principles*, 6th ed. McGraw-Hill, 2008. © McGraw-Hill Education.)

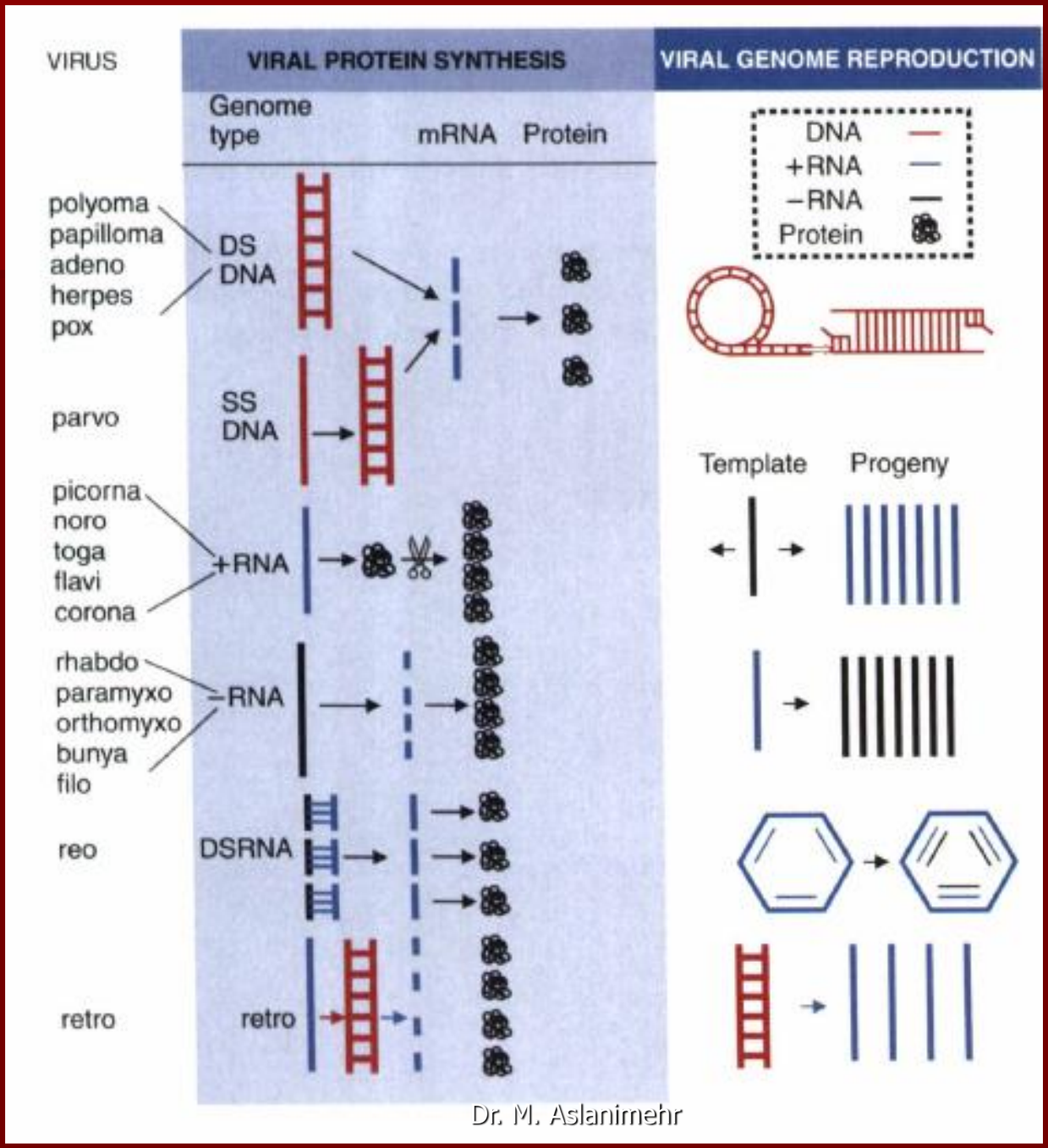
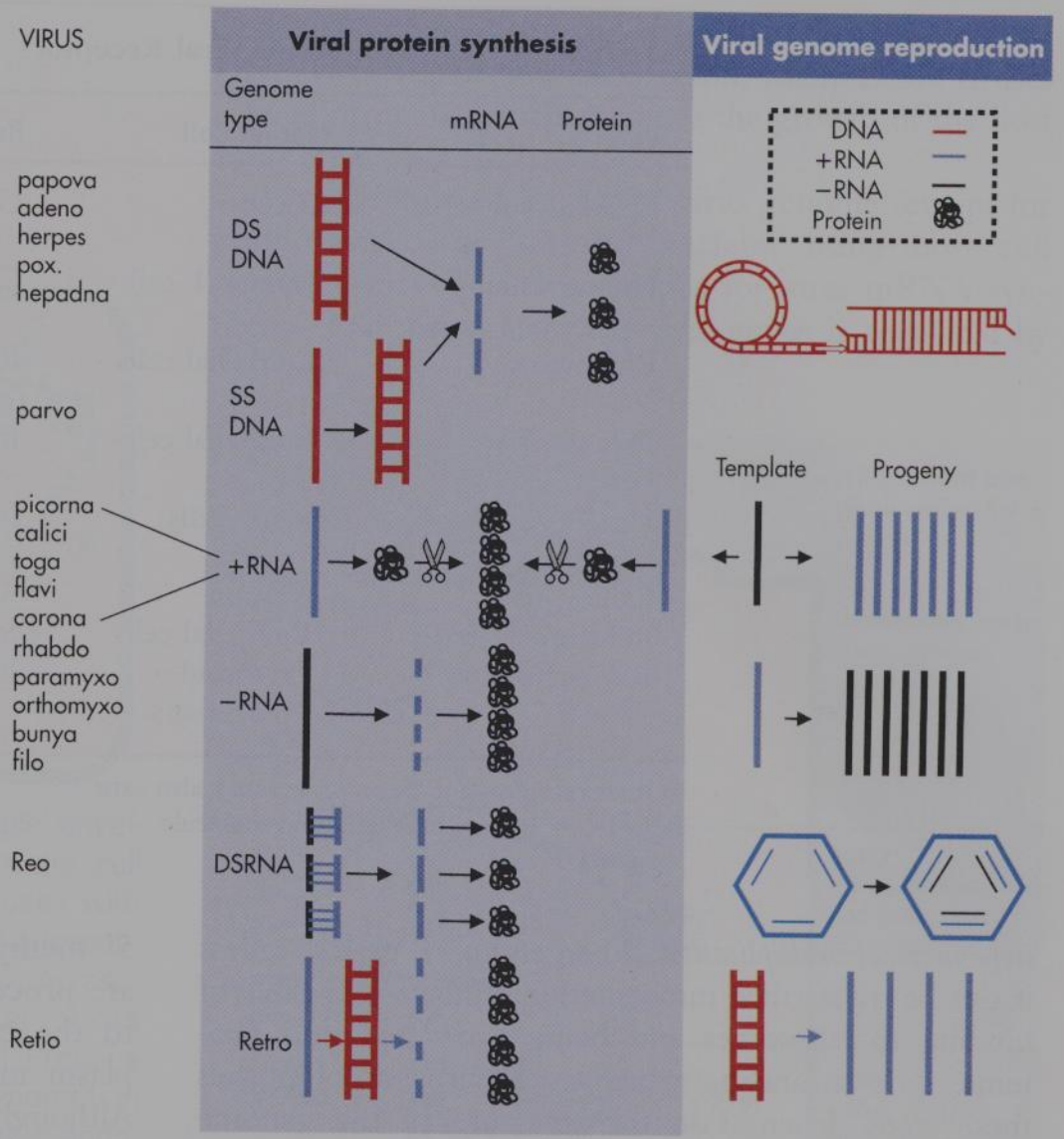
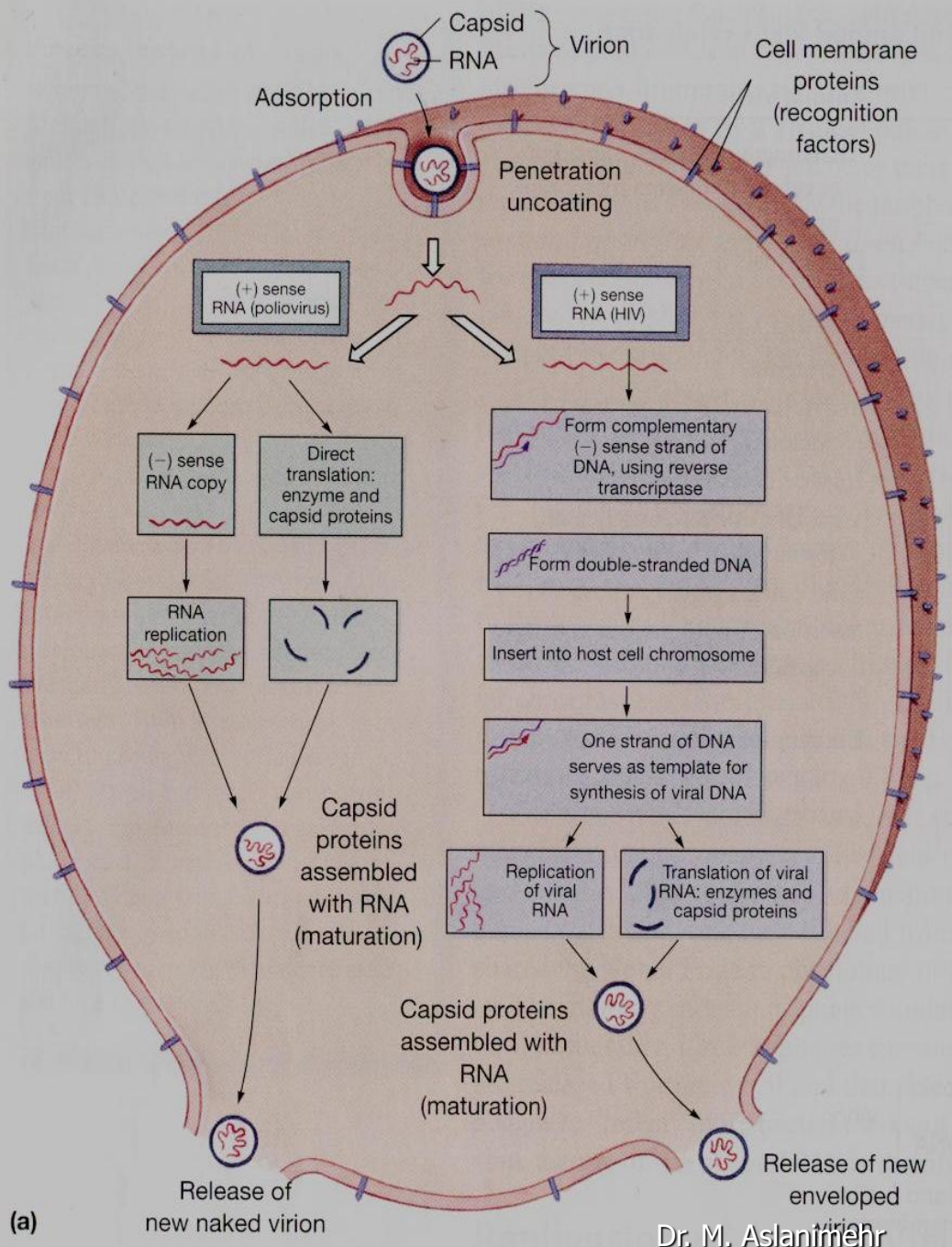
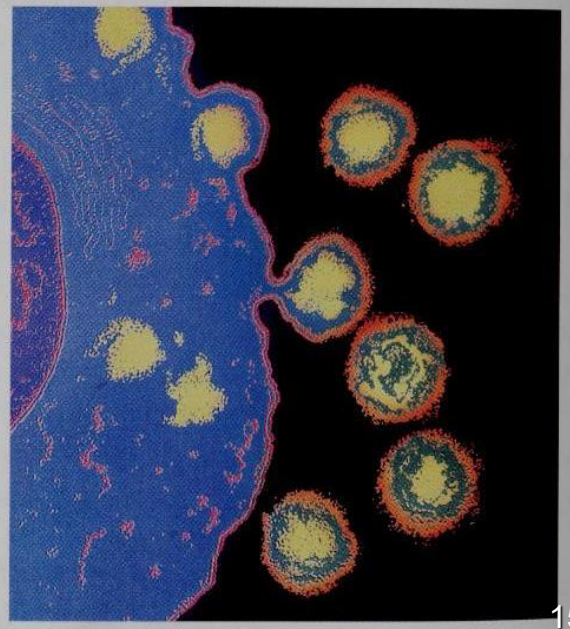

