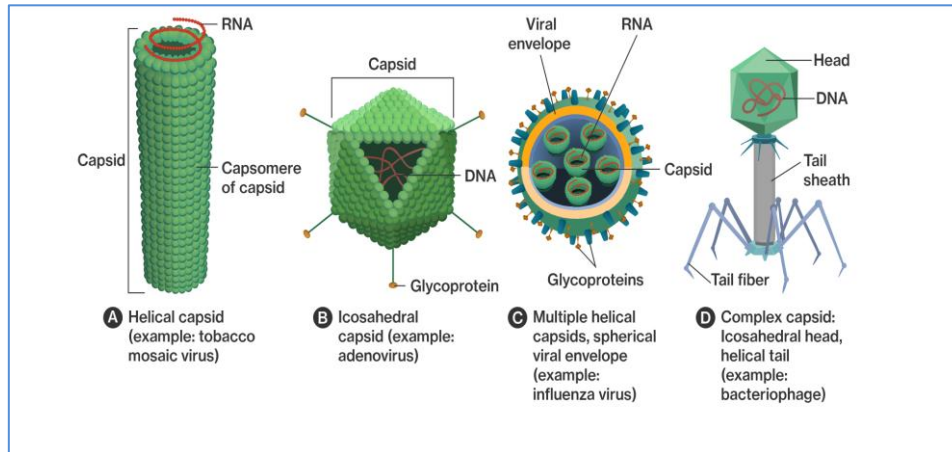


## Classification of Medically Important Viruses

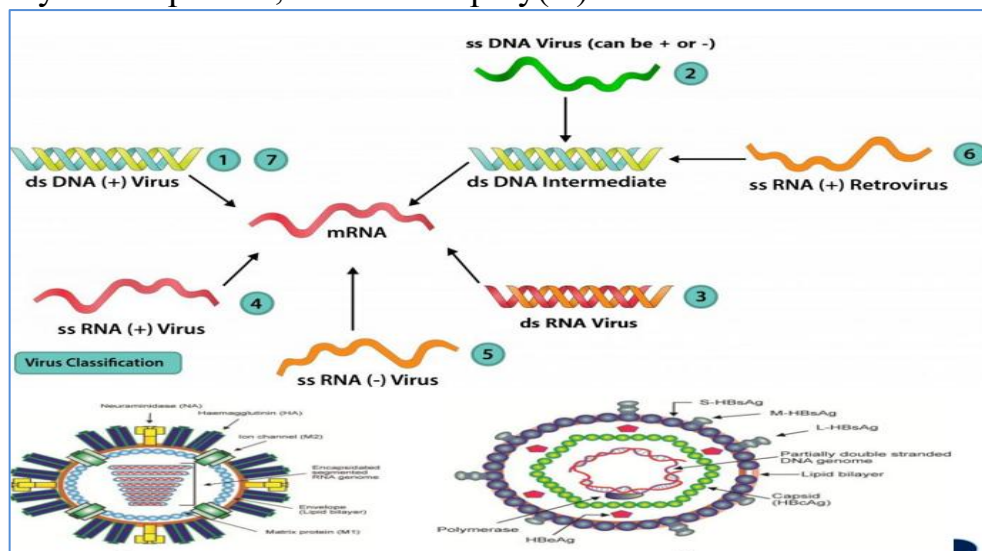
- Before genome sequencing was routine, viruses were classified using a combination of the following observable properties.

1. **Virion morphology**, including size, shape, type of symmetry, presence or absence of peplomers, and presence or absence of membranes.



2. **Virus genome properties**, including type of

- nucleic acid (DNA or RNA),
- size of the genome,
- strandedness (single or double),
- whether linear or circular,
- sense (positive, negative, ambisense),
- Segments (number, size),
- nucleotide sequence, percent GC content, and presence of special features (repetitive elements, isomerization, 5' -terminal cap, 5'-terminal covalently linked protein, 3'-terminal poly(A) tract)



3. **Genome organization and replication**, including gene order, number and position of **open reading frames**, **strategy of replication** (patterns of transcription, translation), and **cellular sites** (accumulation of proteins, virion assembly, virion release).
4. **Virus protein properties**, including number, size, amino acid sequence, modifications (glycosylation, phosphorylation), and functional activities of structural and nonstructural proteins (transcriptase, reverse transcriptase, neuraminidase, fusion activities).
5. **Antigenic properties**, particularly reactions to various antisera.
6. **Physicochemical properties of the virion**, including molecular mass, pH stability, thermal stability, and susceptibility to physical and chemical agents, especially solubilizing agents and detergents.
7. **Biologic properties**, including natural host range, mode of transmission, vector relationships, pathogenicity, tissue tropisms, and pathology.

