Chapter 28

Viral Structure

Comparison with bacteria

-- Bacteria live and grow independently whereas **viruses can grow only intracellularly** although they **can survive outside a cell**.

-- Bacteria contain both RNA and DNA but a **virus can contain only one nucleic acid.**

-- The average virus is about **one-hundredth the size of the average bacterium.**

-- Most viruses that have been studied have a diameter between **10 and 300 nanometres.**

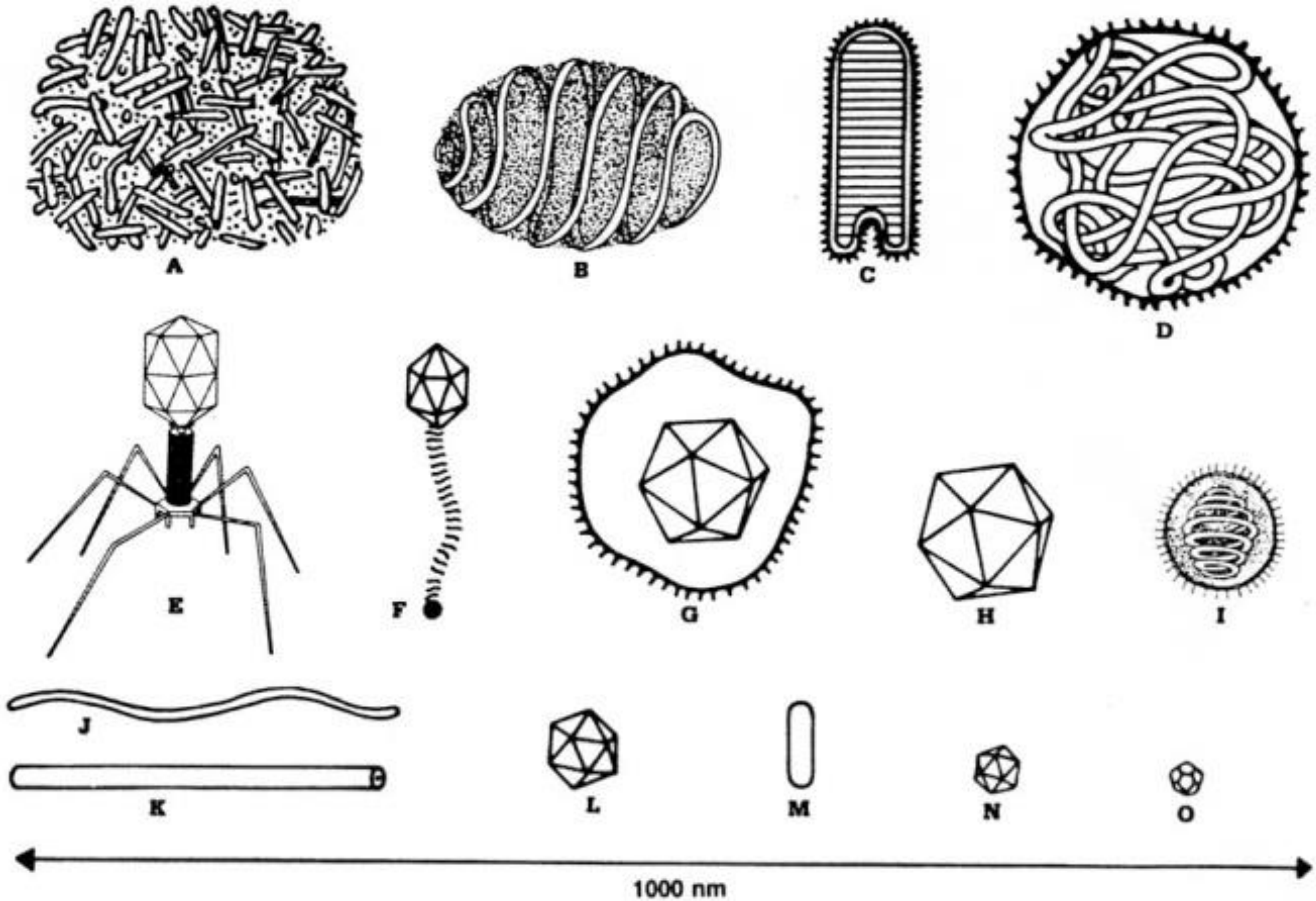
-- Some **filoviruses** have a total **length of up to 1400 nm**; their **diameters are only about 80 nm.**

-- **Mimivirus** is the **largest known virus**, with a capsid **diameter of 400 nm.** Protein filaments measuring 100 nm projects from its surface.

Shape

-- Shapes are referred to in common terms such as **spheres, rods, bullets** etc but actually viruses are **complex structures** of precise geometric symmetry.

-- Shape is determined by repeating subunits that form the protein coat, called **capsid**.


A
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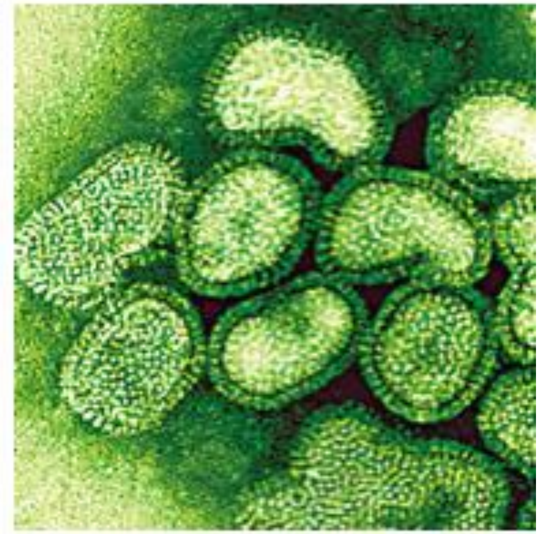


Centers for Disease Control & Prevention

A virus has three basic structures:

1. **Nucleic acid**

2. **Protein coating (capsid)**

3. **Envelope -- which may or may not be present**

Viral nucleic acid

-- The genetic material is made from **either DNA or RNA**.