VIRUS
VIRAL PROTEIN SYNTHESIS
VIRAL GENOME REPRODUCTION
Genome type
mRNA
Protein
DNA
+RNA
−RNA
Protein
polyoma
papilloma
adeno
herpes
pox
DS DNA
parvo
SS DNA
picorna
noro
toga
flavi
corona
+RNA
rhabdo
paramyxo
orthomyxo
bunya
filo
−RNA
reo
DSRNA
retro
retro
Template
Progeny

FIGURE 6–11. Viral macromolecular synthesis steps: The mechanism of viral mRNA and protein synthesis and genome replication are determined by the structure of the genome. 1. Double-stranded DNA (DS DNA) utilizes host machinery in the nucleus (except poxviruses) to make mRNA, which is translated by host cell ribosomes into proteins. Replication of viral DNA occurs by semiconservative means, by rolling circle, linear, and in other ways. 2. Single-stranded DNA (SS DNA) is converted into DS DNA and replicates like DS DNA. 3. +RNA resembles an mRNA that binds to ribosomes to make a polyprotein that is cleaved into individual proteins. One of the viral proteins is an RNA polymerase that makes a (−)RNA template and then more +RNA genome progeny and mRNAs. 4. −RNA is transcribed into mRNAs and a full-length +RNA template by an RNA polymerase carried in the virion. The (+)RNA template is used to make (−)RNA genome progeny. 5. DS RNA acts like −RNA. The (−) strands are transcribed into mRNAs by an RNA polymerase in the capsid. +RNAs get encapsidated and −RNAs are made in the capsid. 6. Retroviruses are +RNA that are converted to DNA (cDNA) by reverse transcriptase carried in the virion. cDNA integrates into the host chromosome, and the host makes mRNAs, proteins, and full-length RNA genome copies.





➢ Figure 10.13 **Replication of RNA viruses.** (a) Two of the replication mechanisms used by different (+) sense RNA animal viruses. *Left:* In the poliovirus the viral (+) sense RNA serves as mRNA—it is translated immediately to produce proteins needed for reproduction of the virus. A (−) sense RNA copy is then made, which serves as a template for the production of more viral (+) sense RNA molecules. Mature polioviruses lyse the cell during release. *Right:* In HIV each (+) sense RNA, copied with the help of reverse transcriptase, forms an ssDNA, which serves as template for the synthesis of the complementary strand. The dsDNA is then inserted into the host chromosome, where it can remain for some time. When virus replication occurs, one strand of the DNA becomes the template for the synthesis of viral (+) sense RNA molecules. Mature HIV particles usually do not lyse the cell but rather bud off the cell surrounded by an envelope. (b) HIV viruses budding from a T-4 lymphocyte.



