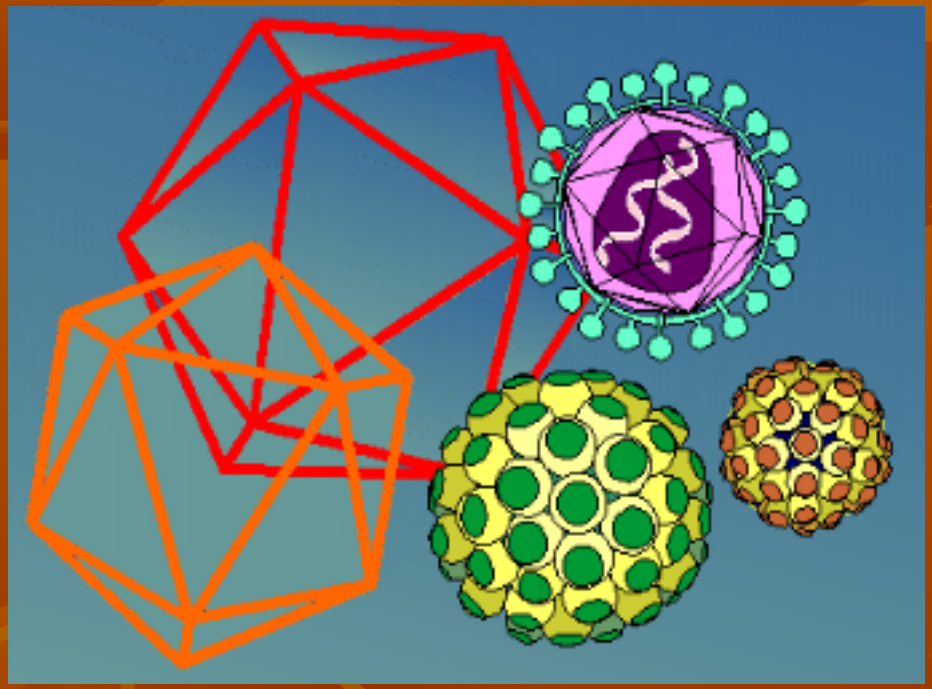
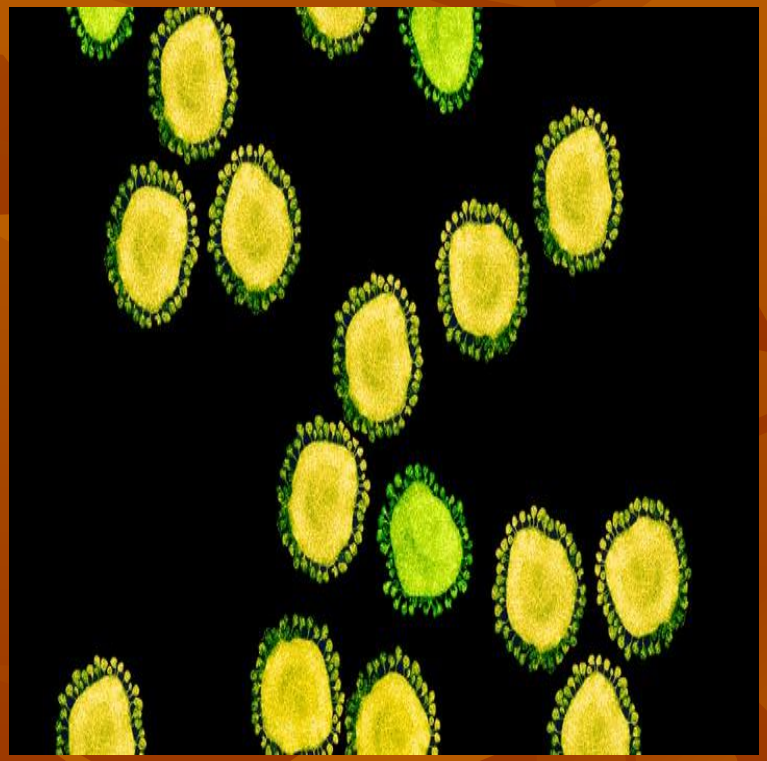
Qazvin University of Medical Sciences

# Viral Structure





Dr. M. Aslanimehr

Dr. M. Aslanimehr

# Size of viruses

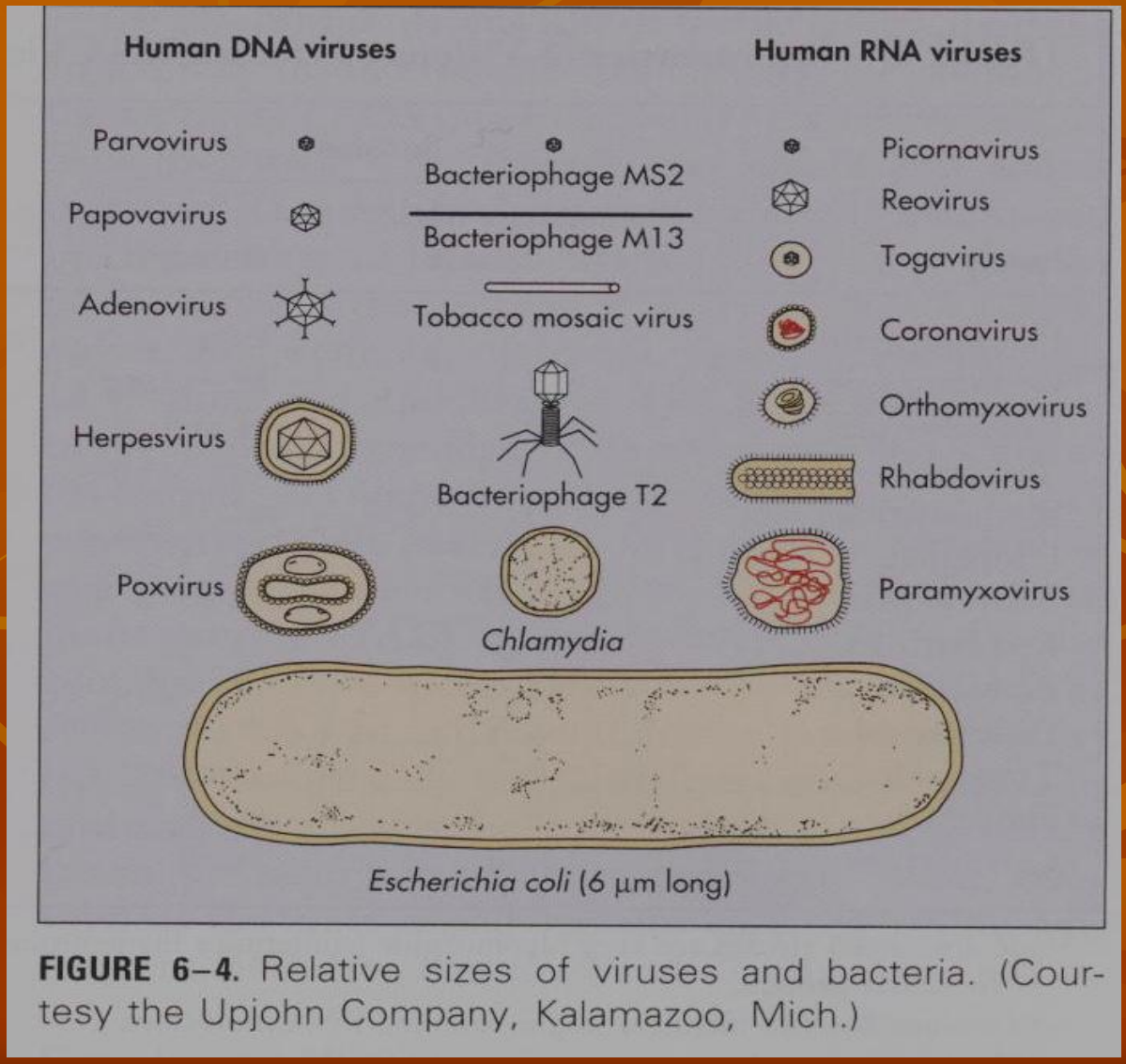
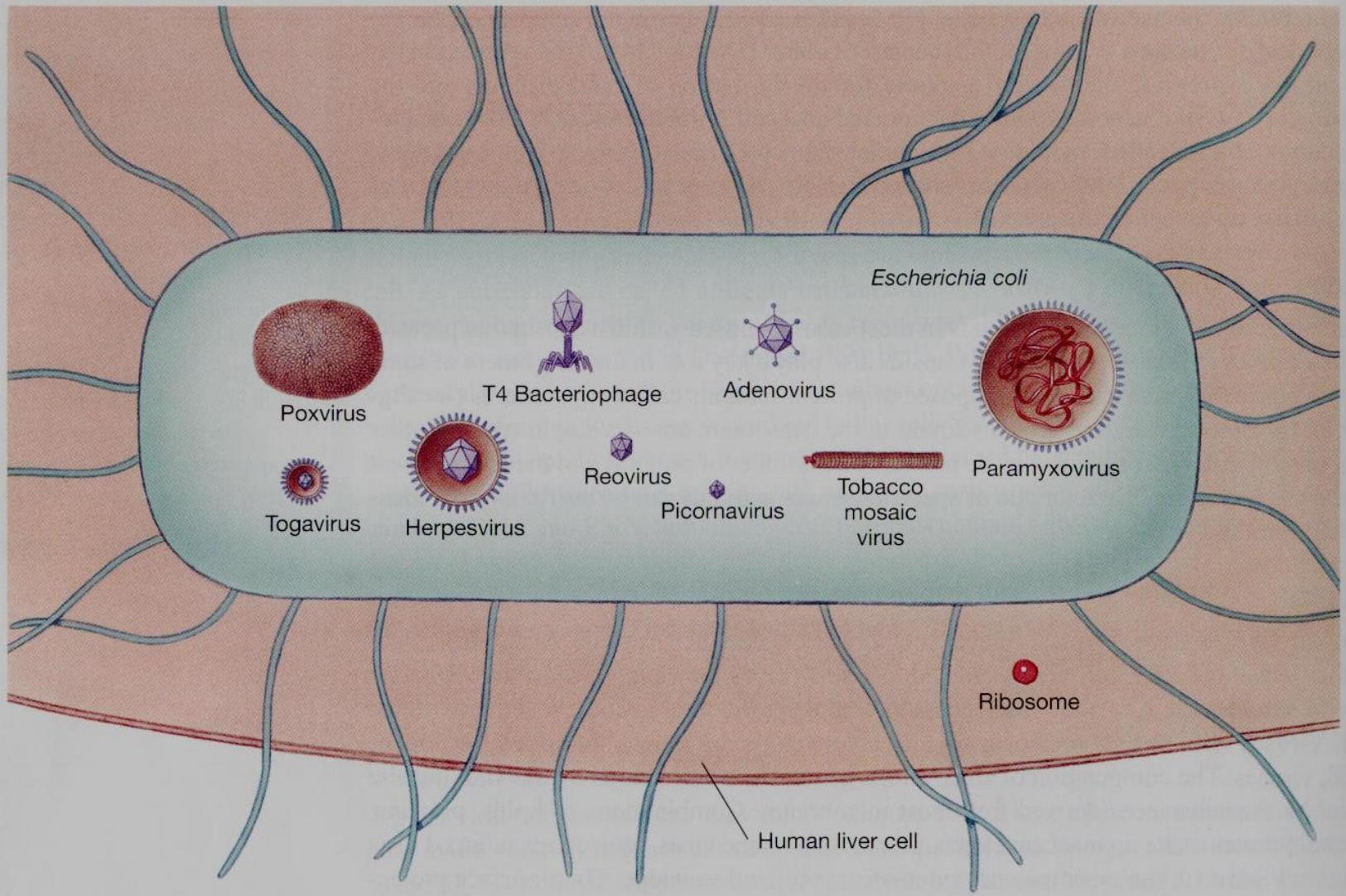



**FIGURE 6–4.** Relative sizes of viruses and bacteria. (Courtesy the Upjohn Company, Kalamazoo, Mich.)



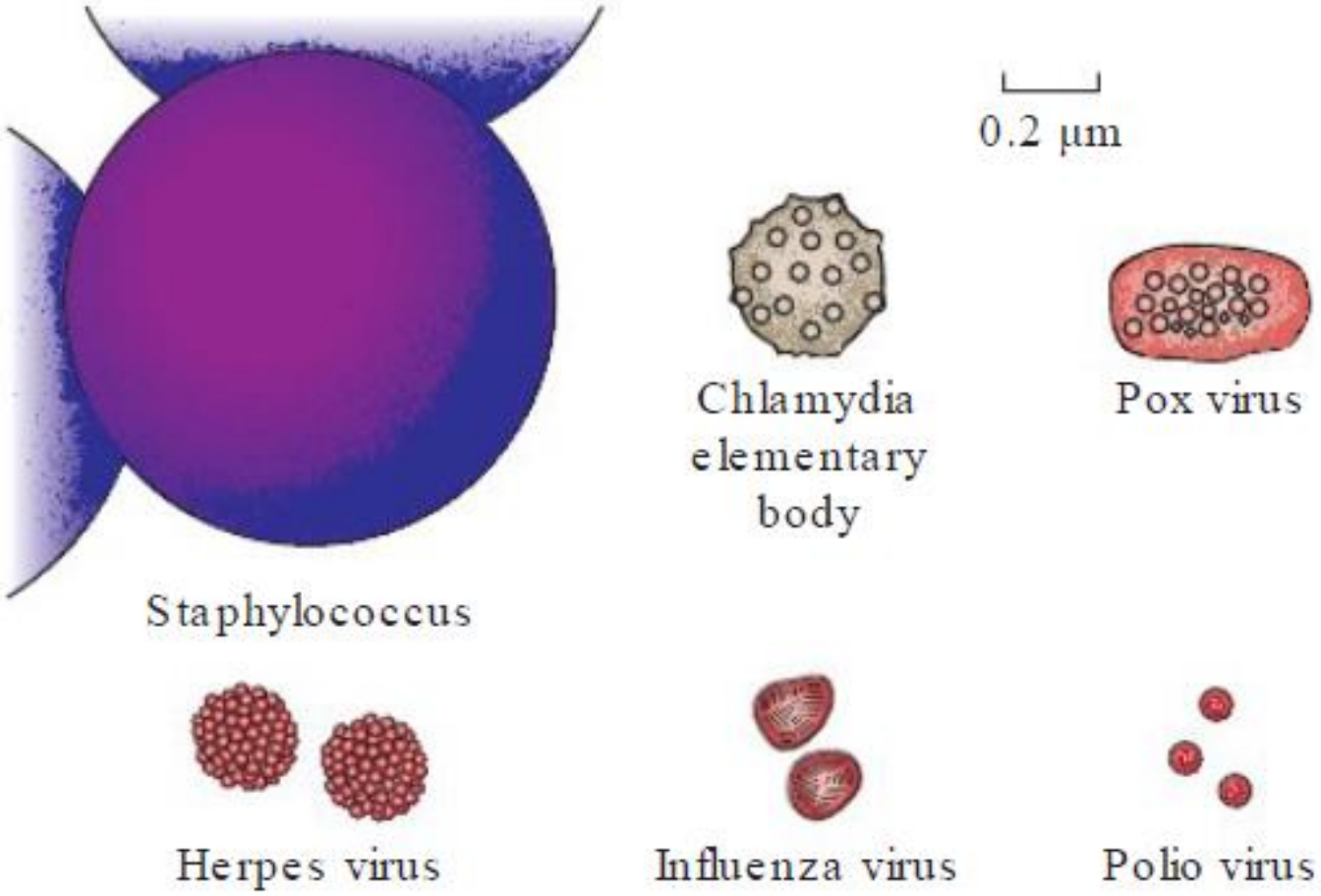

➢ Figure 10.2 **Viral sizes and shapes.** Variations in shapes and sizes of viruses compared with a bacterial cell, an animal cell, and a eukaryotic ribosome.

