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Aly Moussa

EDITOR

RESEARCH INTEREST

- Virology :
- Visualization by electron microscope
- Proteins detection using analytical and/or immuno-detection techniques
- Nucleic acids detection and identification by hybridization, PCR…etc.

BIOGRAPHY

- Aly MOUSSA has obtained his BVSc from Cairo University, Egypt; Dr. Vet. Med. From Justus Liebig university, Germany and PhD from Claude Bernard University, France. He worked 4 years at IFFA-Mérieux Laboratory; Lyon- France, for 20 years was the chief of virology service at the French Bovine Pathology laboratory. Then for 8 years he was concerned at the national agency for sanitary security of aliments with research on the pathogenic prion proteins. He has published many papers in the fields of Virology and Transmissible Spongiform Encephalopathies. By the end of 2005 he is retired. During activity he was member of the biotechnology group at the Office International des Epizooties, member of the CEE group on Infectious Bovine Rhinotrachitis and he was a founding member of the European veterinary virology society.

VIROLOGY

INTRODUCTION TO THE VIRUSES

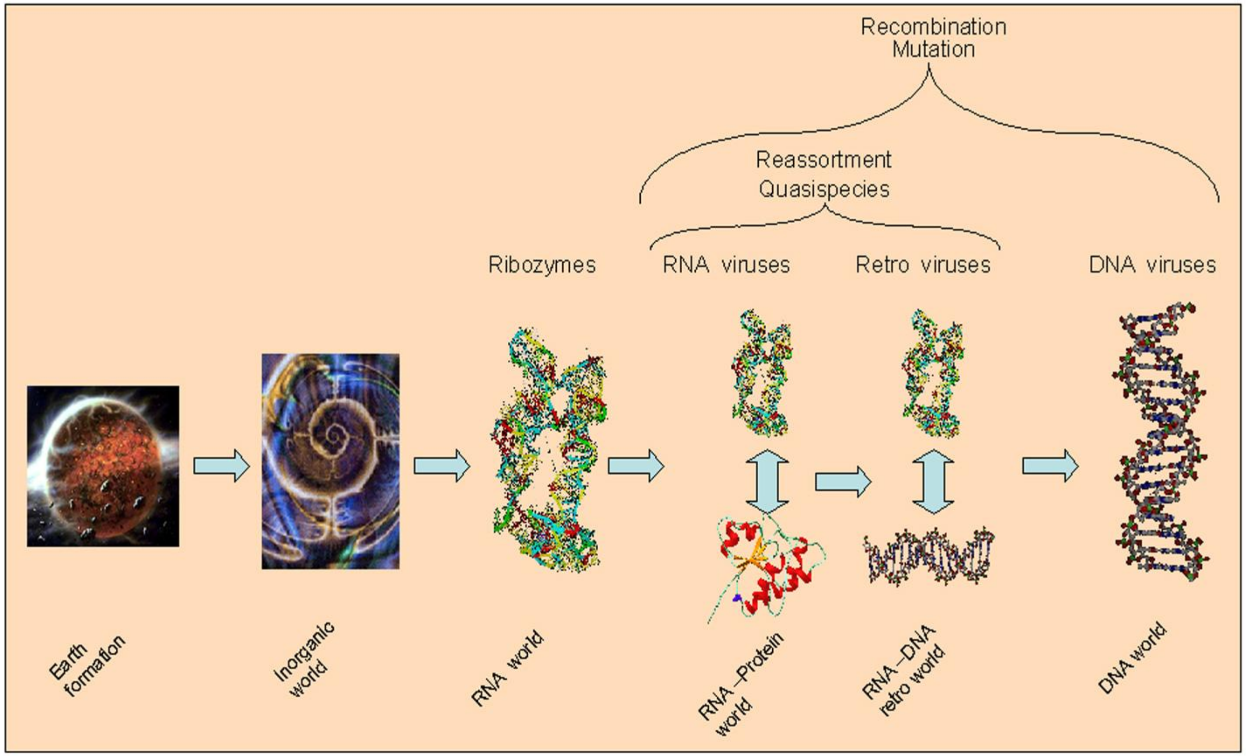
EDWARD JENNER

- Vaccinations
- Cowpox
  - cross protection against small pox
    - Variola virus
      - Major
        - Blisters
        - Blindness
        - Death
      - Minor
    - Poxviridae
    - dsDNA

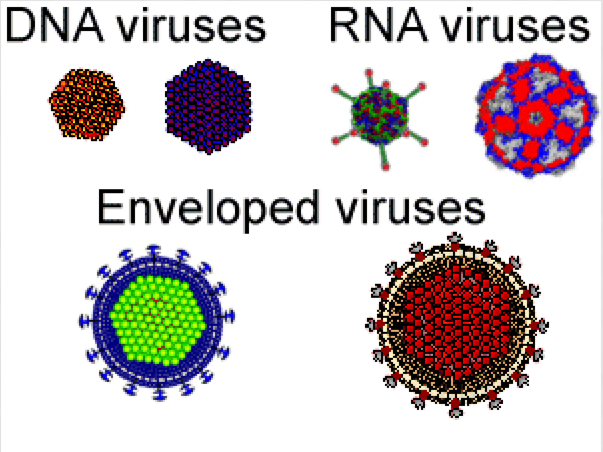
VIRUSES

- Define
- Classification
  - Group
    - NA
  - Family
    - -viridae
  - Genus
    - -virus
  - Species
    - Name

Summary figure: Schematic representation of the evolution of viruses and evolutionary forces acting on them



HOST RANGE: ANIMALS

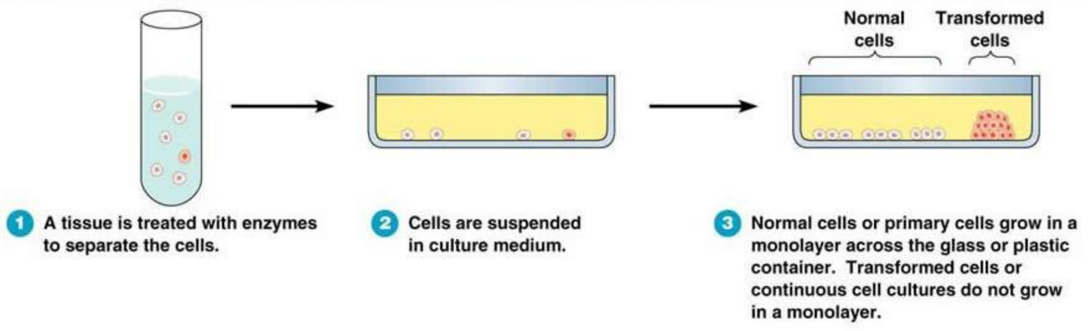


DNA ANIMAL VIRUS EXAMPLES

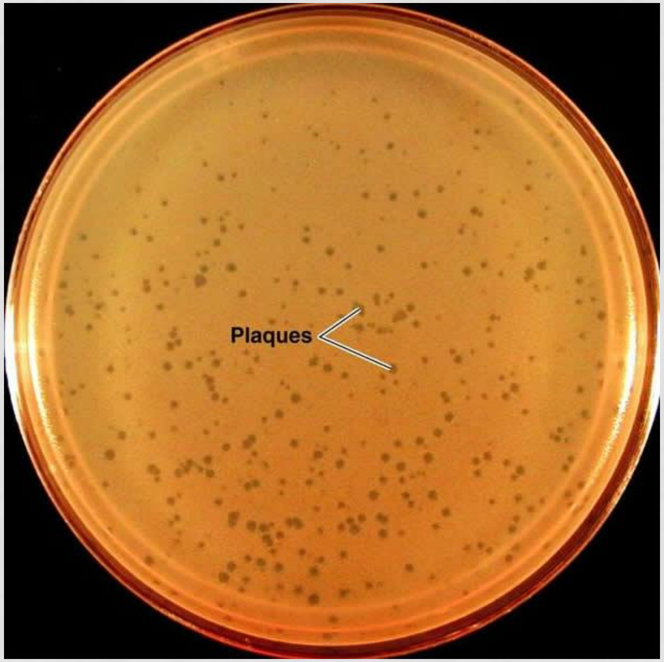
TABLE 41-1 Chemical and Morphologic Properties of Animal Virus Families Relevant to Human Disease

	Virion							
Family	Viral Genome: Type, Configuration[a] and Number of Bases per strand ($x 10^3$)	Shape[b]	Diameter (nm)	Enveloped[c]	Capsid Symmetry	Number of Capsomeres[d]	Site of Capsid Assembly	Enzymes, e.g. Transcriptase present in Virion
Circoviridae	ssDNA, circular; 0.6-1.2	s	17-22	0	Icosahedral	32?	Nucleus	None
Parvoviridae	ssDNA, linear, sense or antisense; 4-6	s	18-26	0	Icosahedral	32	Nucleus	None
Papovaviridae	dsDNA, circular; 5.1 / 7.9	s	45 / 55	0	Icosahedral	72	Nucleus	None
Adenoviridae	dsDNA, linear; 35-40	s	75-80	0	Icosahedral	252	Nucleus	None
Herpesviridae	dsDNA, linear; 124-235	s	120-200	+	Icosahedral	162	Nucleus	Thymidine kinase
Iridoviridae	dsDNA, linear; 170-200	s	125-300	+	Icosahedral	ca. 1,500	Cytoplasm	DNA-dependent RNA polymerase
Poxviridae	dsDNA, linear, covalently closed; 130-370	x	240x300	+	Complex	–	Cytoplasm	DNA-dependent RNA polymerase Protein kinase
Hepadnaviridae	dsDNA, circular, 1 ss-region; 3.0-3.3/2.0	s	40-48	+	Icosahedral	180	Nucleus	DNA-dependent DNA polymerase

VIRAL CULTURE

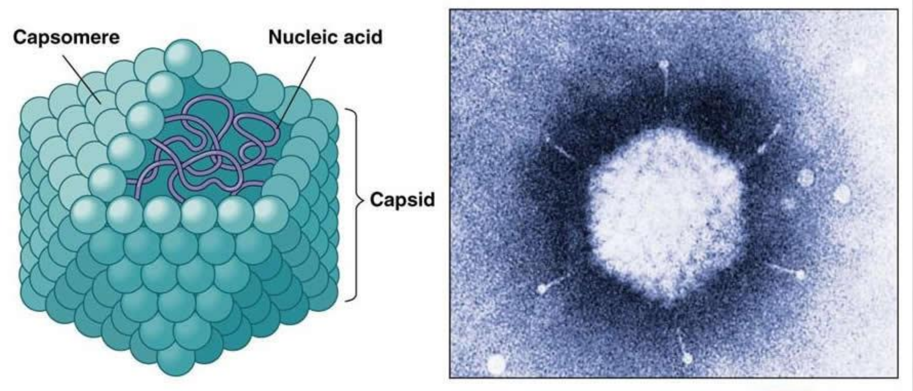


- Tissue Culture
  - Chick Embryos
  - Animal Cells/Tissue
- Assays
  - Hemagglutination
  - Plaque

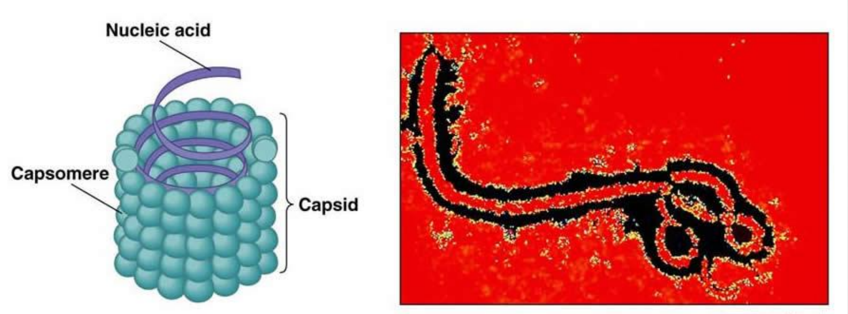


VIRAL CAPSID

- Function
  - Protect NA
  - Aids in transfer to host
- Structure
  - Protein coat
  - Capsomere arrange
    - Helical
    - Polyhedral
    - Complex

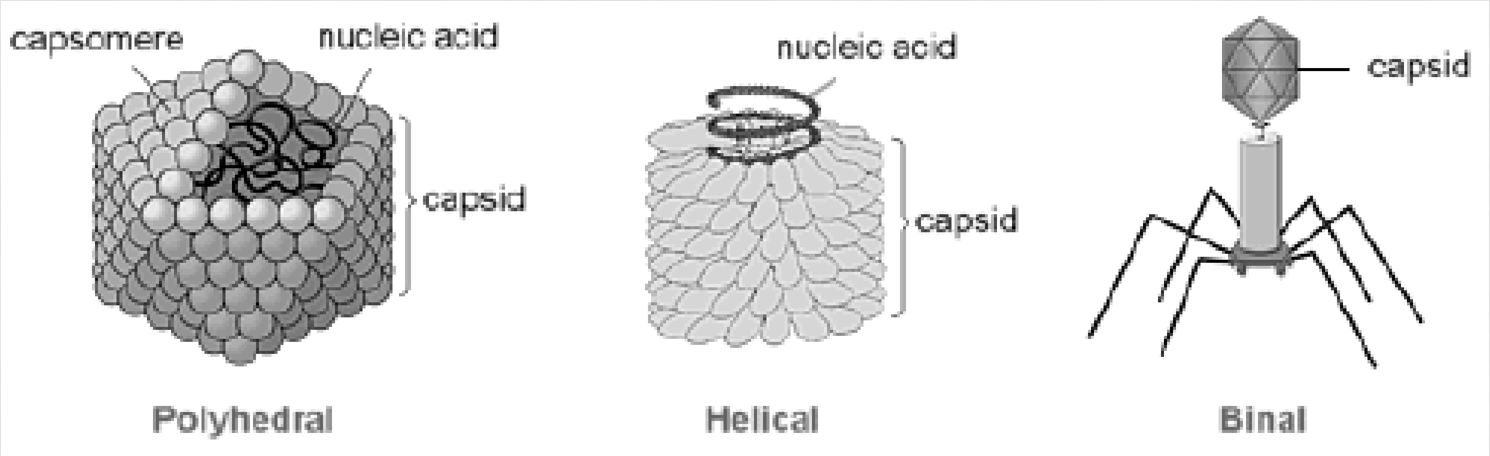


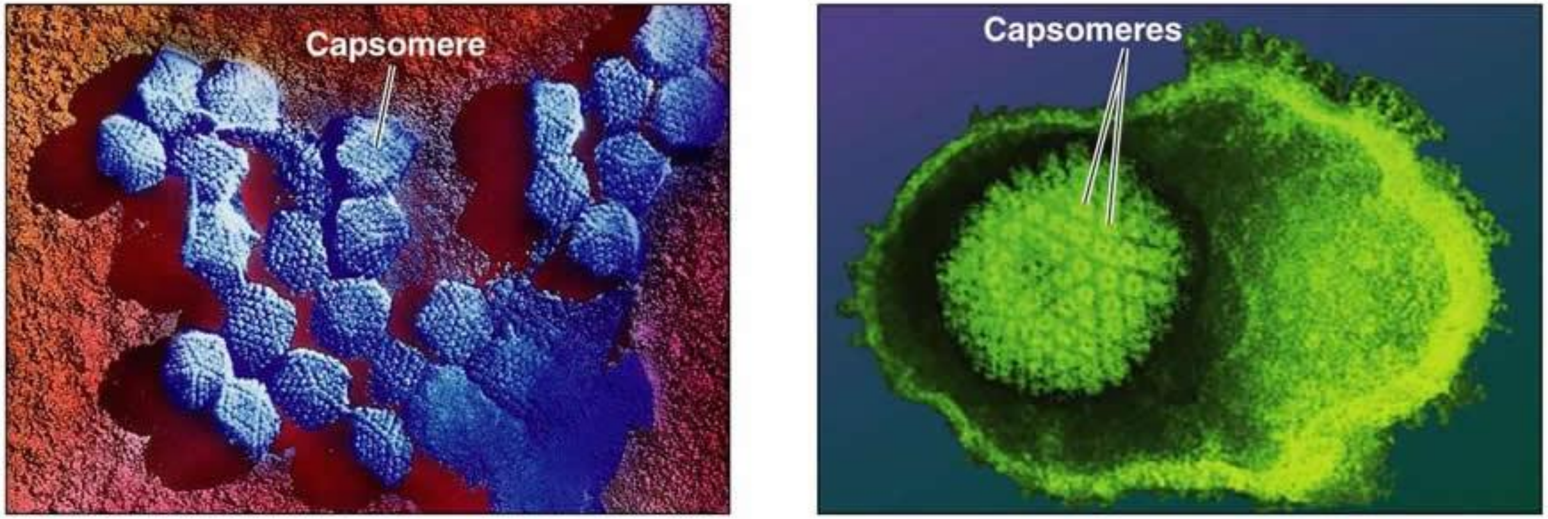
(a) A polyhedral virus (b) *Mastadenovirus*