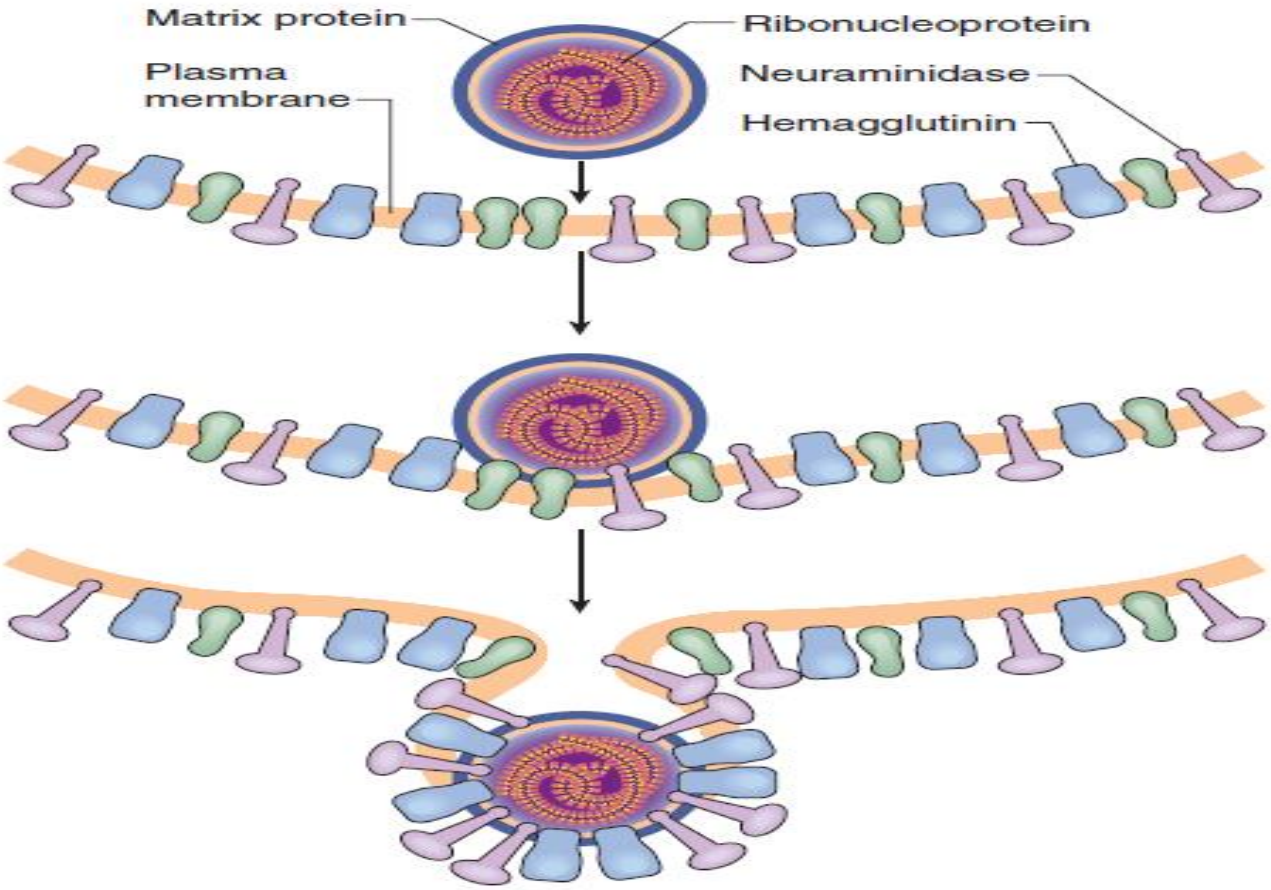


FIGURE 29-3 Release of influenza virus by plasma membrane budding. First, viral envelope proteins (hemagglutinin and neuraminidase) are inserted into the host plasma membrane. Then the nucleocapsid approaches the inner surface of the membrane and binds to it. At the same time, viral proteins collect at the site, and host membrane proteins are excluded. Finally, the plasma membrane buds to simultaneously form the viral envelope and release the mature virion. (Reproduced with permission from Willey JM, Sherwood LM, Woolverton CJ: *Prescott, Harley, and Klein's Microbiology,* 7th ed. McGraw-Hill, 2008. © The McGraw-Hill Companies, Inc.)

TABLE 29-2 Pathways of Nucleic Acid Transcription for Various Virus Classes

Type of Viral Nucleic Acid	Intermediates	Type of mRNA	Example	Comments
± ds DNA	None	+ mRNA	Most DNA viruses (eg, herpesvirus, adenovirus)	
+ ss DNA	± ds DNA	+ mRNA	Parvoviruses	
± ds RNA	None	+ mRNA	Reoviruses	Virion contains RNA polymerase that transcribes each segment to mRNA
+ ss RNA	± ds RNA	+ mRNA	Picornaviruses, togaviruses, flaviviruses	Viral nucleic acid is infectious and serves as mRNA. For togaviruses, smaller + mRNA is also formed for certain proteins
– ss RNA	None	+ mRNA	Rhabdoviruses, paramyxoviruses, orthomyxoviruses	Viral nucleic acid is not infectious; virion contains RNA polymerase, which forms + mRNAs smaller than the genome. For orthomyxoviruses, + mRNAs are transcribed from each segment
+ ss RNA	– DNA, ± DNA	+ mRNA	Retroviruses	Virion contains reverse transcriptase; viral RNA is not infectious, but complementary DNA from transformed cell is

–, negative strand; +, positive strand; ±, a helix containing a positive and a negative strand; ds, double stranded; ss, single stranded.

TABLE 29-3 Comparison of Replication Strategies of Several Important RNA Virus Families

Characteristic	Grouping Based on Genomic RNA[a]					
	Positive-Strand Viruses			Negative-Strand Viruses		Double-Stranded Viruses
	Picornaviridae	Togaviridae	Retroviridae	Orthomyxoviridae	Paramyxoviridae and Rhabdoviridae	Reoviridae
Structure of genomic RNA	ss	ss	ss	ss	ss	ds
Sense of genomic RNA	Positive	Positive	Positive	Negative	Negative	
Segmented genome	0	0	0[b]	+	0	+
Genomic RNA infectious	+	+	0	0	0	0
Genomic RNA acts as messenger	+	+	+	0	0	0
Virion-associated polymerase	0	0	+[c]	+	+	+
Subgenomic messages	0	+	+	+	+	+
Polyprotein precursors	+	+	+	0	0	0

[a]+, indicated property applies to that virus family; 0, indicated property does not apply to that virus family; ds, double stranded; negative, complementary to mRNA; positive, same sense as mRNA; ss, single stranded.

[b]Retroviruses contain a diploid genome (two copies of nonsegmented genomic RNA).

[c]Retroviruses contain a reverse transcriptase (RNA-dependent DNA polymerase).

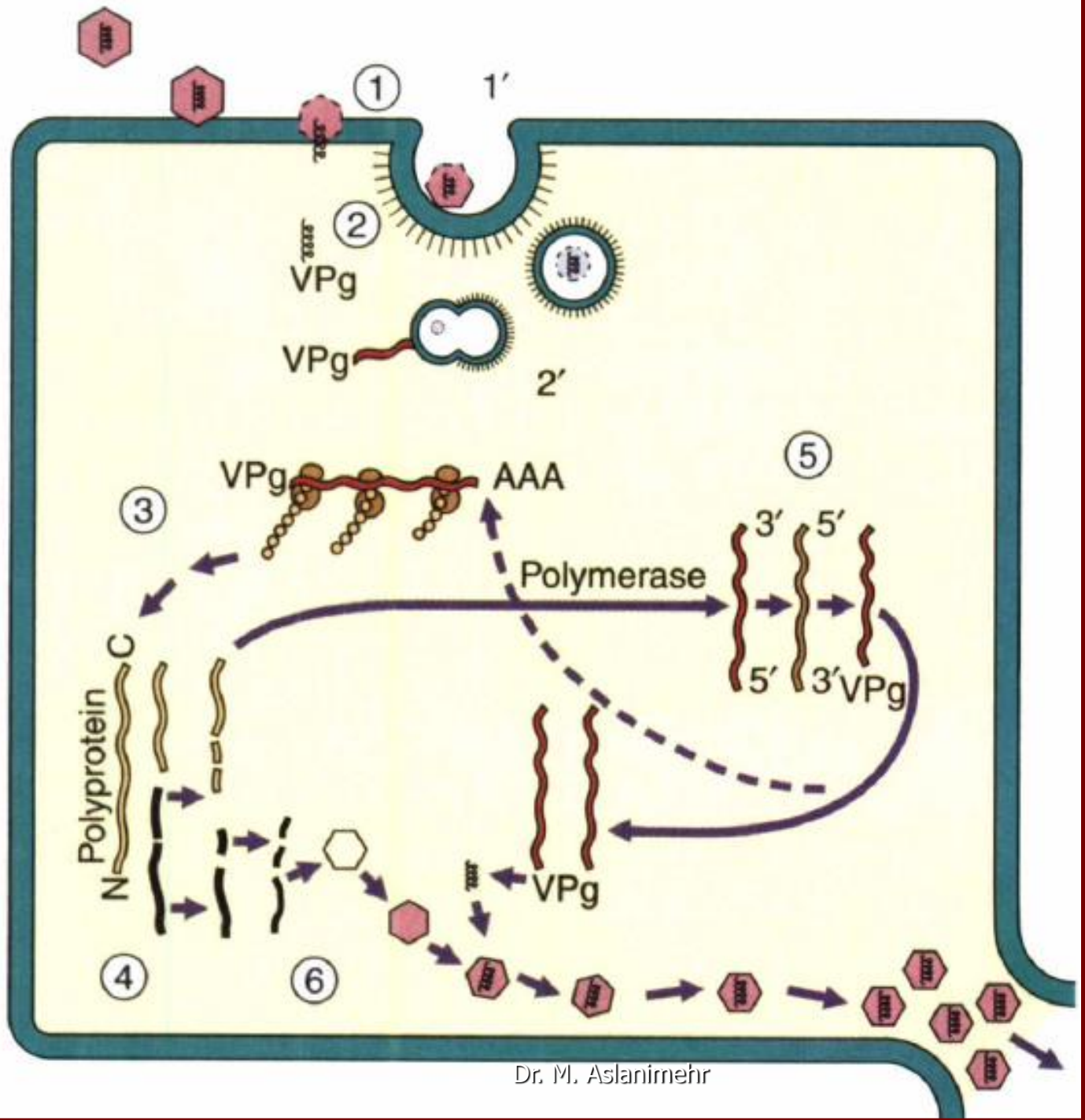
TABLE 29-4 Summary of Replication Cycles of Major Virus Families