### Universal System of Virus Taxonomy

ICTV Classification The International Committee on Taxonomy of Viruses began to devise and implement rules for the naming and classification of viruses early in the 1970s, an effort that continues to the present.

Viral classification starts at the level of order and continues as follows.

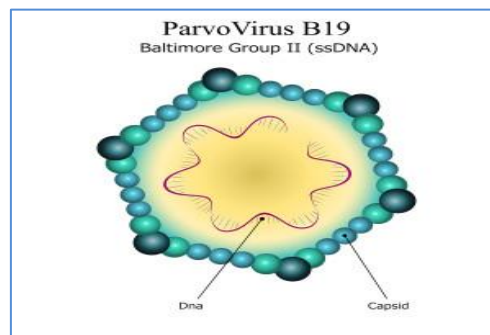
**Order** (-virales)  
**Family** (-viridae)  
**Subfamily** (-virinae)  
**Genus** (-virus)  
**Species**

### DNA Viruses

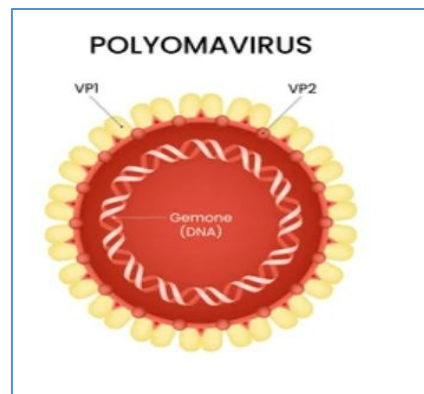
The families of DNA viruses are described in Table –1. The four **naked** (i.e., nonenveloped) icosahedral virus families—the parvoviruses, polyomaviruses, papillomaviruses, and adenoviruses—are presented in order of increasing particle size, as are the three **enveloped** families. The hepadnavirus family, which includes hepatitis B virus and the herpesviruses, are enveloped icosahedral viruses. The largest viruses, the poxviruses, have a complex internal symmetry.

**Parvoviruses:** (18–26 nm).

- Size : Smallest DNA viruses.
- Symmetry: Cubic symmetry, with 32 capsomeres,
- No envelope (Naked).
- The genome is linear, single-stranded DNA, averaging 5 kb in size.
- Replication occurs only in actively dividing cells.
- capsid assembly in the nucleus
- Human parvovirus B19 replicates in immature erythroid cells and causes several adverse consequences, including aplastic crisis, **fifth disease**, and fetal death

**Polyomaviruses : (45 nm)**

- Small , nonenveloped
- Heat-stable
- Cubic symmetry, with 72 capsomeres.
- The genome is circular, double-stranded DNA, about 5 kb in size.
- These agents have a slow growth cycle, stimulate cell DNA synthesis, and replicate within the nucleus.
- The most wellknown human polyomaviruses are
- JC virus, the causative agent of progressive multifocal leukoencephalopathy.
- BK virus, associated with nephropathy in transplant recipients;
- Merkel cell virus, found associated with the majority of Merkel cell skin carcinomas.
- SV40, a primate virus, can also infect humans.