# Measuring the Sizes of Viruses

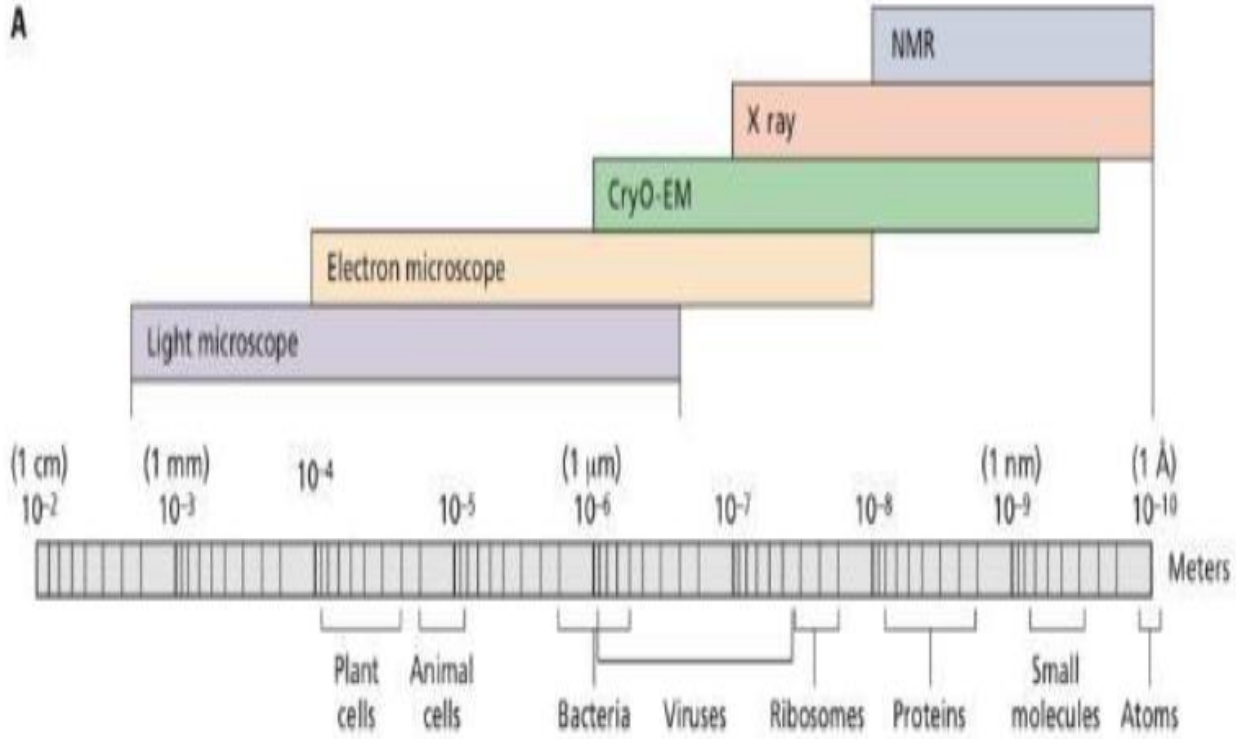
- ***Small size*** and the ability to pass through filters that hold back bacteria are classic attributes of viruses.
  - However, because some bacteria may be smaller than the largest viruses, filterability is not regarded as a unique feature of viruses.
- Direct ***observation in the electron microscope*** is the ***most widely used method*** for estimating particle size.
  - Viruses can be visualized in preparations from tissue extracts and in ultrathin sections of infected cells.
  - Another method that can be used is ***sedimentation*** in the ultracentrifuge.
  - The relationship between the **size and shape** of a particle and its rate of sedimentation permits determination of particle density.

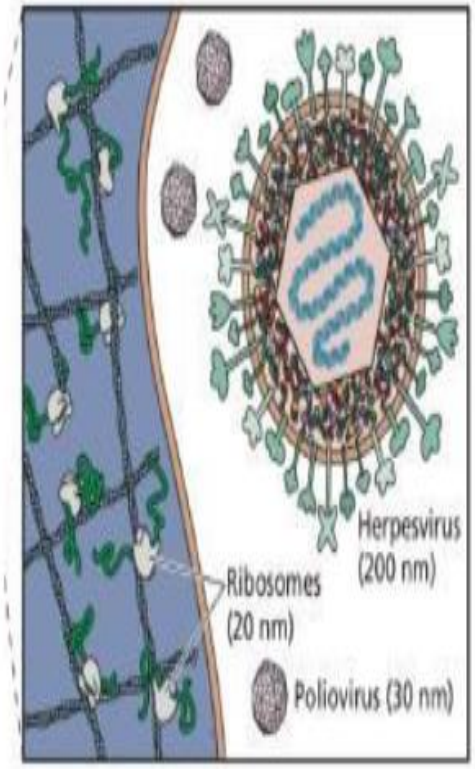
# Comparative Measurements

- Viruses range in diameter from **about 20 to 300 nm** . For purposes of comparison, the following data should be recalled:
  - (1) **Staphylococcus** species have a diameter of about **1000 nm** (1 μm).
  - (2) Bacterial viruses (**bacteriophages**) vary in size (10–100 nm). Some are spherical or hexagonal and have short or long tails.
  - (3) Representative **protein molecules** range in diameter from serum albumin (5 nm) and globulin (7 nm) to certain hemocyanins (23 nm).
  - (4) **Eukaryotic ribosomes** are about 25–30 nm in size, with mitochondria being much larger (1–10 μm).
  - (5) **Red blood cells** are about 6–8 μm in diameter.
  - (6) The **width of a human hair** is about **100 μm**.




■ FIGURE 23-1 Viruses are the smallest of infectious agents. The relative size of a bacterium, Staphylococcus, is compared with Chlamydia, with the largest virus group (poxvirus), and with one of the smallest viruses (poliovirus, a member of the enterovirus group).



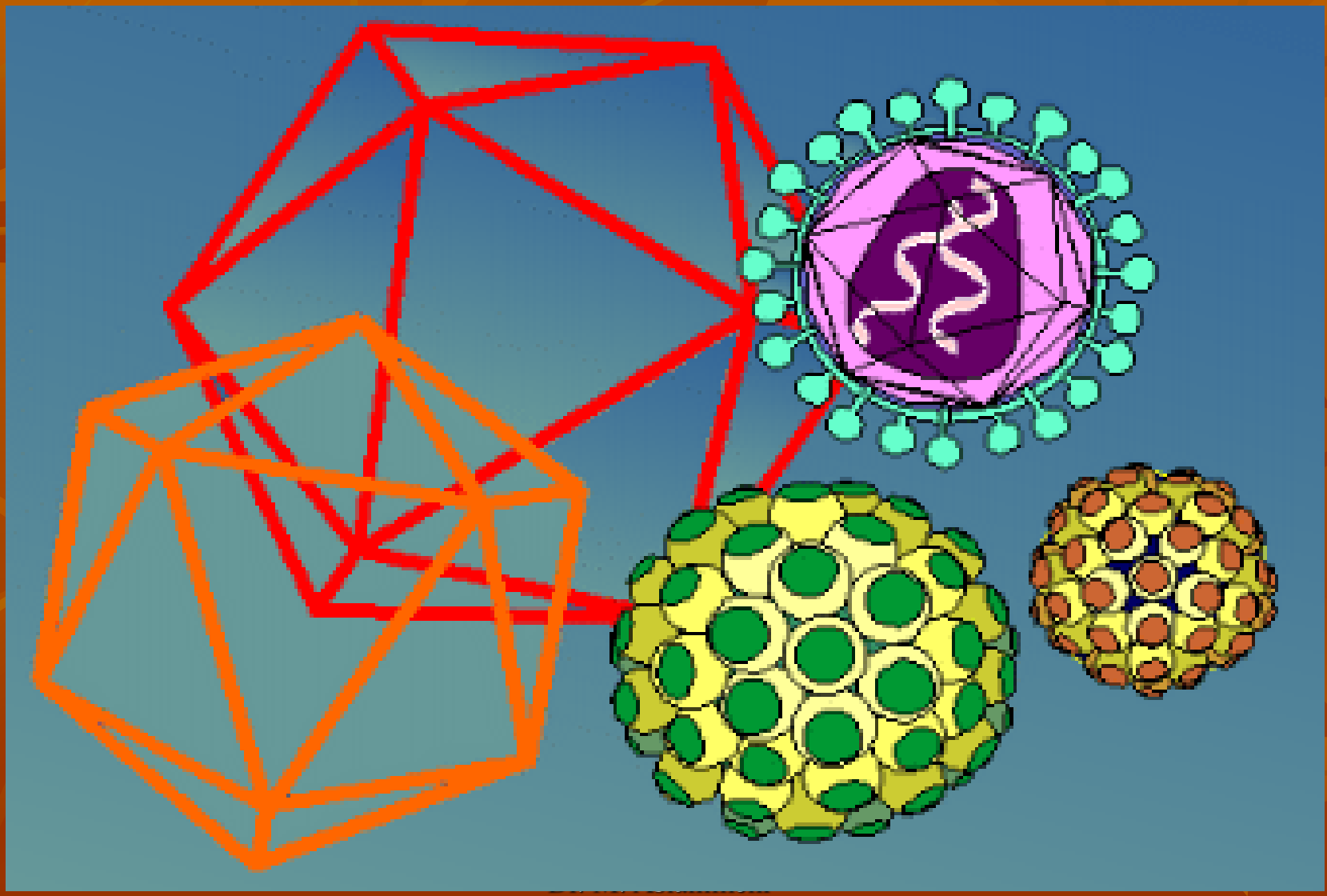




# Size of viruses

# Viruses

- Viruses are the one of  smallest infectious particles,
- The units for measurement of virion size are nanometers (nm). The clinically important viruses range from 18 nm (parvoviruses) to 300 nm (poxviruses)
- (most viruses are less than 200 nm and cannot be seen with a light microscope).

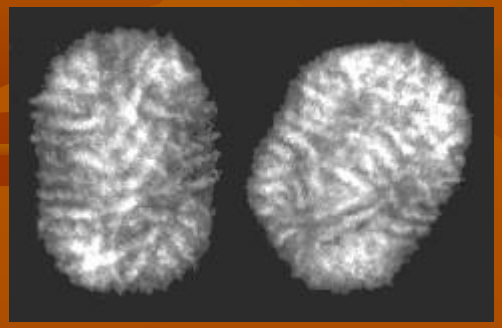
# Viral Structure

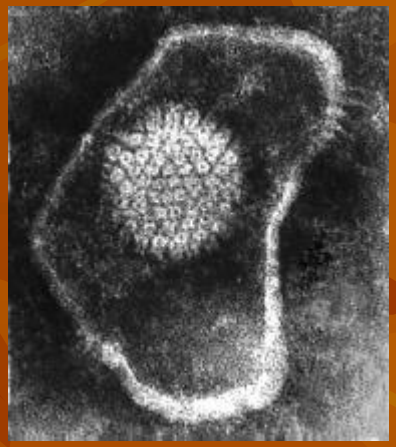


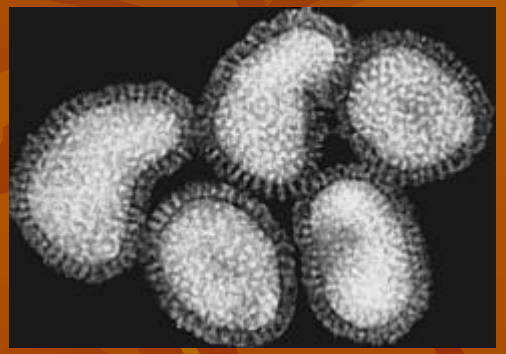
# Viruses

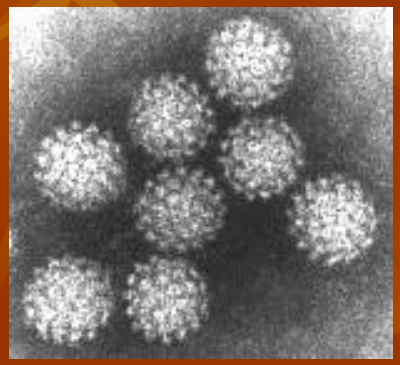
- Viruses typically contain either (DNA) or (RNA) but not both;
- while the recently discovered Mimivirus contains both RNA and DNA.
- The viral nucleic acids and proteins required for replication and pathogenesis are enclosed in a protein coat with or without
- a lipid membrane coat.
- Viruses are true parasites, requiring host cells for replication.
- The cells they infect and the host response to the infection dictate the nature of the clinical manifestation.
- however, prions do not contain any detectable nucleic acids (see Chapter 66),

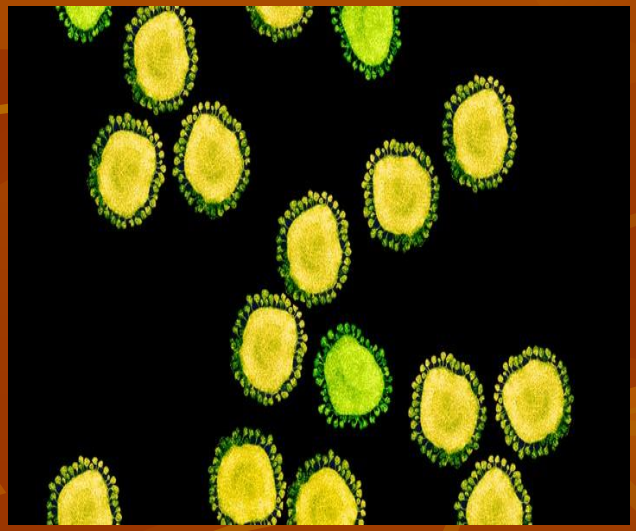
# What is virion ?

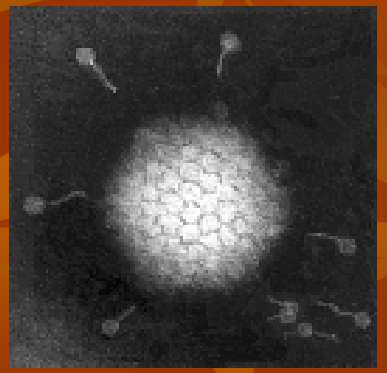












# TERMS AND DEFINITIONS IN VIROLOGY

**Capsid:** The protein shell, or coat, that encloses the nucleic acid genome.

**Capsomeres:** Morphologic units seen in the electron microscope on the surface of icosahedral virus particles. Capsomeres represent clusters of polypeptides, but the morphologic units do not necessarily correspond to the chemically defined structural units.

**Defective virus:** A virus particle that is functionally deficient in some aspect of replication.

**Envelope:** A lipid-containing membrane that surrounds some virus particles. It is acquired during viral maturation by a budding process through a cellular membrane. Virus-encoded glycoproteins are exposed on the surface of the envelope. These projections are called **peplomers**.

**Nucleocapsid:** The protein–nucleic acid complex representing the packaged form of the viral genome. The term is commonly used in cases in which the nucleocapsid is a substructure of a more complex virus particle.

**Structural units:** The basic protein building blocks of the coat. They are usually a collection of more than one nonidentical protein subunit. The structural unit is often referred to as a **protomer**.

**Subunit:** A single folded viral polypeptide chain.

**Virion:** The complete virus particle. In some instances (eg, papillomaviruses, picornaviruses), the virion is identical with the nucleocapsid. In more complex virions (herpesviruses, orthomyxoviruses), this includes the nucleocapsid plus a surrounding envelope. This structure, the virion, serves to transfer the viral nucleic acid from one cell to another.

