Virology: An introduction

Introduction

- Viruses can cause a variety of diseases from common cold and the flu to serious illnesses such as AIDS, dengue fever, measles, small pox and bird flu.
- All viruses infect cells and hijack the host cellular machinery for their own benefit.
- Learning about the biology and structure of viruses can help us better understand the diseases that they cause, their prevention and treatment.

- Viruses have shaped the history and evolution of their hosts.
- Viral infections of humans have altered the history of mankind.
- Virtually all living organisms have viral parasites.

- Virus particles have evolved to transfer genetic material between cells and to encode information sufficient to ensure their own continued propagation.

- They are, in effect, extracellular organelles.

- They contain most or all of the molecular machinery necessary for efficient and specific packaging of viral genomes, escape from an infected cell, survival of transfer to a new host cell, attachment, penetration, and initiation of a new replication cycle.

- In many cases, the molecular machinery works in part by subverting more elaborate elements of the host cell apparatus for carrying out related processes.
- The principles of virus structure thus arise from the requirements imposed by the functions of viral molecular architecture.
- There is more biological diversity within viruses than in all the rest of the bacterial, plant, and animal kingdoms put together.

- **Viruses are submicroscopic obligate intracellular parasites that differ from all other organisms**:-

*** Virus particles are produced from the assembly of preformed components**

*** Viruses lack the genetic information for the generation of metabolic energy for protein synthesis**

- **Viroids**

  Circular RNA molecules (200-400 nt) with a rod-like structure. They have no capsid or envelope and are associated with certain plant disease.

- **Virusoids**

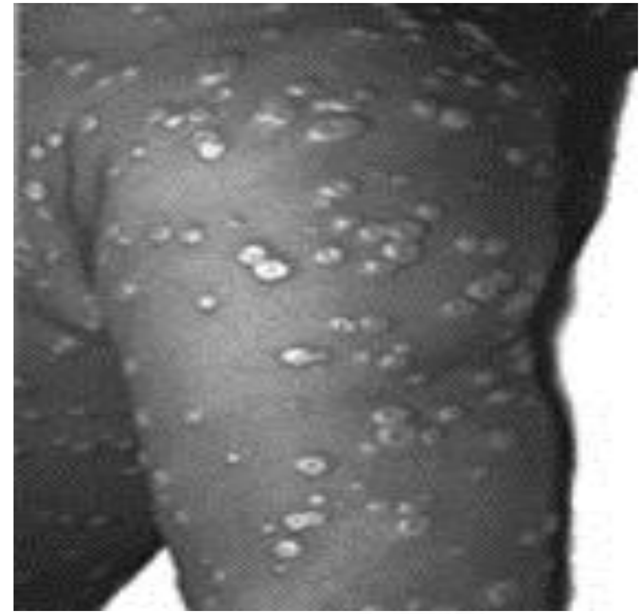
  Satellite, viroid - like molecules,(1000 nt) packaged into virus capsids as passengers**.**

- **Prions**

  Generally believed to consist of a single type of protein molecule with no nucleic acid component.

The Origin of virology

- Virology is a " new" discipline in biology.
- Ancient people were aware of the effects of virus infection.
- 1400 BC: A hieroglyph from Memphis depicts a temple priest showing clinical signs of paralytic poliomyelitis.
- 1196 Bc: The Pharoh Ramses V is believed to have succumbed to smallpox.



- Henle was the first to propose the existence of viruses in 1840.

- Failure of Henle Koch postulates to explain all cases paved the way to discover viruses.

- 19th /20th century: The concept of filtrable agents developed.

- 1909: The first demonstration of a virus being a cause of human disease by Landsteiner and Popper who showed that poliomyelitis was caused by a filtrable agent.
- 1939: The first electron micrograph of a virus (TMV) followed by the demonstration of many filtrable agents from animals and humans.
- 1949: Isolation of viruses in cell culture.

- Later years witnessed the elucidation of both the structure and chemical composition of viruses.
- In the 1950’s and 1960’s there was an explosion in the discovery of new viruses.
- Prompted by a rapidly growing mass of data, several individuals and committees independently advanced classification schemes which led to confusion and controversy.

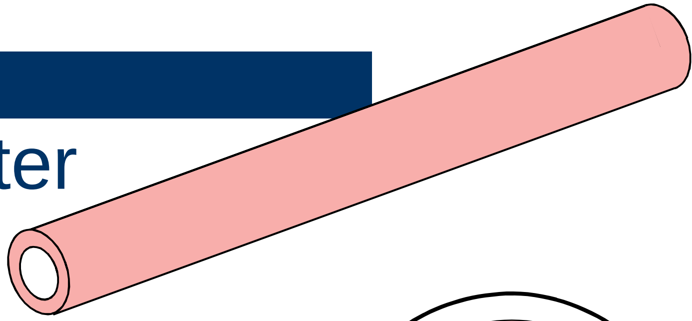
- **In summary**
- Viruses are commonly defined as " the smallest (20-300 nm) infectious agents that are obligate intracellular parasites, contain either DNA or RNA and depend on the biochemical machinery of living cells to copy themselves."
- Viruses cannot be regarded as microorganisms for they are not cells, they have no ribosomes, mitochondria or other organelles, and are metabolically inert.

Virus Structure

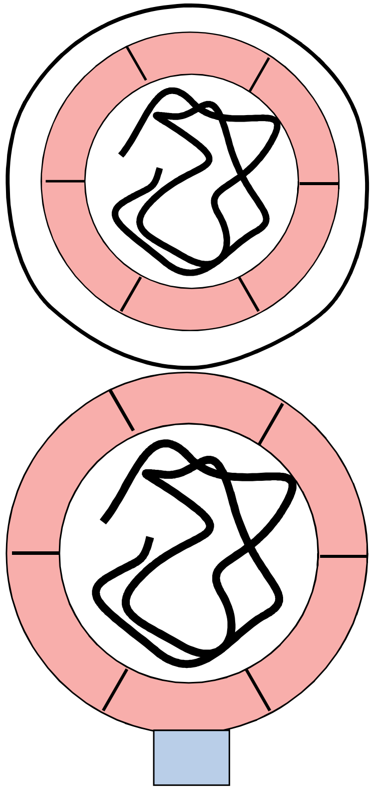
- Virus particles form regular geometric shapes
  And they come in a great variety of shapes and sizes.

- Structural features are determined by requirements for assembly, exit, transmission, attachment and other functions of viruses.