-- **DNA is always a single molecule.**

-- **RNA can exist either as a single molecule or in several segments**, e.g., **influenza virus** and **rotavirus**.

-- All viruses are **haploid** except **retroviruses** which are diploid.

Viral capsid

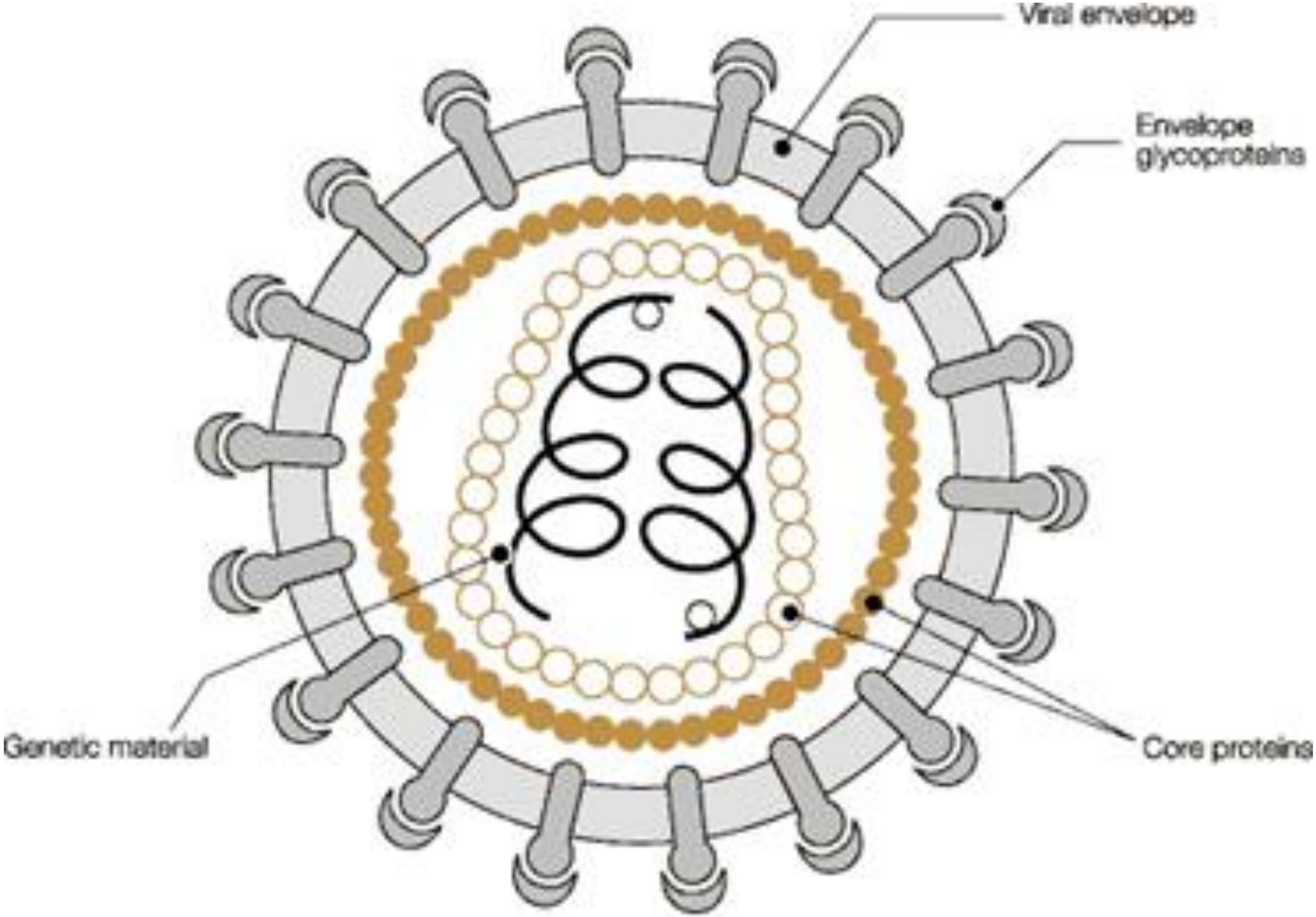
-- A protein coat that protects these genes is called a **capsid**.

-- Capsids are formed from identical protein subunits called **capsomeres.**

-- **Arrangement** of capsomeres gives a virus its **characteristic** shape.

-- Capsid and genetic material are collectively called **nucleocapsid**.

-- In some cases an **envelope of lipids** is present that surrounds the protein coat when virions are outside a cell.


Viral envelope
Envelope glycoproteins
Genetic material
Core proteins

-- Capsid also determines the **shape** of the virion.