(a) A helical virus (b) Ebola virus

CAPSOMERES ARE CAPSID SUBUNITS

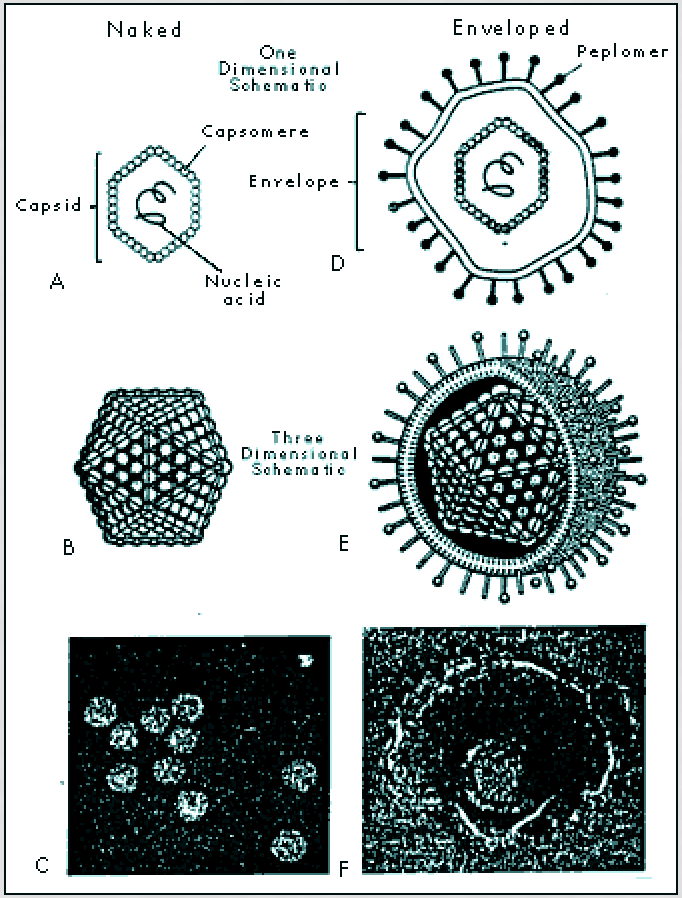




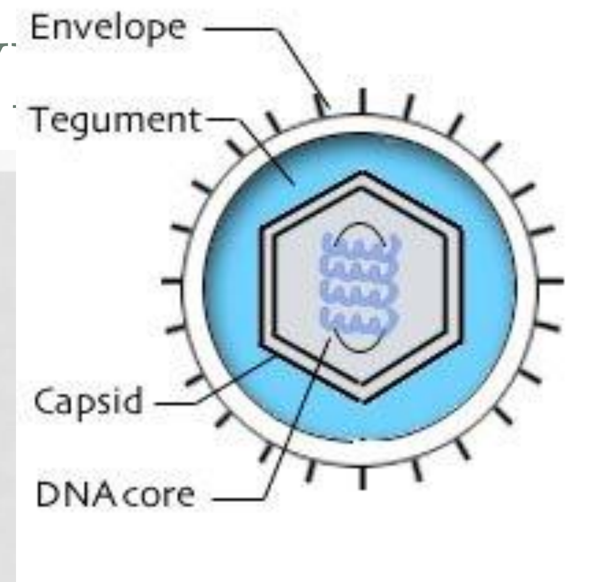
(a) *Mastadenovirus*

(b) *Herpesvirus*

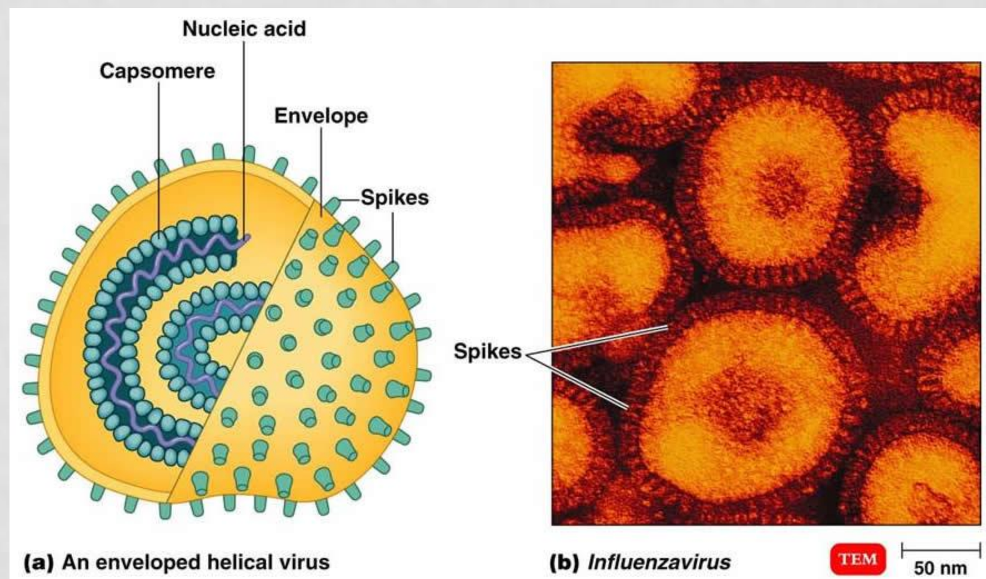
NAKED VS. ENVELOPED VIRUSES



VIRAL ENV

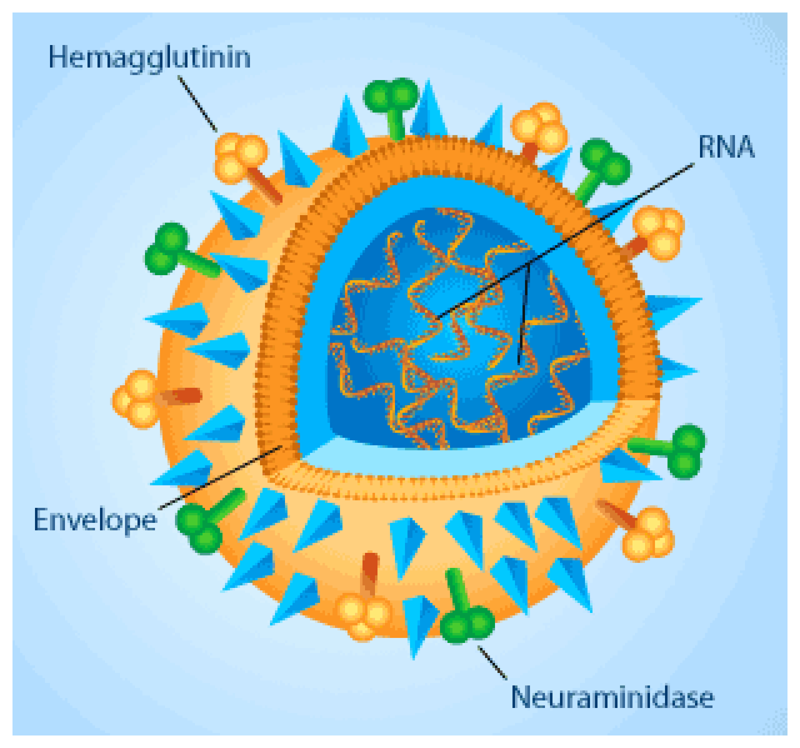


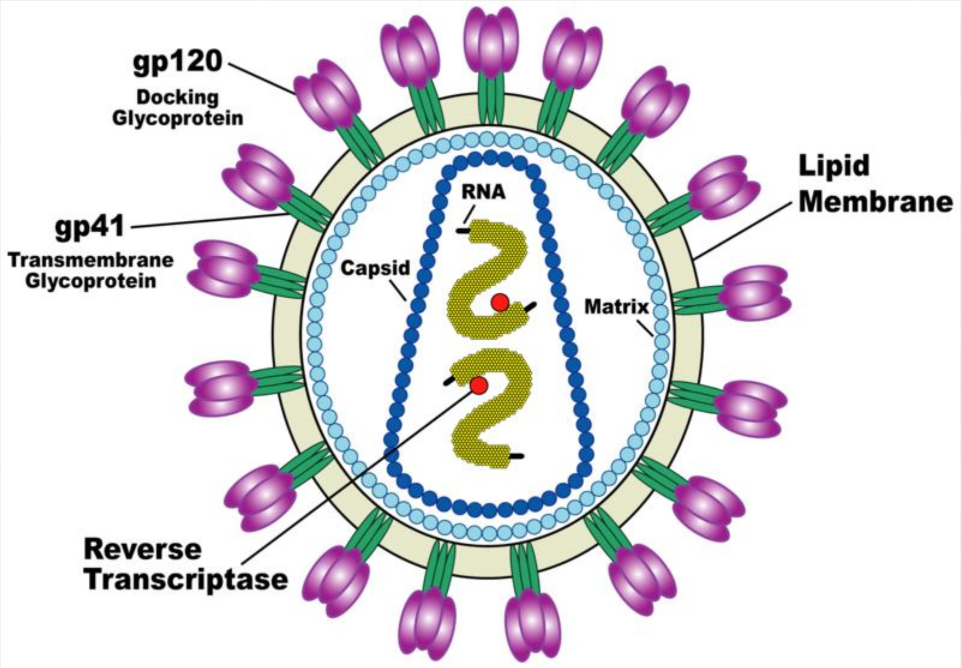
- Presence
  - Enveloped
  - Naked (non-enveloped)
- Location
  - Surrounds capsid
- Source
  - Host plasma membrane
  - Nuclear membrane
  - Endoplasmic reticulum
- Components
  - Phospholipid
  - Proteins
  - Glycoprotein spikes (+/-)
- Examples
  - Influenza
  - Rabies
  - Herpes
  - HIV



(a) An enveloped helical virus **(b)** *Influenzavirus*

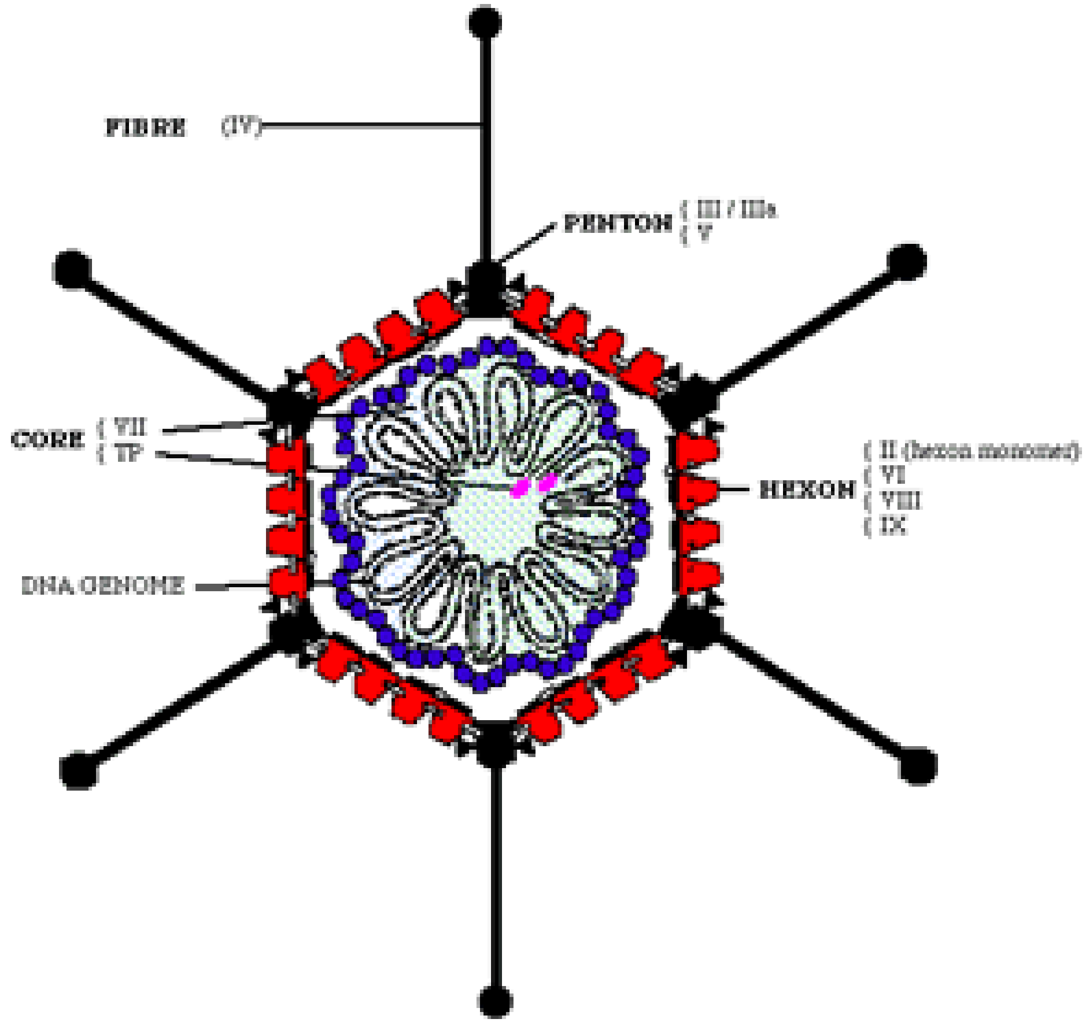
ENVELOPE GLYCOPROTEIN SPIKES





VIRAL NA

- DNA OR RNA
- Shape
  - Circular
  - Linear
- Number
  - One
  - Or more
- Strands
  - ss
  - ds
  - + or - if RNA