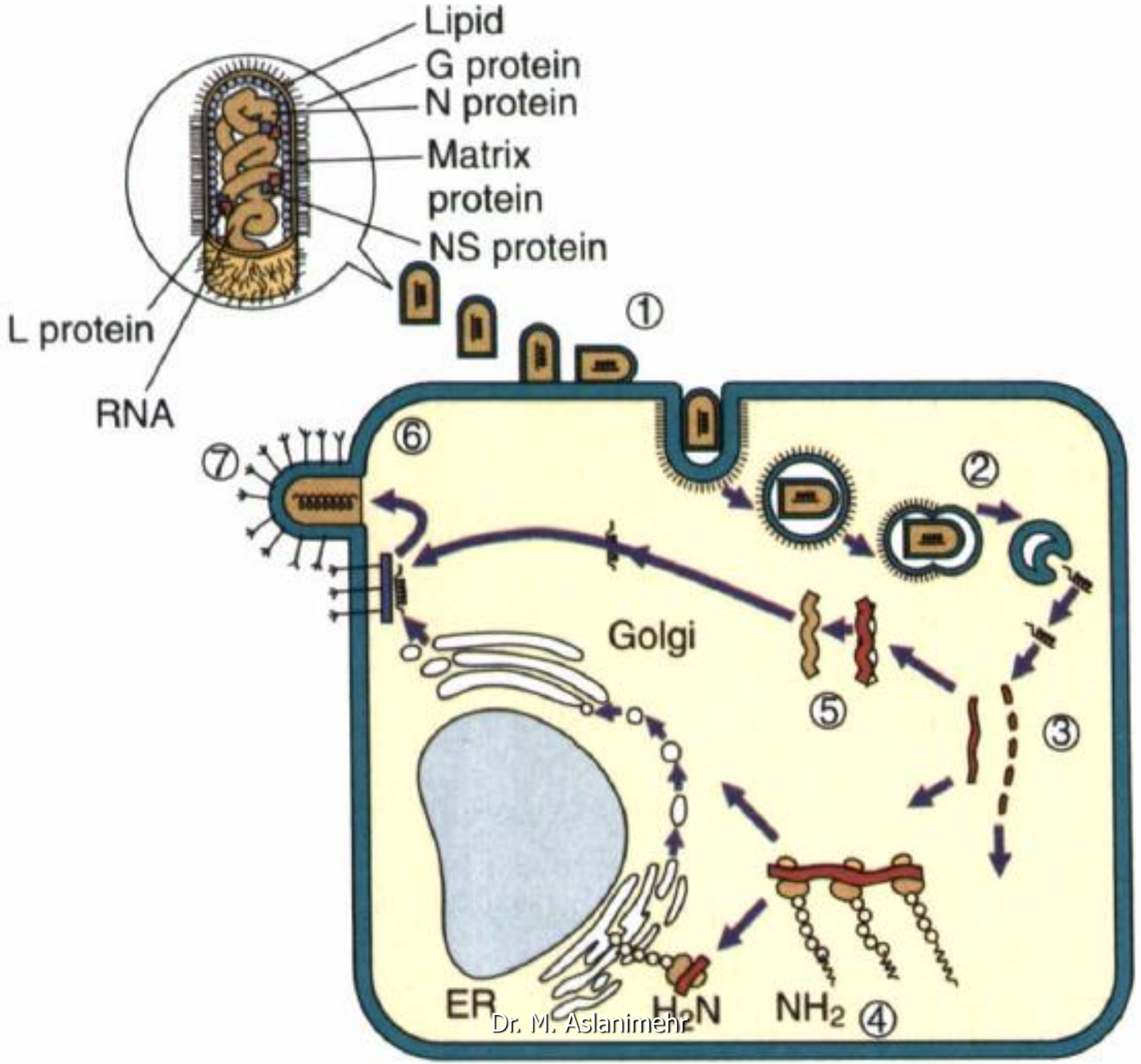
Virus Family	Presence of Virion Envelope	Intracellular Location			Multiplication Cycle (Hours)[b]
		Replication of Genome	Formation of Nucleocapsid[a]	Virion Maturation	
DNA viruses					
Parvoviridae	0	N	N	N	
Polyomaviridae	0	N	N	N	48
Adenoviridae	0	N	N	N	25
Hepadnaviridae	+	N	C	M–E	
Herpesviridae	+	N	N	M	15–72
Poxviridae	0	C	C	C	20
RNA viruses					
Picornaviridae	0	C	C	C	6–8
Reoviridae	0	C	C	C	15
Togaviridae	+	C	C	M–P	10–24
Flaviviridae	+	C	C	M–E	
Retroviridae	+	N	C	M–P	
Bunyaviridae	+	C	C	M–G	24
Orthomyxoviridae	+	N	N	M–P	15–30
Paramyxoviridae	+	C	C	M–P	10–48
Rhabdoviridae	+	C	C	M–P	6–10

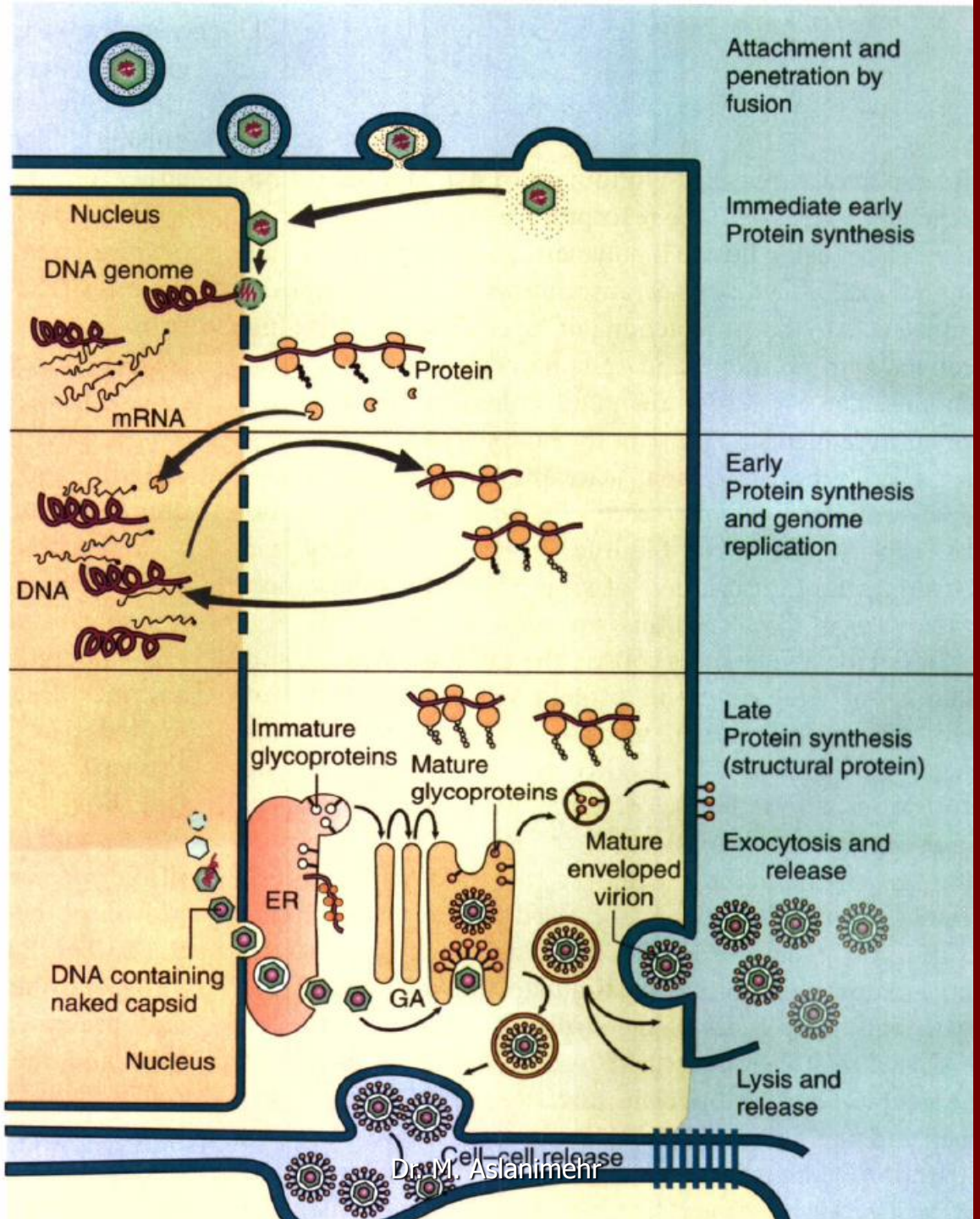
[a]The synthesis of viral proteins always occurs in the cytoplasm.

[b]The values shown for duration of the multiplication cycle are approximate; ranges indicate that various members within a given family replicate with different kinetics. Different host cell types also influence the kinetics of viral replication.

C, cytoplasm; M, membranes; M–E, endoplasmic reticulum membranes; M–G, Golgi membranes; M–P, plasma membranes; N, nucleus.