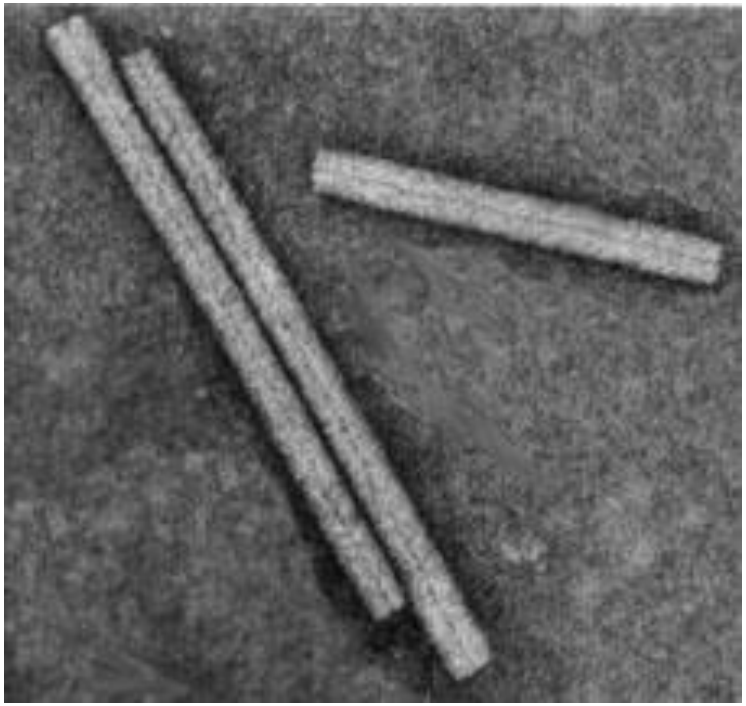
-- The shapes of viruses range from simple **helical (rod)** and **icosahedral (spherical)** forms to more complex structures.

-- The rod shape is due to the **linear array of the nucleic acid** and the protein subunits making up the capsid.

-- The sphere shape is actually a **20-sided polygon (icosahedron).**

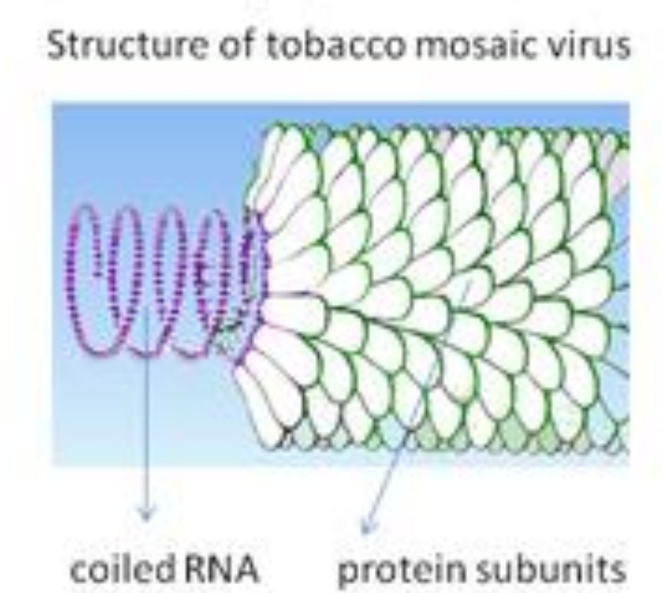
Helical viruses

-- These viruses are composed of a **single type of capsomer stacked around a central axis** to form a helical structure, which may have a **central cavity, or hollow tube**.



-- Overall, the **length** of a helical capsid is related to the **length of the nucleic acid** contained within it and the **diameter** is dependent on the **size and arrangement of capsomeres**.

-- The well-studied **tobacco mosaic virus** is an example of a helical virus.



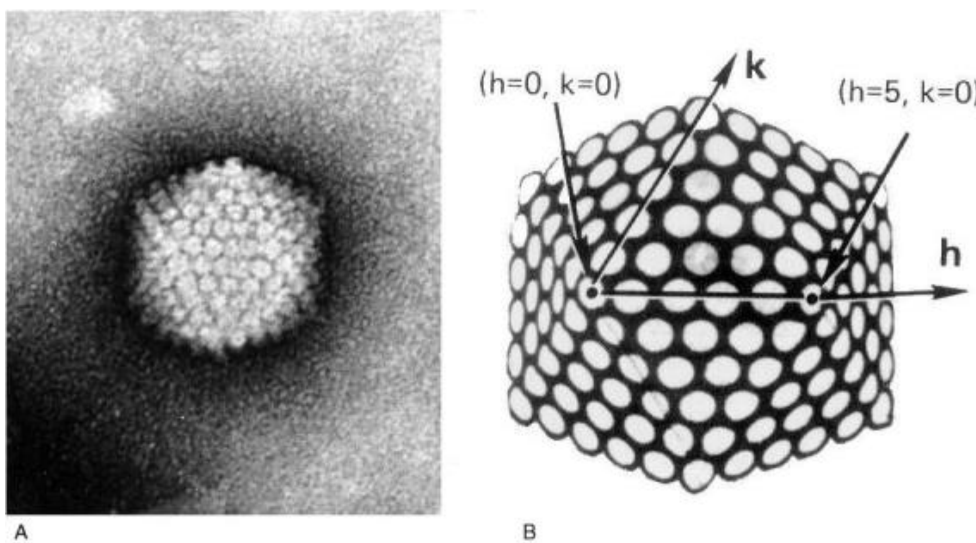
-- **There is no helical human virus that is not covered with an envelope.**

Icosahedral

-- Most **animal viruses** are **icosahedral or near-spherical** with icosahedral symmetry.

-- A regular icosahedron is the **optimum** way of forming a **closed shell** from identical sub-units.

-- These viruses may **either be enveloped or nake**d.



The advantage of building the virus particles from identical subunits is **twofold**:

1. It reduces **need for genetic information**

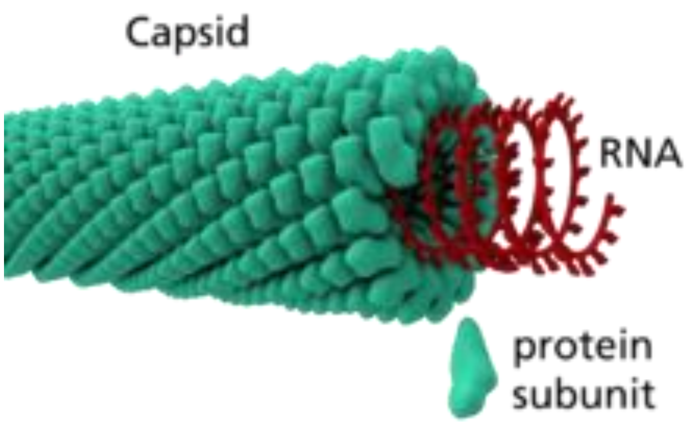
1. It **promotes self assembly** (without enzymes or energy).