VIRAL CLASSIFIC

- dsDNA
  - pox
  - Herpes
  - Papilloma
- ssDNA
  - Parvo
- DsRNA
  - Reovirus
  - Rotavirus
- ssRNA
  - Polio
  - Rhino
  - Corona
  - Measles, mumps
  - Rabies
  - Influenza
  - Parainflenza
  - Retroviruses

TABLE 13.2 Families of Viruses That Affect Humans

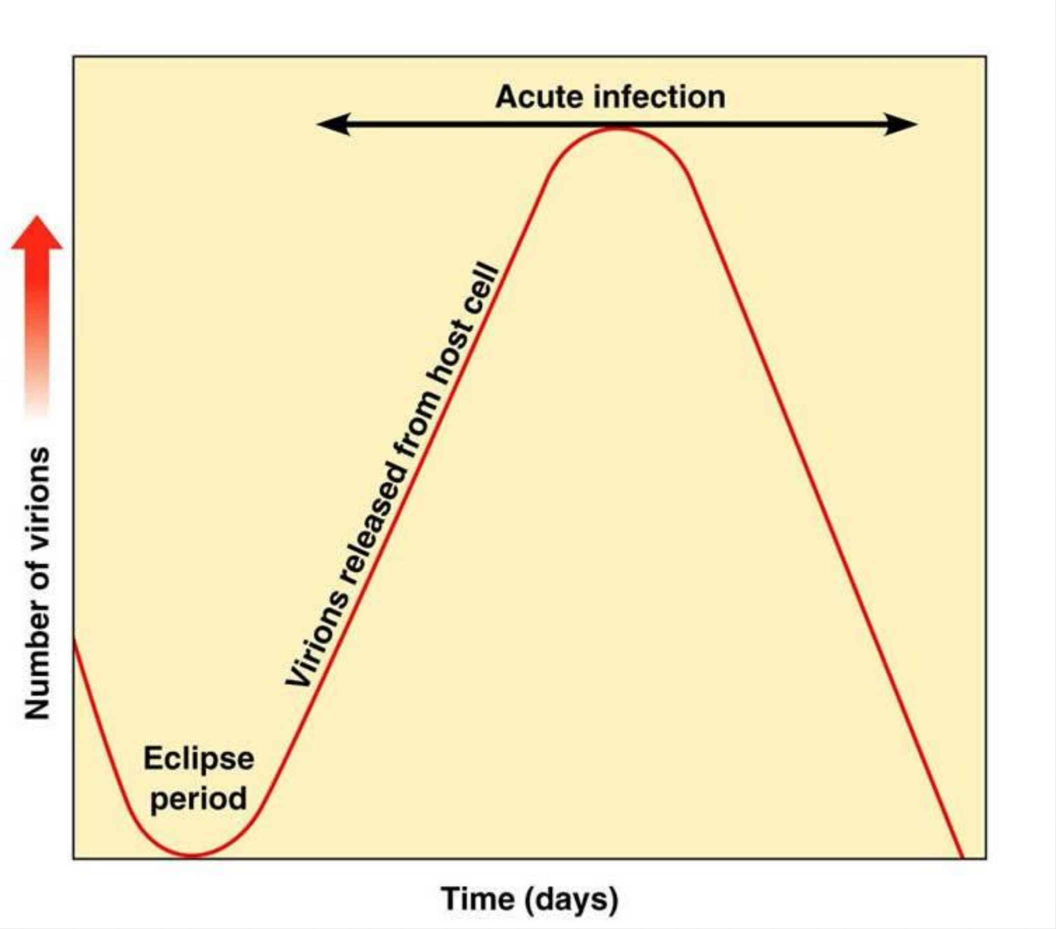
Characteristics/ Dimensions	Viral Family	Important Genera	Clinical or Special Features
Single-stranded DNA nonenveloped 18–25 nm	Parvoviridae	Human parvovirus B19	Fifth disease; anemia in immunocompromised patients. Refer to Chapter 21.
Double-stranded DNA nonenveloped 70–90 nm	Adenoviridae	*Mastadenovirus*	Medium-sized viruses that cause various respiratory infections in humans; some cause tumors in animals.
40–57 nm	Papovaviridae	*Papillomavirus* (human wart virus) *Polyomavirus*	Small viruses that induce tumors; the human wart virus (papilloma) and certain viruses that produce cancer in animals (polyoma and simian) belong to this family. Refer to Chapters 21 and 26.
Double-stranded DNA enveloped 200–350 nm	Poxviridae	*Orthopoxvirus* (vaccinia and smallpox viruses) *Molluscipoxvirus*	Very large, complex, brick-shaped viruses that cause diseases such as smallpox (variola), molluscum contagiosum (wartlike skin lesion), and cowpox. Refer to Chapter 21.
150–200 nm	Herpesviridae	*Simplexvirus* (HHV-1 and 2) *Varicellovirus* (HHV-3) *Lymphocryptovirus* (HHV-4) *Cytomegalovirus* (HHV-5) *Roseolovirus* (HHV-6) HHV-7 Kaposi's sarcoma (HHV-8)	Medium-sized viruses that cause various human diseases, such as fever blisters, chickenpox, shingles, and infectious mononucleosis; causes a type of human cancer called Burkitt's lymphoma. Refer to Chapters 21, 23, and 26.
Double-stranded DNA enveloped 42 nm	Hepadnaviridae	*Hepadnavirus* (hepatitis B virus)	After protein synthesis, hepatitis B virus uses reverse transcriptase to produce its DNA from mRNA; causes hepatitis B and liver tumors. Refer to Chapter 25.
Single-stranded RNA, + strand nonenveloped 28–30 nm	Picornaviridae	*Enterovirus* *Rhinovirus* (common cold virus) Hepatitis A virus	At least 70 human enteroviruses are known, including the polio-, coxsackie-, and echoviruses; more than 100 rhinoviruses exist and are the most common cause of colds. Refer to Chapters 22, 24, and 25.
35–40 nm	Caliciviridae	Hepatitis E virus *Norovirus*	Includes causes of gastroenteritis and one cause of human hepatitis. Refer to Chapter 25.
Single-stranded RNA, + strand enveloped 60–70 nm	Togaviridae	*Alphavirus* *Rubivirus* (rubella virus)	Included are many viruses transmitted by arthropods (*Alphavirus*); diseases include eastern equine encephalitis (EEE) and western equine encephalitis (WEE). Rubella virus is transmitted by the respiratory route. Refer to Chapters 21, 22, and 23.
40–50 nm	Flaviviridae	*Flavivirus* *Pestivirus* Hepatitis C virus	Can replicate in arthropods that transmit them; diseases include yellow fever, dengue and St. Louis and West Nile encephalitis. Refer to Chapters 22, 23, and 25.
Nidovirales 80–160 nm	Coronaviridae	*Coronavirus*	Associated with upper respiratory tract infections and the common cold; SARS virus. Refer to Chapter 24.
Mononegavirales − strand, one strand of RNA 70–180 nm	Rhabdoviridae	*Vesiculovirus* (vesicular stomatatis virus) *Lyssavirus* (rabies virus)	Bullet-shaped viruses with a spiked envelope; cause rabies and numerous animal diseases. Refer to Chapter 22.
80–14,000 nm	Filoviridae	*Filovirus*	Enveloped, helical viruses; Ebola and Marburg viruses are filoviruses. Refer to Chapter 23.
150–300 nm	Paramyxoviridae	*Paramyxovirus* *Morbillivirus* (measleslike virus)	Paramyxoviruses cause parainfluenza, mumps, and Newcastle disease in chickens. Refer to Chapters 21, 24, and 25.
− strand, one strand of RNA 32 nm	Deltaviridae	Hepatitis D	Depend on coinfection with hepadnavirus. Refer to Chapter 25.
− strand, multiple strands of RNA 80–200 nm	Orthomyxoviridae	Influenza virus A, B, and C	Envelope spikes can agglutinate red blood cells. Refer to Chapter 24.
90–120 nm	Bunyaviridae	*Bunyavirus* (California encephalitis virus) *Hantavirus*	Hantaviruses cause hemorrhagic fevers such as Korean hemorrhagic fever and *Hantavirus* pulmonary syndrome; associated with rodents. Refer to Chapters 22, 23.
110–130 nm	Arenaviridae	*Arenavirus*	Helical capsids contain RNA-containing granules; cause lymphocytic choriomeningitis, Venezuelan hemorrhagic fever, and Lassa fever. Refer to Chapter 23.
Produce DNA 100–120 nm	Retroviridae	Oncoviruses *Lentivirus* (HIV)	Includes all RNA tumor viruses. Oncoviruses cause leukemia and tumors in animals; the *Lentivirus* HIV causes AIDS. Refer to Chapter 19.
Double-stranded RNA nonenveloped 60–80 nm	Reoviridae	*Reovirus* *Rotavirus*	Involved in mild respiratory infections and gastroenteritis; an unclassified species causes Colorado tick fever. Refer to Chapter 25.

VIRAL REPLICATION DIFFERENCES

TABLE 13.3 Bacteriophage and Viral Multiplication Compared

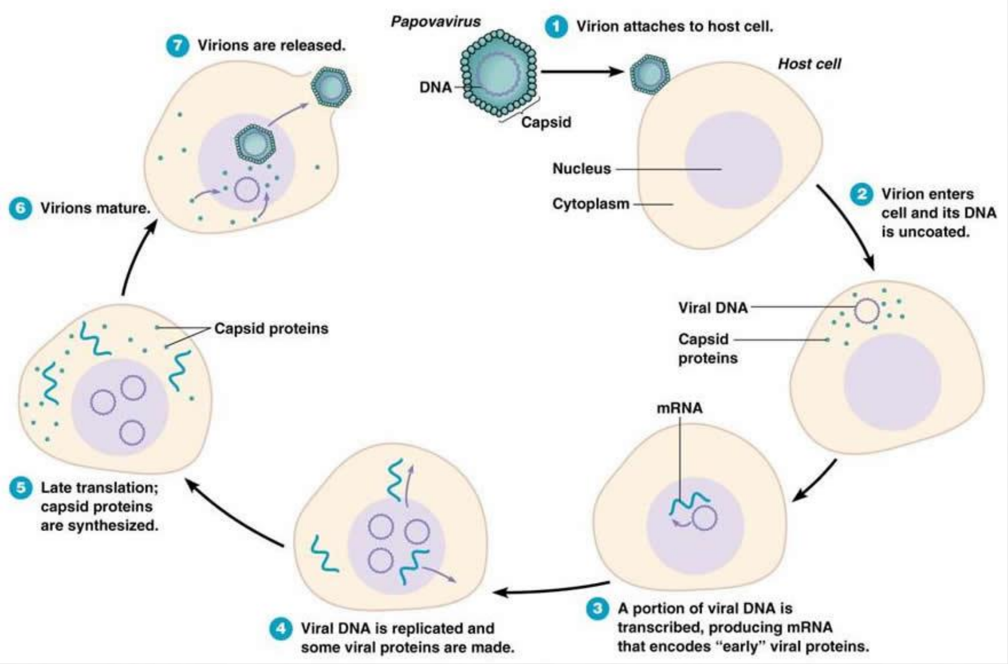
Stage	Bacteriophages	Animal Viruses
Attachment	Tail fibers attach to cell wall proteins	Attachment sites are plasma membrane proteins and glycoproteins
Entry	Viral DNA injected into host cell	Capsid enters by endocytosis or fusion
Uncoating	Not required	Enzymatic removal of capsid proteins
Biosynthesis	In cytoplasm	In nucleus (DNA viruses) or cytoplasm (RNA viruses)
Chronic infection	Lysogeny	Latency; slow viral infections; cancer
Release	Host cell lysed	Enveloped viruses bud out; nonenveloped viruses rupture plasma membrane

VIRAL INFECTIONS



REPLICATION OF ANIMAL VIRUSES

- Attach
- Entry
  - Direct Penetration
  - Membrane fusion
  - Endocytosis
- Uncoating
- Synthesis
- Assembly
- Release