1
1′
2
VPg
VPg
2′
3
VPg
AAA
5
3′
5′
Polymerase
5′
3′VPg
Polyprotein
C
N
VPg
4
6


Lipid
G protein
N protein
Matrix protein
NS protein
L protein
RNA
①
②
③
④
⑤
⑥
⑦
Golgi
ER
H_2N
NH_2


Attachment and penetration by fusion
Nucleus
DNA genome
Immediate early Protein synthesis
Protein
mRNA
Early Protein synthesis and genome replication
DNA
Late Protein synthesis (structural protein)
Immature glycoproteins
Mature glycoproteins
Mature enveloped virion
Exocytosis and release
ER
GA
DNA containing naked capsid
Nucleus
Lysis and release
Cell–cell release

Replication of herpes simplex virus

- A complex enveloped DNA virus.
- The virus binds to specific receptors and fuses with the plasma membrane.
- The nucleocapsid then delivers the DNA genome to the nucleus.
- Transcription and translation occur in three phases:
- immediate early. early, and late. Immediate early proteins promote the takeover of the cell; early proteins consist of enzymes. including the DNA-dependent DNA polymerase; and the late proteins are structural
- proteins. including the viral capsid and glycoproteins.
- The genome is replicated before transcription of the late genes. Capsid proteins migrate into the nucleus, assemble into icosadeltahedral capsids, and are filled with the DNA genome.
- The capsids filled with genomes bud through the nuclear and endoplasmic reticulum membranes into the cytoplasm, acquire tegument proteins.
- and then acquire their envelope as they bud through the viral glycoprotein modified membranes of the trans-Golgi network.
- The virus is released by exocytosis or cell lysis. (Ref: Murray 2009)

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Reoviridae	0	C	C	C	15
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Flaviviridae	+	C	C	M–E	
Retroviridae	+	N	C	M–P	
Bunyaviridae	+	C	C	M–G	24
Orthomyxoviridae	+	N	N	M–P	15–30
Paramyxoviridae	+	C	C	M–P	10–48
Rhabdoviridae	+	C	C	M–P	6–10

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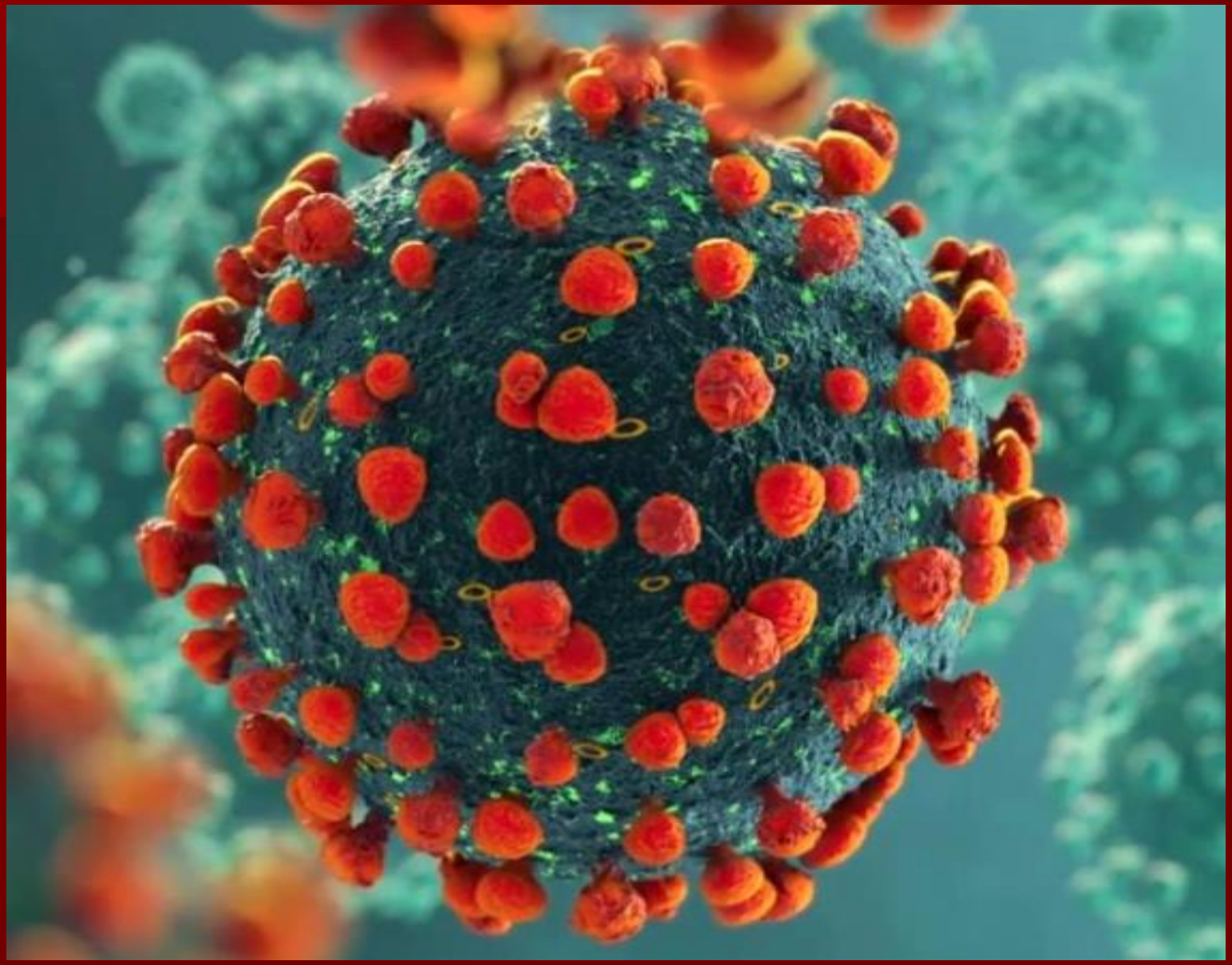
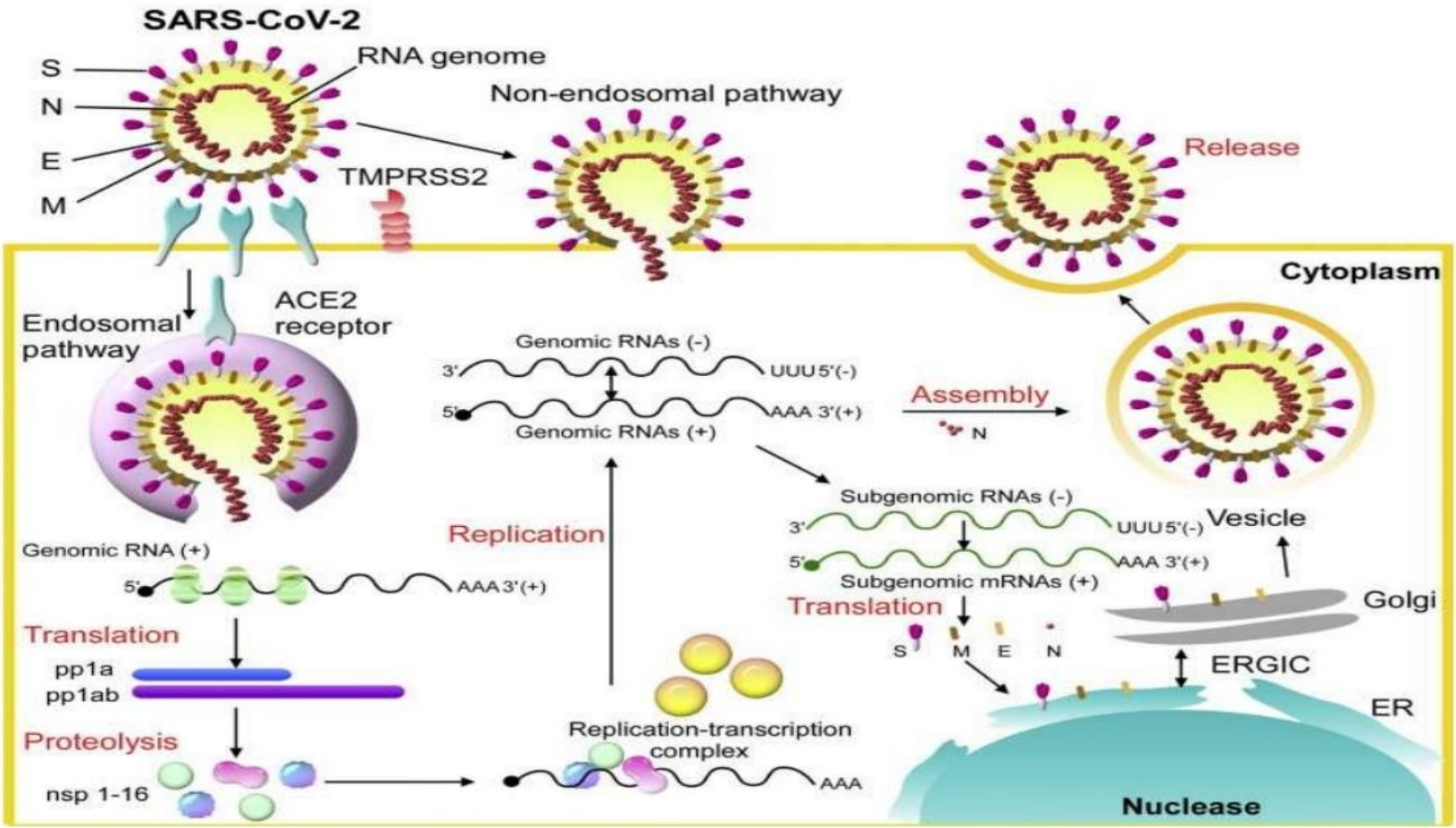