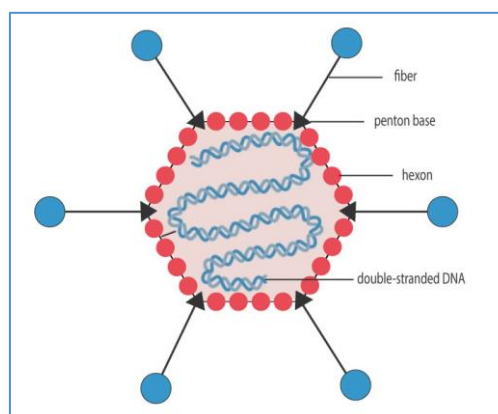


**Papillomaviridae:**(55–60 nm).

- Non-enveloped, icosahedral structure
- Circular double-stranded DNA genome
- is a very common virus, often sexually transmitted, that causes warts and is linked to several cancers

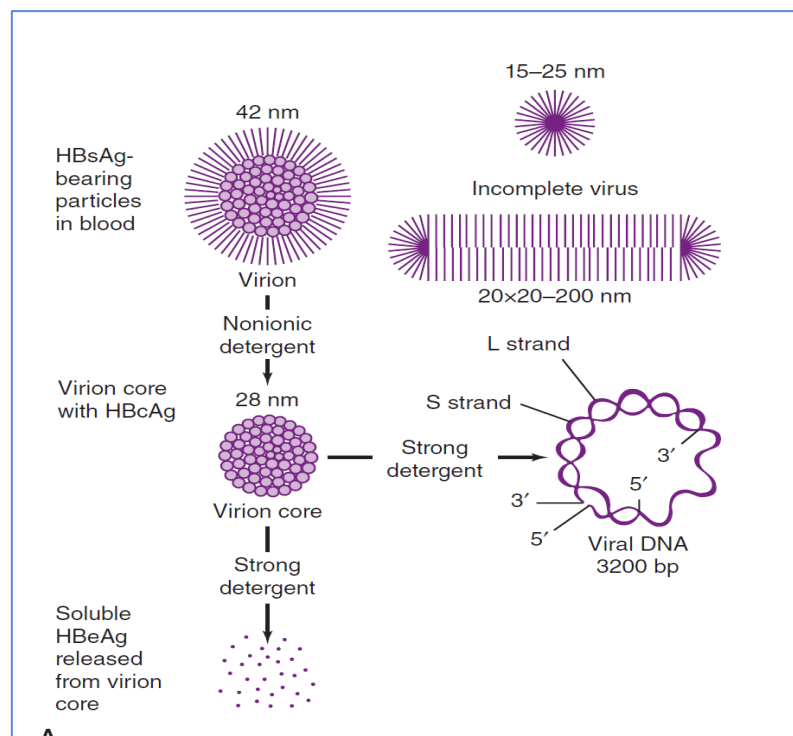
**Adenovirus:** (70–90 nm),

- Non-enveloped viruses
- Cubic symmetry, with fiber spikes protruding from capsomers that aid in attachment.
- The genome is linear, double-stranded DNA, 26–48 kb in size.
- Replication occurs in the **nucleus**.
- At least 67 types infect humans, especially in mucous membranes,
- Some types can persist in lymphoid tissue.
- Adenoviruses can cause **acute respiratory** diseases, **conjunctivitis**, and **gastroenteritis**.



Hepadnaviridae: (40–48 nm),

- Enveloped viruses
- Circular, partially double-stranded DNA molecules that are about 3.2 kbp in size.
- Replication involves repair of the single-stranded gap in the DNA, transcription of RNA, and reverse transcription of the RNA to make genomic DNA.
- The virus consists of a 27-nm icosahedral nucleocapsid core within a closely adherent envelope that contains lipid and the viral surface antigen.
- The surface protein is characteristically overproduced during replication of the virus, which takes place in the liver, and is shed into the bloodstream.
- **Hepatitis B virus** can cause acute and chronic hepatitis

Herpesviruses :(150–200 nm )

- large viruses.
- They possess an **icosahedral nucleocapsid** (100 nm, 162 capsomeres) surrounded by a **lipid-containing envelope**
- The genome is linear, double-stranded DNA, 120–240 kb in size.
- **Latent infections** may last for the life span of the host,
- Human herpesviruses include
  1. Herpes simplex types 1 and 2 (oral and genital lesions),
  2. Varicella-zoster virus (chickenpox and shingles), cytomegalovirus,
  3. Epstein-Barr virus (infectious mononucleosis)
  4. Human herpesviruses 6 and 7 (T cell lymphotropic),
  5. Human herpesvirus 8 (associated with Kaposi sarcoma).