VIRAL ATTACHMENT

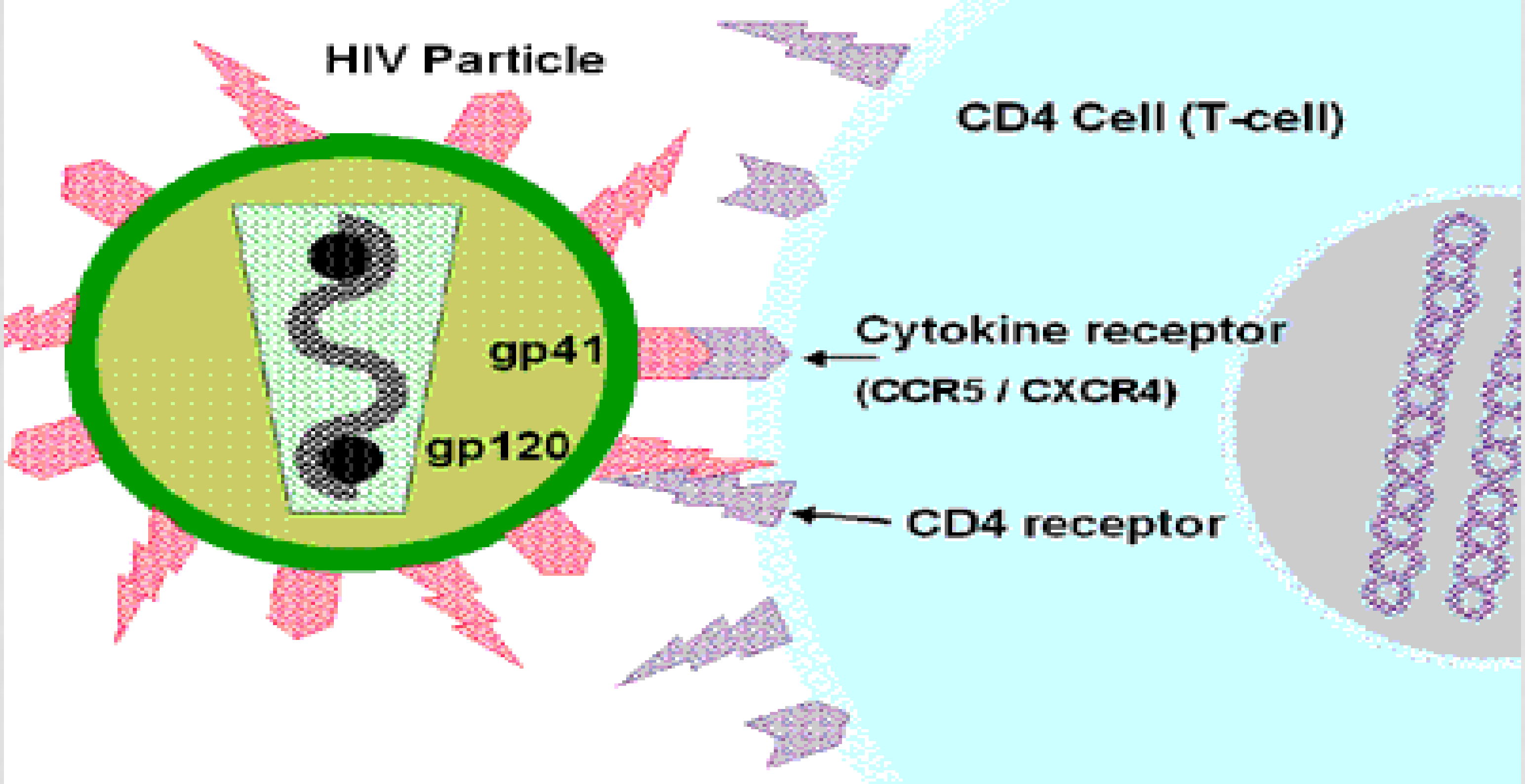
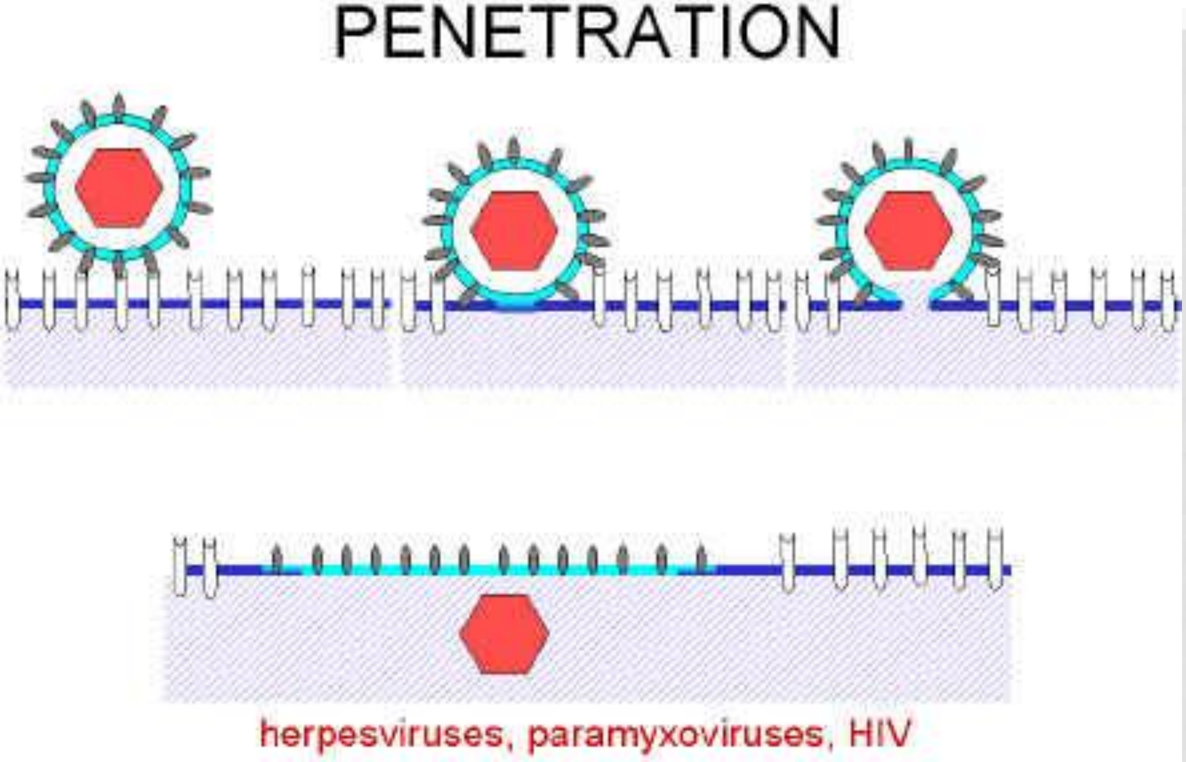
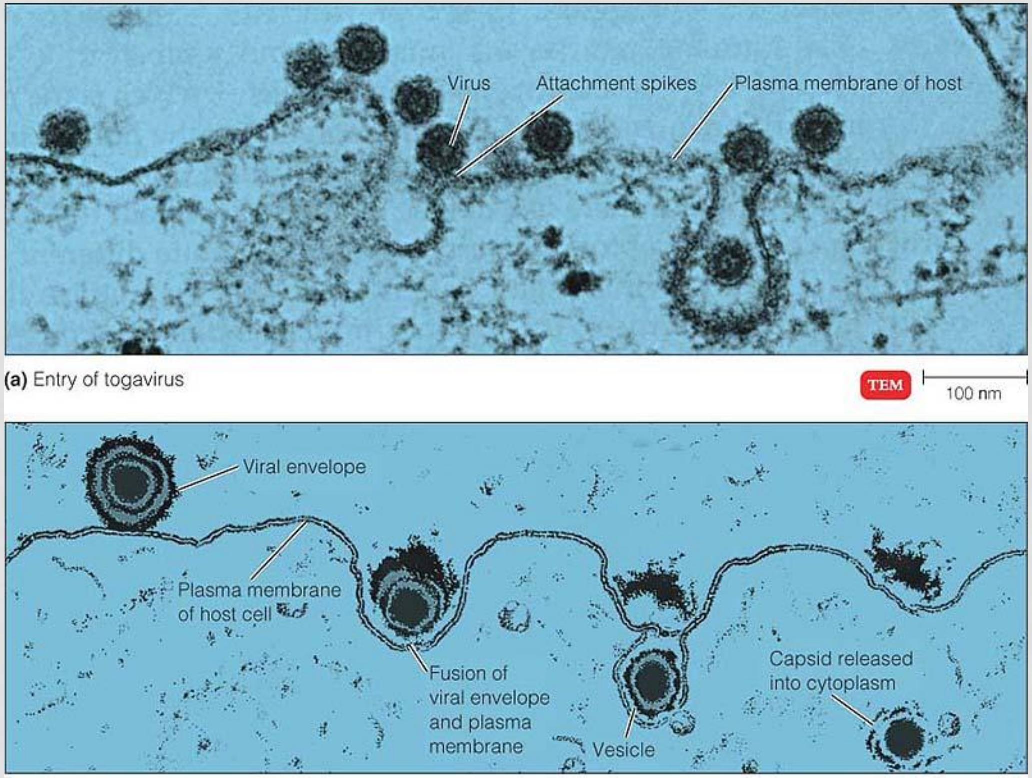


Figure 2. **Viral Attachment**

Direct



ENDOCYTOSIS VS. MEMBRANE FUSION

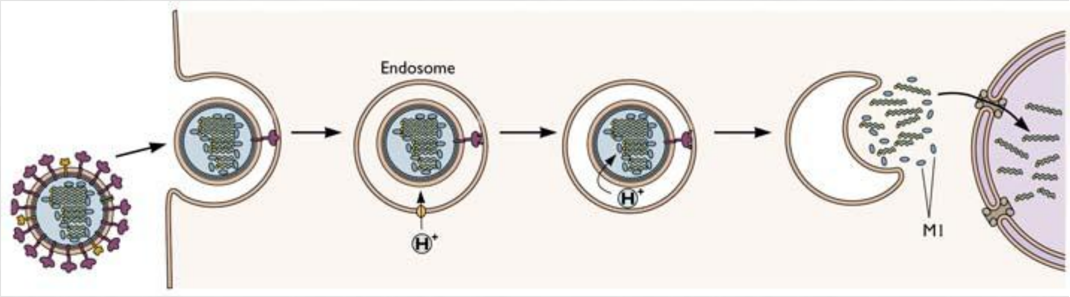


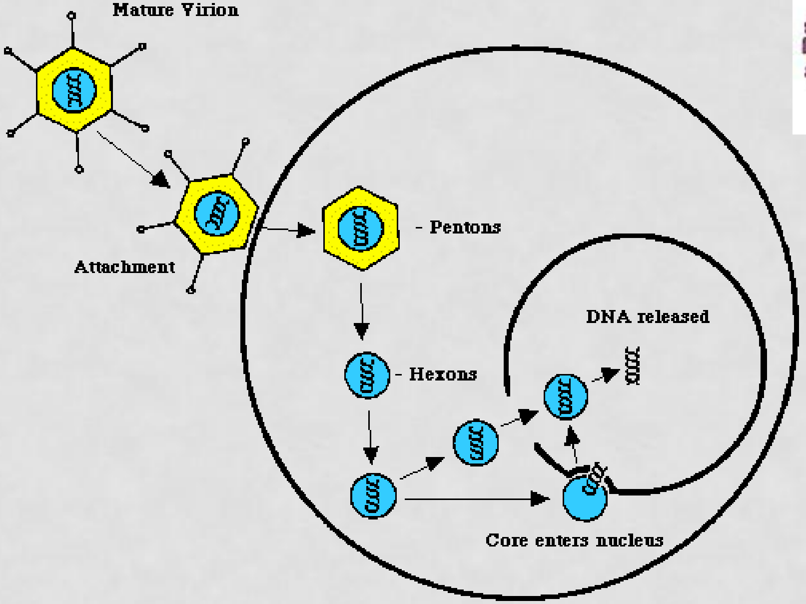
(a) Entry of togavirus

(b) Entry of herpesvirus

RELEASE OF GENOME (UNCOATING)

Influenza Virus





Adenovirus uncoating

Endosome formation
pH drop due to H+ pump
Fusion peptide to PM
Conformational change
Release of NA

NA SYNTHESIS

- dsDNA: usual replication (for most)
- ssDNA
  - complementary strand
  - Normal replication
- dsRNA
  - + strand = mRNA
  - Template and copy
- +ssRNA
  - + strand = mRNA
  - Complimentary strand for template
- -ssRNA
  - Viral enzymes make + strand
  - Template for mRNA and -ss
- Retroviruses
  - +ssRNA (mRNA to make DNA)
  - Reverse transcriptase
  - DNA is template for new +ssRNA