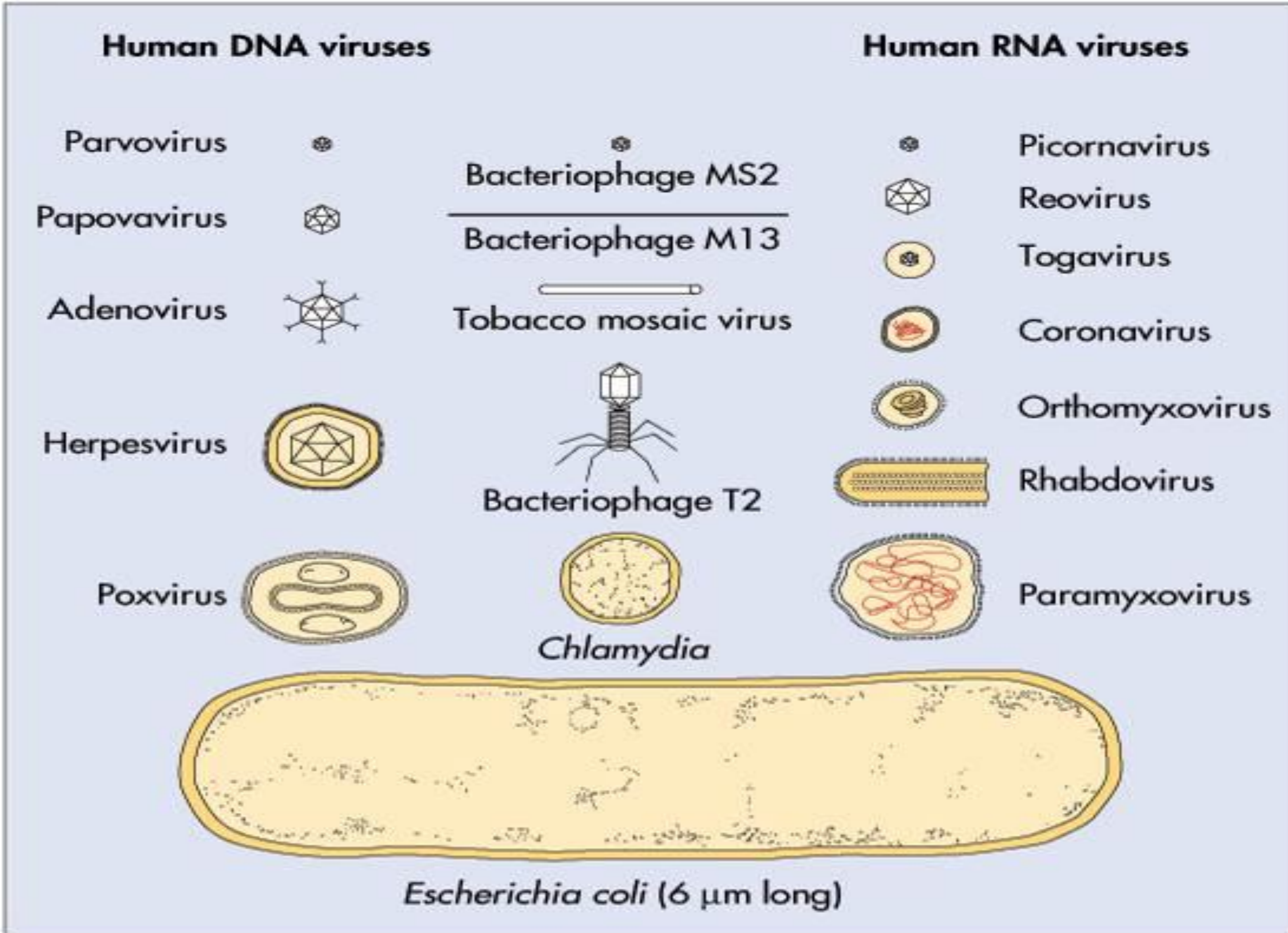
Virus Structure

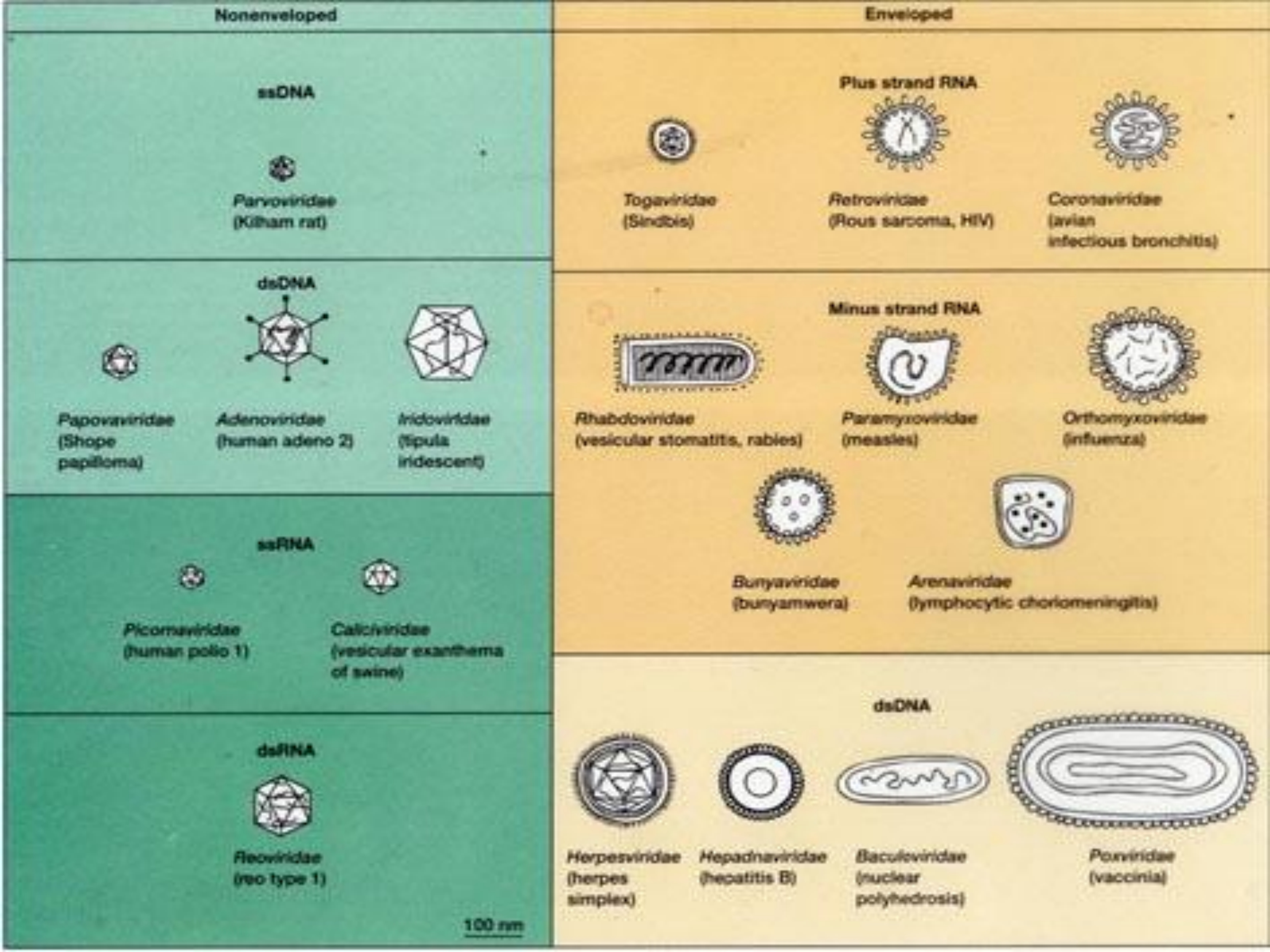


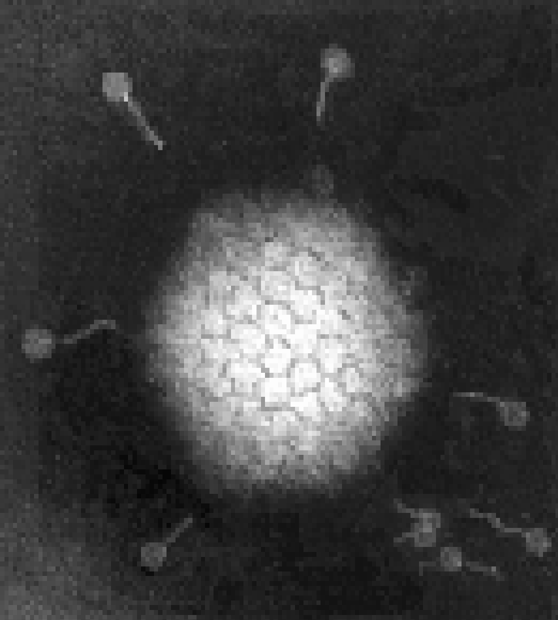
- Size: 17 nm – 3000 nm diameter
- Basic shape
  - Rod-like or “Spherical”
- Protective Shell - Capsid
  - Made of many identical protein subunits
  - <u>Symmetrically</u> organized
  - 50% of weight
  - Enveloped or non-enveloped
  - Genomic material
  - DNA or RNA
  - Single- or double-stranded