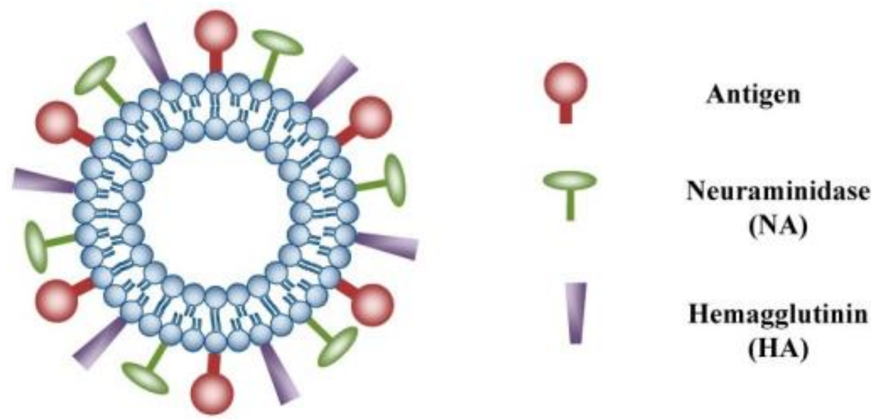
Viral proteins

-- These serve several important functions.

-- The **capsid proteins** protect the genome from **degradation by nucleases**.

-- **Surface proteins** mediate **attachment to specific receptors** on cell surface **defining organ specificity.**





-- These surface proteins also **induce antibody and activate T cells** to kill virus infected cells. Conversely they serve as targets for antibodies for neutralization.

-- **“Serotype”** is the term used to describe a subcategory of virus based on surface antigens.

Rhinoviruses have over 100 serotypes.

-- A person can become **immune to one serotype** and can **still get disease from other serotype**.

-- So the vaccines need to be **polyvalent**.

-- **Internal proteins** can either be **structural (capsid)** or **enzymes** (e.g., polymerases that synthesize mRNA).

-- Some viruses have **DNA or RNA polymerase** attached to the genome; others do not.

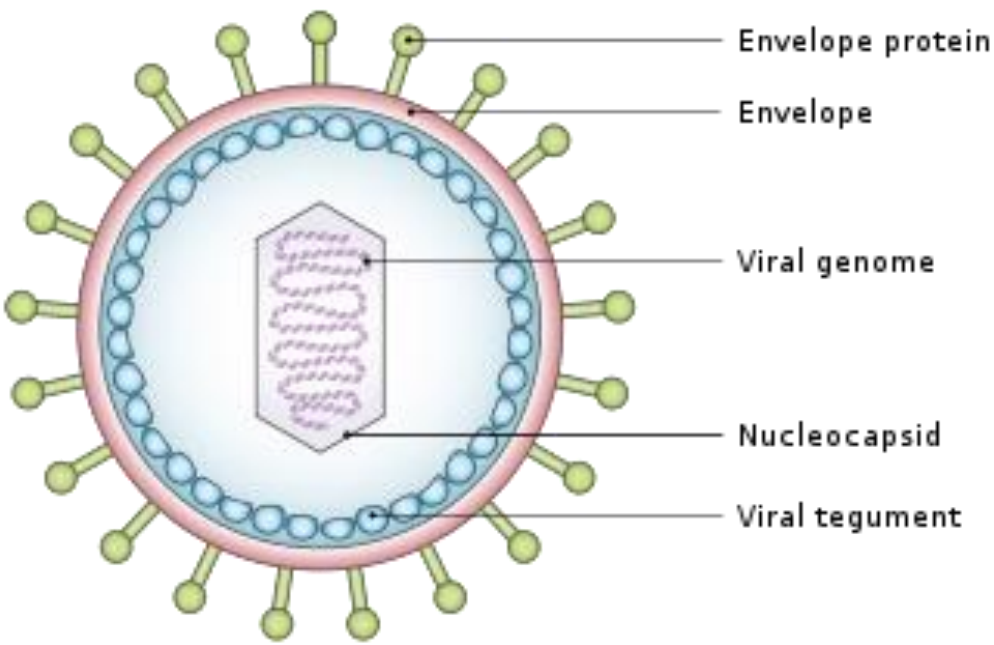
-- Some viruses produce **superantigens**. These include **Epstein-Barr virus** and **cytomegalovirus**.

-- Probably, the superantigens are produced to **activate CD4 +ve cells in a way to favor viral replication.**

-- Some viruses contain **regulatory proteins** called **tegument or matrix proteins** located between nucleocapsid and the envelope.