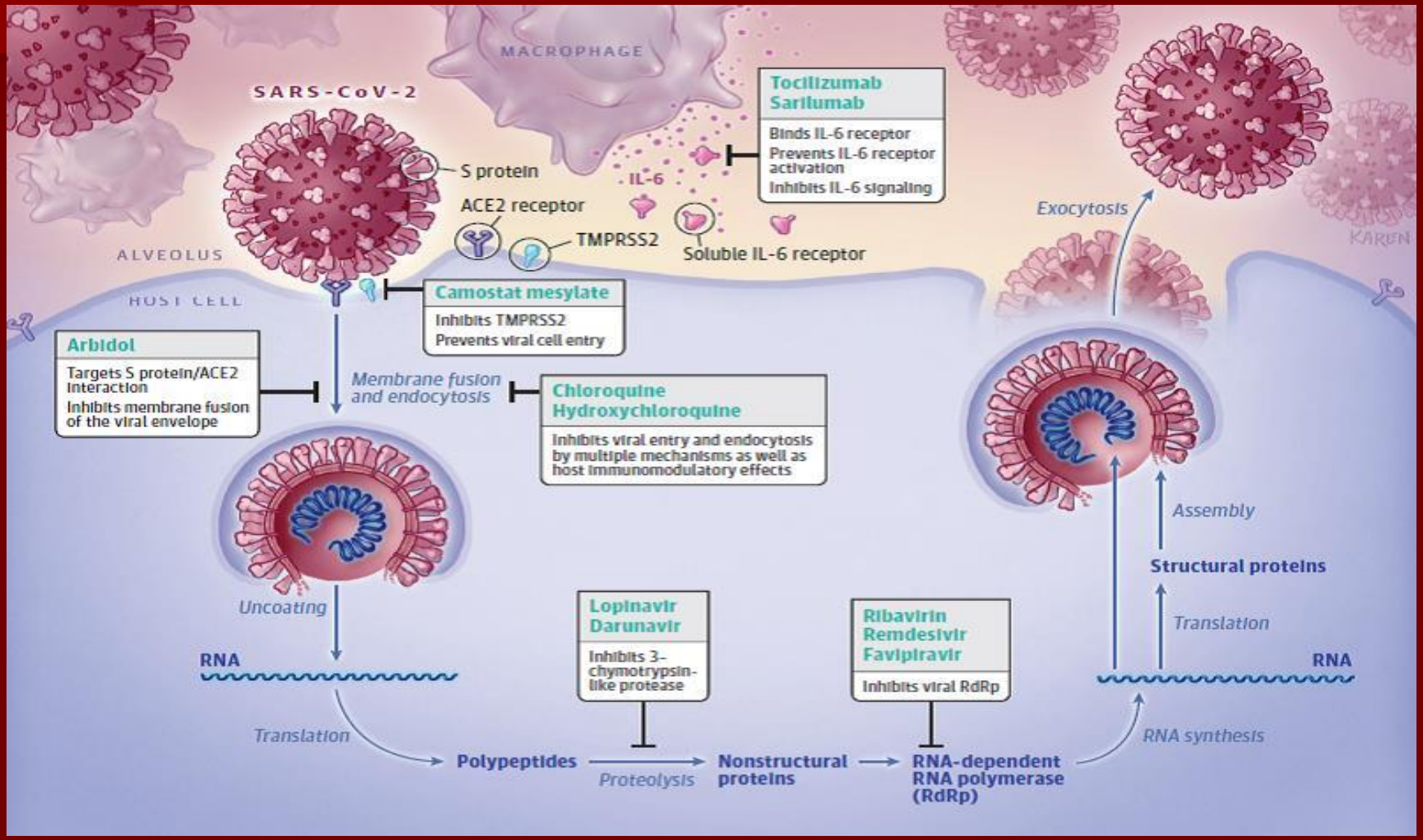
SARS-CoV-2

Qazvin University of Medical Sciences



شکل ۳: ورود ویروس SARS-CoV-2 به سلول میزبان و چرخه زندگی آن در این سلول (۳۱)

SARS-CoV-2 Viral Lifecycle and Potential Drug Targets



SARS-CoV-2 Viral Lifecycle Potential Drug Targets

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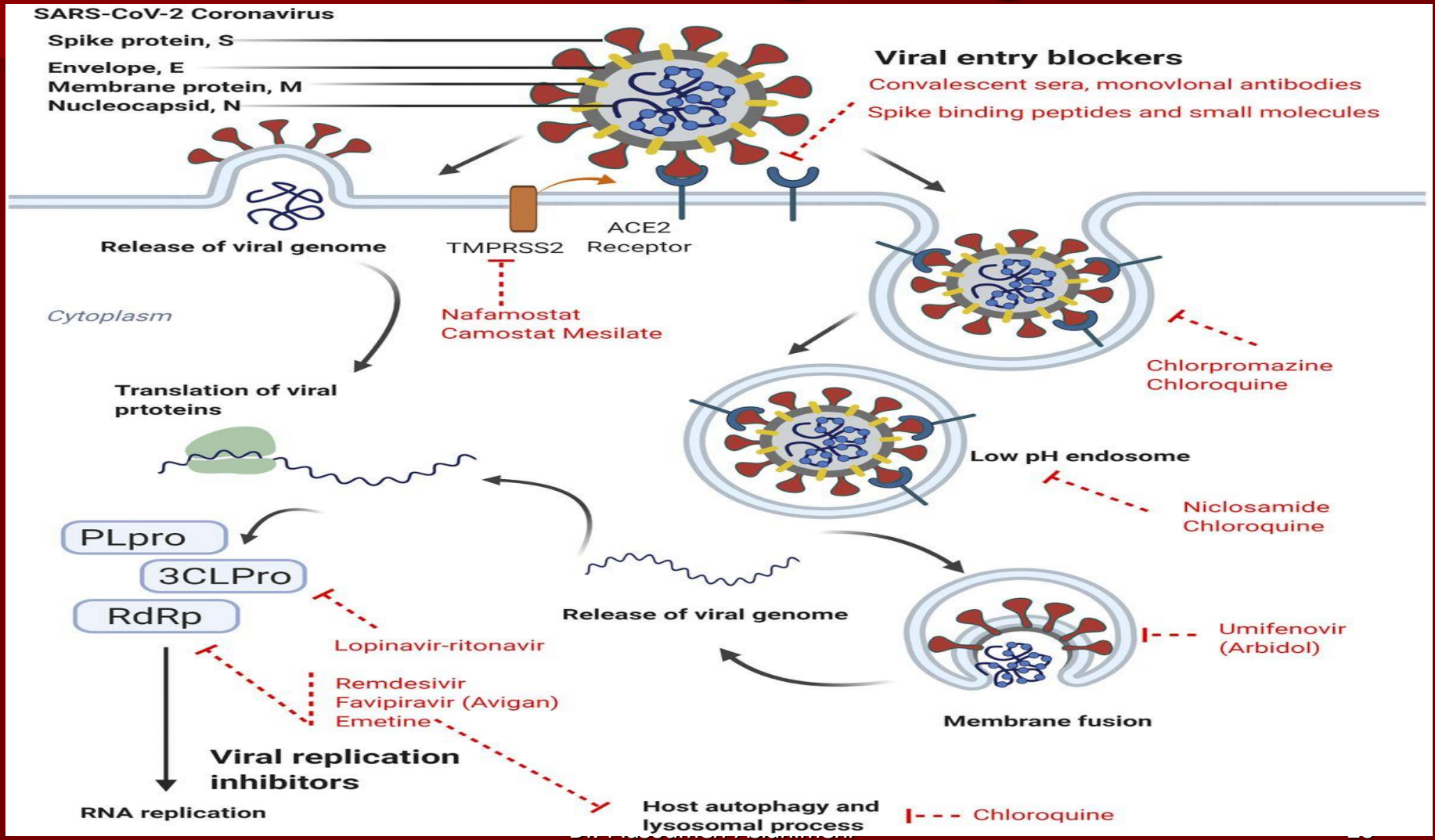
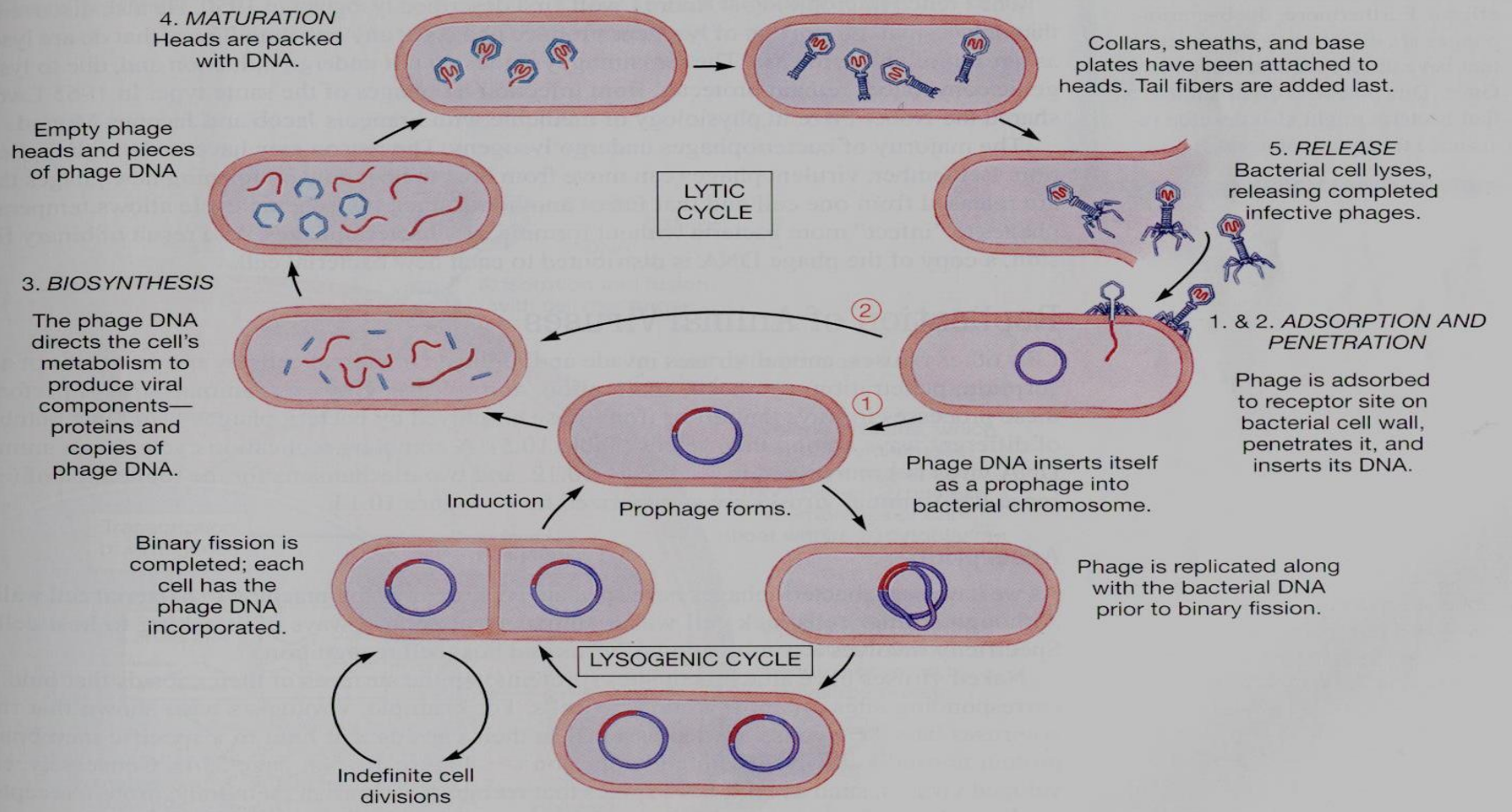