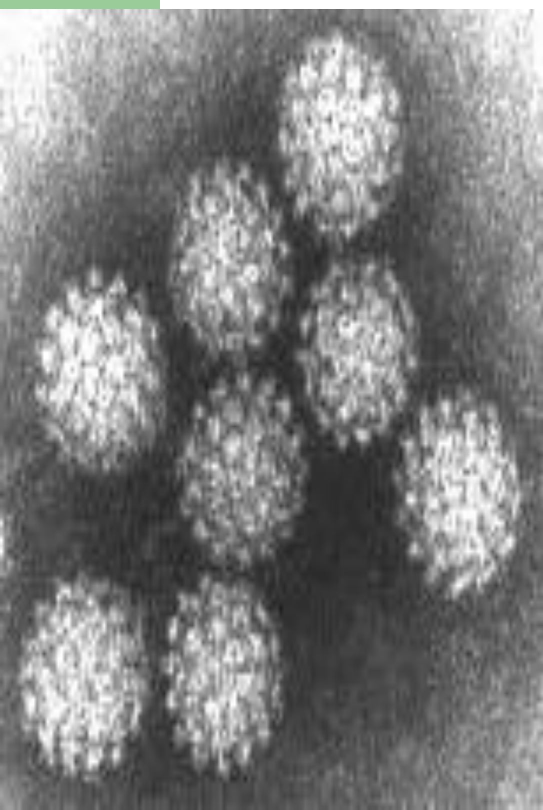


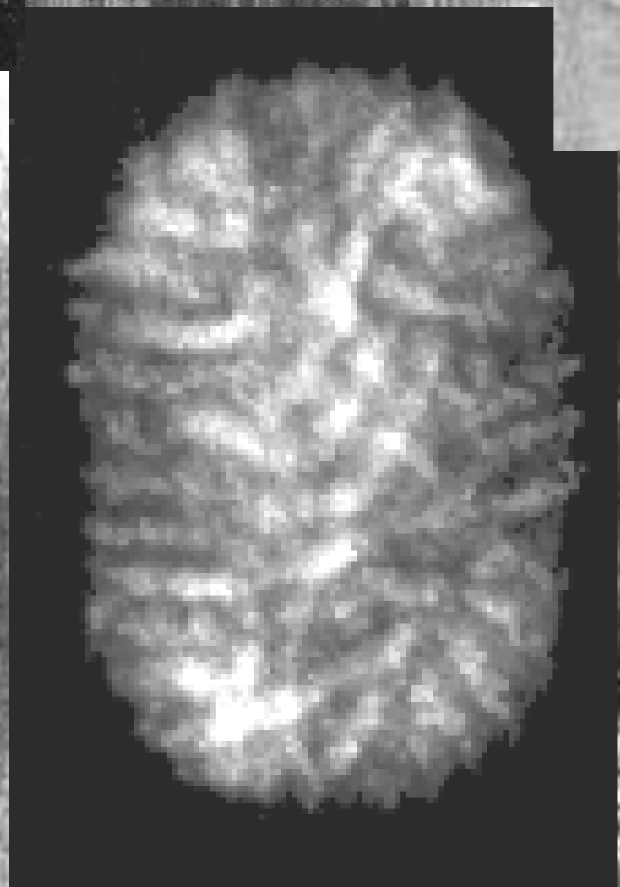
Structures compared

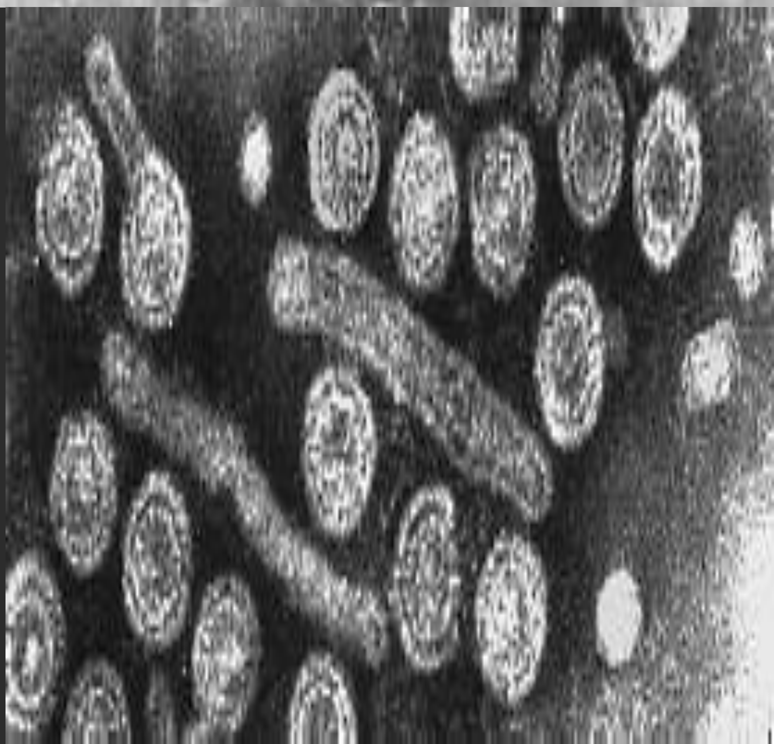


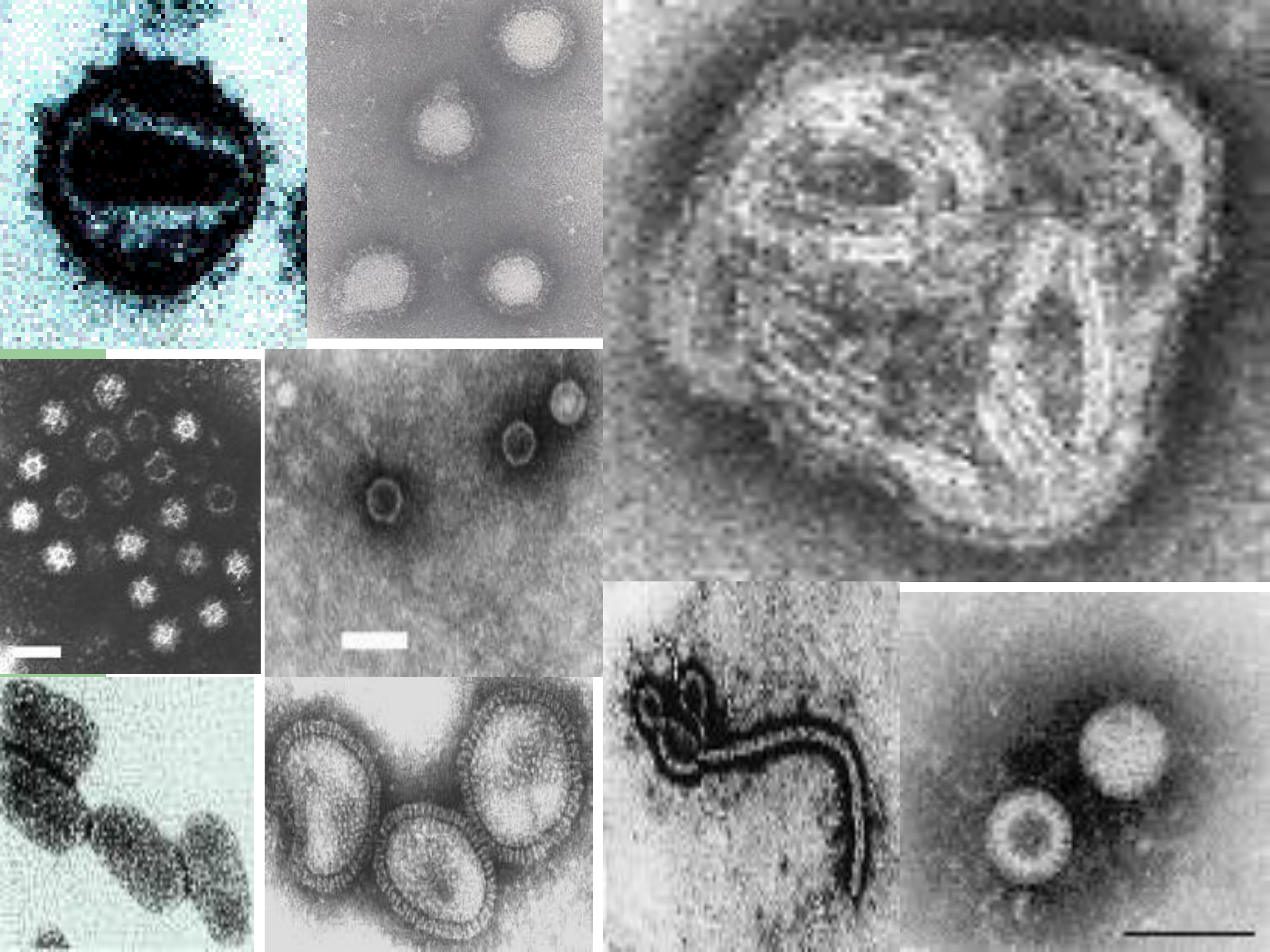

Nonenveloped
Enveloped
ssDNA
Parvoviridae
(Kilham rat)
dsDNA
Papovaviridae
(Shope
papilloma)
Adenoviridae
(human adeno 2)
Iridoviridae
(tipula
iridescent)
ssRNA
Picornaviridae
(human polio 1)
Caliciviridae
(vesicular exanthema
of swine)
dsRNA
Reoviridae
(reo type 1)
100 nm
Plus strand RNA
Togaviridae
(Sindbis)
Retroviridae
(Rous sarcoma, HIV)
Coronaviridae
(avian
infectious bronchitis)
Minus strand RNA
Rhabdoviridae
(vesicular stomatitis, rabies)
Paramyxoviridae
(measles)
Orthomyxoviridae
(influenza)
Bunyaviridae
(bunyamwera)
Arenaviridae
(lymphocytic choriomeningitis)
dsDNA
Herpesviridae
(herpes
simplex)
Hepadnaviridae
(hepatitis B)
Baculoviridae
(nuclear
polyhedrosis)
Poxviridae
(vaccinia)











- **Viral structural components include**:-
- **Capsid** : The protein shell directly surrounding viral nucleic acid (coat, shell). Composed of capsomeres.
- **Genome** : Nucleic acid of the virus (RNA or DNA).