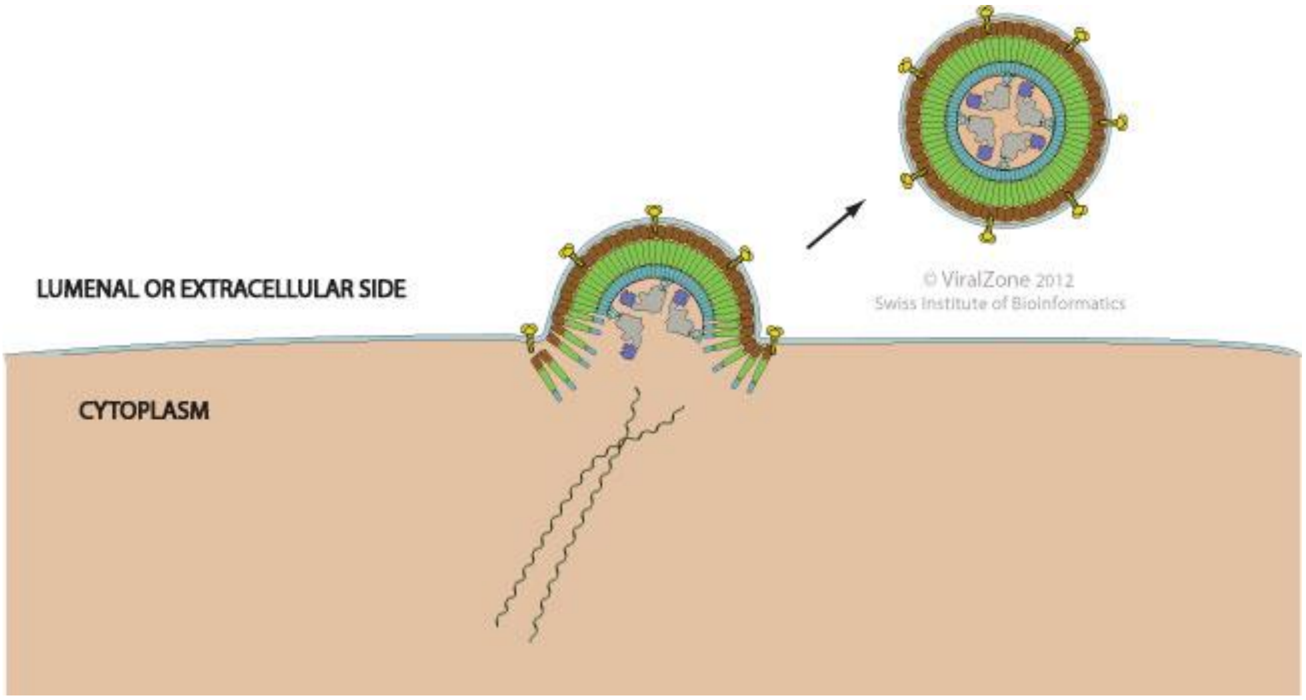
-- These include **transcription and translation vectors** that control either viral or cellular processes.

-- **Herpes simplex** and **cytomegaloviruses** have **teguments**.



Viral envelope

-- Some species of virus **envelope** themselves in **mostly the outer membrane** surrounding an infected host cell, or **internal membranes such as nuclear membrane** (e.g. herpes viruses) or **endoplasmic reticulum,** thus gaining an outer lipid bilayer known as a viral envelope by a process called **"budding".**



-- The lipid bilayer is interspersed with protein molecules and may contain material from the membrane of a **host cell as well as that of viral origin.**

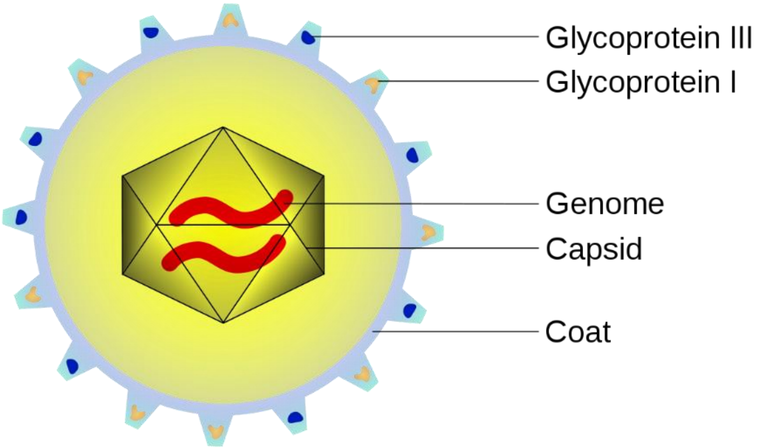
-- The lipid membrane itself and any carbohydrates present **originate entirely from the host.**

Envelope Proteins

For better attachment and infectivity, viruses modify their lipid envelopes by the **synthesis of several classes of proteins.** These include:

> **Matrix Proteins or teguments:** These are internal virion proteins whose function is effectively to link the internal nucleocapsid assembly.
>
> **Glycoproteins:** These are present on the surface. They identify and bind to receptor sites on the host's membrane.

Scheme of a CMV virus



-- **Generally the presence of an envelope confers instability on the virus.**

-- Enveloped viruses are **more sensitive to heat, drying, detergents, and lipid solvents** such as alcohol or ether.

-- Virtually all viruses transmitted by **fecal-oral route** are **naked**, e.g, **hepatitis A** and **poliovirus**.

-- **Enveloped viruses** are **usually transmitted by direct contact** such as blood, e.g., **HIV** and **hepatitis B and C** viruses, **or by insect**(**dengue**) or **animal** (**rabies**) bite.

-- Viruses **transmitted by aerosols are mostly enveloped**, e.g., **influenza** and **measles** viruses.

-- **Rhinoviruses** also **transmitted by aerosols are naked** and **can survive for long periods in atmosphere.**

Atypical Virus-Like Agents

Defective viruses

-- **Defective viruses cannot replicate without a "helper virus"** because of a mutation or a deletion in their genetic material.

-- During the growth of human viruses, **defective viruses outnumber infectious viruses by as much as 100:1.**

-- They may actually **aid in recovery** from an infection by limiting the ability of the infectious particles to grow.

Pseudovirions

-- **Pseudovirions** contain **host cell DNA instead of viral DNA** when the host cell DNA is fragmented and its pieces are incorporated within the capsid protein.