## Poxviruses

- Large brick-shaped or ovoid
- Enveloped viruses
- Complex symmetry
- Genome is linear, double stranded DNA
- Replication occurs entirely within the cell cytoplasm.
- (smallpox, vaccinia, molluscum contagiosum)

Table –1 Classification of DNA Viruses

Virus Family	Envelope Present	Capsid Symmetry	Virion Size (nm)	DNA Structure <sup>1</sup>	Medically Important Viruses
<b>Parvovirus</b>	No	Icosahedral	22	SS, linear	B19 virus
<b>Polyomavirus</b>	No	Icosahedral	45	DS, circular, supercoiled	JC virus, BK virus
<b>Papillomavirus</b>	No	Icosahedral	55	DS, circular, supercoiled	Human papilloma virus
<b>Adenovirus</b>	No	Icosahedral	75	DS, linear	Adenovirus
<b>Hepadnavirus</b>	Yes	Icosahedral	42	DS, incomplete circular	Hepatitis B virus
<b>Herpesvirus</b>	Yes	Icosahedral	100 <sup>2</sup>	DS, linear	Herpes simplex virus, varicella-zoster virus, cytomegalovirus, Epstein-Barr virus
<b>Poxvirus</b>	Yes	Complex	250 x 400	DS, linear	Smallpox virus, molluscum contagiosum virus

<sup>1</sup>SS = single-stranded; DS = double-stranded.

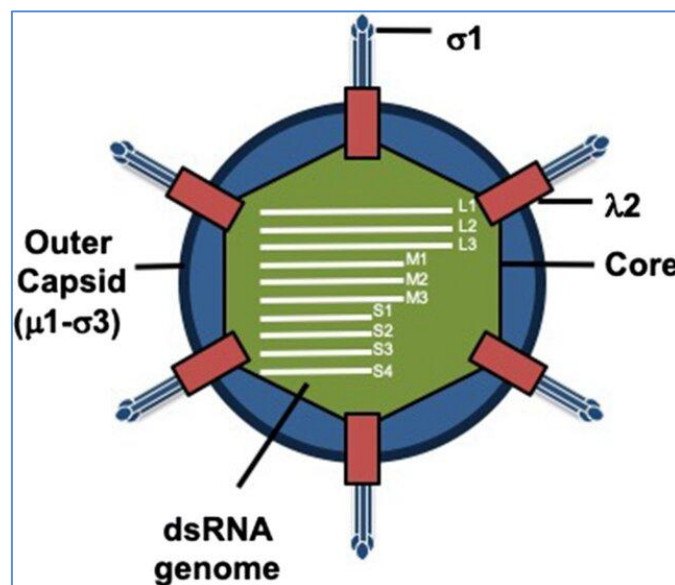
<sup>2</sup>The herpesvirus nucleocapsid is 100 nm, but the envelope varies in size. The entire virus can be as large as 200 nm in diameter.

## RNA Viruses

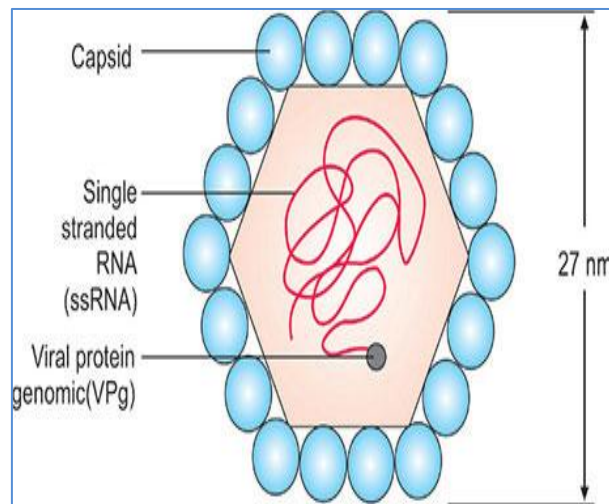
The 14 families of RNA viruses are described in Table 2. The three **naked icosahedral** virus families are listed first and are followed by the three **enveloped icosahedral** viruses. The remaining eight families are **enveloped helical** viruses; the first five have single-stranded linear RNA as their genome, whereas the last three have single-stranded circular RNA.