- **Nucleocapsid** : the complete protein – nucleic acid complex.
- **Envelope:** The lipid bilayer and associated glycoproteins that surround some viruses.
- **Virion:** The entire infectious virus particle.

VIRUS STRUCTURE

- Basic rules of virus architecture, structure, and assembly are the same for all families
- Some structures are much more complex than others, and require complex assembly and disassembly
- The **capsid** (coat) protein is the basic unit of structure; functions that may be fulfilled by the capsid protein are to:
  - Protect viral nucleic acid
  - Interact *specifically* with the viral nucleic acid for packaging
  - Interact with vector for specific transmission
  - Interact with host receptors for entry to cell
  - Allow for release of nucleic acid upon entry into new cell
  - Assist in processes of viral and/or host gene regulation

Capsid symmetry and Virus Architecture

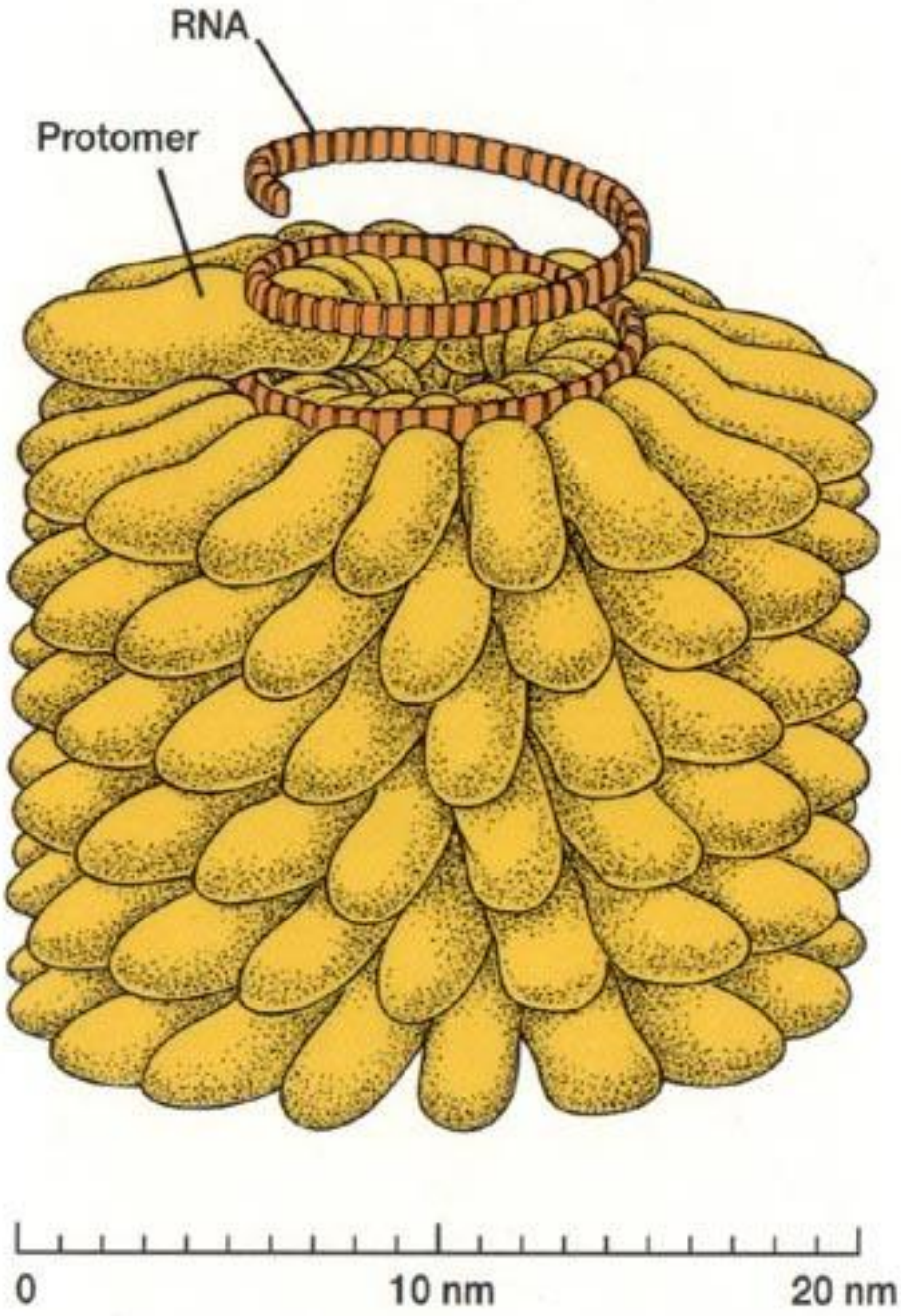
- **Virus capsid must be made up of multiple protein molecules (subunit construction) and viruses must overcome the problem of how these subunits are arranged.**