# Terms and defeniation in virology

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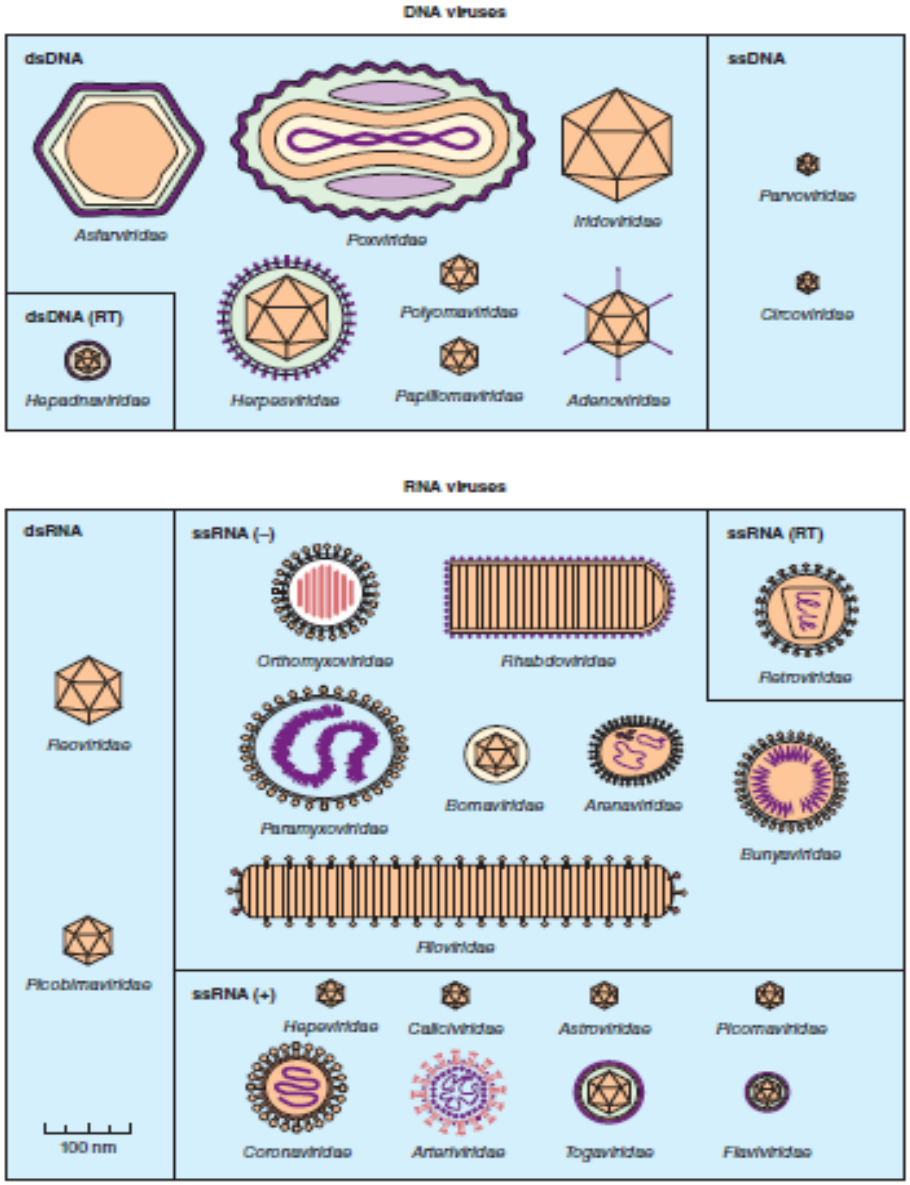
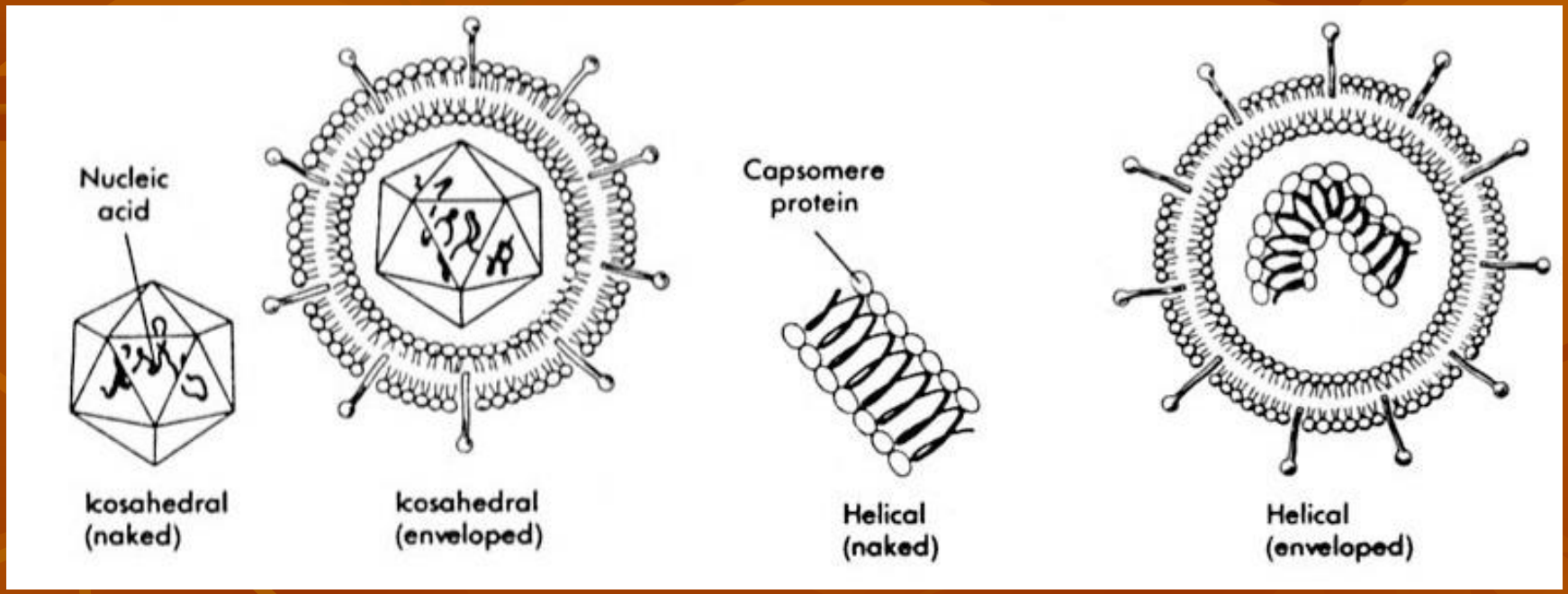



**FIGURE 29-2** Shapes and relative sizes of animal viruses of families that infect vertebrates. In some diagrams, certain internal structures of the particles are represented. Only those families that include human pathogens are listed in Table 29-1 and described in the text. (Reproduced with permission from van Regenmortel MHV, Fauquet CM, Bishop DHL, et al [editors]: *Virus Taxonomy: Classification and Nomenclature of Viruses. Seventh Report of the International Committee on Taxonomy of Viruses*. Academic Press, 2000.)

# Viral Structure



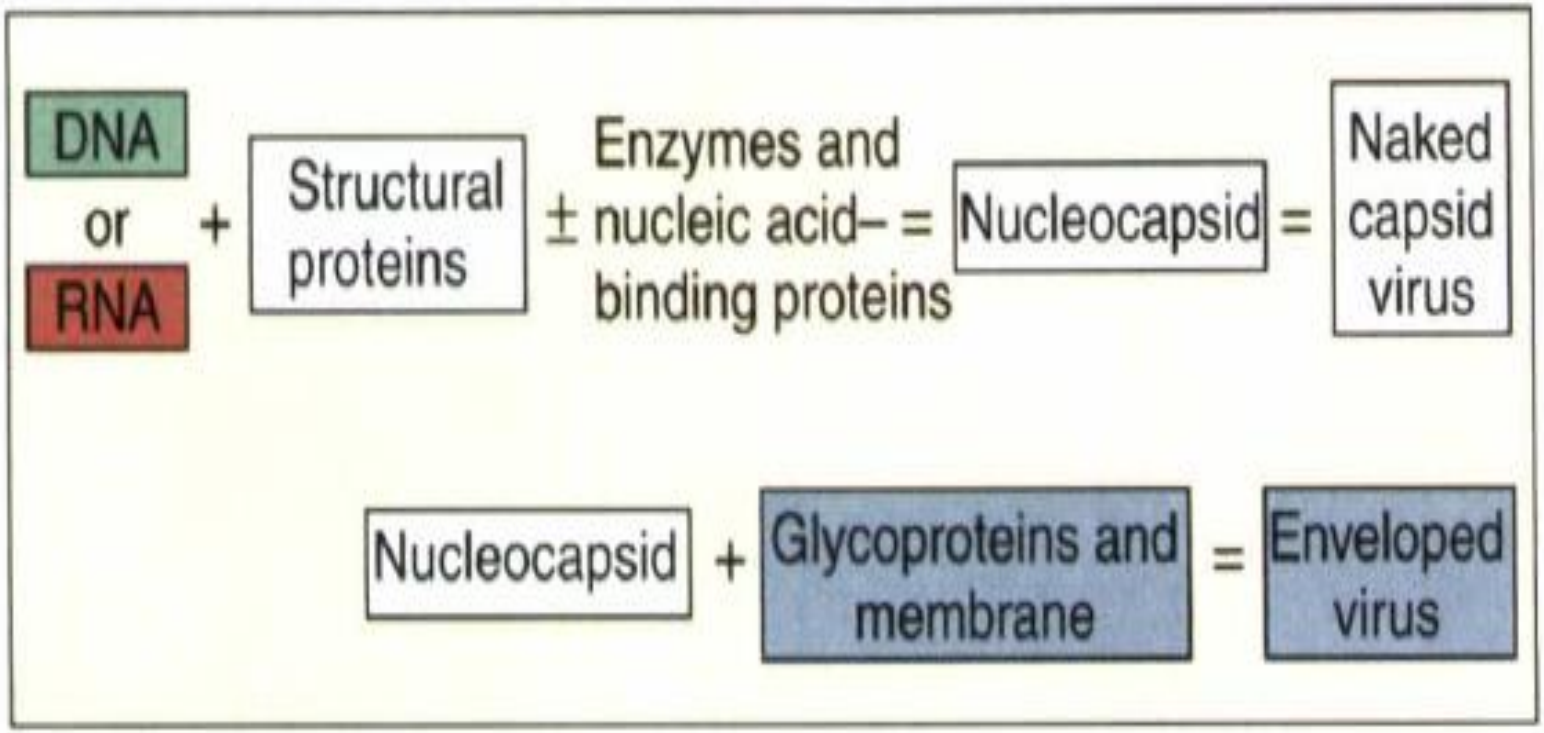



**Figure 4–1.** Components of the basic virion.

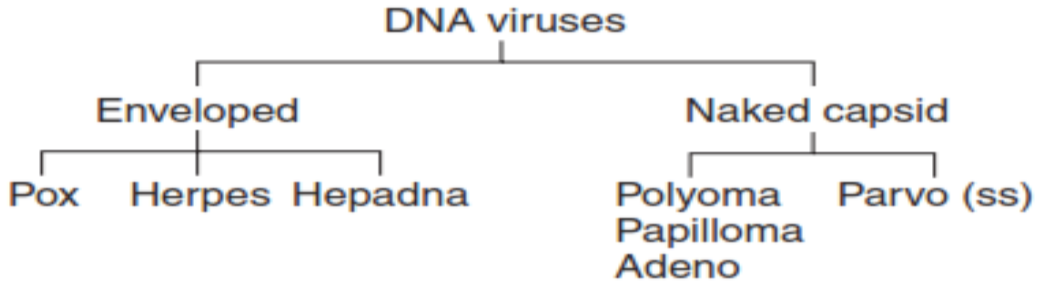



**Fig. 36.2** DNA viruses and their morphology. The viral families are determined by the structure of the genome and the morphology of the virion. *ss,* Single-stranded genome.

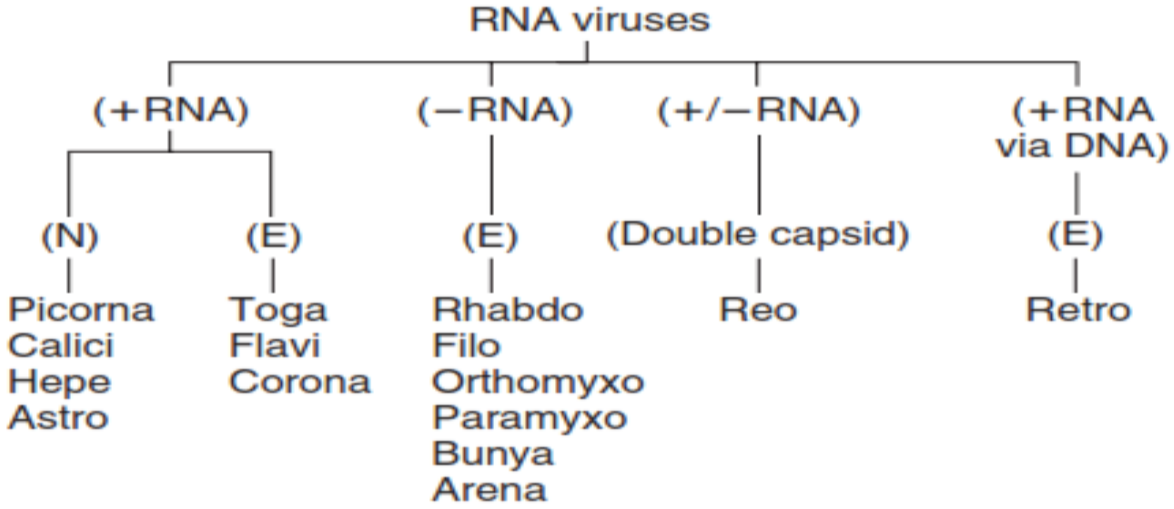



**Fig. 36.3** RNA viruses, their genome structure, and their morphology. The viral families are determined by the structure of the genome and the morphology of the virion. *E,* Enveloped; *N,* naked capsid.

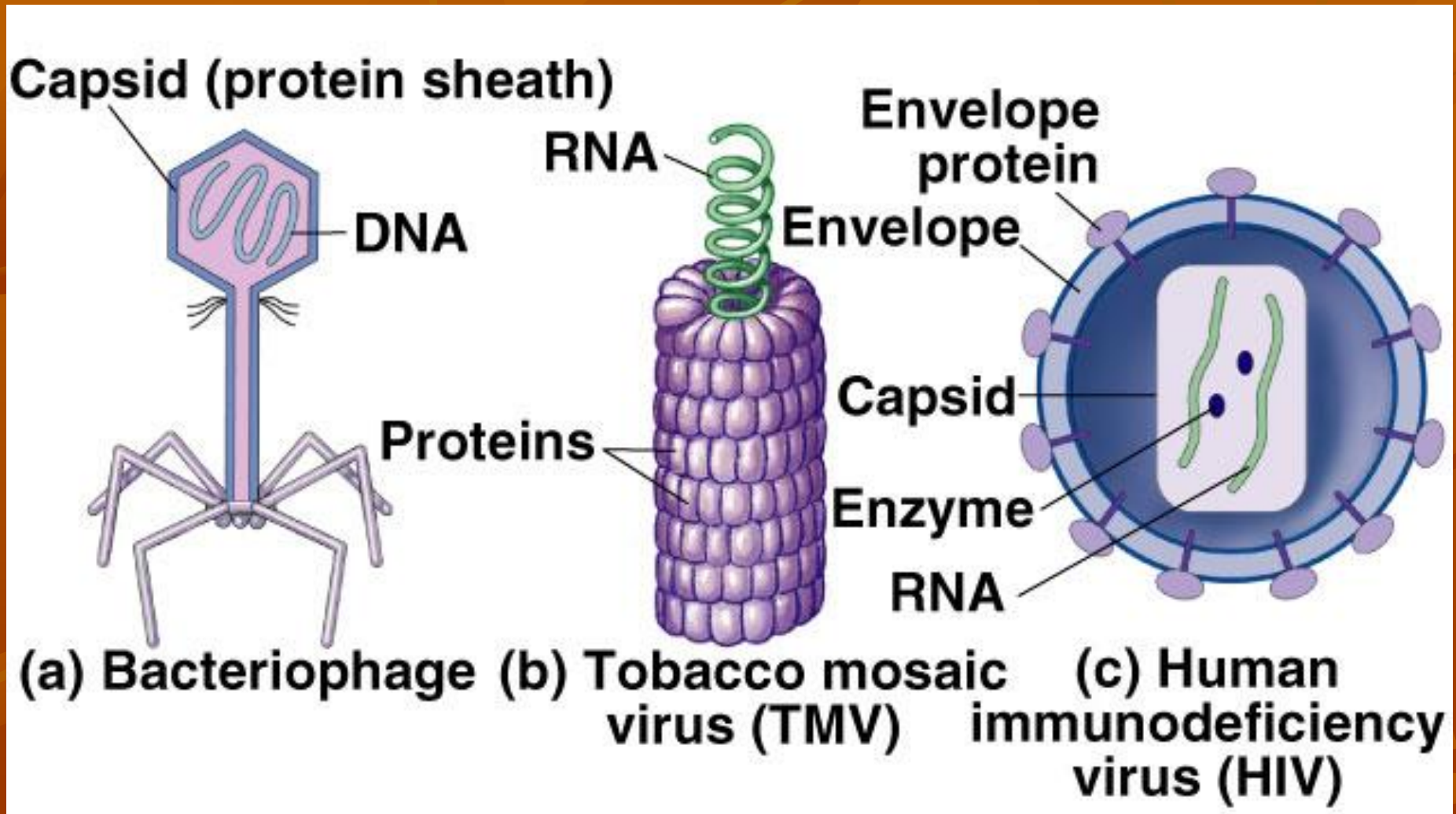
# Types of Symmetry of Virus Particles

- **X-ray crystallography** can provide **atomic resolution** information, generally at a ***level of 0.2–0.3 nm***. The specimen must be **crystalline**, and this has only been achieved with small, nonenveloped viruses.

  - ***Viral architecture*** can be grouped into three types based on the arrangement of morphologic subunits:

    - (1) **cubic symmetry** (eg, adenoviruses),
    - (2) **helical symmetry** (eg, orthomyxoviruses), and
    - (3) **complex structures** (eg, poxviruses).

# Viral Structure



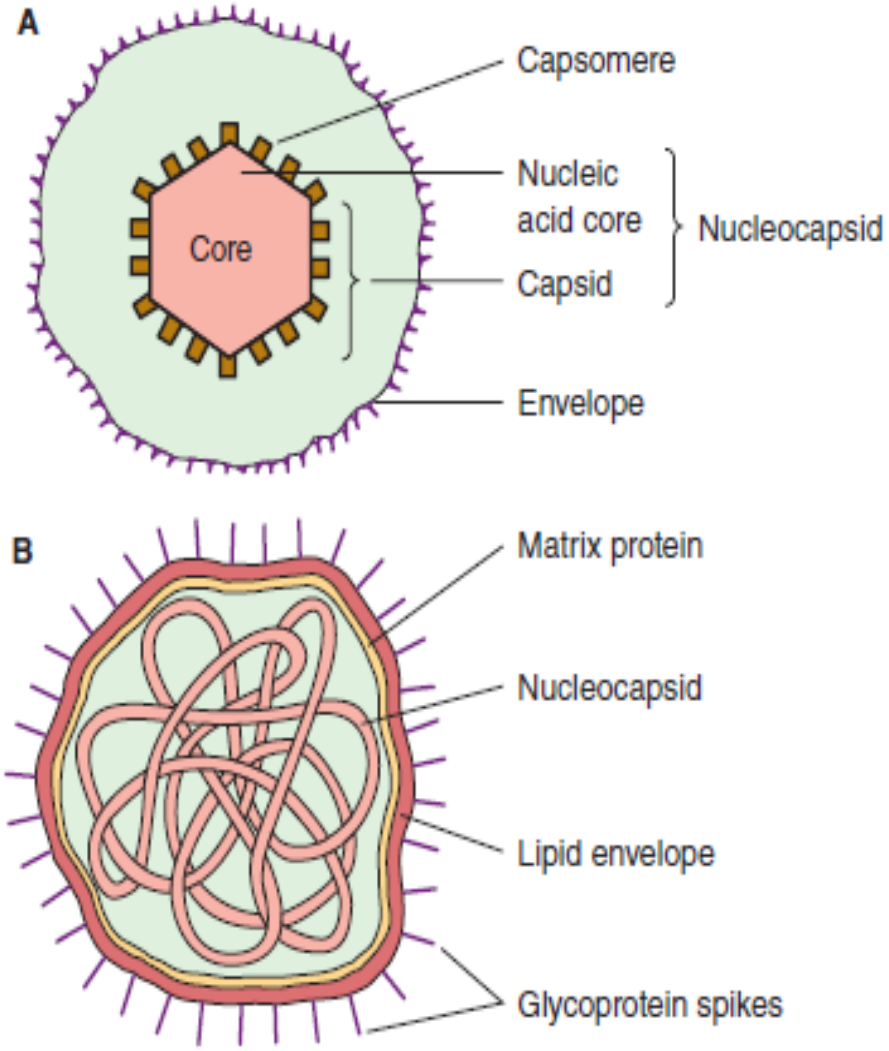



**FIGURE 29-1** Schematic diagram illustrating the components of the complete virus particle (the virion). **A:** Enveloped virus with icosahedral symmetry. Not all icosahedral viruses have envelopes. **B:** Virus with helical symmetry.