-- **They can infect cells but do not replicate.**

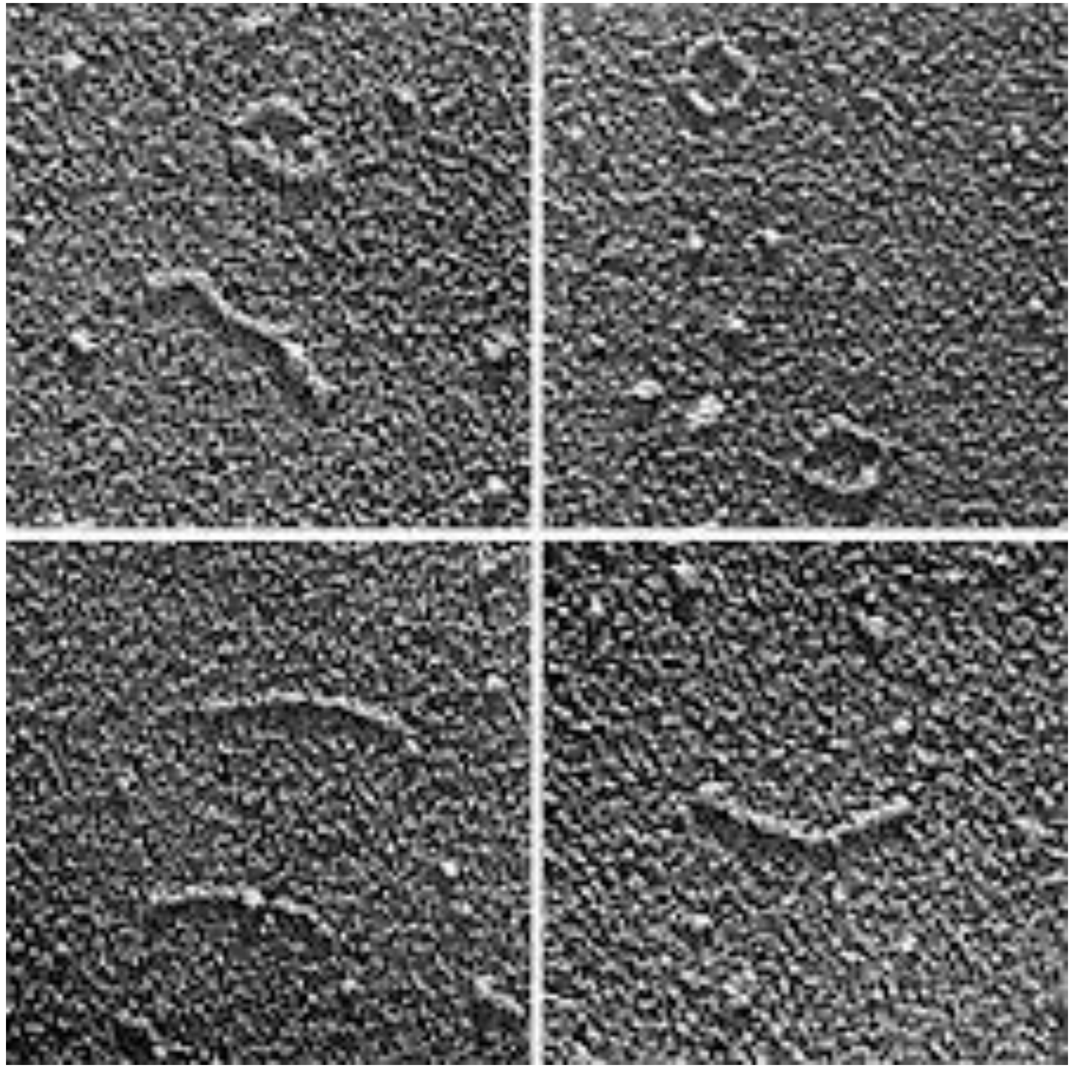
Viroids

-- **Viroids** are **plant pathogens** that consist of a short stretch (a few hundred nucleobases) of circular, single- stranded RNA.

-- The human pathogen **Hepatitis D virus** is similar to viroids.

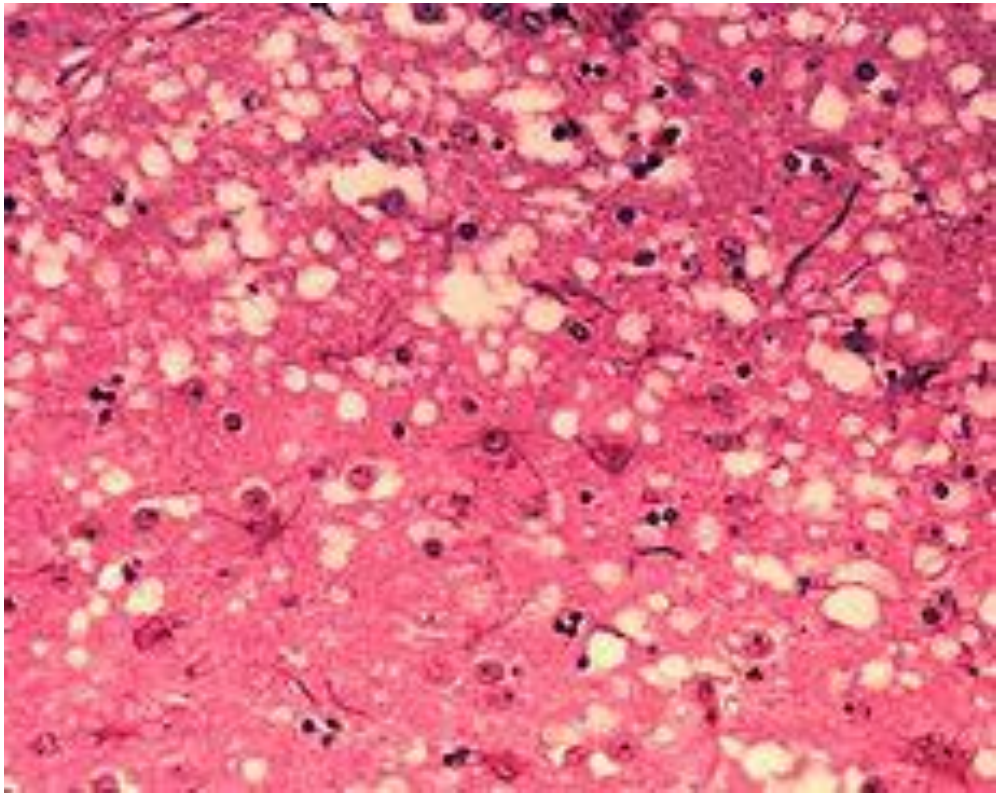
-- Viroids are **extremely small in size**, ranging from 246 to 467 nucleotide (nt) long genome and consisting of fewer than 10,000 atoms.