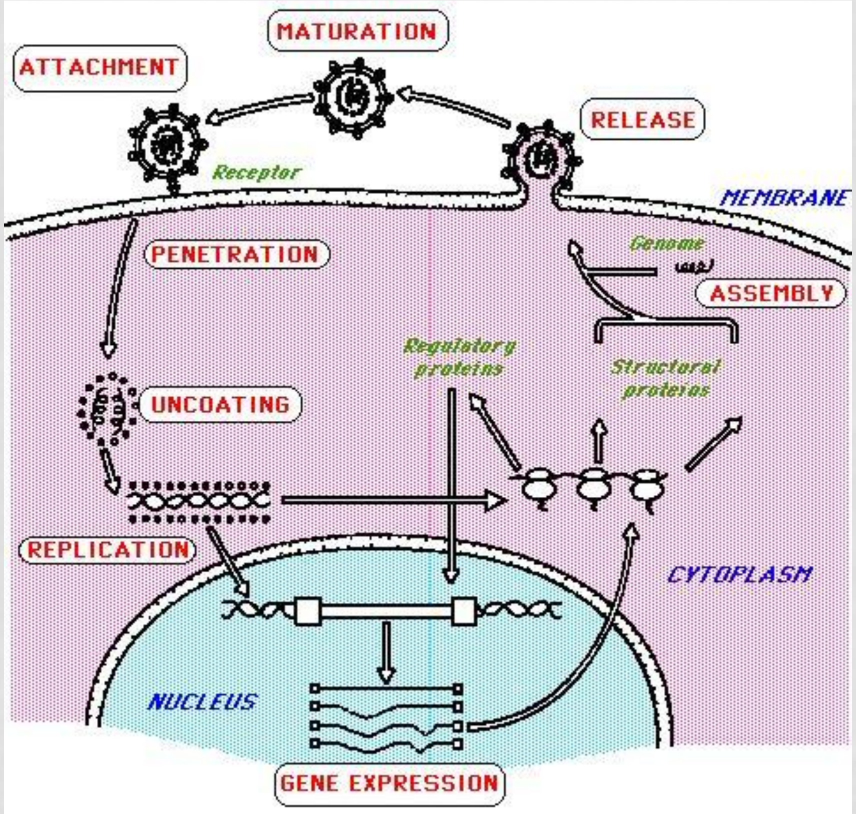
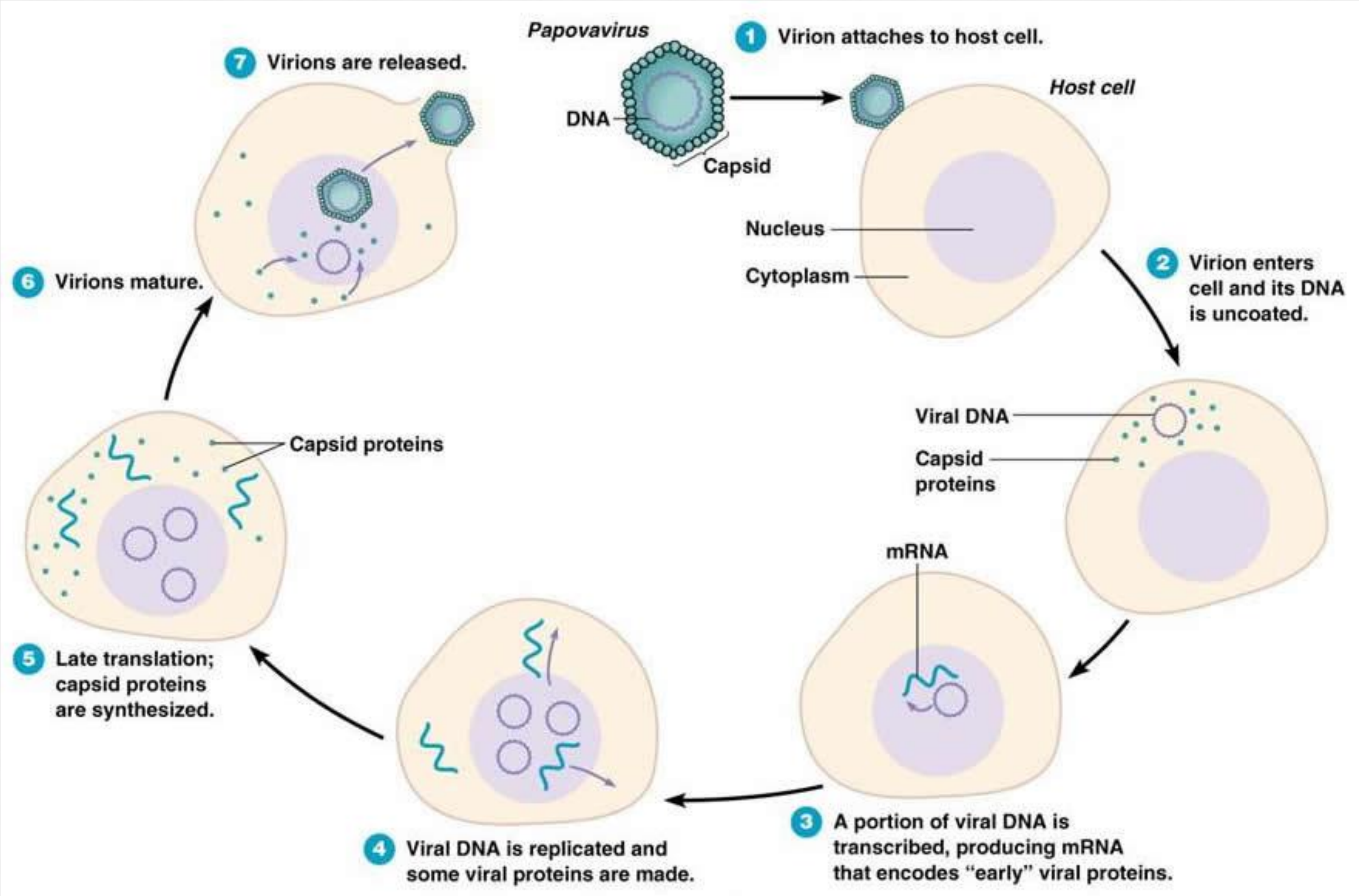
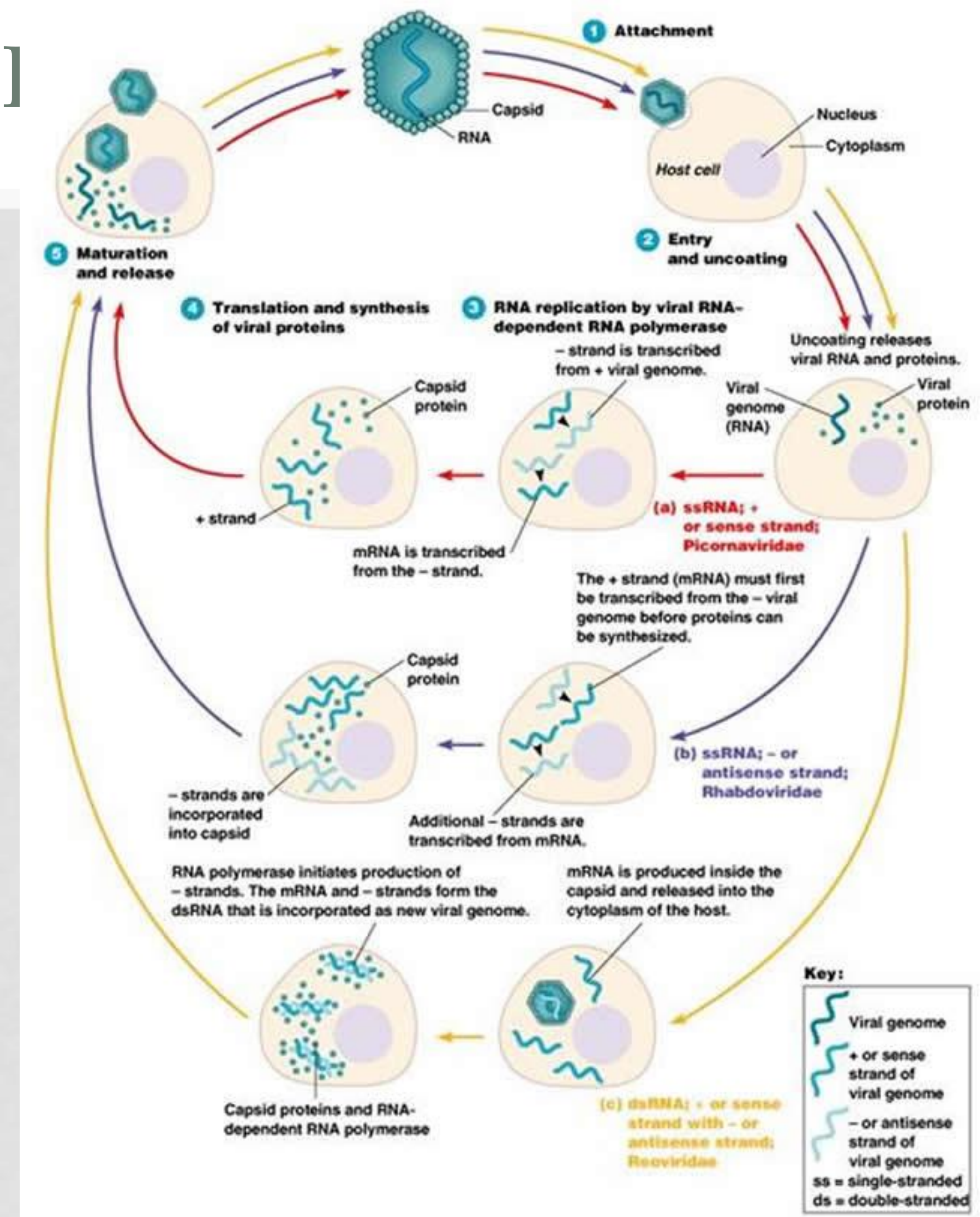


TABLE 13.4 The Biosynthesis of DNA and RNA Viruses Compared

Viral Nucleic Acid	Virus Family	Special Features of Biosynthesis
DNA, single-stranded	Parvoviridae	Cellular enzyme transcribes viral DNA in nucleus
DNA, double-stranded	Herpesviridae Papovaviridae	Cellular enzyme transcribes viral DNA in nucleus
	Poxviridae	Viral enzyme transcribes viral DNA in virion, in cytoplasm
DNA, reverse transcriptase	Hepadnaviridae	Cellular enzyme transcribes viral DNA in nucleus; reverse transcriptase copies mRNA to make viral DNA
RNA, + strand	Picornaviridae Togaviridae	Viral RNA functions as a template for synthesis of RNA polymerase which copies − strand RNA to make mRNA in cytoplasm
RNA, − strand	Rhabdoviridae	Viral enzyme copies viral RNA to make mRNA in cytoplasm
RNA, double-stranded	Reoviridae	Viral enzyme copies − strand RNA to make mRNA in cytoplasm
RNA, reverse transcriptase	Retroviridae	Viral enzyme copies viral RNA to make DNA in cytoplasm; DNA moves to nucleus

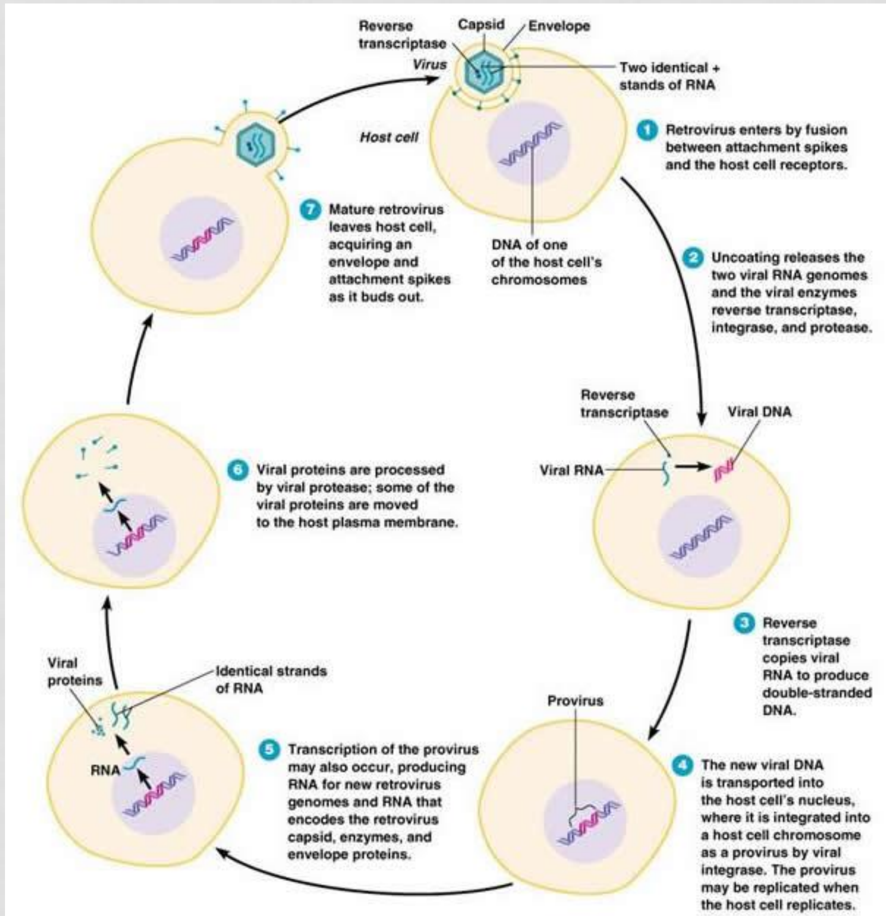
DNA VIRUS BIOSYNTHESIS





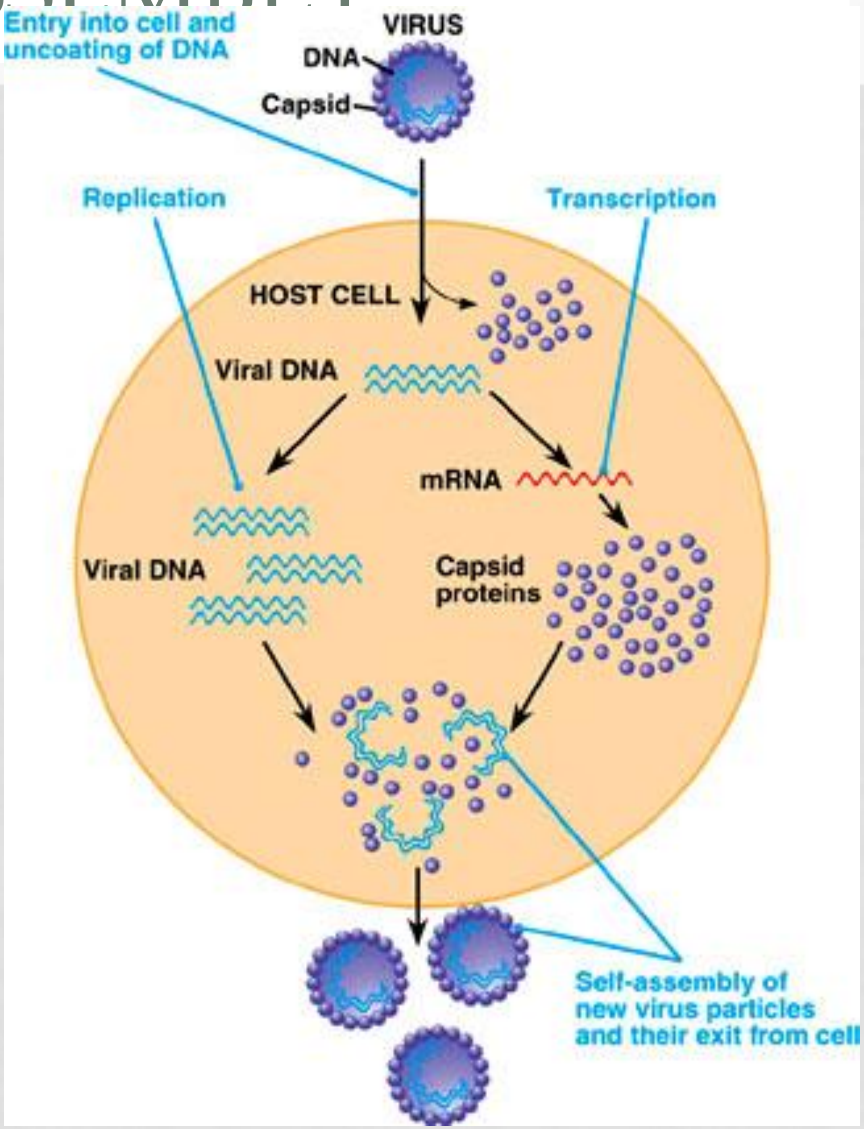
1 Attachment
Capsid
RNA
Nucleus
Cytoplasm
Host cell
2 Entry and uncoating
5 Maturation and release
4 Translation and synthesis of viral proteins
3 RNA replication by viral RNA-dependent RNA polymerase
– strand is transcribed from + viral genome.
Uncoating releases viral RNA and proteins.
Viral genome (RNA)
Viral protein
Capsid protein
+ strand
mRNA is transcribed from the – strand.
(a) ssRNA; + or sense strand; Picornaviridae
The + strand (mRNA) must first be transcribed from the – viral genome before proteins can be synthesized.
Capsid protein
– strands are incorporated into capsid
Additional – strands are transcribed from mRNA.
(b) ssRNA; – or antisense strand; Rhabdoviridae
RNA polymerase initiates production of – strands. The mRNA and – strands form the dsRNA that is incorporated as new viral genome.
mRNA is produced inside the capsid and released into the cytoplasm of the host.
Capsid proteins and RNA-dependent RNA polymerase
(c) dsRNA; + or sense strand with – or antisense strand; Reoviridae
Key:
Viral genome
+ or sense strand of viral genome
– or antisense strand of viral genome
ss = single-stranded
ds = double-stranded