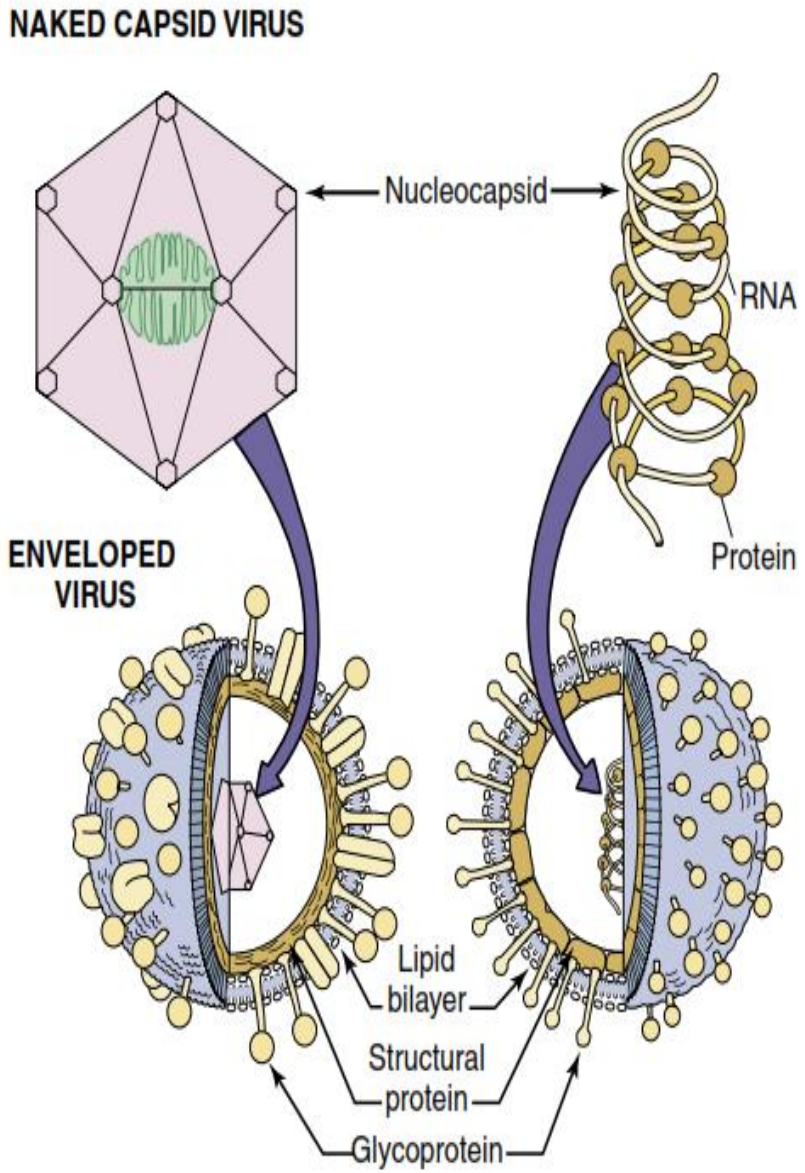
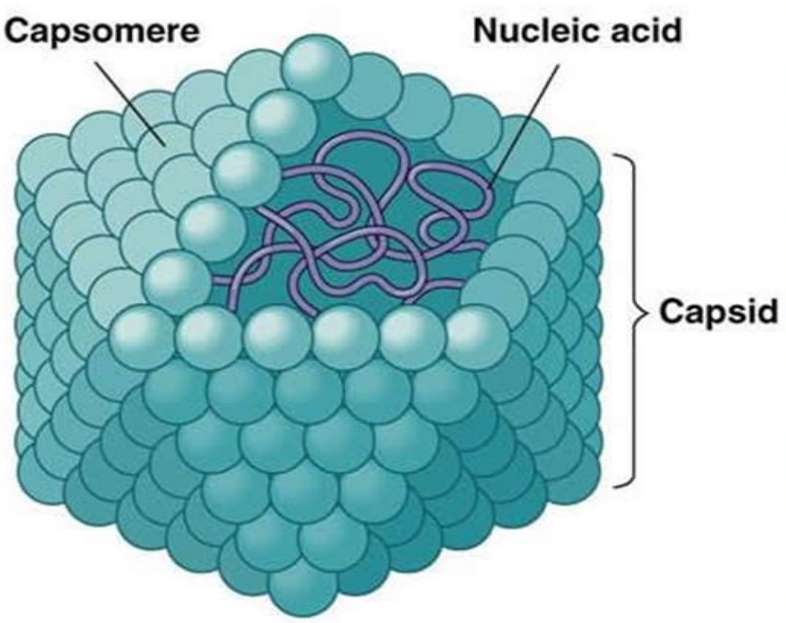
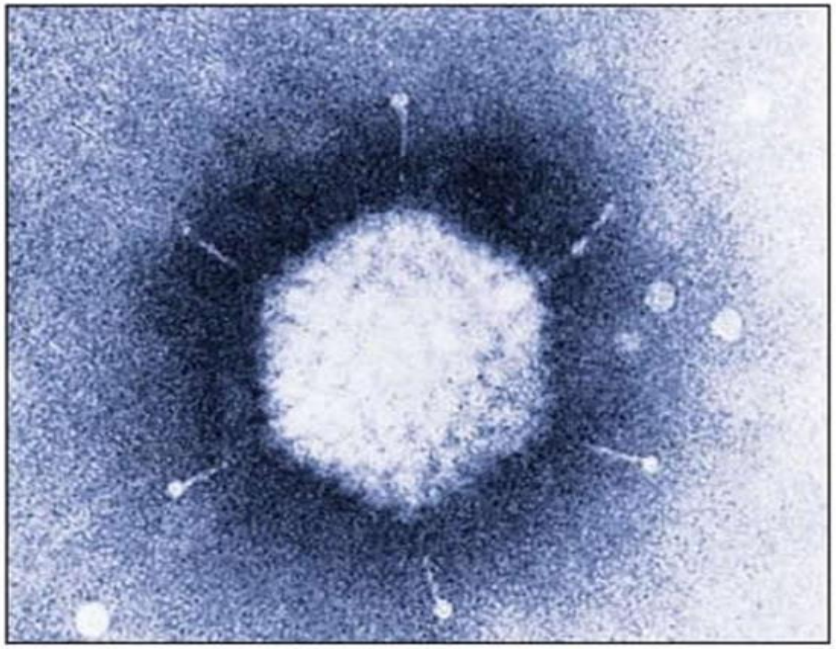


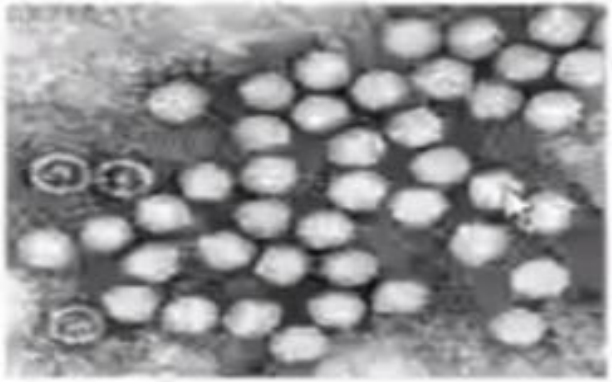

**Fig. 36.4** Structures of a naked icosahedral capsid virus *(top left)* and enveloped viruses *(bottom)* with an icosahedral *(left)* nucleocapsid or a helical *(right)* ribonucleocapsid. Helical nucleocapsids are always enveloped for human viruses.

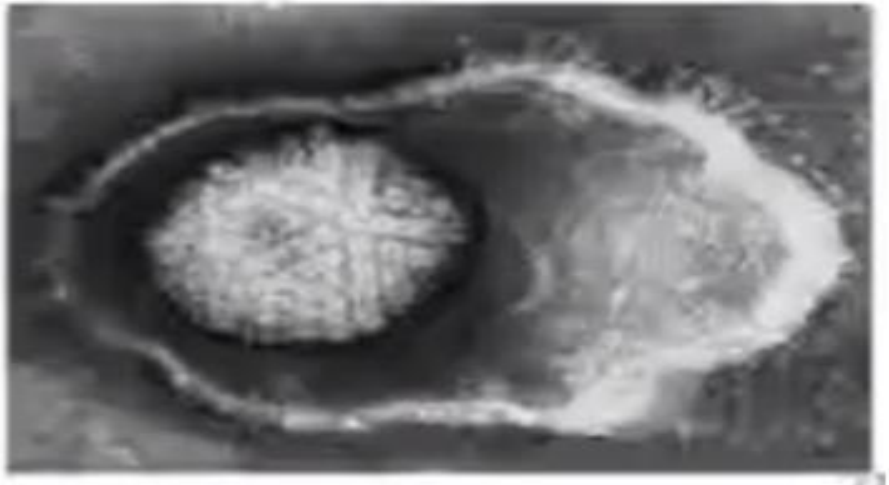



(a) A polyhedral virus




(b) *Mastadenovirus*



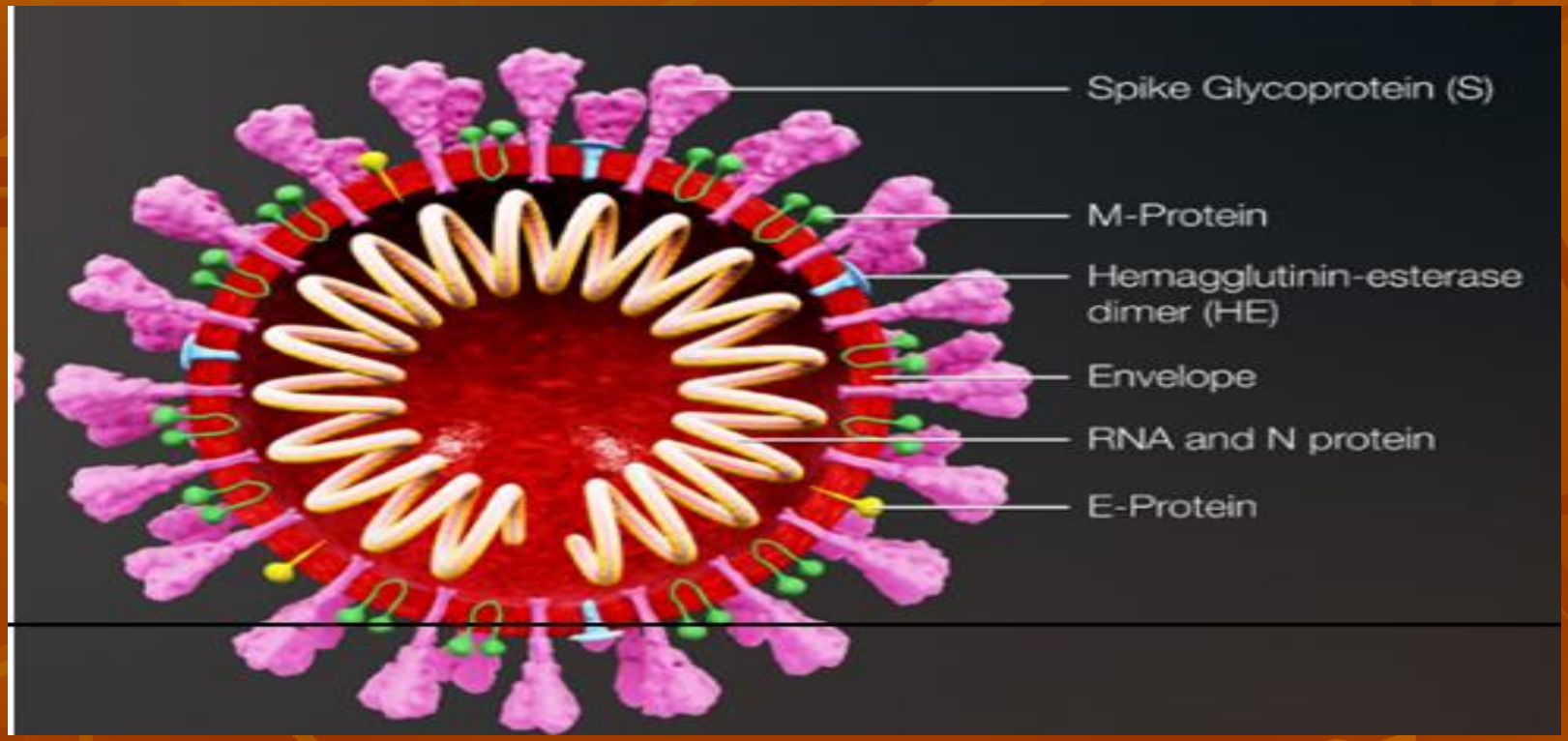


Icosahedral symmetric in Naked Capsid (left) and Envelope virus (right)

# Enveloped Viruses Structure

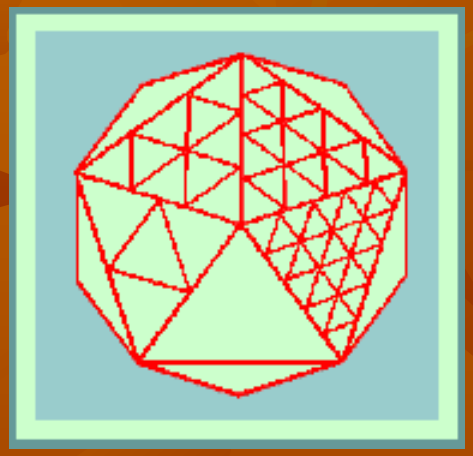
Qazvin University of Medical Sciences

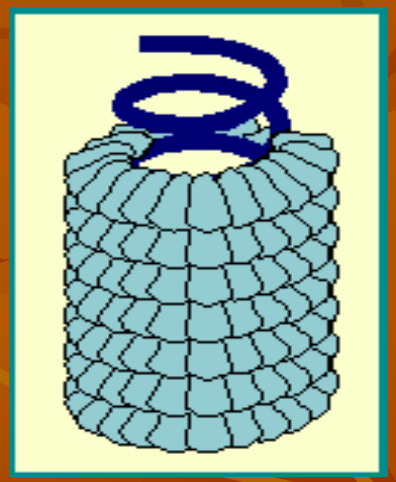
## ويژگيهاي آنتي ژنيک , و ساختاری ويروس SARS-CoV- 2

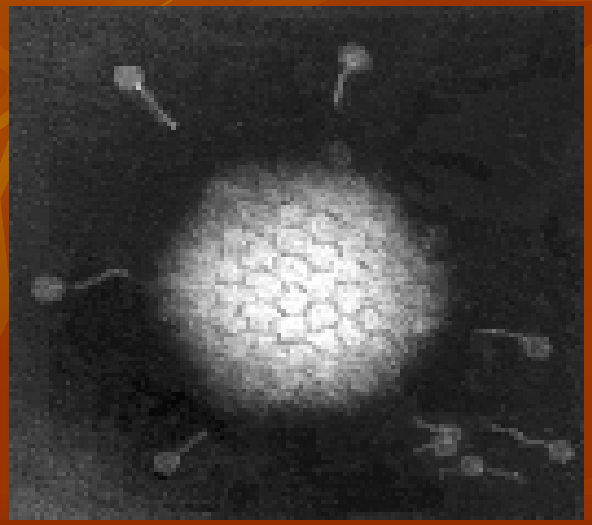


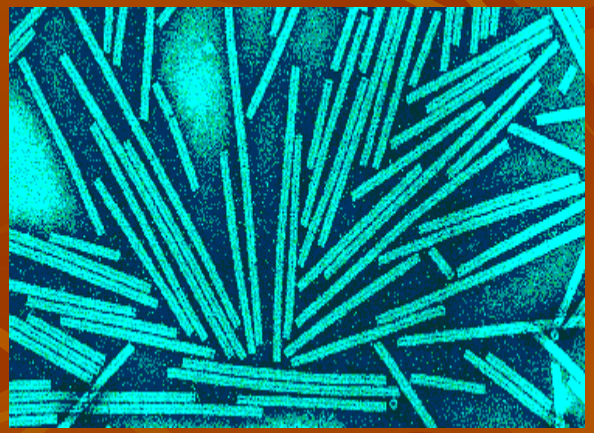

- SARS-CoV-2 دارای 15 پروتئين غير ساختماني، و 5 پروتئين ساختاری است.