- **It was demonstrated that when mixtures of purified virus nucleic acid and coat proteins were incubated together, virus particle formed.**

- **Stability is an important feature of the virus particle.**
- **The forces, which drive assembly of virus particles, include hydrophobic and electrostatic interactions.**
- **Only rarely are covalent bonds involved in holding together the multiple subunits.**
- **In biological terms, this means that protein – protein, protein – nucleic acid, and protein – lipid interactions are used.**

Helical Capsids

- **Close examination of helical viruses revealed that the structure of the capsid actually consists of a helix rather than a pile of stacked disks.**
- **Some helices are rigid, but some helical viruses demonstrate considerable flexibility and longer helical viruses are often curved or bent.**
- **Helical naked animal viruses do not exist. All, however, have a similar design (- ss RNA and basic structural features).**



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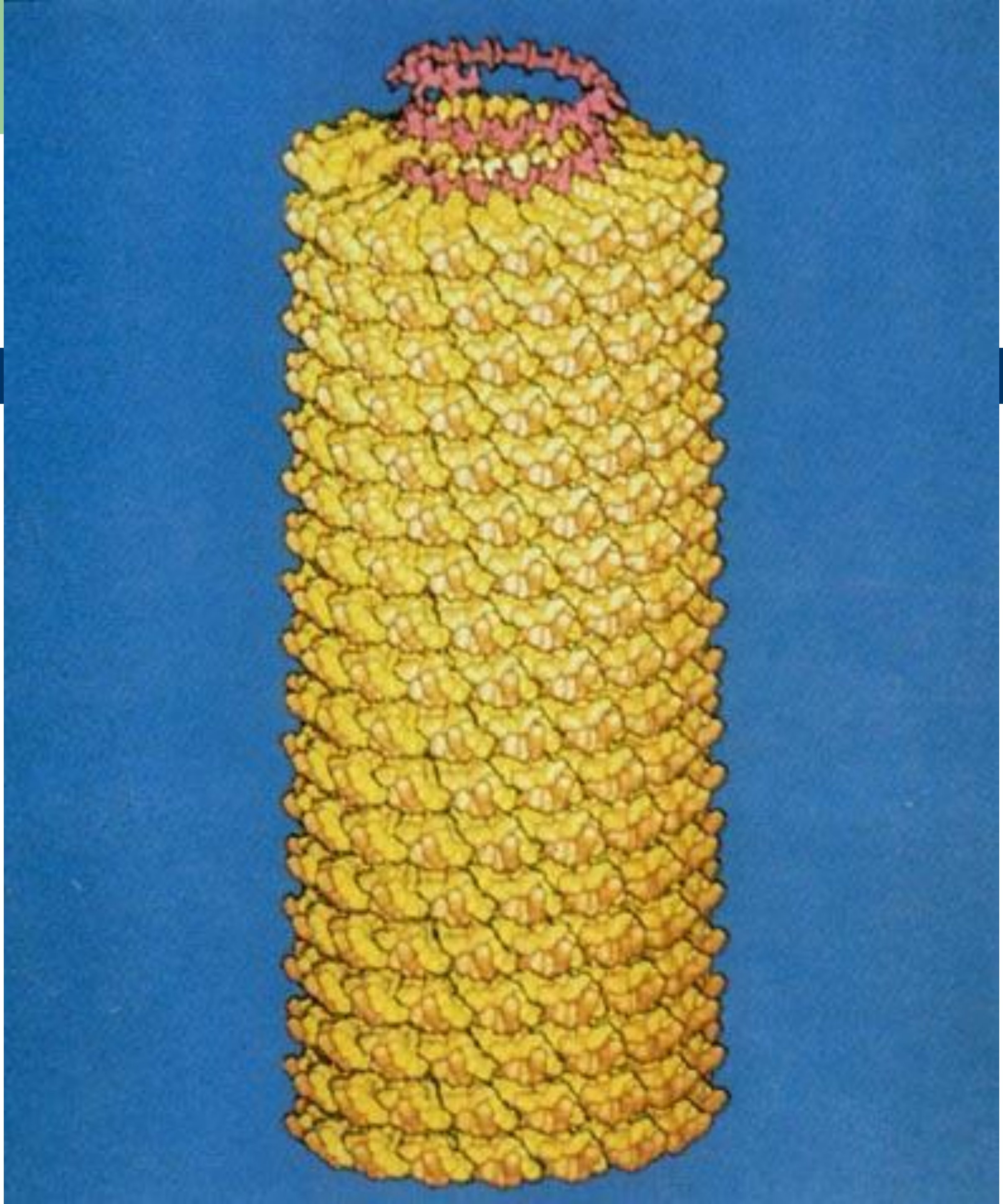