RETROVIRUSES

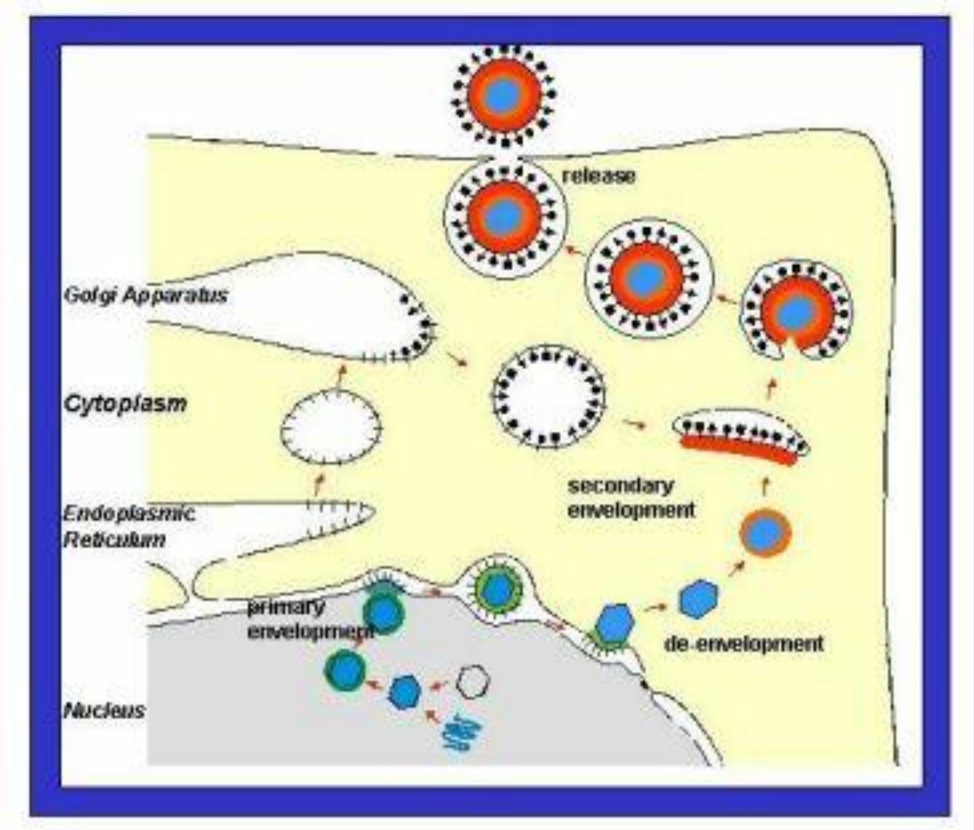


VIRAL ASSEMBLY

- DNA
  - Nucleus
  - Moves to cytoplasm
- RNA
  - cytoplasm



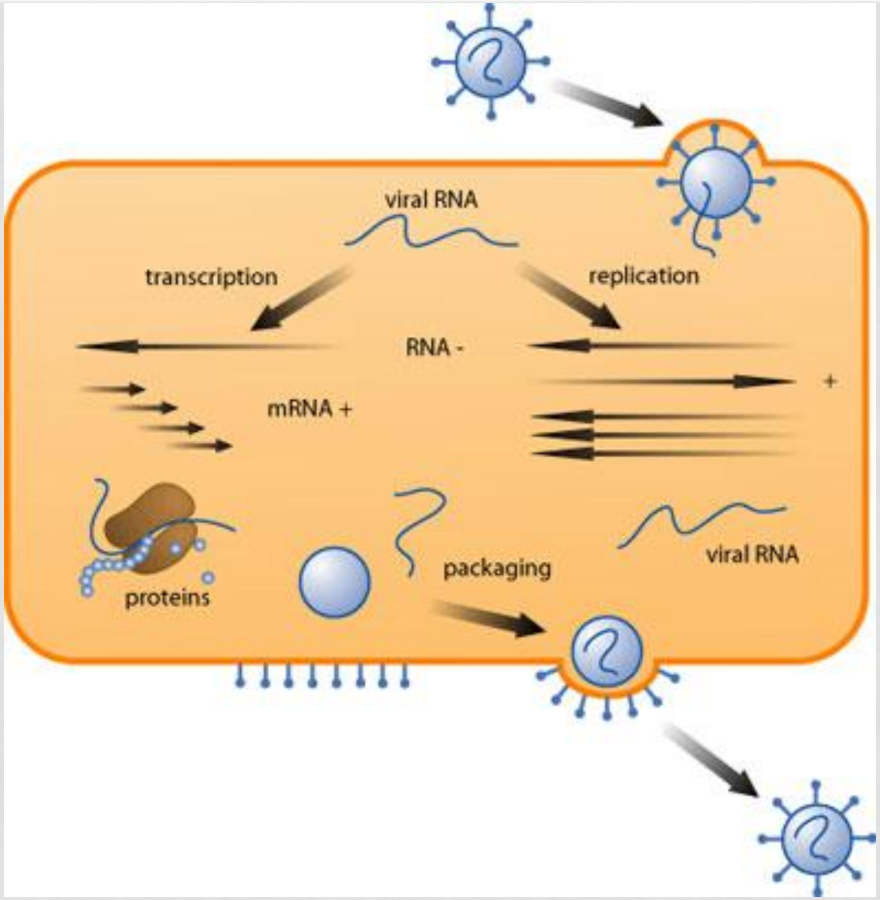
USE OF ER AND GOLGI



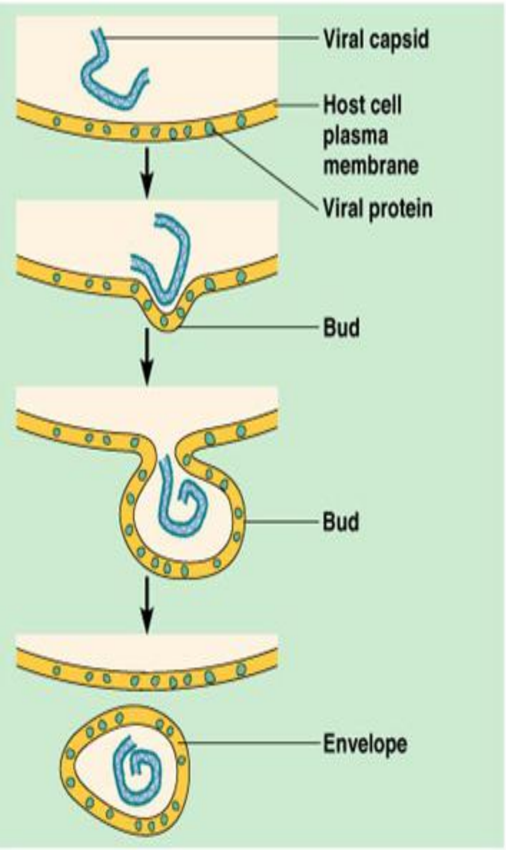
Herpes

VIRAL RELEASE

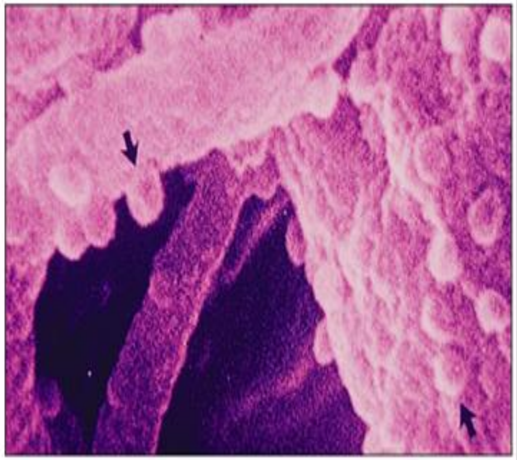
- Types
  - Budding
    - Acquire membranes
    - envelope
  - Exocytosis
  - Lysis
- Latency



BUDDING



(a) Release by budding



(b) *Alphavirus*

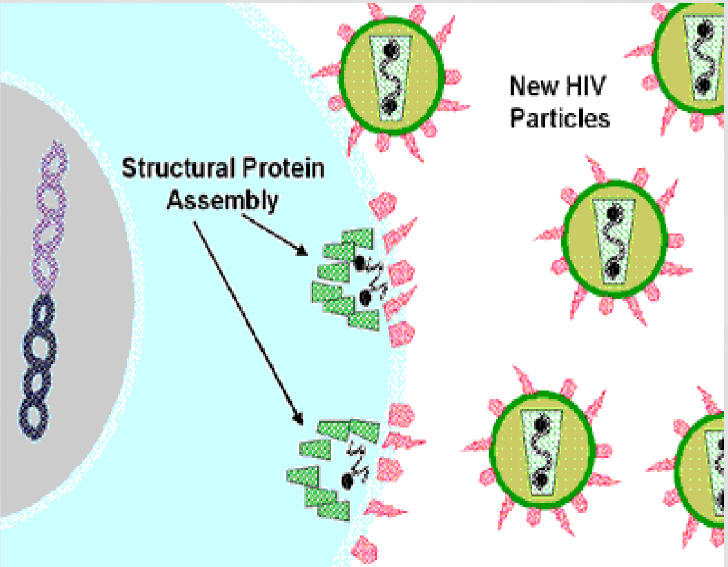
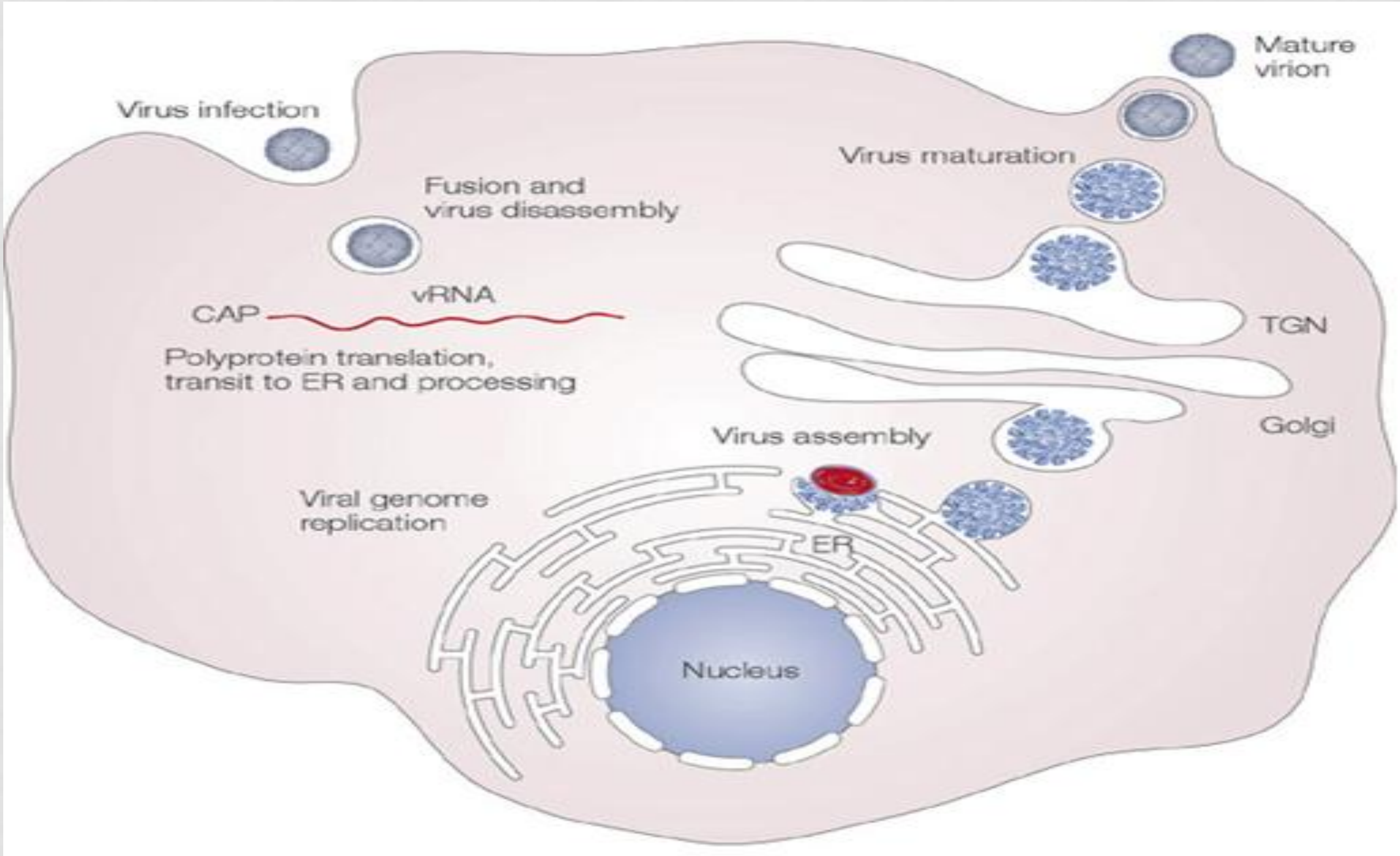
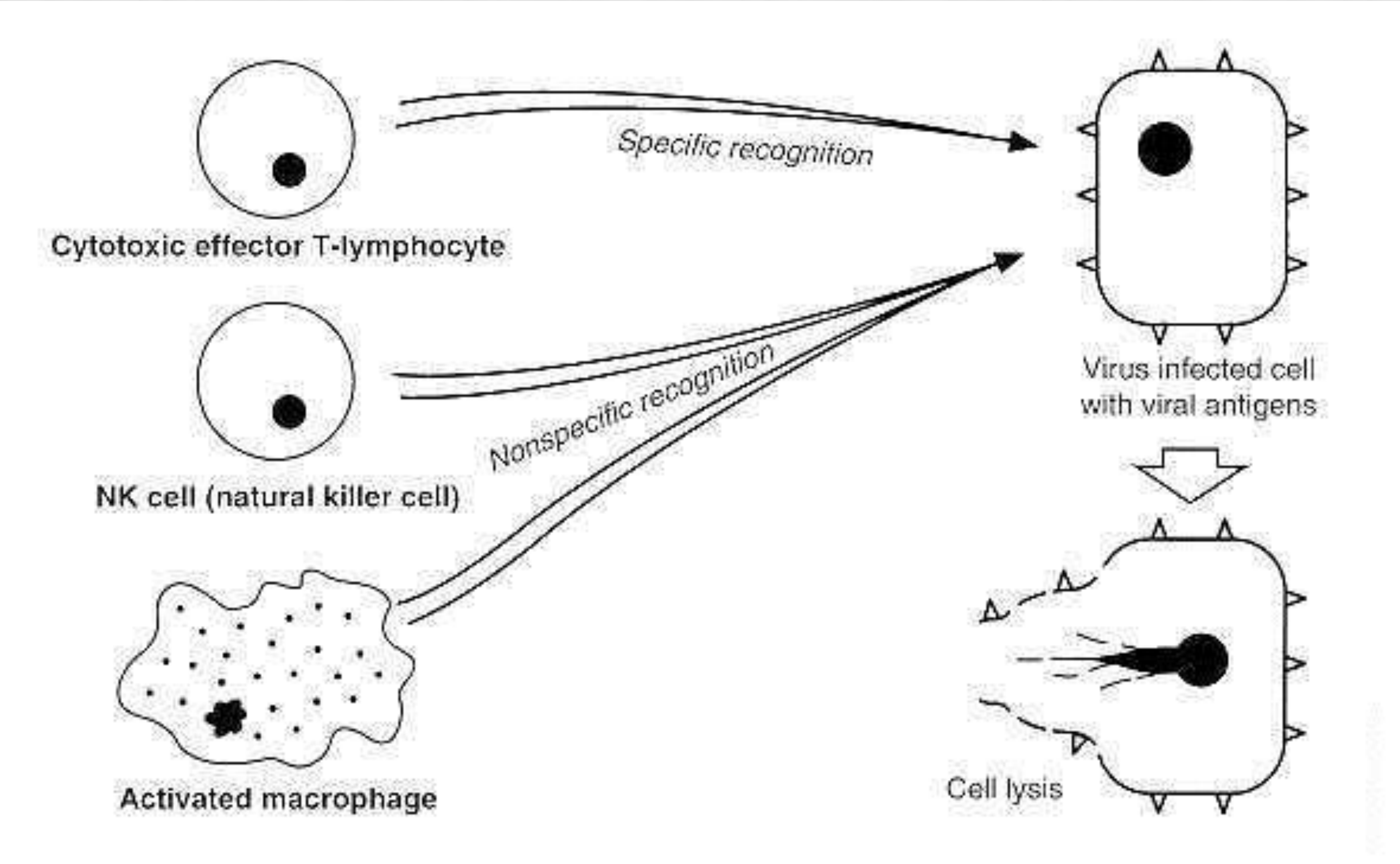