# Capsid Symmetry









# Symmetry of Virus Particles determined By:

- ***Electron microscopy***, ***cryoelectron*** **microscopy**, and ***x-ray diffraction*** **techniques** have made it possible to resolve fine differences in the basic morphology of viruses.
  - The study of viral symmetry by standard electron microscopy requires the use of **heavy metal stains** (eg, **potassium phosphotungstate**) to emphasize surface structure.
- The **heavy metal adsorbs** to virus particles and brings out the surface structure of viruses by virtue of "negative staining." The typical level of resolution is 3–4 nm. (The size of a DNA double helix is 2 nm.)
- However, ***conventional methods*** of sample preparation often cause distortions and changes in particle morphology.
  - ***Cryoelectron microscopy*** uses virus samples quickly frozen in vitreous ice; fine structural features are preserved, and the use of negative stains is avoided.
- ***Three-dimensional structural information*** can be obtained by the use of computer image processing procedures.

# Cubic Symmetry

- All ***cubic symmetry*** observed with animal viruses is of the **icosahedral** pattern, the most efficient arrangement for subunits in a closed shell.
  - The icosahedron has ***20 faces*** (each an equilateral triangle***), 12 vertices,*** and ***fivefold***, ***threefold***, and ***twofold*** axes of rotational symmetry.
- The vertex units have five neighbors (**pentavalent**), and all others have six (**hexavalent**).
  - There are **60 identical subunits** on the surface of an icosahedron. To build a particle size adequate to encapsidate viral genomes, viral shells are often composed of multiples of 60 structural units.
- Larger capsid structures are formed in some cases to accommodate the size of the viral genome with the association of additional protein subunits.

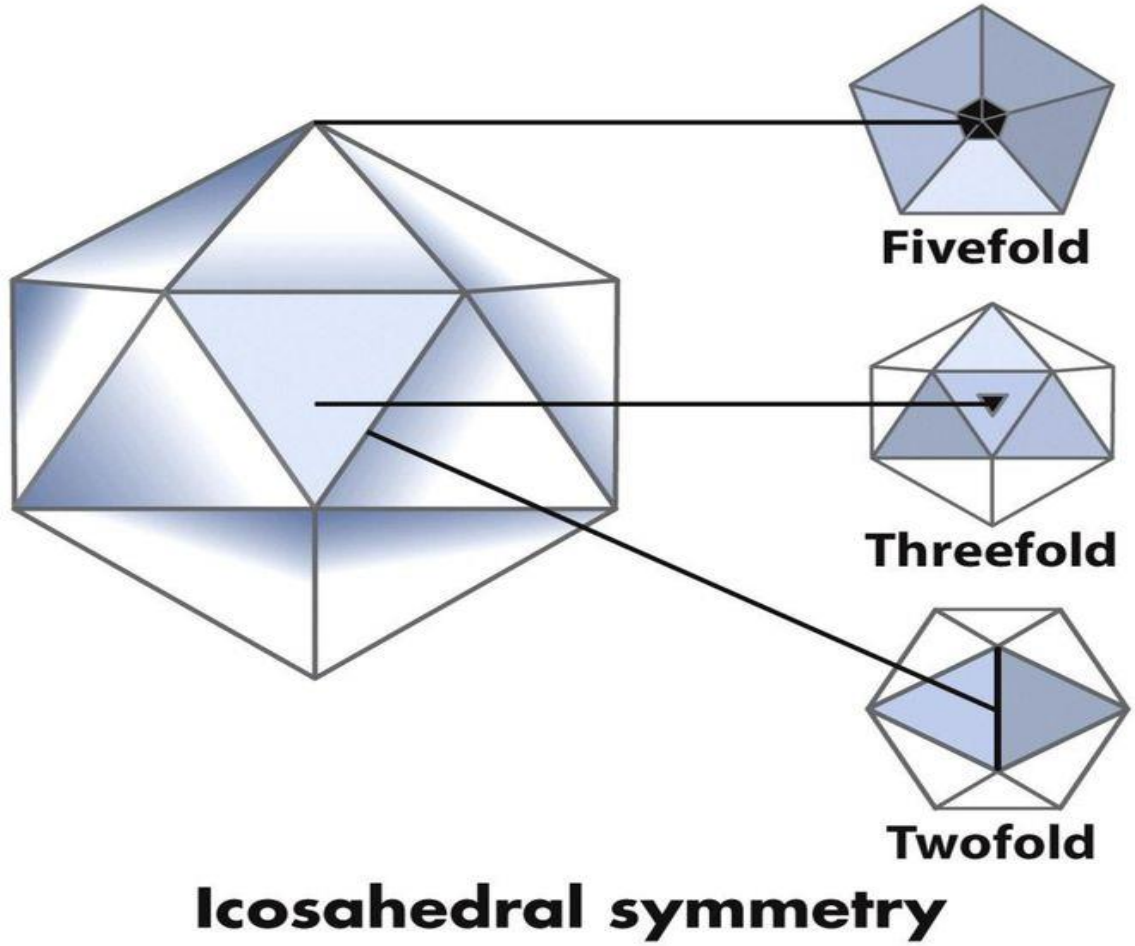



**Figure 4-23c**
*Lehninger Principles of Biochemistry, Fifth Edition*


# محورهای چرخشی تقارن دوتایی، سه تایی و پنج تایی

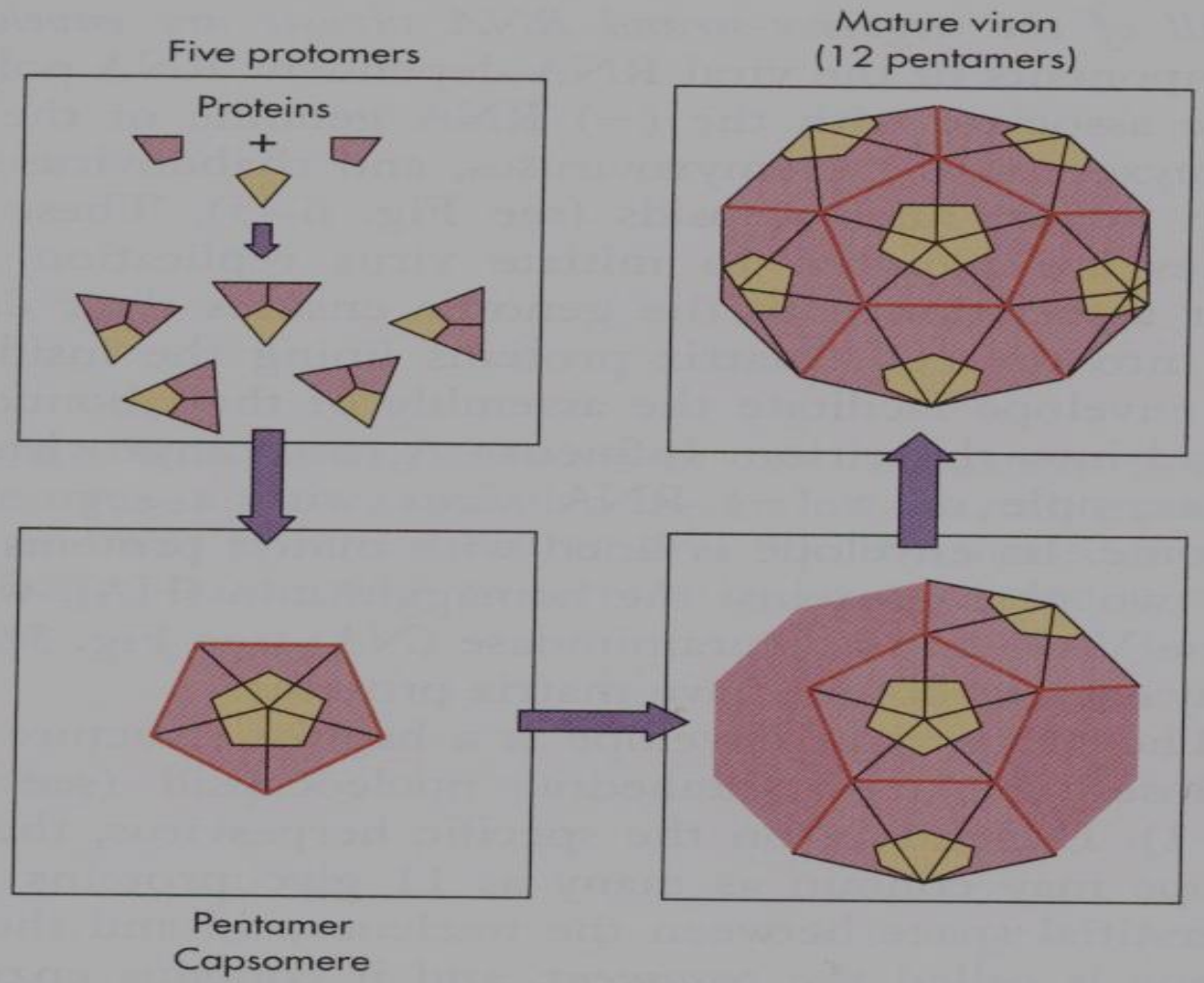
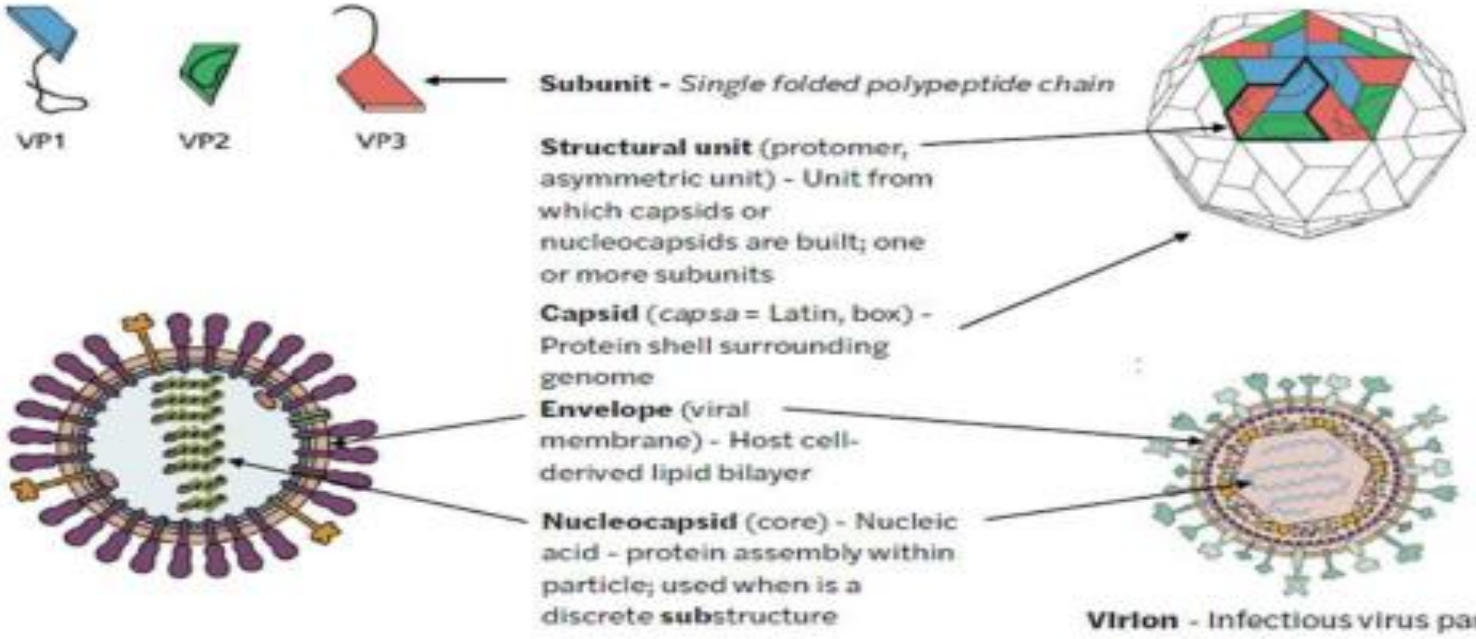
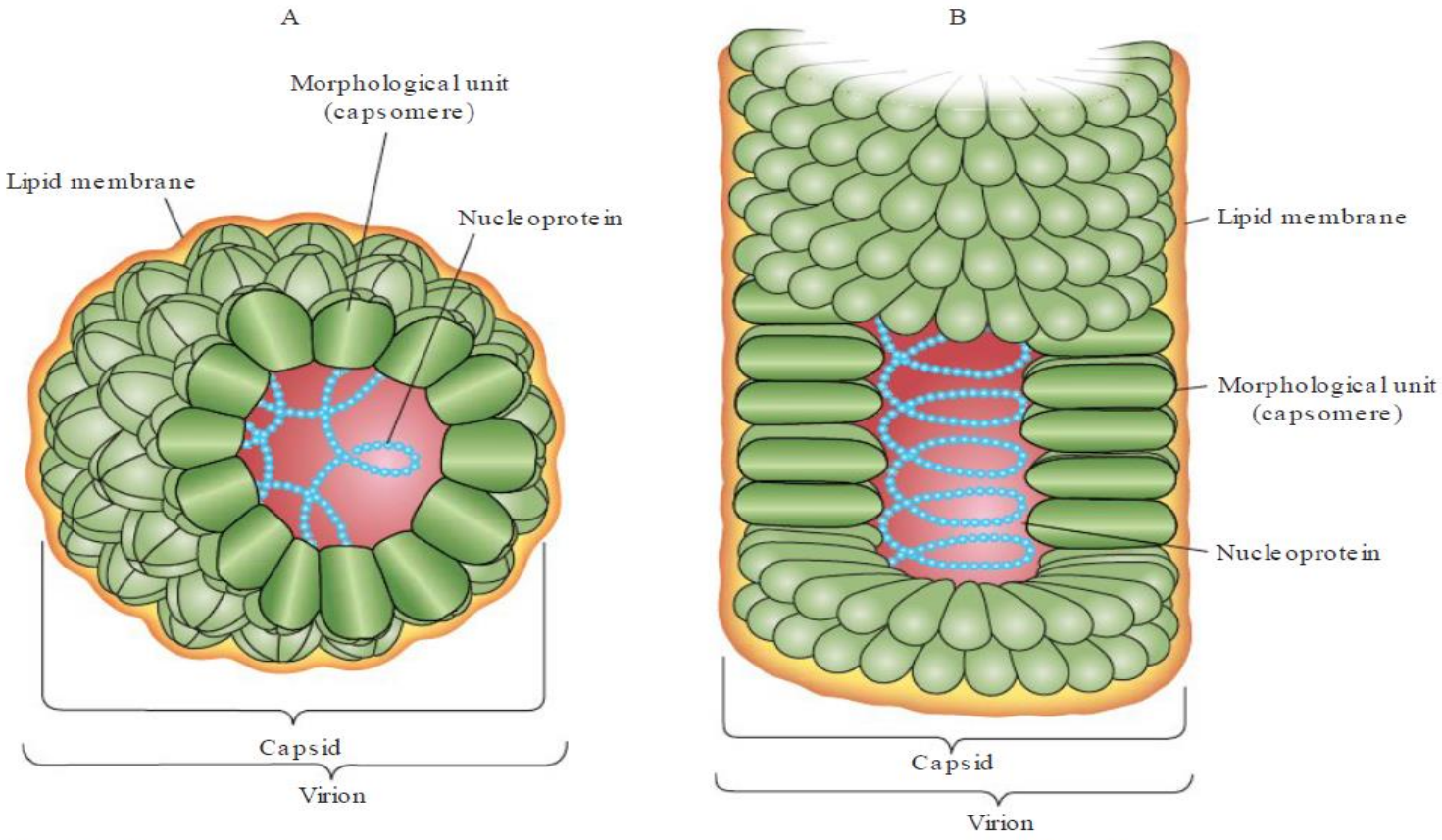



**FIGURE 6–6.** Capsid assembly of the icosahedral capsid of a picornavirus. Individual proteins associate into subunits, which associate into protomers, capsomeres, and an empty procapsid. Inclusion of the (+) RNA genome triggers its conversion to the final capsid form.




- Subunit : کوچکترین زیرواحد سازنده آن پوسته پروتئینی یا کپسید ویروس ها است.
- Stractural unit : زیرواحد میتواند یک پلی پپتید و یا یک زنجیره پلی پپتید باشد که دچار تاخوردگی شده است. این زنجیره های پلی پپتیدی میتوانند کنار یکدیگر قرار بگیرند و زیر واحدی بنام واحد ساختمانی تشکیل بدهند. این stractural unit از چند زیرواحد تشکیل شده است که کنار یکدیگر قرار گرفته اند. این واحد های ساختمانی با یکدیگر کپسید ویروس را میسازند .
- Capsid : کپسید همان پوسته پروتئینی است که ژنوم ویروس را در بر میگیرد .
- Envelope : در بعضی ویروس ها غشای لیپیدی دور کپسید را فرا گرفته است. ویروس ها این غشا را معمولا از میزبان بر میدارند. ویروس ها هیچ اطلاعاتی برای ساختن غشای لیپیدی، ندارند .
- Nucleocapsid : به مجموع ژنوم و کپسید ویروس نیز نوکلئوکپسید میگویند.