Icosahedral (Isometric) capsids

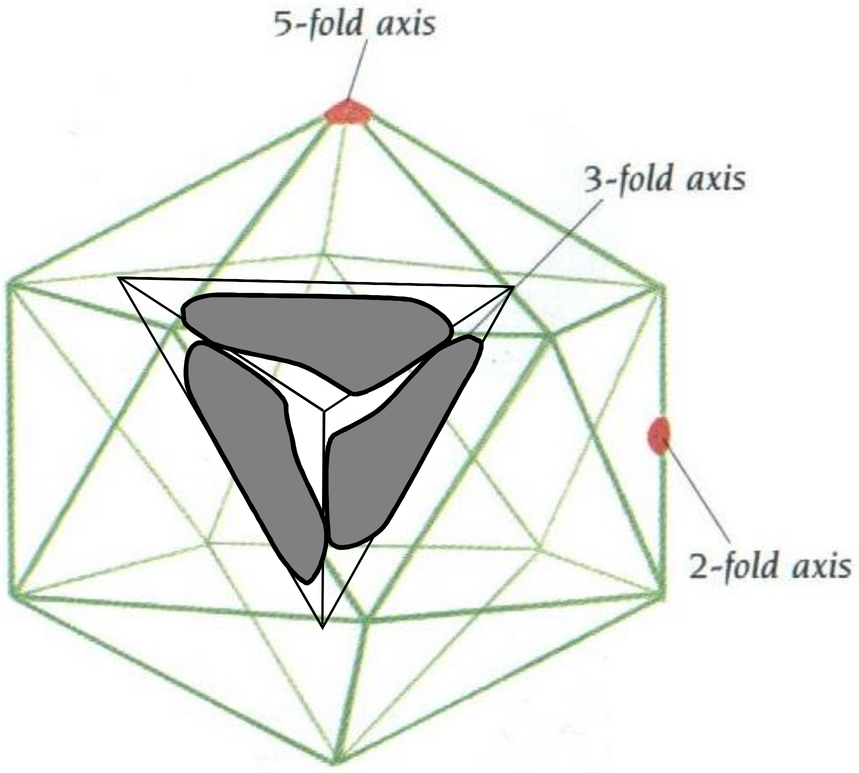
- An Icosahedron is a solid shape consisting of 20 triangular faces arranged around the surface of a sphere. It has 12 vertices and 30 edges.

- Since protein molecules are irregularly shaped and are not regular equilateral triangles, the simplest icosahdral capsids are built up by using three identical subunits to form each triangular faces.

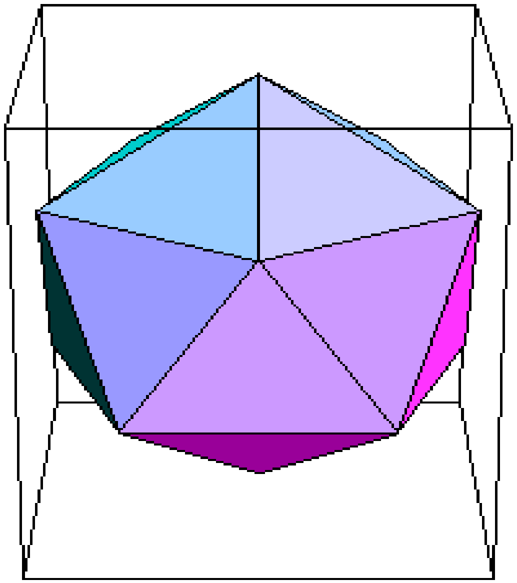
- This means that (60) identical subunits are required to form a complete capsid.

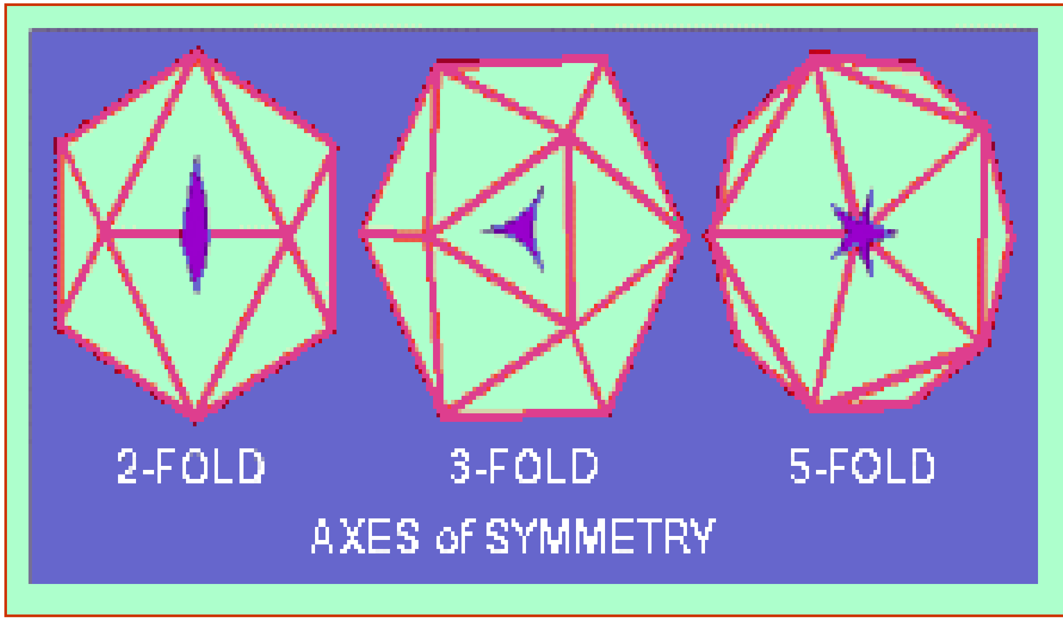
Icosahedral Symmetry

- 12 vertices
- 20 faces
  (equilateral triangles)
- 5-3-2 symmetry axes
- 60 identical subunits
  in identical environments
  can form icosahedral shell