Figure 9. **Viral Assembly / Budding**

VIRAL EXOCYTOSIS



VIRAL LYSIS



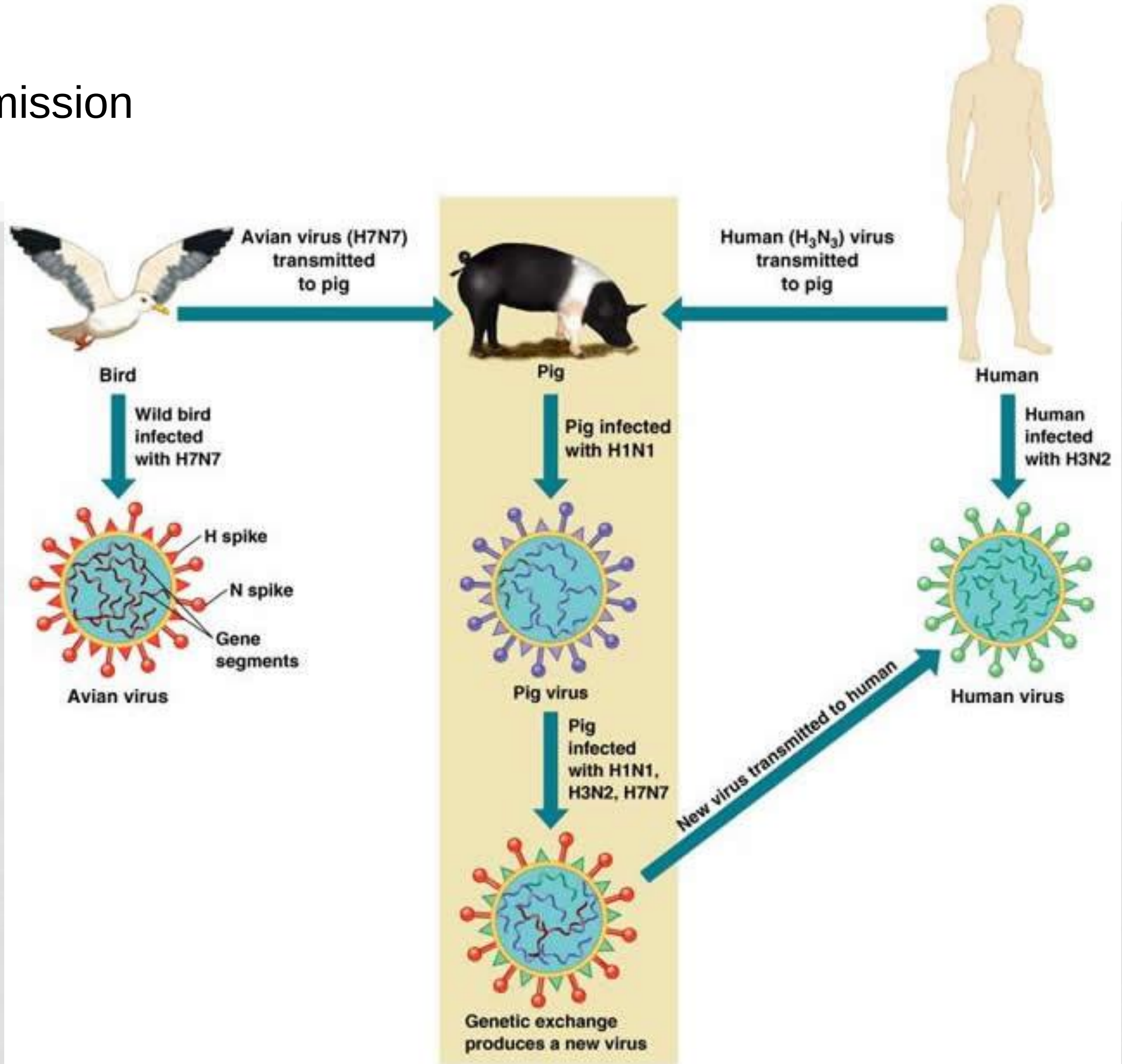
Cytotoxic effector T-lymphocyte
Specific recognition
NK cell (natural killer cell)
Nonspecific recognition
Activated macrophage
Virus infected cell
with viral antigens
Cell lysis

VIRAL DAMAGE

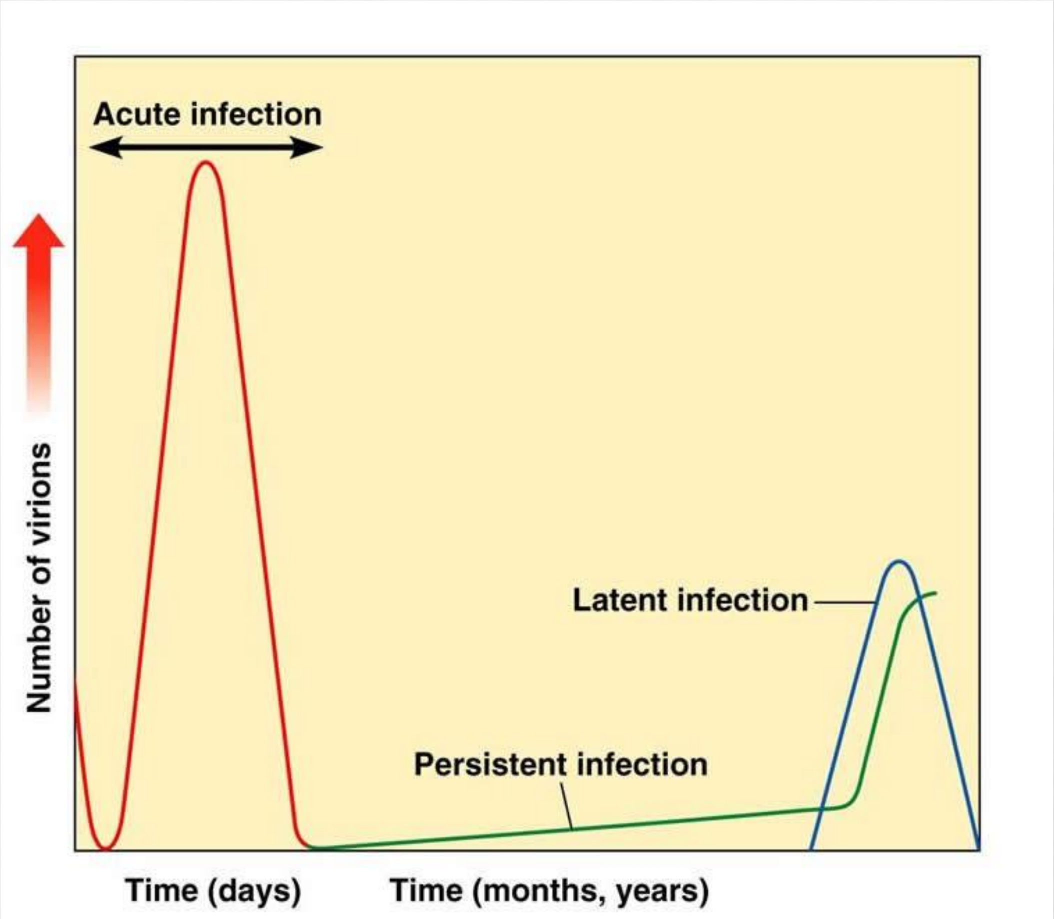
TABLE 15.4 Cytopathic Effects of Selected Viruses

Virus (Genus)	Cytopathic Effect
Poliovirus *(Enterovirus)*	Cytocidal (cell death)
Papovavirus (family Papovaviridae)	Acidophilic inclusion bodies in nucleus
Adenovirus *(Mastadenovirus)*	Basophilic inclusion bodies in nucleus
Rhabdovirus (family Rhabdoviridae)	Acidophilic inclusion bodies in cytoplasm
Cytomegalovirus	Acidophilic inclusion bodies in nucleus and cytoplasm
Measles virus *(Morbillivirus)*	Cell fusion
Polyomavirus	Transformation
HIV *(Lentivirus)*	Destruction of T cells