Replication of Bacteriophage



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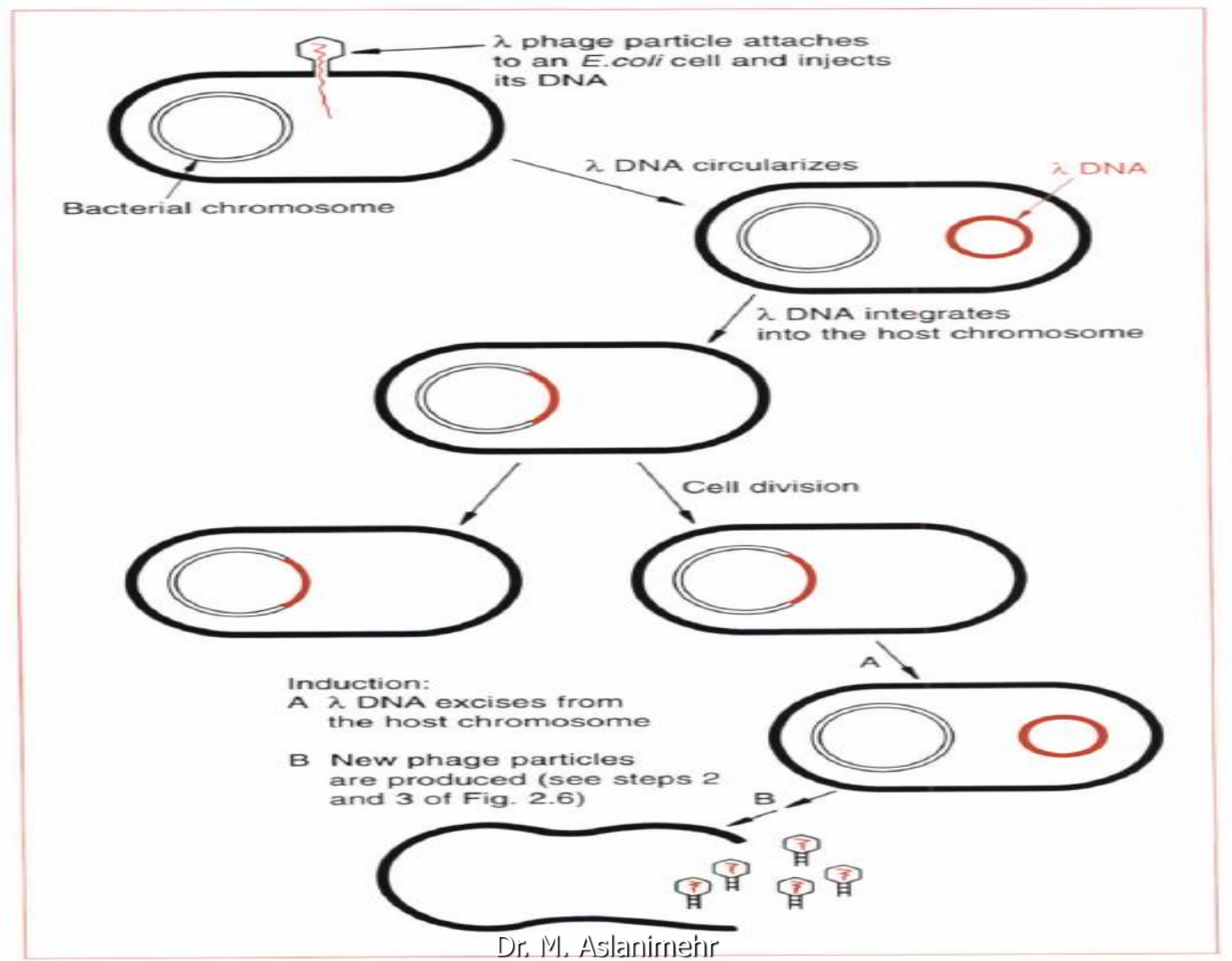
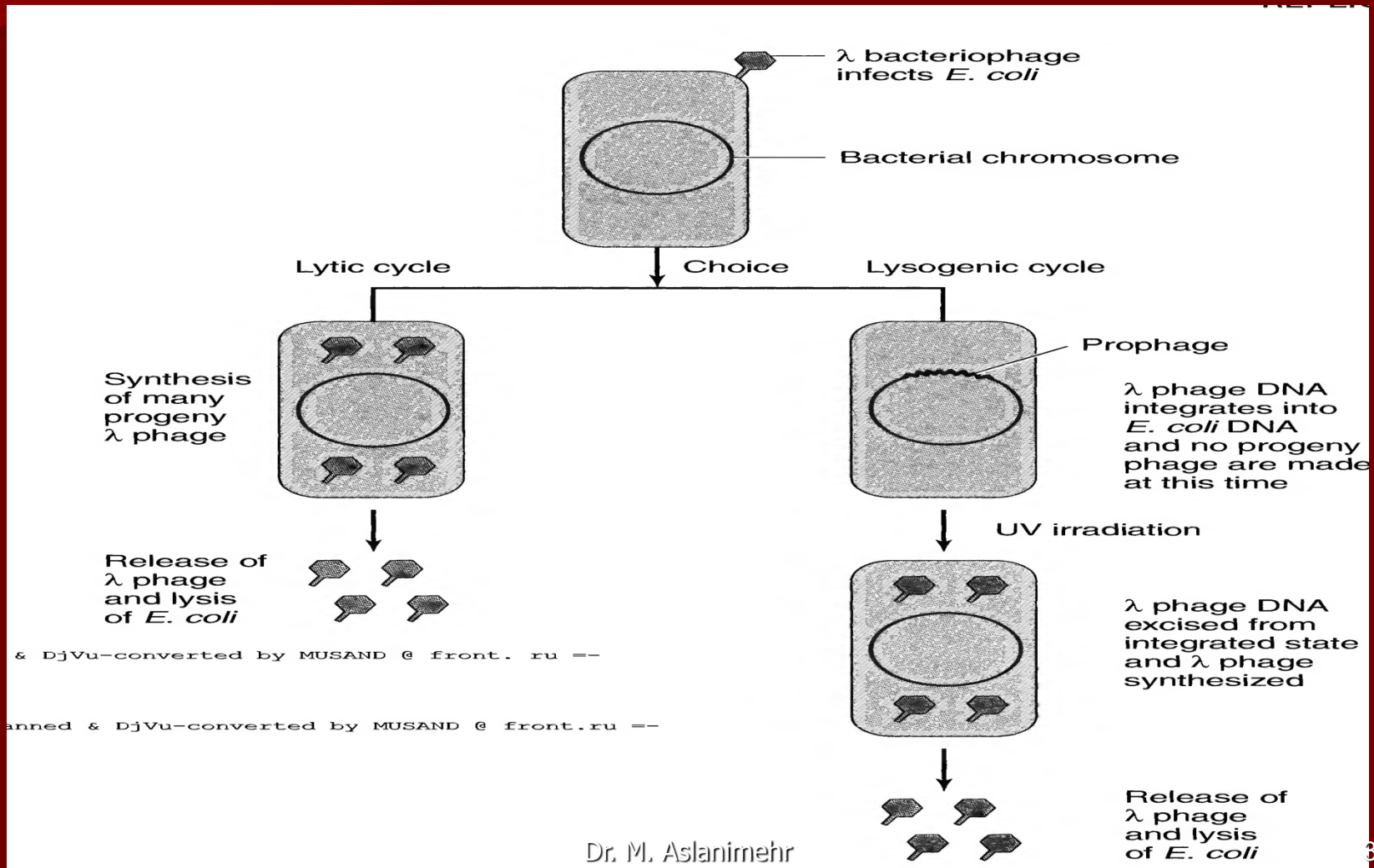
Bacteriophage λ