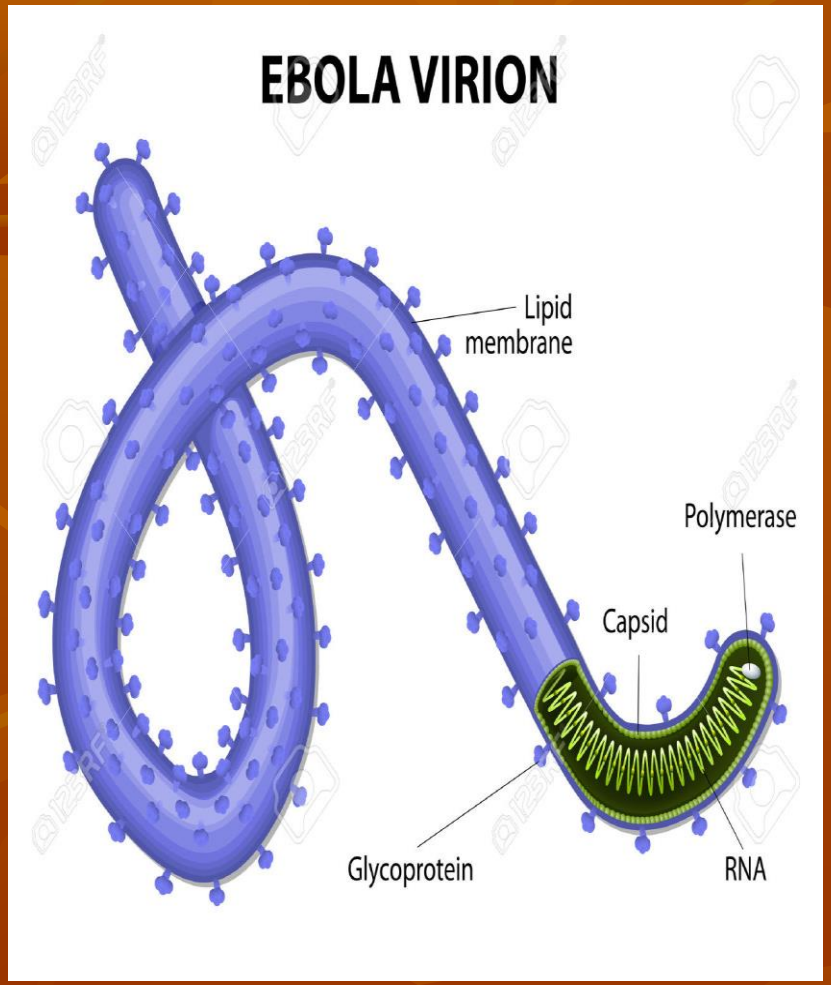


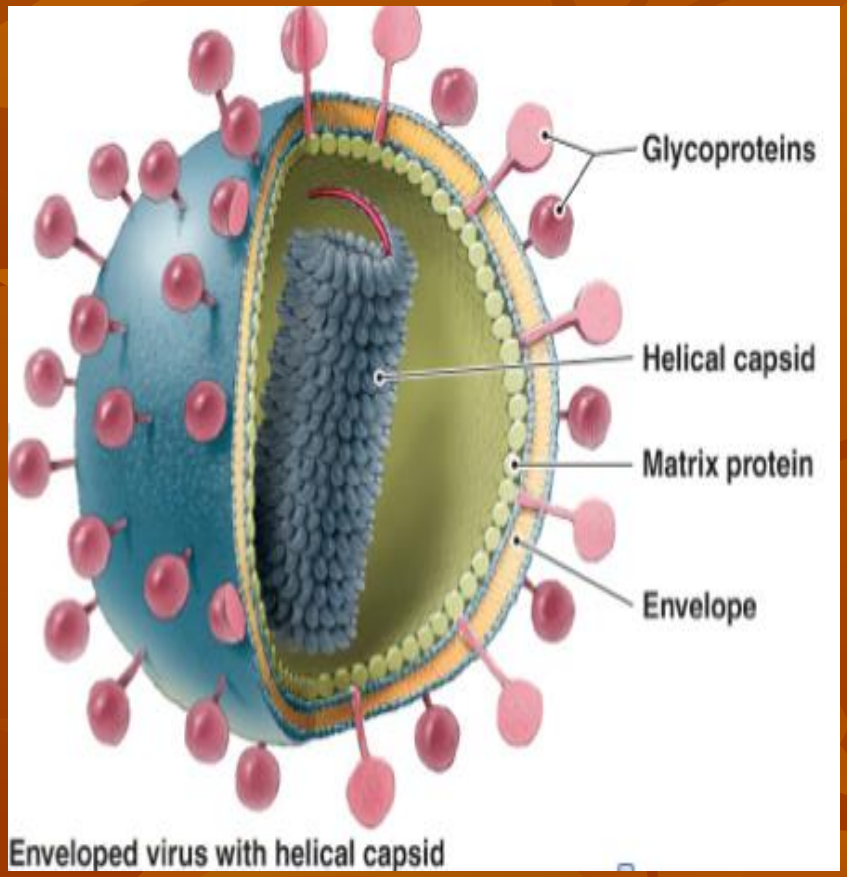

■ FIGURE 23-2 Virus morphology. Viruses are constructed with great economy. A central nucleoprotein core is surrounded by a protein capsid, which is made up of individual capsomeres. Some viruses also have a host-derived lipoprotein membrane around the nucleocapsid. The two most common organizational patterns of symmetry are icosahedral **(A)** and helical **(B)**. Ultrastructurally, the icosahedral viruses appear round, although the facets may occasionally be visualized (see the illustration of adenovirus in Table 23-2).

# Helical Symmetry

Dr. M. Aslanimehr

# Schematic diagram of the virion with Helical Symmetry in enveloped viruses



# Cubic Symmetry

- The viral nucleic acid is condensed within the isometric particles; **virus-encoded core proteins—or**, in the case of polyomaviruses and papillomaviruses, **cellular histones—are** involved in condensation of the nucleic acid into a form suitable for packaging.
  - "**Packaging sequences**" on viral nucleic acid are involved in assembly into virus particles.
- Icosahedral capsids are formed **independently** of nucleic acid.
- Expression of capsid proteins from cloned genes often results in self-assembly and formation of empty "**virus-like particles**."
  - Both DNA and RNA viral groups exhibit examples of cubic symmetry.

# Helical Symmetry

- In cases of ***helical symmetry***, protein subunits are bound in a periodic way to the viral nucleic acid, winding it into a helix.
- The ***filamentous viral nucleic acid–protein complex*** (nucleocapsid) is then coiled inside a lipid-containing envelope.
  - Thus, as is not the case with icosahedral structures, there is a regular, periodic interaction between capsid protein and nucleic acid in viruses with helical symmetry. It is not possible for "empty" helical particles to form.
- All known examples of animal viruses with helical symmetry **contain RNA genomes** and, with the exception of **rhabdoviruses**, have flexible nucleocapsids that are wound into a ball inside envelopes

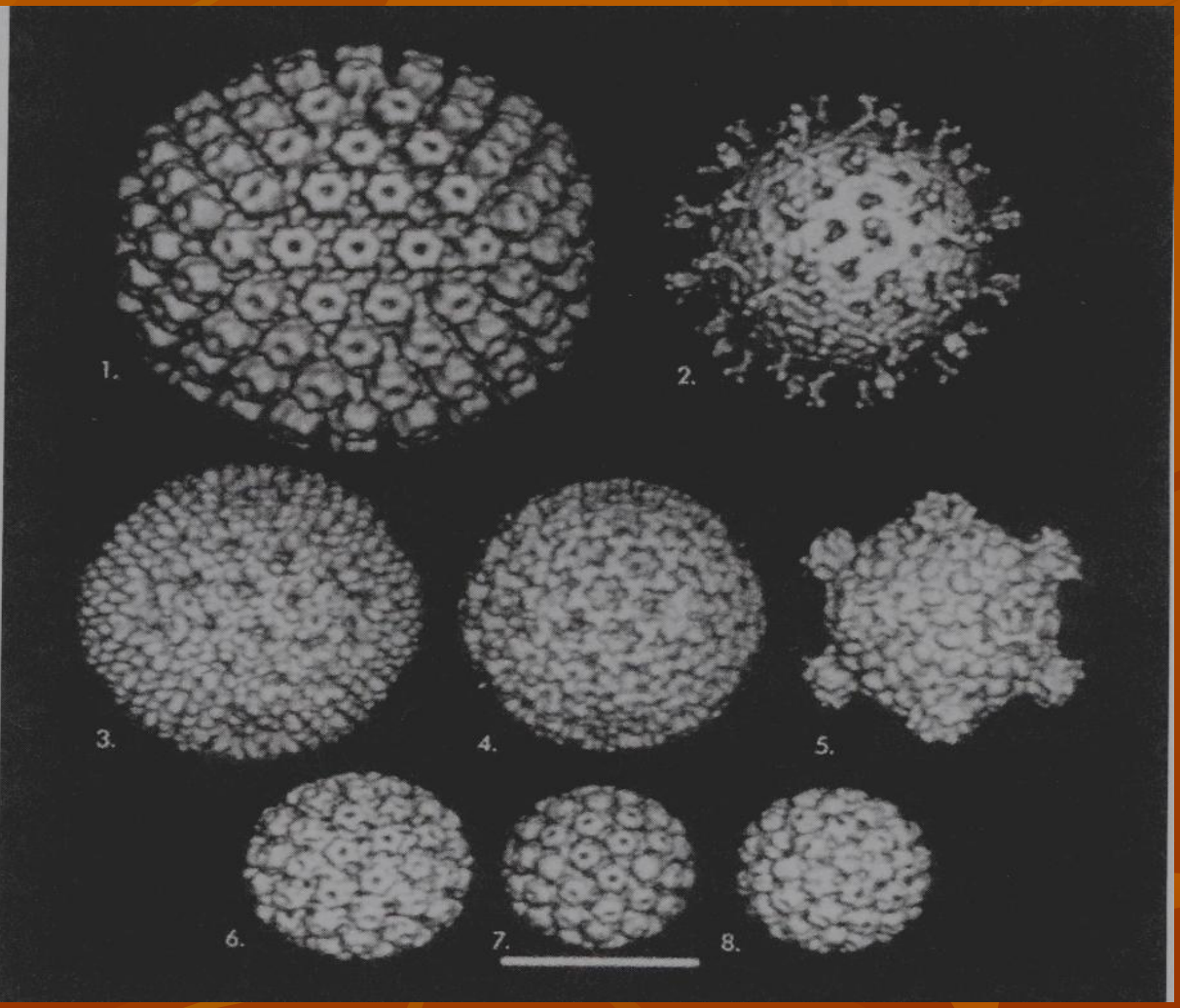
# Complex Structures

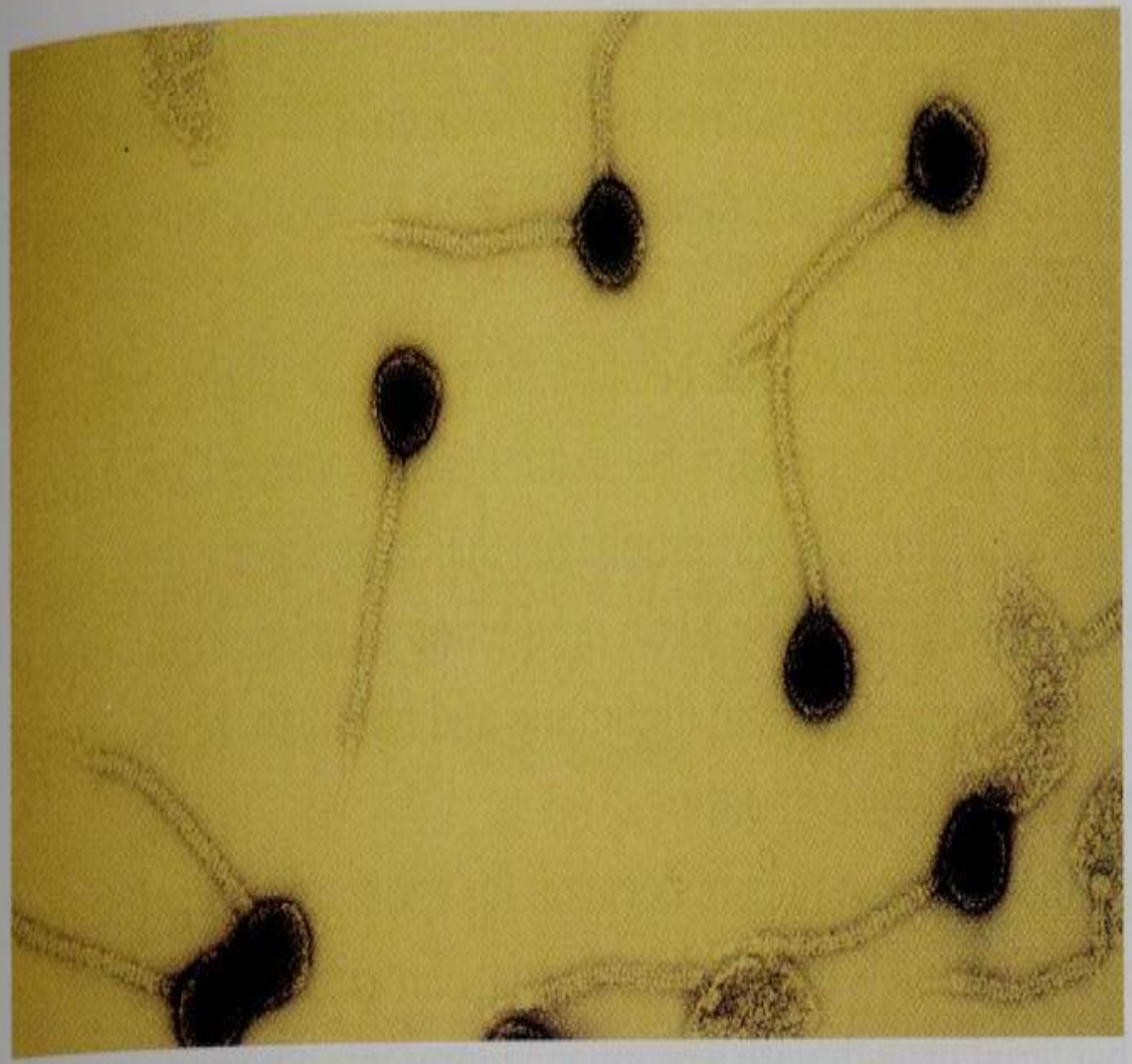
- Some virus particles do not exhibit simple cubic or helical symmetry but are more complicated in structure.

- For example, **poxviruses** are brick shaped, with ridges on the external surface and a core and lateral bodies inside

# Capsomer

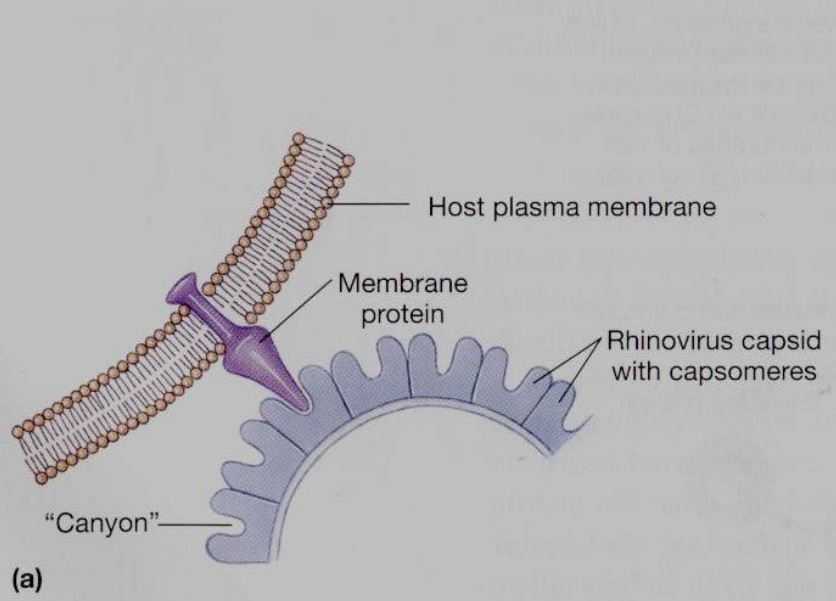
**FIGURE 6–7.** Cryoelectron microscopy and computer-generated three-dimensional image reconstructions of several icosahedral capsids. These images show the symmetry of capsids and the individual capsomeres. During assembly, the genome may fill the capsid through the holes in the herpesvirus and papovavirus capsomeres. 1, Equine herpesvirus nucleocapsid; 2, simian rotavirus; 3, reovirus type 1 (Lang) virion; 4, intermediate subviral particle (reovirus); 5, core (inner capsid) particle (reovirus); 6, human papillomavirus type 19 (papovavirus); 7, mouse polyomavirus (papovavirus); 8, cauliflower mosaic virus. (Bar = 50 nm.) (Courtesy Dr. Tim Baker, Purdue University.)