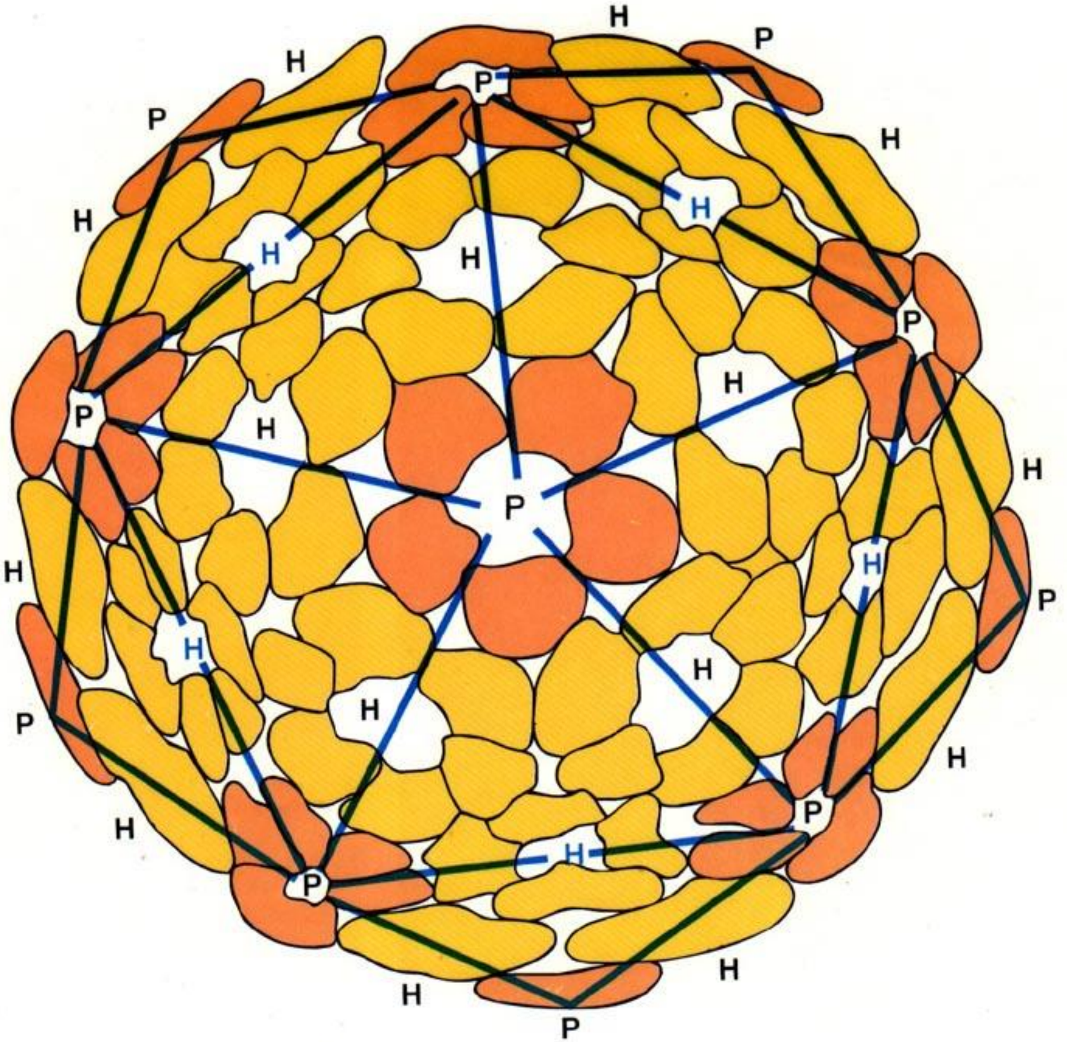


What is an Icosahedron?

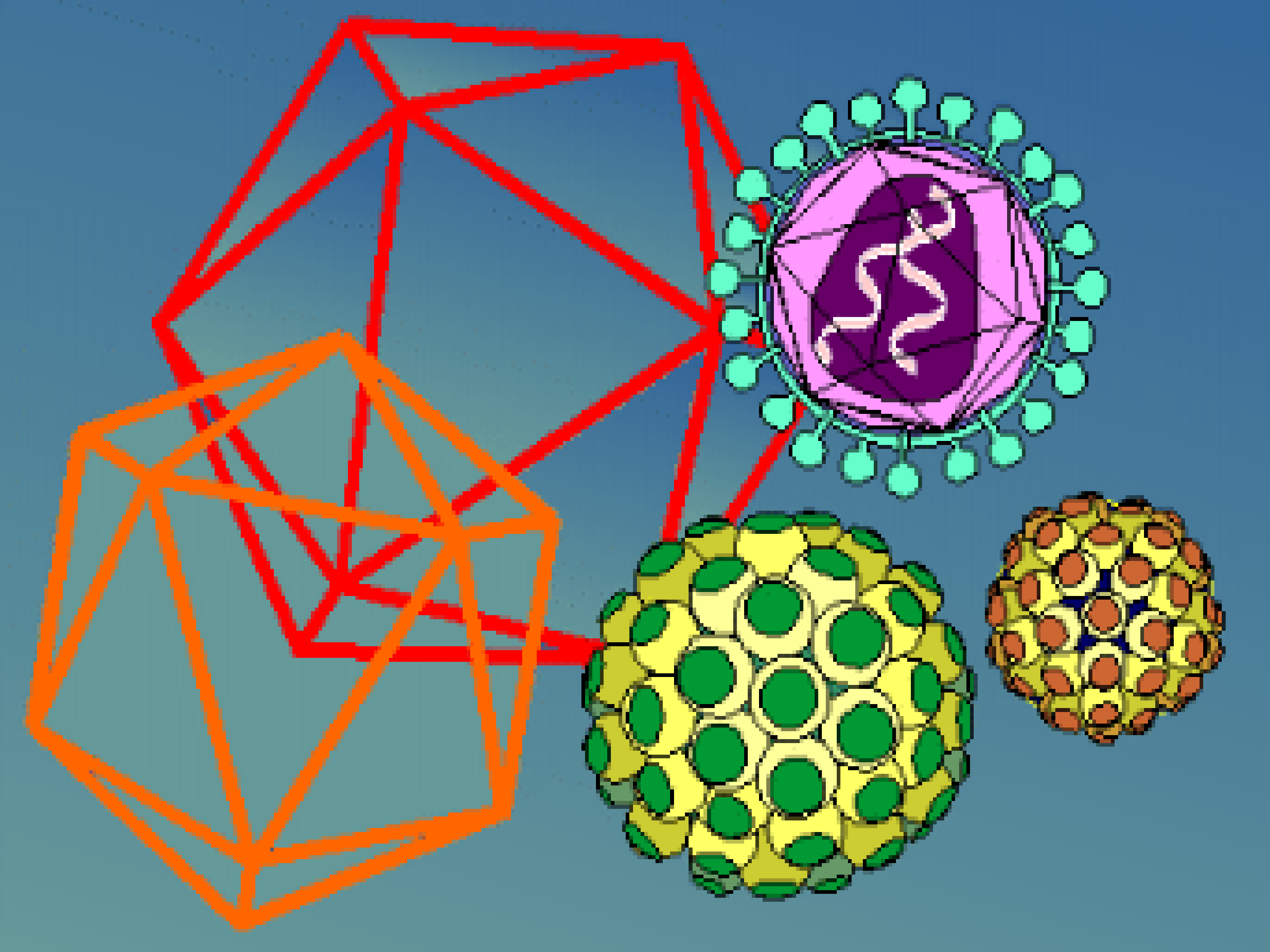




Icosahedron: a geometric solid with twenty faces. Each face is an equilateral triangle and every vertex of the icosahedron is formed by five triangular faces. Edges 30; Vertices 12; Faces 20



49 **The Structure of an Icosahedral Capsid**
Figure 17.13



Complex structure

- Such viruses often consist of several layers of protein and lipid.
- The larger and more complex viruses can not be simply defined by a mathematical equation.
- Because of complexity, they have defied attempts to determine detailed atomic structures using the techniques used for viral studies.

Enveloped viruses

- Viruses have devised strategies to effect an exit from the infected cell without its total destruction.
- Viruses leaving the cell must allow cell membrane to remain intact. This is achieved by extrusion (budding) of the particle through the membrane
- The envelope may be acquired from intracellular structures.

- **Viruses modify their lipid envelope with several classes of proteins**:

- **Matrix proteins**

  Internal virion proteins that link nucleocapsid to envelope.

- **Glycoproteins**

  Transmembrane proteins of two types:-

- **External glycoproteins** (spikes).
- **Transport channel proteins**

  They enable the virus to alter permeability of the membrane(M2 of influenza) .

Naked Viruses (protein)

Properties

- **Environmentally stable to drying , heat, acid, protease and detergents**
- **Released from infected cells by lysis**

Consequences

- **Can be spread easily**

(fomites, hand, dust,etc…..)