-- **Viroid RNA does not code for any protein.**



Prions

Prions are responsible for the transmissible **spongiform encephalopathies** in a variety of mammals.



-- These include **bovine spongiform encephalopathy** (**BSE**, also known as **"mad cow disease"**) in cattle and **Creutzfeldt-Jakob disease (CJD)** in humans.

-- **All known prion diseases affect the structure of the brain or other neural tissue and all are currently untreatable and universally fatal.**

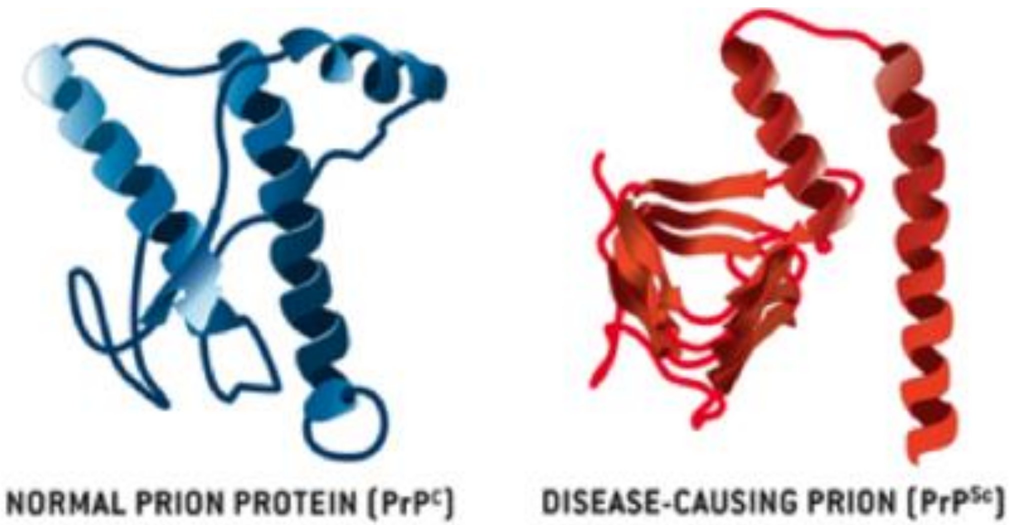
-- A prion in the **Scrapie form (PrPSc)** is an **infectious agent composed of protein in a misfolded form.**

-- This is the central idea of the **Prion Hypothesis**, which **remains debated.**

-- **This would be in contrast to all other known infectious agents (which must contain nucleic acid).**

-- **Prions propagate by transmitting a misfolded protein state.**

-- When a prion enters a healthy organism, it **induces existing, properly folded proteins to convert into the disease-associated, prion form.**



-- The prion **acts as a template** to guide the **misfolding of more proteins** into prion form.

-- These newly formed prions can then go on to convert more proteins themselves; this triggers a **chain reaction** that produces large amounts of the prion form.

Transmission

-- It has been recognized that prion diseases can arise in **three** different ways: **acquired, familial, or sporadic**.

-- It is thought that prions may be deposited in the environment through the **remains of dead animals and via urine, saliva, and other body fluids.**

-- They may then survive in the soil by **binding to clay and other minerals**.

Diagnosis

-- There continues to be a very practical problem with diagnosis of prion diseases, including **BSE** and **CJD**.

-- They have an **incubation period of months to decades** during which there are **no symptoms, even though the pathway of converting the normal brain PrP protein into the toxic, disease-related PrPSc form has started.**

-- At present, there is virtually **no way to detect PrPSc** reliably except by examining the brain using neuropathological and immunohistochemical methods **after death**.

-- Accumulation of the abnormally folded PrPSc form of the PrP protein is a characteristic of the disease, but it is present at **very low levels** in easily accessible body fluids like blood or urine.

Sterilization

-- Sterilizing prions requires the **denaturation of the protein to a state where the molecule is no longer able to induce the abnormal folding** of normal proteins.

-- Prions are generally **quite resistant to proteases, heat, radiation, and formalin treatments**, although their infectivity can be reduced by such treatments.

-- **Effective prion decontamination relies upon protein hydrolysis or reduction or destruction of protein tertiary structure.**

Examples include **bleach, caustic soda, and strongly acidic detergents**.

Chapter 31

Classification of medically important viruses

Principles of classification

Major components used in classification are:

1. **Nucleic acid -----** mol. wt and structure
2. **Capsid -----** size, symmetry, envelope

DNA viruses

Parvoviruses

These are very small (**22 nm** in diameter) **naked icosahedral viruses** with **single-stranded linear DNA.**

Defective parvoviruses (e.g. adeno-associated viruses) are **unusual because positive and negative strands of DNA are carried in separate particles.**

Non defective parvoviruses are represented by **B19 virus** which cause aplastic crises in **sickle cell anemia patients**.