**Reoviridae (60-80nm)**

- Non-enveloped viruses having icosahedral symmetry
- have two or three protein shells with channels extending from the surface to the core; short spikes extend from the virion surface.
- The genome is linear, double-stranded, segmented RNA (10–12 segments)
- Replication occurs in the cytoplasm
- rotaviruses, cause Gastroenteritis

**Picornaviridae: ( 28-30 nm)**

- Small ether-resistant viruses with cubic symmetry.
- Genome :Single-stranded ,positive-sense RNA
- Human-Infecting Groups:
- Enteroviruses :Includes polioviruses ,coxsackieviruses ,echoviruses , (parechoviruses ,and rhinoviruses) over 100 serotypes causing common colds, Hepatovirus :Causes hepatitis A.

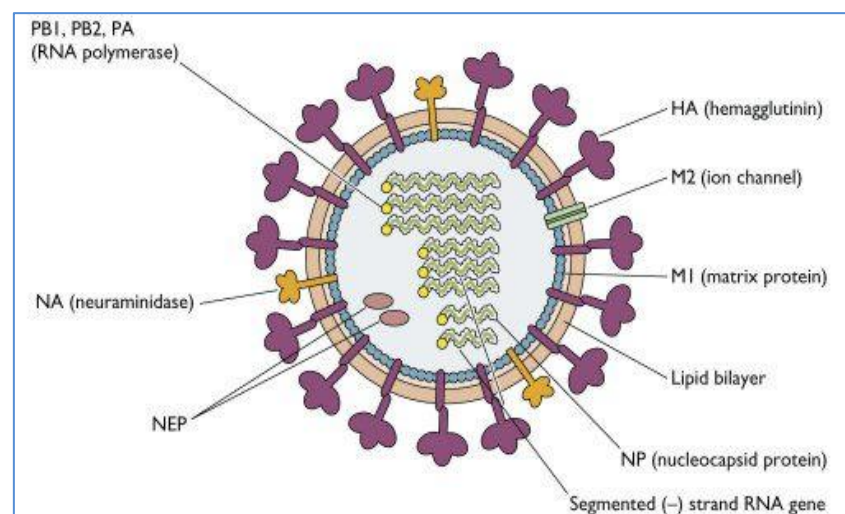


## Hepviridae (23-42 nm)

- Naked with an icosahedral capsid
- Particle Characteristics :Small and either resistant.
- Genome :Single-stranded ,positive-sense RNA,
- Unique Feature :Lacks a genome-linked protein (VPg).
- Key Example :Human **hepatitis E virus** belongs to this group.

## Orthomyxoviruses (80-120nm)

- Enveloped with Helical symmetry.
- Particles are round or filamentous.
- surface projections contain hemagglutinin (HA) or neuraminidase (NA) activity
- Genome: Linear, segmented (6–8 segments), negative-sense, single-stranded RNA,
- Includes influenza viruses that infect humans or animals



**Coronaviruses :(120-160nm)**

- These are enveloped viruses with a helical nucleocapsid
- Unsegmented, linear positive single-stranded RNA.
- The term "corona" refers to the prominent halo of spikes protruding from the envelope.
- Coronaviruses cause respiratory tract infections, such as the common cold, SARS (severe acute respiratory syndrome), and covid -19 in humans.

**Paramyxoviruses (150–300 nm)**

- These are enveloped viruses with a helical nucleocapsid
- Nonsegmented, linear, negative single-stranded RNA.
- The important human pathogens are measles, mumps, parainfluenza, and respiratory syncytial viruses.

**Rhabdoviruses**

- These are bullet-shaped enveloped viruses with a helical nucleocapsid
- single-stranded, linear, unsegmented, negative-sense RNA.
- The term "rhabdo" refers to the bullet shape.
- Rabies virus is the only important human pathogen.