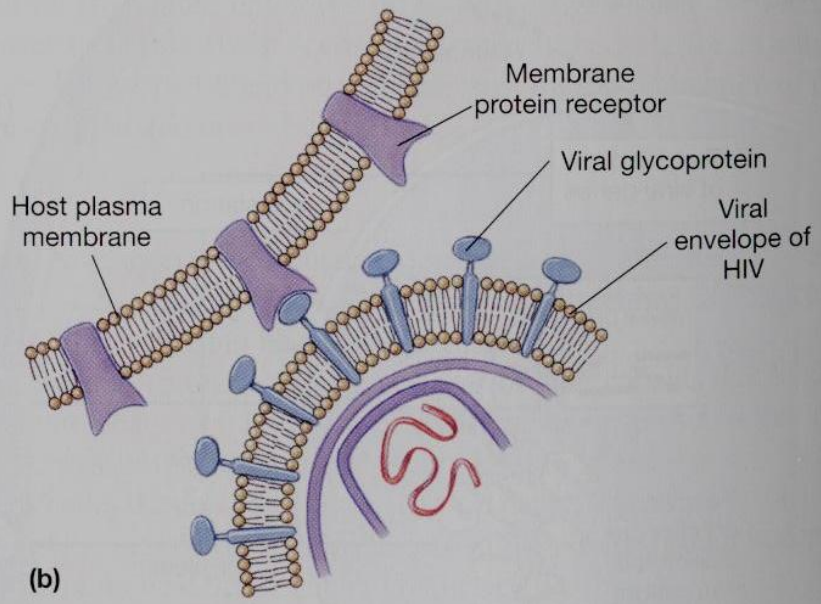




➢ Figure 10.10 **False-color TEM of the temperate lambda phage (84,000ZX).** This virus infects the bacterium *Escherichia coli.*

# Viral Attachment protein ( VAP )




➢ Figure 10.14 **Viral recognition of an animal host cell.** (a) Rhinoviruses have "canyons," or depressions, in the capsid that attach to specific membrane proteins on the host cell membrane. (b) HIV has specific envelope spikes (viral glycoproteins) that attach to a membrane protein receptor on the surface of specific host immune defense cells.

# Spike and RBD (Receptor Binding Domain)

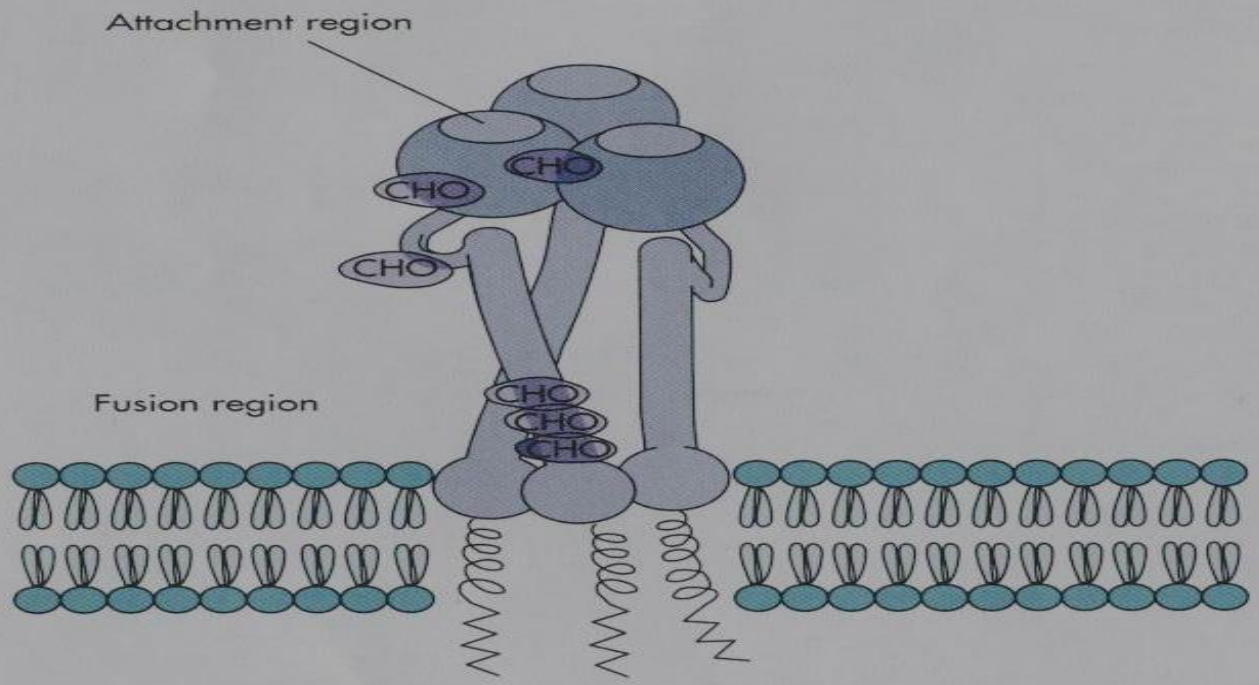
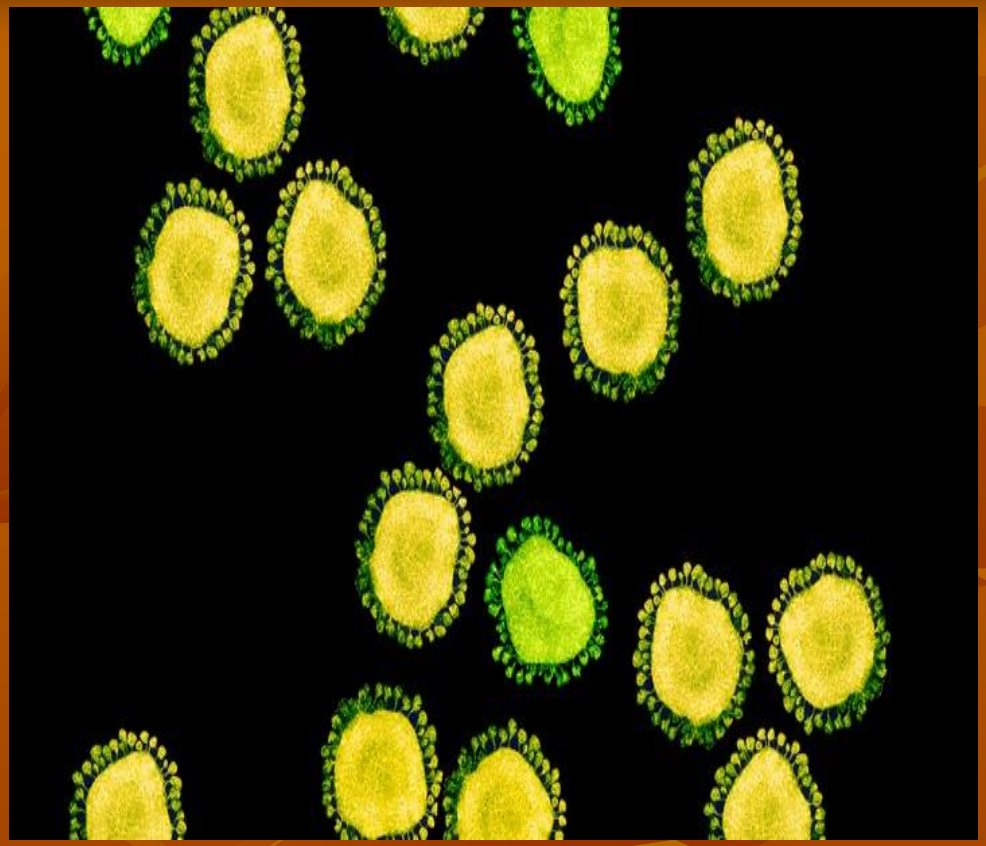
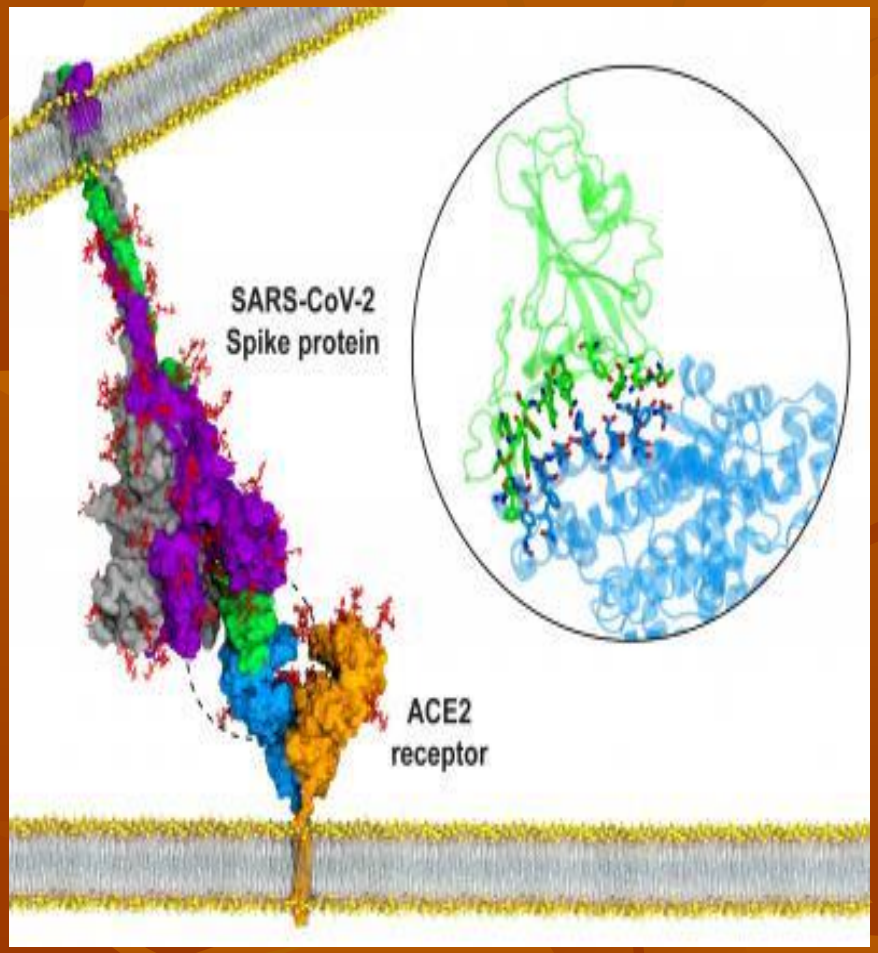


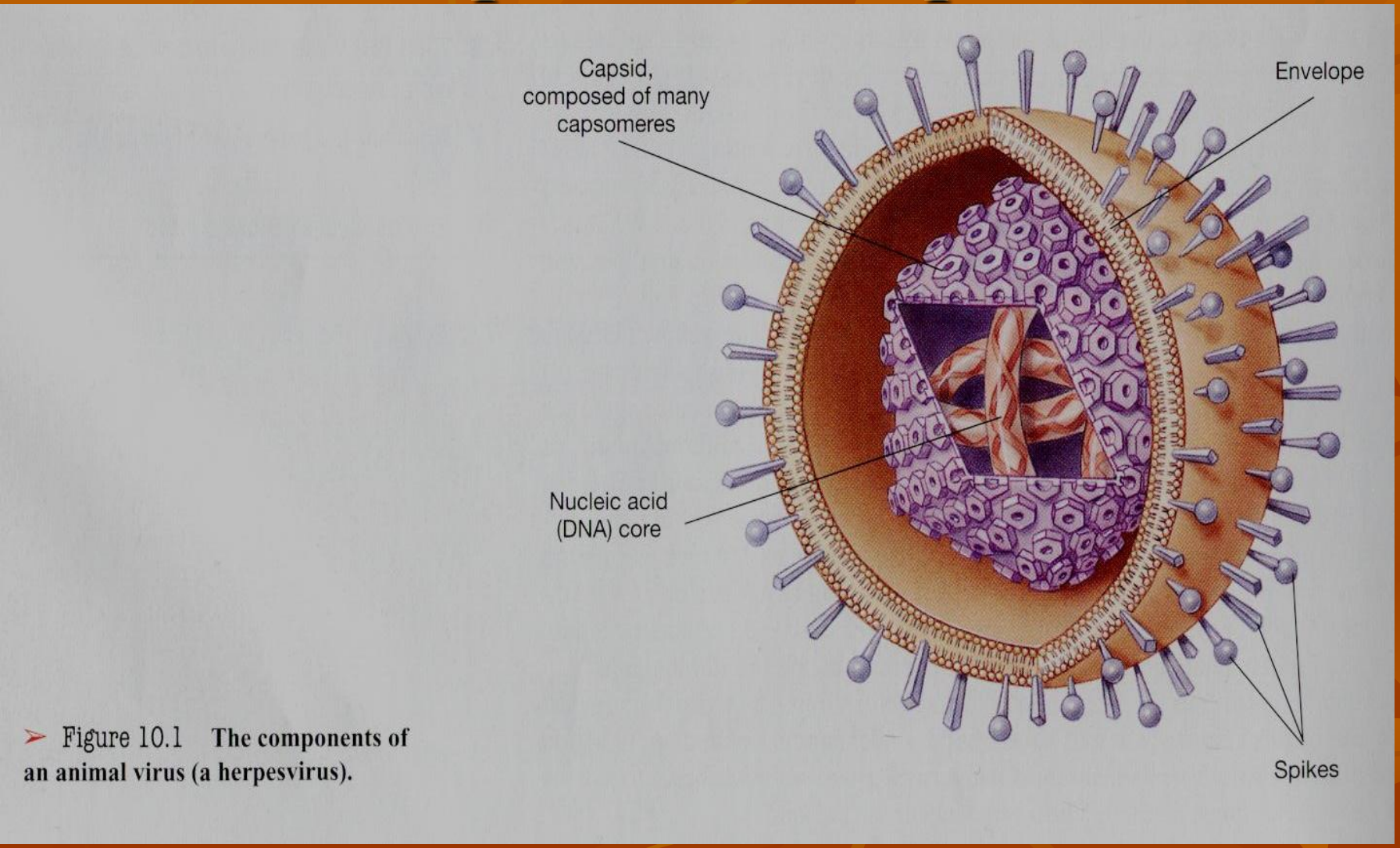

**FIGURE 6–8.** Diagram of the hemagglutinin glycoprotein trimer of influenza A virus, a representative spike protein. The region for attachment to the cellular receptor is exposed on the spike protein's surface. Under mild acidic conditions, the hemagglutinin changes conformation to expose a hydrophobic sequence at the "fusion region." CHO, *N*-linked carbohydrate attachment sites. (Modified from Schlesinger MJ, Schlesinger S: Domains of virus glycoproteins *Adv Virus Res* 33:1–44, 1987.)





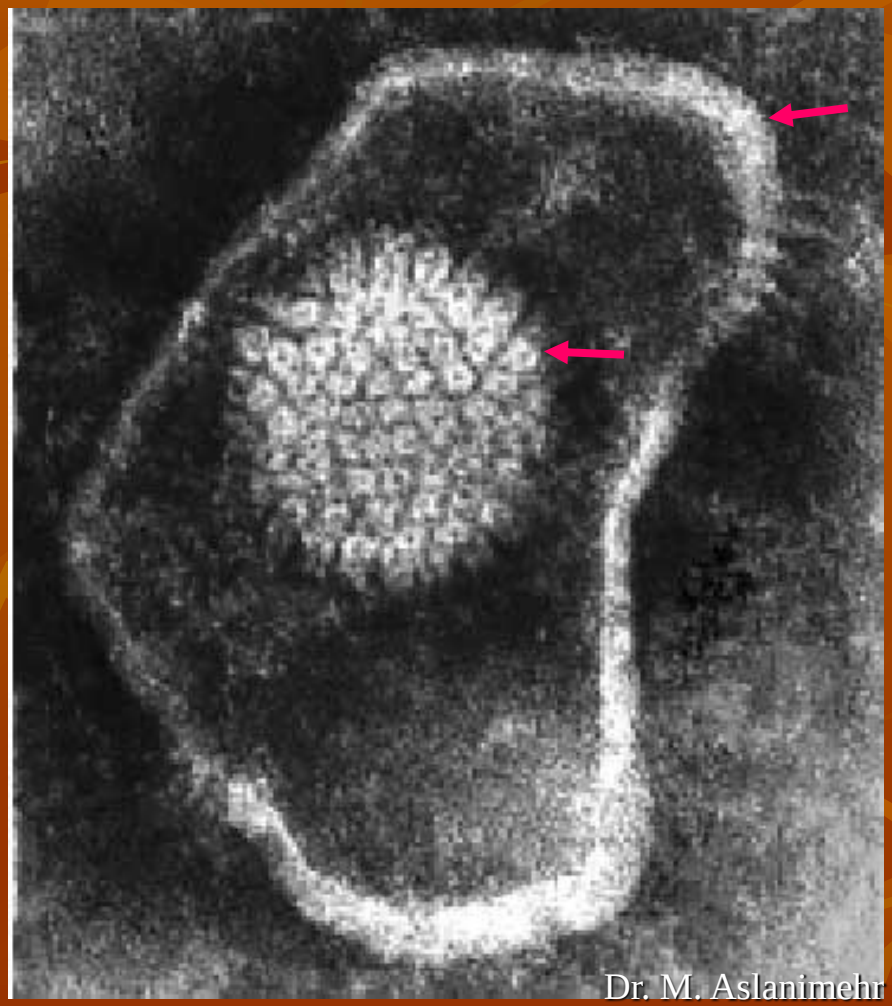

# SARS-CoV-2 Spike

# Peplomer & Spikes




➢ Figure 10.1 **The components of an animal virus (a herpesvirus).**

# Herpesvirus Particle




envelope

icosahedral capsid

## BOX 36.4 Virion Structure: Naked Capsid

**Component**

Protein

**Properties**[a]

Is environmentally stable to the following:
- Temperature
- Acid
- Proteases
- Detergents
- Drying

Is released from cell by lysis

**Consequences**[a]

Can be spread easily (on fomites, from hand to hand, by dust, by small droplets)
Can dry out and retain infectivity
Can survive the adverse conditions of the gut
Can be resistant to detergents and poor sewage treatment
Antibody may be sufficient for immunoprotection

[a]Exceptions exist.