Lytic Cycle

The Lysogenic Infection cycle of Bacteriophage λ



Lysogeny



6. Comparison of the lytic and lysogenic cycles of bacteriophage (phage) replication.

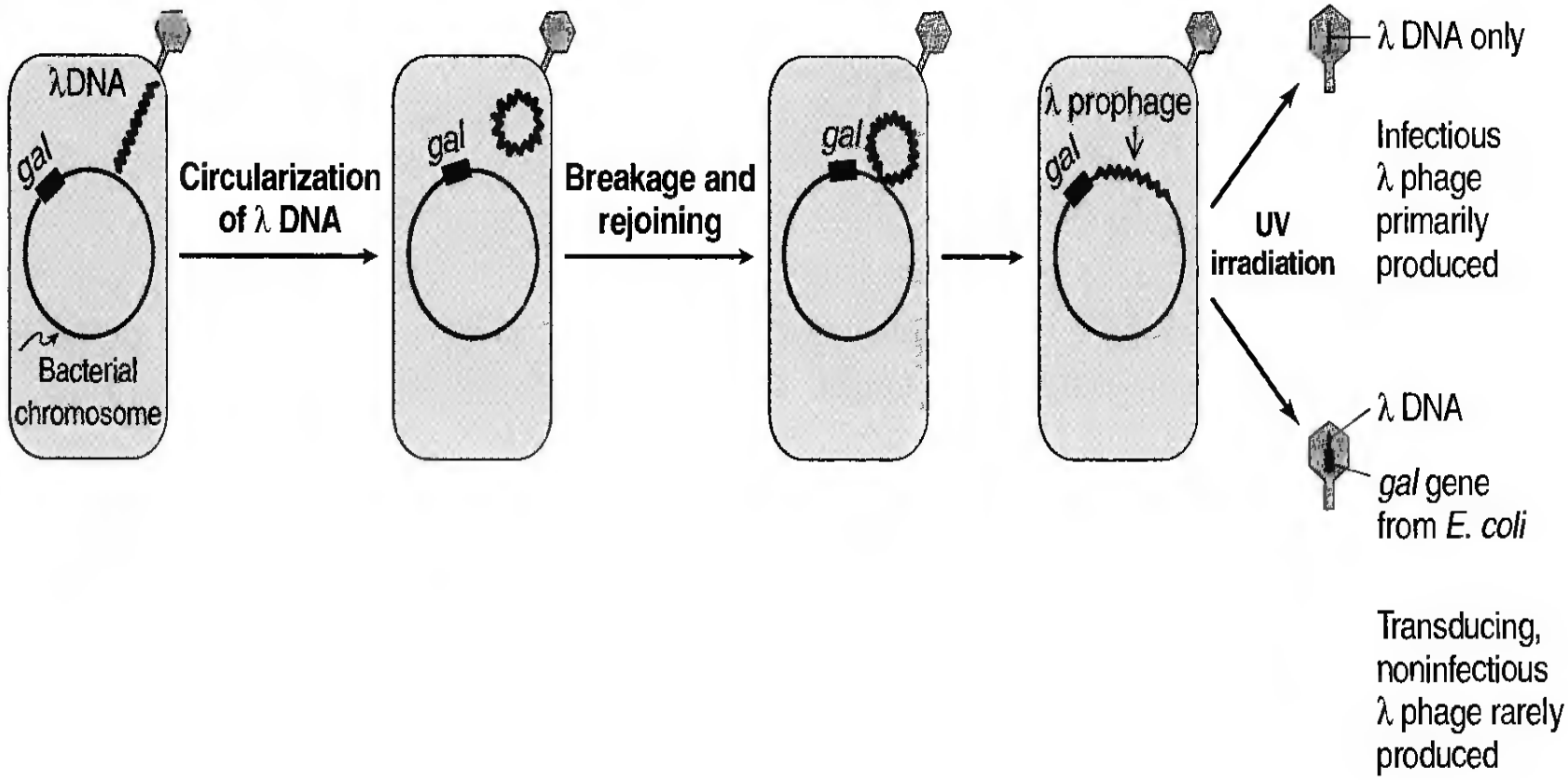
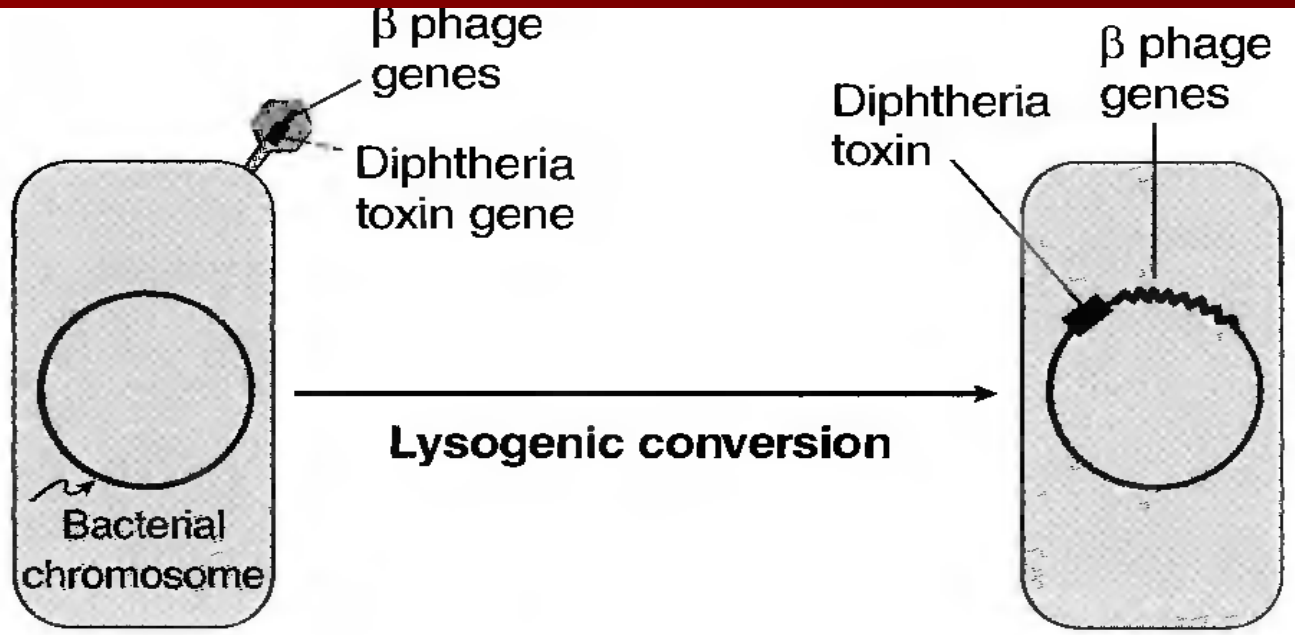


Figure 29–8. Lysogeny. The linear lambda phage DNA is injected into the bacterium, circularizes, and then integrates into the bacterial DNA. When integrated, the phage DNA is called a prophage. When the prophage is induced to enter the replicative cycle, aberrant excision of the phage DNA can occur; ie, part of the phage DNA and part of the bacterial DNA including the adjacent *gal* gene are excised. The *gal* gene can now be transduced to another bacterium. Transduction is also described in Figure 4–4. (Reproduced, with permission, from Jawetz E et al: *Review of*



β phage carrying diphtheria toxin gene infects *C. diphtheriae* not lysogenized by β phage; bacterium is nonpathogenic prior to infection by β phage.

Diphtheria toxin genes integrated into chromosome of *C. diphtheriae*; bacterium becomes pathogenic.