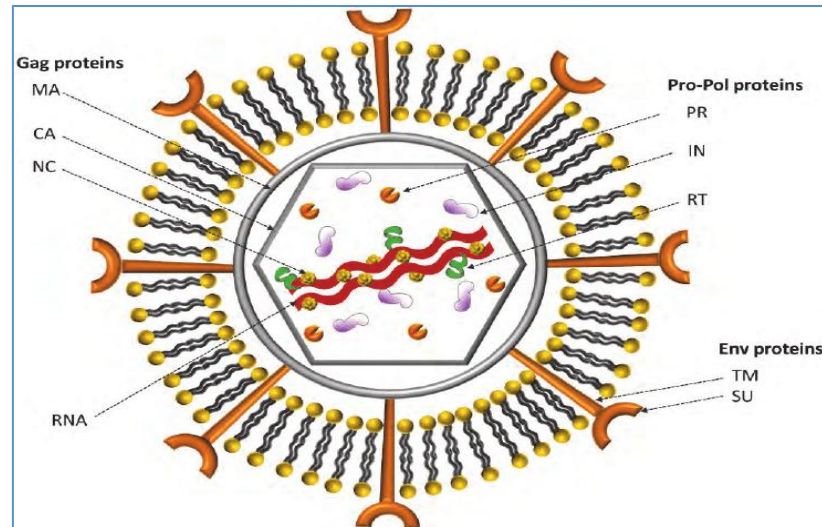
### Filoviruses

- These are enveloped viruses with a helical nucleocapsid
- single-stranded, linear, unsegmented, negative sense RNA.
- They are highly pleomorphic, they may appear very long and like threads. The term "filo" means "thread" and refers to the long filaments.
- The two human pathogens are Ebola virus and Marburg virus.



### Retroviruses

- Enveloped viruses with an icosahedral capsid.
- Two identical strands (said to be "diploid") of single-stranded, linear, positive-sense RNA.
- The term "retro" pertains to the reverse transcription of the RNA genome into DNA.
- There are two medically important groups:
  1. Human T-cell leukemia virus (HTLV) causes sarcoma and leukemia
  2. the lentivirus ("slow virus") group, which includes human immunodeficiency virus (HIV).



### Flaviviruses

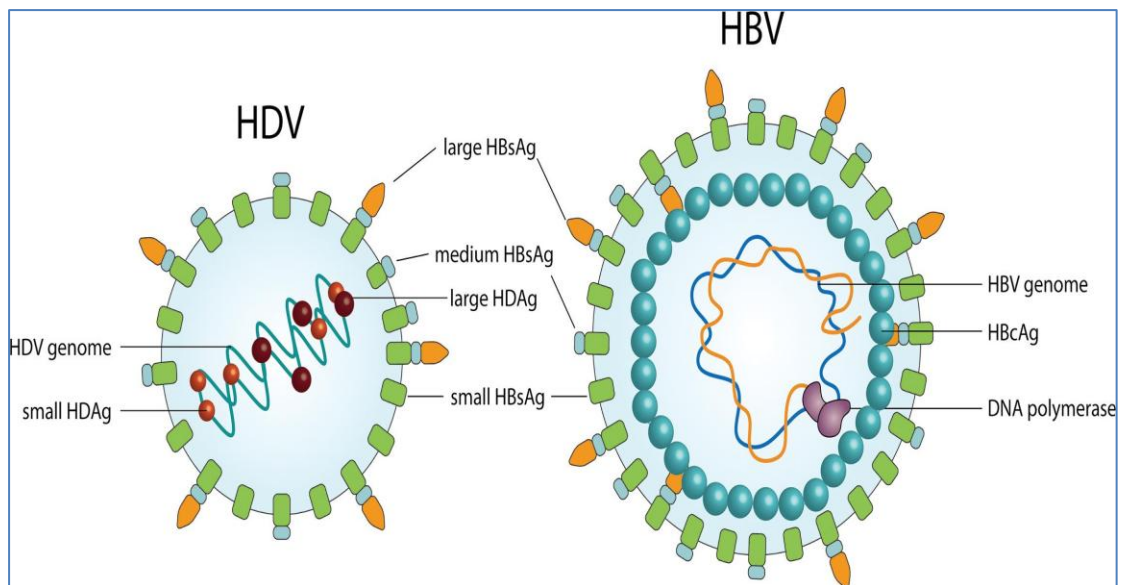
- These are enveloped viruses with an icosahedral capsid
- single-stranded, linear, unsegmented, positive-sense RNA.
- The flaviviruses include hepatitis C virus, yellow fever virus, dengue virus, West Nile virus, and St. Louis and Japanese encephalitis viruses.