- **Can dry out and retain infectivity**
- **Can survive adverse conditions in the gut.**
- **Resist poor sewage treatment**
- **Can elicit a protective antibody response**

Enveloped Viruses (membrane lipids, proteins, glycoproteins)

Properties

- **Environmentally labile, disrupted by acid, detergents, drying and heat**
- **Modify cell membrane during replication**
- **Released by budding and cell lysis**

Consequences

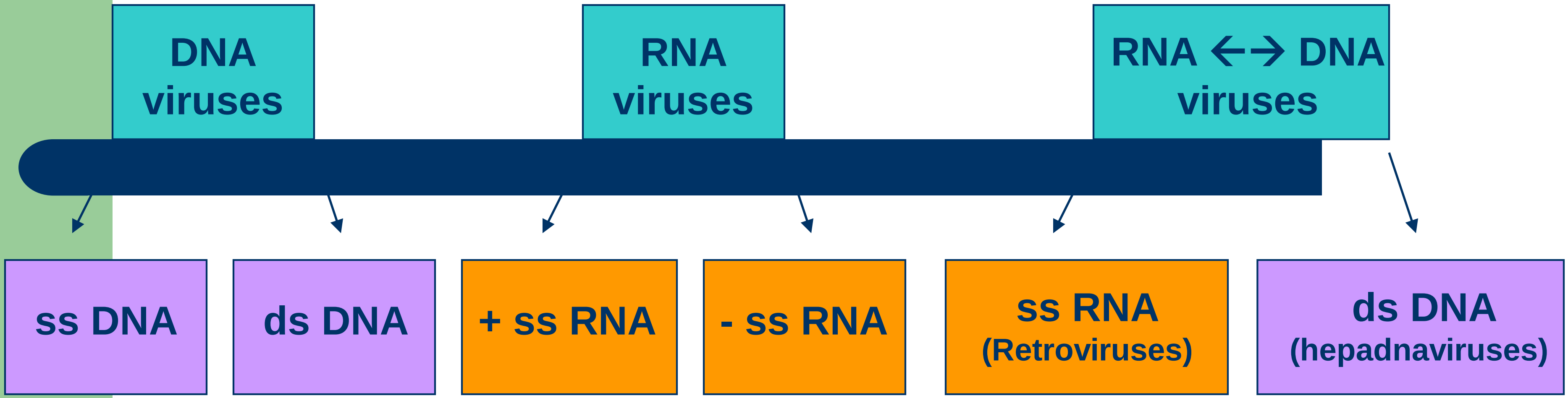
- **Cannot survive in the GI tract**
- **Must stay wet(**Spread in large droplets, secretions, and organ transplants or blood transfusion.)
- **Need not kill the cell to spread**
- **Initiate a CMIR**

(Pathogenesis is often due to hypersensitivity and inflammation initiated by CMI)

Genomes

- The genome may be DNA or RNA, SS or ds, in a linear, circular or segmented configuration.
- Single – stranded virus genomes may be either (+) sense, (-) sense or ambience.
- Genome size ranges from 3500 nucleotides to 470000 (235 KPB) nucleotides.
- The Physical nature of nucleic acid dictates the strategy of replication and forms a basis for classification.

Viral genomes



- genome can function as mRNA
- genome is template for mRNA
- genome is template for DNA synthesis ("retrovirus")

Effects of Physical and chemical Agents

- **Vital dyes**

  Neutral red, toluidine blue and Proflavin .

  Photodynamic inactivation.

- **Proteolytic enzymes**

  Pronase inactivates viruses whereas GI enzymes(trypsin, chemotrypsin, and pepsin) are inefficient.

- **Ether and chloroform**

  Inactivate enveloped viruses.

- **Detergents, iodine, chlorine, and alcohol:** Variable effects.

- **Phenol:** Most viruses are relatively stable.

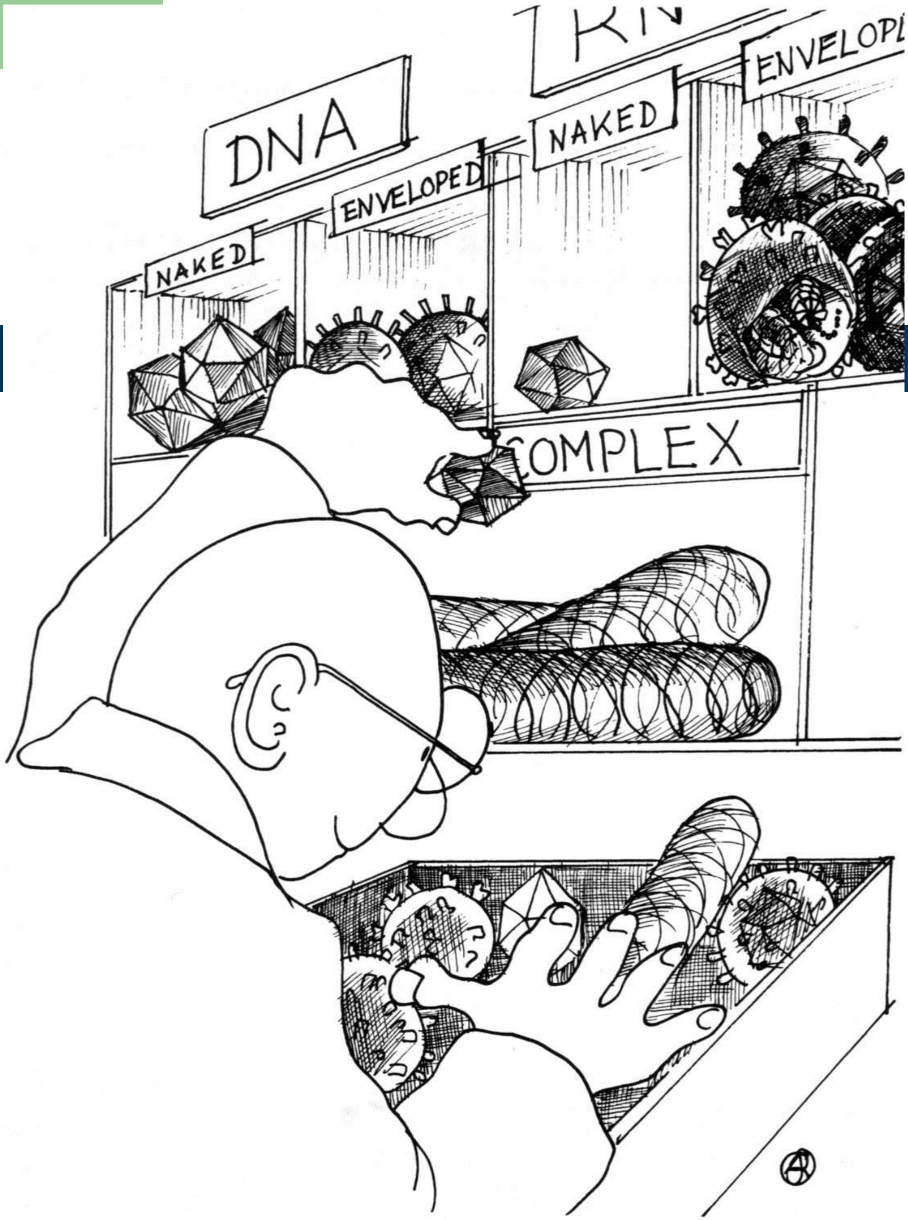
- **PH:** All viruses are stable at a pH of 5 to 9.

- **Salts and glycerol:** Stabilize viruses.

Classification of Viruses

Different Bases

- Type of nucleic acid
- Size and morphology
- Presence of an envelope
- Effect of Ether
- Clinical
- Epidemiology



CLASSIFIED MATERIAL