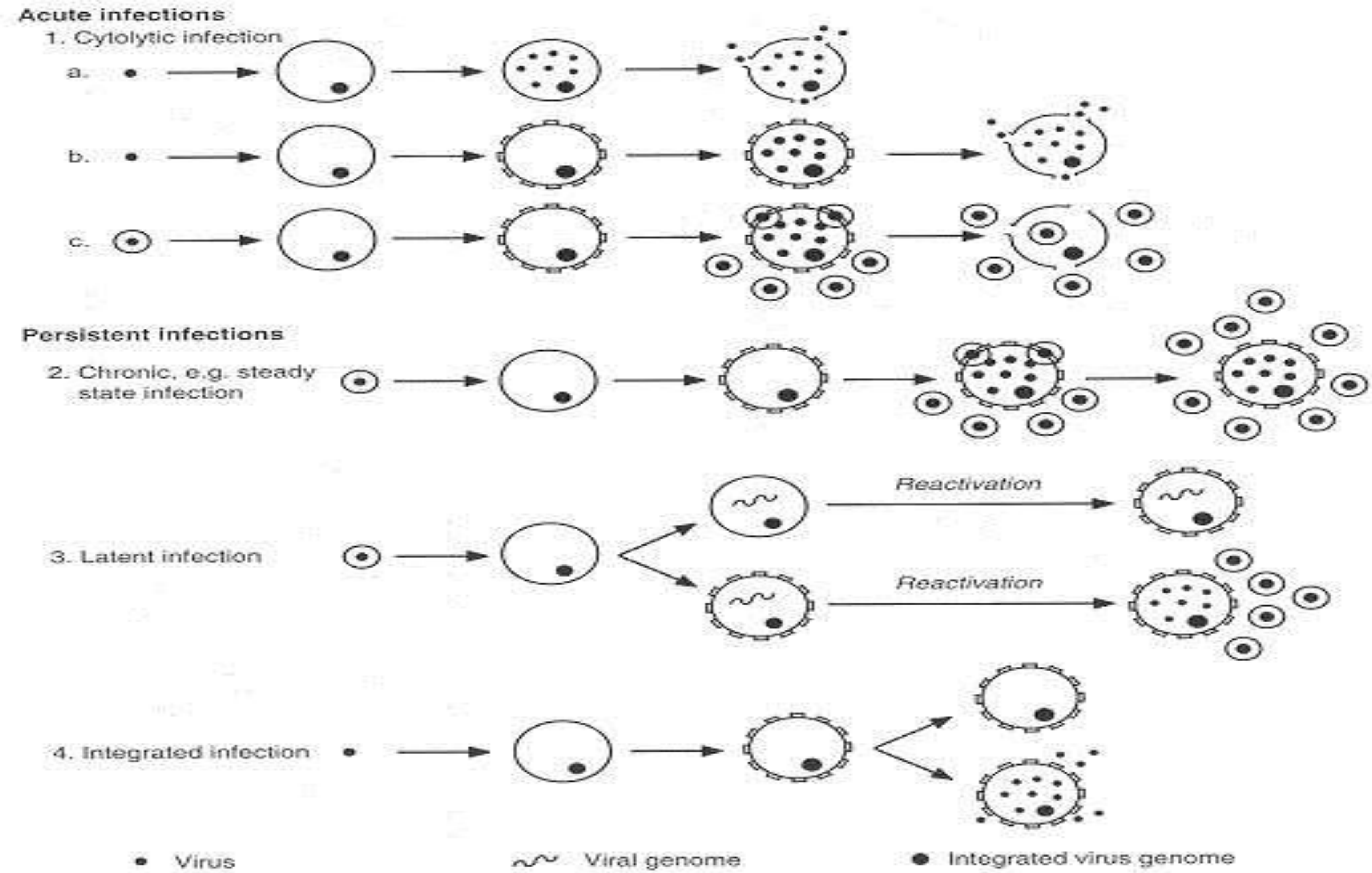
Viral Transmission



ACUTE VS. LATENT

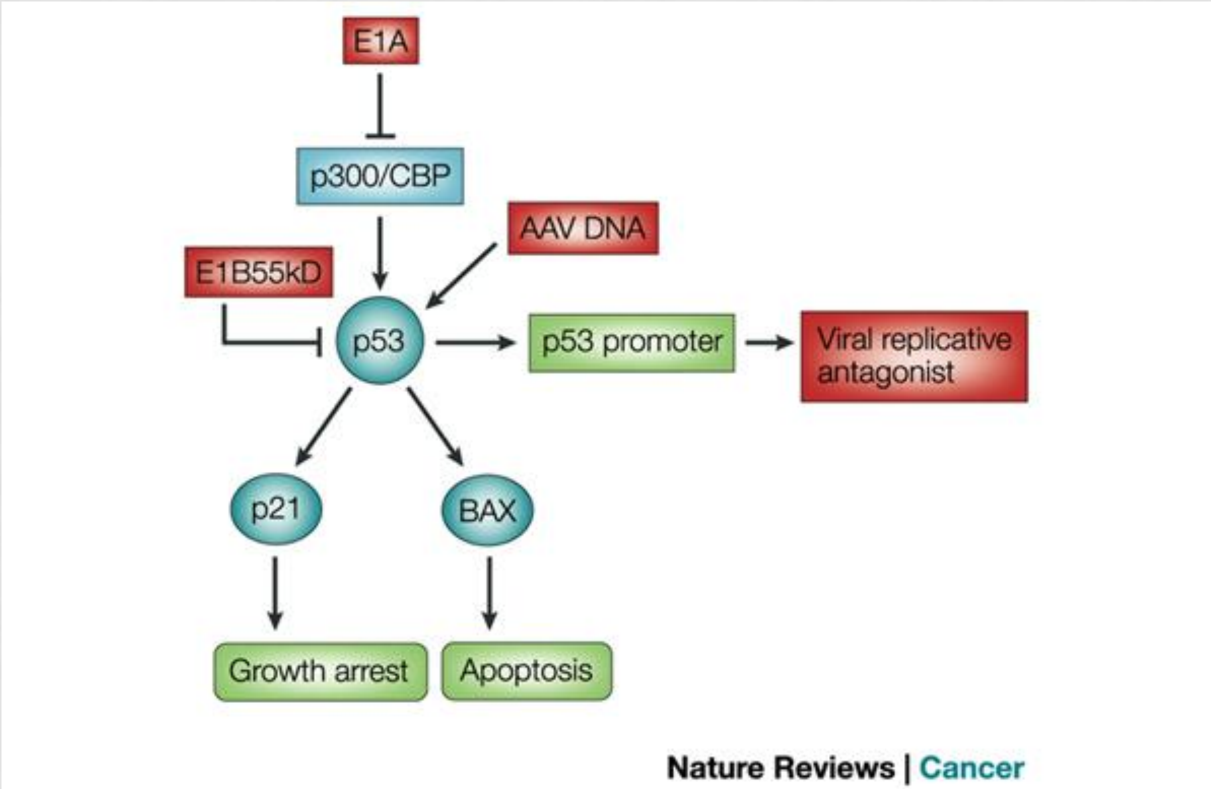


Viral Infections

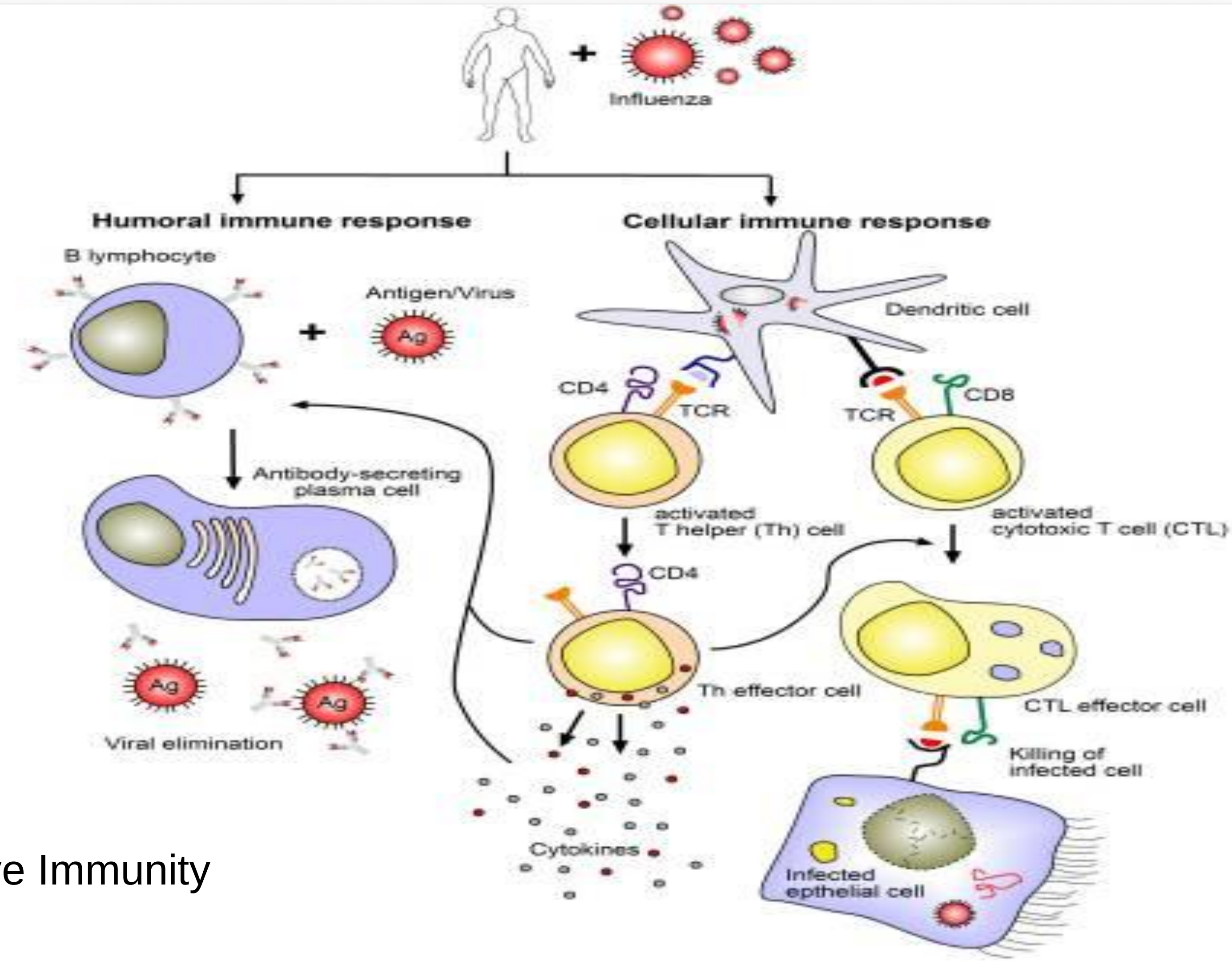


VIRUSES AND CANCER

- Definitions
  - Oncogenes
  - Activation
    - Mutation
    - Transduction
- Tumor
  - Types
    - Benign
    - Malignant
  - Characteristics
- Examples
  - DNA
    - Adenovirus
    - Herpes
    - Poxviruses
    - Papoviruses
    - Hepadenaviruses
  - RNA
    - Retroviruses
      - HIV
      - HTLV



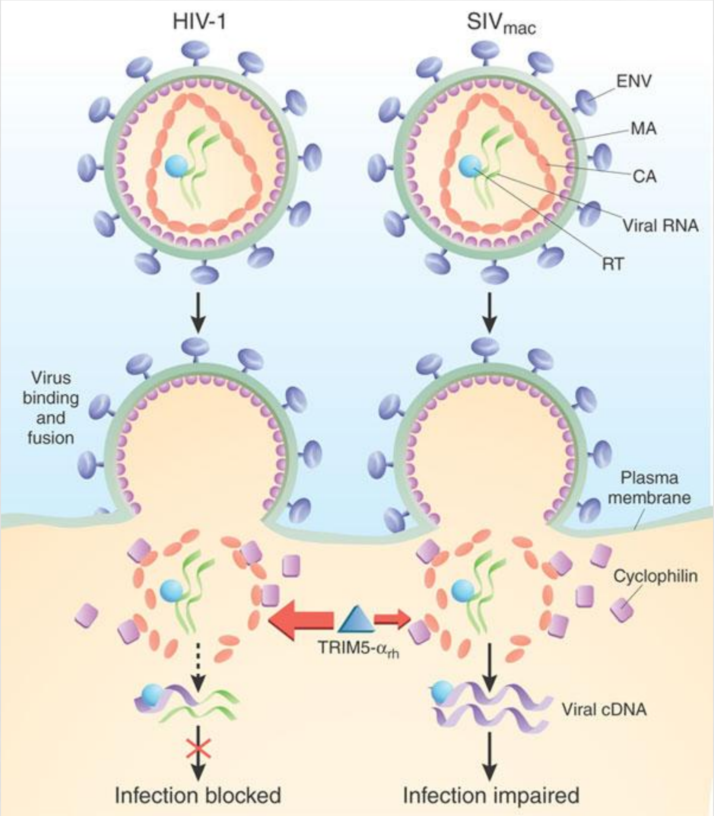
IMMUNE RESPONSE



Adaptive Immunity

ANTI-VIRAL DRUGS

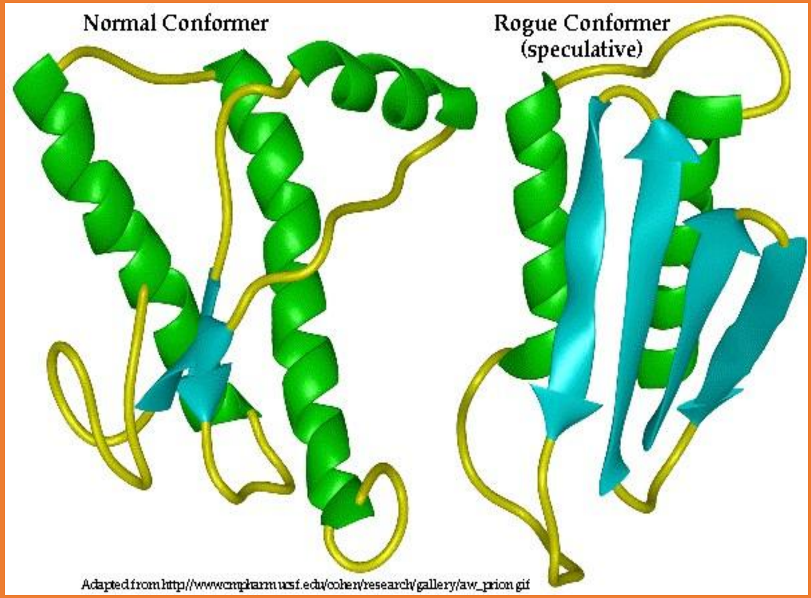
- Attachment antagonists
  - Block attachment molecule
    - Arildone
- Inhibit Uncoating
  - Neutralize acid environment
    - Amantadine
    - Rimantadine
- Inhibit DNA/RNA synthesis
  - Activation by phosphorylation of drug by viral kinases
    - Acyclovir
    - Gancyclovir



PRION PROTEINS

TRIDIMENSIONAL STRUCTURE OF THE PRPC RICH IN ALPHA- HELICES (LEFT) AND THE PRPSC RICH IN BETA-SHEETS PR

PrPc
Sensitive to Proteinase K



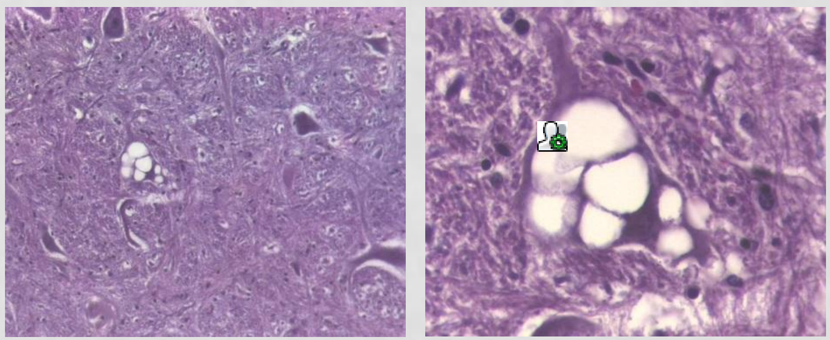
PrPsc PrPsc

proteinase k resistant

Detergant Insoluble

THE PRION IS AN AMYLOID PROTEIN WHICH INDUCES ALONE DISEASES;

THE TRANSMISSIBLE SPONGIFORM ENCEPHALITIS (TSE) ARE SUB-ACUTE, FATAL INFECTIONS AND CHARACTERIZED BY THE PRESENCE OF VACUOLES IN NEURONS



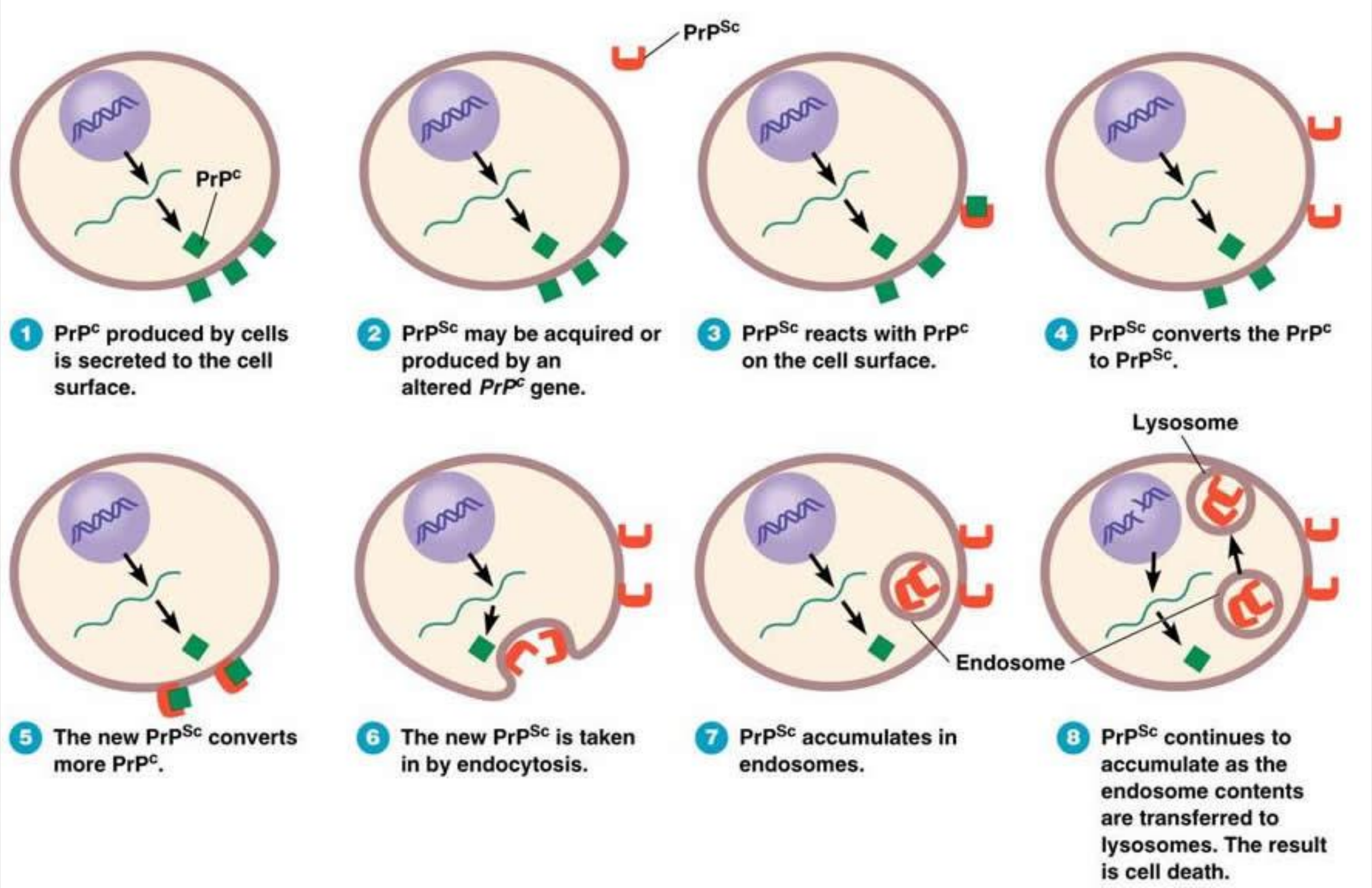
Exp:

Scrapie in sheep& gaots, BSE in cattle, chronic wasting disease in deer and Creutzfeld-Jakob Disease in humans (CJD).

THE PRION PROTEIN (PRP):- PRPC & PRPSC

- The cellular Prion protein PrPc is coded by the prnp Gene situated on the chromosome 20 in humans, 13 in bovine and 2 in mice.
- This gene was found in all vertebrates and invertebrates and is expressed mainly in the CNS and the reticular-endothelial system.
- The gene product (PrPc) is transported outside the cell and anchored on the cell membrane and is associated with signal transduction.
- The pathogenic prion protein PrPsc is produced after conformational transformation of the PrPc induced either by gene mutation or after infection with a PrPsc.

PRION PRODUCTION



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