Polyomaviruses

These are naked icosahedral viruses (**45 nm**) with **double stranded circular supercoiled DNA.**

In humans JC virus has been isolated from patients of leukoencephalopathy and BK virus from urine of immunosuppressed kidney transplant patients.

Papillomaviruses

These are **naked icosahedral** (**55nm**) viruses with **double-stranded supercoiled** DNA. Human pailloma virus (**HPV**) causes **papilloma (warts)** at many body sites and certain strains cause **carcinoma of the cervix**.

Adenoviruses

These are **naked icosahedral viruses** (**75 nm**) with **double stranded linear DNA**. They cause **pharyngitis, upper and lower respiratory tract disease** and a variety of other less common infections.

Hepadnaviruses

These are **double shelled viruses** (**42nm**) with an **icosahedral capsid covered by an envelope.**

Circular, double stranded DNA is unusual because one strand is 25% incomplete.

It has an envelope. Hepatitis B virus is main human pathogen.

Herpesviruses

These are **enveloped viruses** (**100 nm**) with an **icosahedral nucleocapsid** and **double stranded linear DNA**.

They cause **latent infections**. Important human pathogens are **herpes simplex virus types 1 and 2**, **varicella-zoster virus, cytomegalovirus** and **Epstein-Barr virus**.

Poxviruses

These are the **largest viruses (300 nm)** with a **brick like shape, an envelope with an unusual appearance, and a complex capsid symmetry.**

Smallpox virus and **molluscum contagiosum virus** are two important human pathogens.

RNA viruses

There are **14 families**.

Three each are **naked icosahedral** and **enveloped icosahedral**, and **eight** are **enveloped helical viruses**.

Picornaviruses

These are **smallest RNA viruses** (**28 nm**).

They have **single stranded, linear, nonsegmented, positive polarity RNA** within a **naked icosahedral capsid**.

Two groups are of human importance, 1) **enteroviruses** such as **poliovirus, Coxsackie virus, echovirus,** and **hepatitis A virus** and 2) **rhinoviruses**.

Hepeviruses

These are **naked viruses** (**30 nm**) with an **icosahedral nucleocapsid**.

They have **single stranded , linear, nonsegmented, positive polarity RNA**.

Main human pathogen is **hepatitis E virus**.

Calciviruses

These are **naked viruses** (**38 nm**) with an **icosahedral caps**id.

They have **single stranded, linear, non-segmented, positive polarity RNA**.

Main human pathogen is **Norwalk virus or norovirus**.

Reoviruses

These are **naked viruses** (**75 nm**) with **two icosahedral capsid coats**.

They have **10-11 segments of double-stranded linear RNA**.

Main human pathogen is **rotavirus**.

Flaviviruses

These are **enveloped viruses with an icosahedral capsid and single-stranded, linear, nonsegmented, positive polarity RNA.**

Human pathogens include **hepatitis C virus, yellow fever virus, dengue virus**, and **West Nile virus**.

Togaviruses

These are **enveloped viruses** with an **icosahedral capsid** and **single stranded, linear, non-segmented positive polarity RNA.**

There are two groups **alphaviruses** and **rubiviruses**.

Important human pathogen in first group is **Eastern/western encaphilitis virus** and of later is **rubella virus**.

Retroviruses

These are **enveloped viruses** with an **icosahedral capsid** and **two identical strands (diploid) of single stranded, linear, positive polarity RNA.**

Retro refers to **reverse transcription of RNA genome into DNA**.

There are two important groups, **oncoviruses** (include s**arcoma** and **leukemia** viruses) and **lentiviruses (HIV**).

Orthomyxoviruses

These viruses are **enveloped** with a **helical nucleocapsid** and **eight segments of linear, single stranded, negative polarity RNA.**

Influenza virus is main human pathogen.

Paramyxoviruses

These are **enveloped viruses** with a **helical nucleocapsid** and **single-stranded, linear, nonsegmented, negative polarity RNA.**

The important human pathogens are **measles, mumps, parainfluenza**, and **respiratory syncytial viruses**.

Filoviruses

These are **enveloped viruses** with a **helical nucleocapsid** and **single stranded, linear, non-segmented, negative polarity RNA.**

They are **highly pleomorphic**, the filament size range from **80nm to more than thousand nm.**

Two deadly human pathogens **Ebola virus** and **Marburg virus** belong to this group.

Coronaviruses

These are **enveloped viruses** with a **helical nucleocapsid**, and a **single stranded, linear, non-segmented, positive polarity RNA.**

These cause **respiratory tract infections** such as **common cold** and **SARS** (severe acute respiratory syndrome).

Arenaviruses

These are **enveloped viruses** with a **helical nucleocapsid** and a **single stranded circular, negative polarity RNA** in **two segments** (a part of both segments have positive polarity, i.e, it is **ambisense**).

Important pathogens are **lymphocytic choriomeningitis virus** and **Lassa fever virus.**

Bunyaviruses

These are **enveloped viruses** with a **helical nucleocapsid** and a **single stranded circular negative polarity RNA** in **three segment**s.

Some contain **ambisense** RNA.

They cause **encephalitis**. Example is **hantaviruses.**

Deltaviruses

Hepatitis delta virus (HDV) is the only member of this genus.

It is an **enveloped virus** with an RNA genome that is a **single stranded, negative polarity, covalently closed circle. Symmetry is uncertain.**

It is a **defective virus** and **HBV is its helper virus** which provides outer protein coat.

Its RNA genome encodes **only one protein**, the internal core protein called **delta antigen.**


Thank You!