(Murray)

## BOX 36.5 Virion Structure: Envelope

**Components**

Membrane
Lipids
Proteins
Glycoproteins

**Properties**[a]

Is environmentally labile—disrupted by the following:
- Acid
- Detergents
- Drying
- Heat

Modifies cell membrane during replication
Is released by budding and cell lysis

**Consequences**[a]

Must stay wet
Cannot survive the gastrointestinal tract
Spreads in large droplets, secretions, organ transplants, and blood transfusions
Does not need to kill the cell to spread
May need antibody and cell-mediated immune response for protection and control
Elicits hypersensitivity and inflammation to cause immunopathogenesis

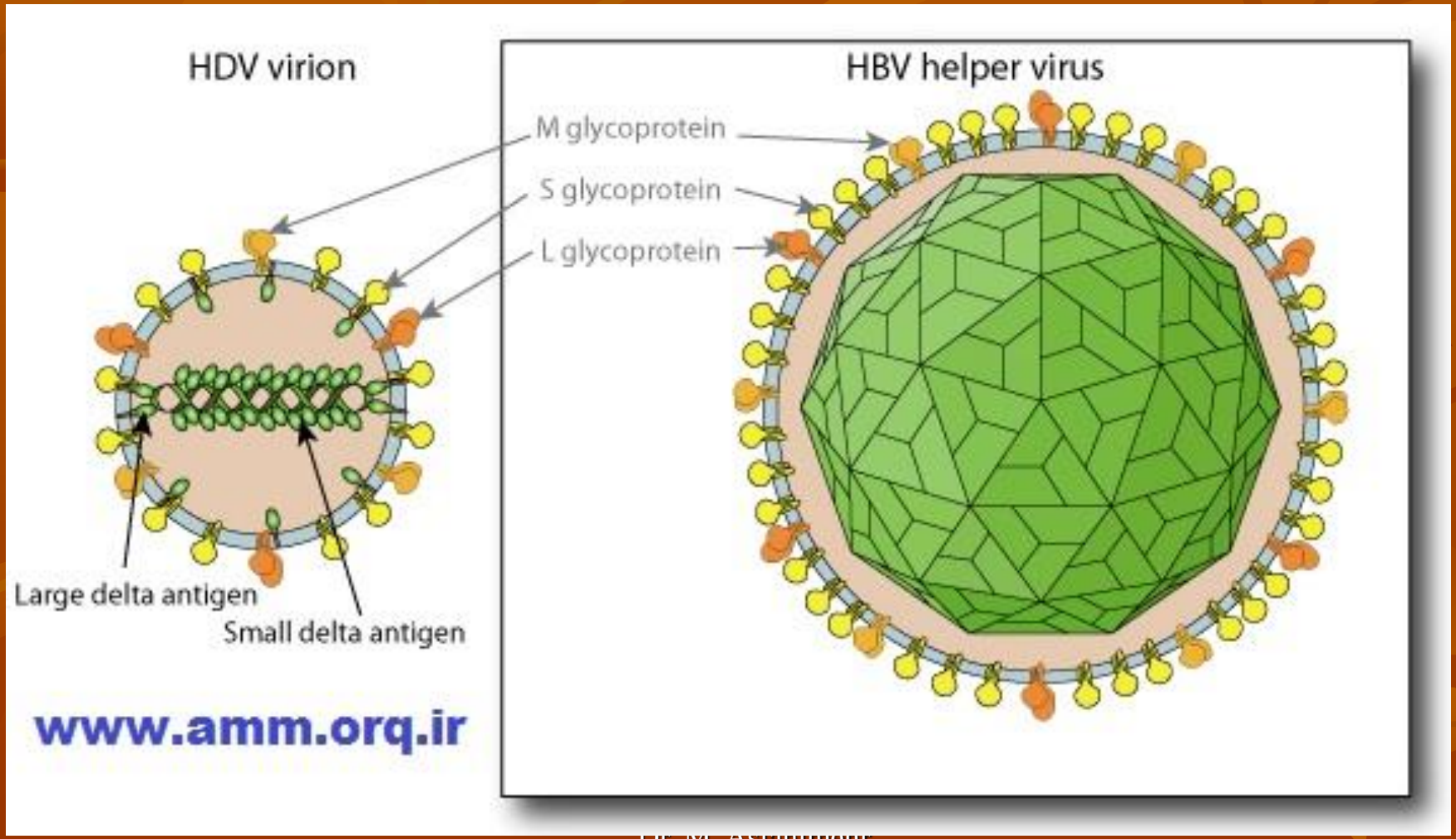
[a]Exceptions exist.

(Murray)

# What are atypical agents?

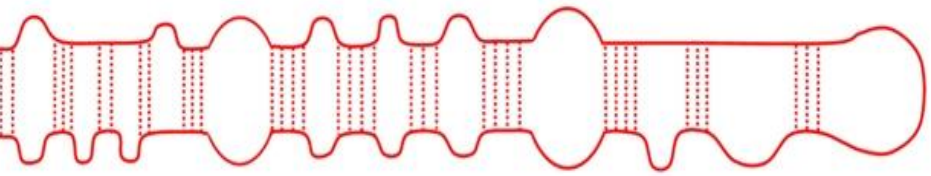
- **Atypic virus like agents**
  1- Defective Viruses
  2- Pseudovirions
- **Atypic agents**
  1- Viroids
  2- **Prions**

# HDV as a defective virus



# Atypic agents

## Viroid



Structure of a viroid – circular single-stranded RNA with some pairing between complementary bases and loops where no such pairing occurs

## Prion

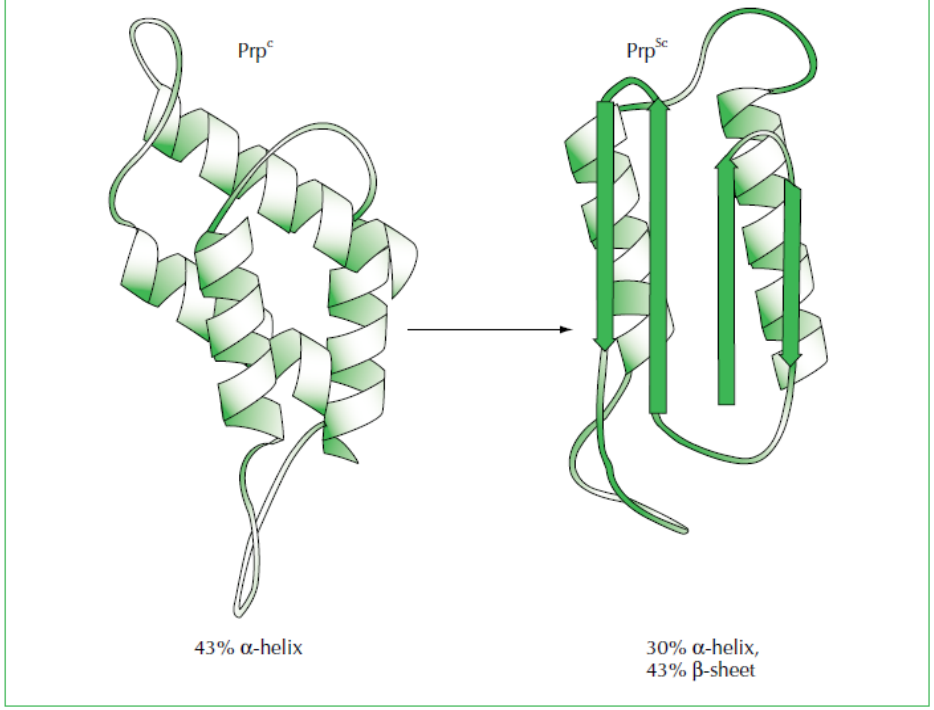



Figure 8.10 Conformational changes in PrP.

# Viroids

- Viroid are small infectious agents that cause diseases of plants.
- Viroids are agents that do not fit the definition of classic viruses. They are nucleic acid molecules without a protein coat.
- Plant viroids are single-stranded, covalently closed circular RNA molecules consisting of about
- 246 to 375 nucleotides and with a highly base-paired rodlike structure.
- Viroid RNA does not encode any protein products; the devastating plant diseases induced by viroids occur by an unknown mechanism. Hepatitis D virus in humans has properties similar to viroids.

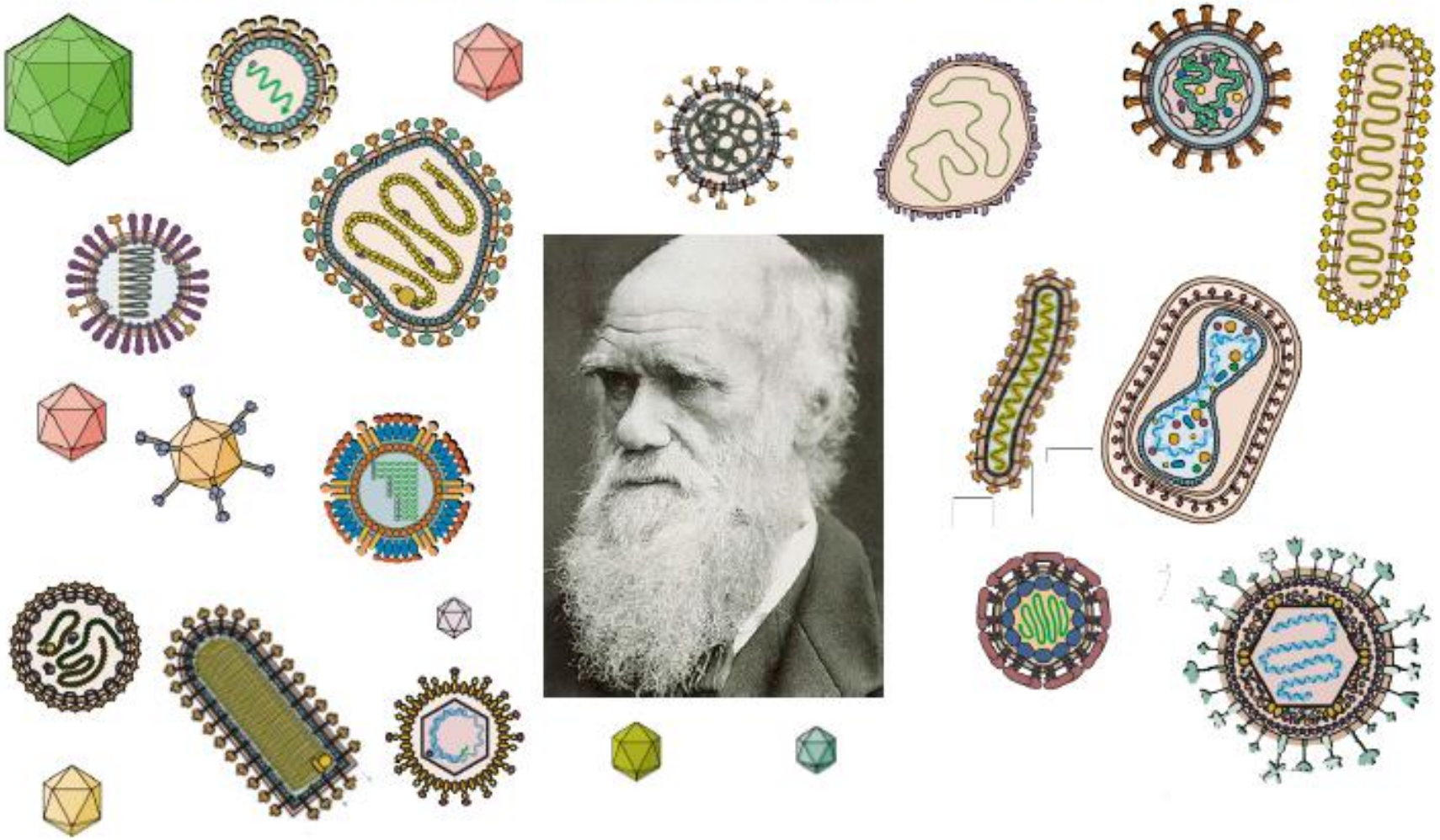
# Viroids

- The extracellular form of the viroid is naked RNA there is no capsid of any kind.
- The RNA molecule contains no protein-encoding genes, and the viroid is therefore totally dependent on host functions for its replication.
- Viroid RNA is replicated by the DNA-dependent RNA polymerase of the plant host; preemption of this enzyme may contribute to viroid pathogenicity

# Prions

- Prions are infectious particles composed solely of protein with no detectable nucleic acid.
- They are highly resistant to inactivation by heat, formaldehyde, and ultraviolet light that inactivate viruses.
- The infectious prion protein is misfolded and able to change the conformation of the native prion protein which is encoded by a single cellular gene.
- Prion diseases, called "transmissible spongiform encephalopathies," include scrapie in sheep, mad cow disease in cattle, and kuru and Creutzfeldt-Jakob disease in humans (see Chapter 42).

# Darwin would have loved viruses!

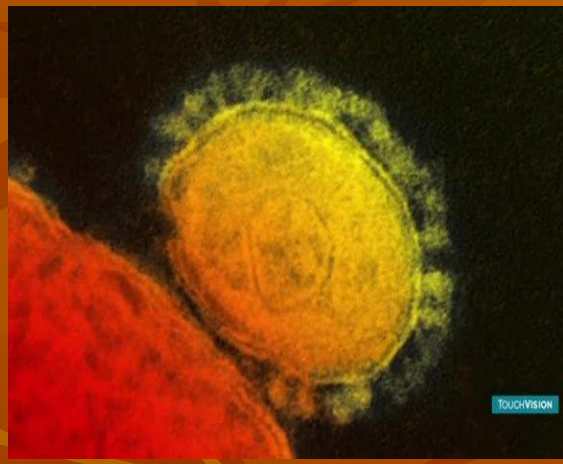


*The best exemplars of evolution by natural selection, and for RNA viruses, evolution is so rapid it can be followed in real time*

# EVOLUTIONARY ORIGIN OF VIRUSES

The origin of viruses is not known. There are profound differences among the DNA viruses, the RNA viruses, and viruses that use both DNA and RNA as their genetic material during different stages of their life cycle. It is possible that different types of agents are of different origins. Two theories of viral origin can be summarized as follows:

1. Viruses may be derived from DNA or RNA nucleic acid components of host cells that became able to replicate autonomously and evolve independently. They resemble genes that have acquired the capacity to exist independently of the cell. Some viral sequences are related to portions of cellular genes encoding protein functional domains. It seems likely that at least some viruses evolved in this fashion.
2. Viruses may be degenerate forms of intracellular parasites. There is no evidence that viruses evolved from bacteria, although other obligately intracellular organisms (eg, rickettsiae and chlamydiae) presumably did so. However, poxviruses are so large and complex that they might represent evolutionary products of some cellular ancestor.



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# Evolutionary Origin of Viruses

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- However, ***Poxviruses*** are so large and complex that they might represent evolutionary products of some cellular ancestor.
- And recently ***Mimi Viruses & Mega viruses***

# Evolutionary of Viruses

- The physical structure and genetics of viruses have been optimized by mutation and selection to infect humans or other hosts.
- To do this, the virus must be capable of transmission between hosts, must traverse the skin or other protective barriers of the host, must be adapted to the biochemical machinery of the host cell for replication, and must escape elimination by the host immune response.
- Knowledge of the structural **(size and morphology) and** genetic **(type and tructure of nucleic acid) features of a** virus provides insight into how the virus replicates, spreads, and causes disease.

# با تشکر از توجه تان

Dr. M. Aslanimehr

تا که بودیم نبودیم کسی
کشت ما را غم بی همنفسی
تا که رفتیم همه یار شدند
خفته ایم و همه بیدارشدند
قدر آینه بدانیم چون هست
نه در آن وقت که اقبال
شکست

میر عماد قزوینی