### Togaviruses

- These are enveloped viruses with an icosahedral capsid
- Single-stranded, linear, unsegmented, positive sense RNA.
- There are two major groups of human pathogens:
- The alphaviruses and rubiviruses. The alphavirus group includes eastern and western encephalitis viruses; the rubivirus group consists only of rubella virus.

**Deltavirus**

- Hepatitis delta virus (HDV) is the only member of this genus.
- It is an enveloped virus
- RNA genome that is a single-stranded, negative-sense , covalently closed circle.
- The symmetry of the nucleocapsid is uncertain.
- It is a defective virus because it cannot replicate unless hepatitis B virus (HBV) is present within the same cell. HBV is required because it encodes hepatitis B surface antigen (HBsAg), which serves as the outer protein coat of HDV.
- The RNA genome of HDV encodes only one protein, the internal core protein called delta antigen.
- 



HBV as a helper virus for HDV.

Hepatitis B virus (HBV) shares its small, medium, and large hepatitis B surface antigens (HBsAg) with hepatitis D virus (HDV).

Table –2 Classification of RNA Viruses

Virus Family	Envelope Present	Capsid Symmetry	Particle Size (nm)	RNA Structure <sup>1</sup>	Medically Important Viruses
<b>Picornavirus</b>	No	Icosahedral	28	SS linear, nonsegmented, positive polarity	Poliovirus, rhinovirus, hepatitis A virus
<b>Hepevirus</b>	No	Icosahedral	30	SS, linear, non-segmented, positive polarity	Hepatitis E virus
<b>Calicivirus</b>	No	Icosahedral	38	SS linear, nonsegmented, positive polarity	Norwalk virus
<b>Reovirus</b>	No	Icosahedral	75	DS linear, 10 or 11 segments	Rotavirus
<b>Flavivirus</b>	Yes	Icosahedral	45	SS linear, nonsegmented, positive polarity	Yellow fever virus, dengue virus, West Nile virus, hepatitis C virus
<b>Togavirus</b>	Yes	Icosahedral	60	SS linear, nonsegmented, positive polarity	Rubella virus
<b>Retrovirus</b>	Yes	Icosahedral	100	SS linear, 2 identical strands (diploid), positive polarity	HIV, human T-cell leukemia virus
<b>Orthomyxovirus</b>	Yes	Helical	80–120	SS linear, 8 segments, negative polarity	Influenza virus
<b>Paramyxovirus</b>	Yes	Helical	150	SS linear, nonsegmented, negative polarity	Measles virus, mumps virus, respiratory syncytial virus
<b>Rhabdovirus</b>	Yes	Helical	75 x 180	SS linear, nonsegmented, negative polarity	Rabies virus
<b>Filovirus</b>	Yes	Helical	80 <sup>3</sup>	SS linear, nonsegmented, negative polarity	Ebola virus, Marburg virus
<b>Coronavirus</b>	Yes	Helical	100	SS linear, nonsegmented, positive polarity	Coronavirus
<b>Arenavirus</b>	Yes	Helical	80–130	SS circular, 2 segments with cohesive ends, negative polarity	Lymphocytic choriomeningitis virus
<b>Bunyavirus</b>	Yes	Helical	100	SS circular, 3 segments with cohesive ends, negative polarity	California encephalitis virus, hantavirus
<b>Deltavirus</b>	Yes	Uncertain <sup>4</sup>	37	SS circular, closed circle, negative polarity	Hepatitis delta virus

<sup>1</sup>SS = single-stranded; DS = double-stranded.

<sup>2</sup>Retrovirus RNA contains 2 identical molecules of MW  $3.5 \times 10^6$ .

<sup>3</sup>Particles are 80 nm wide but can be thousands of nanometers long.

<sup>4</sup>The nucleocapsid appears spherical but its symmetry is unknown.

## Reaction to physical & chemical agents

### Temperature

**Heat** - there is great variability in the heat stability of different viruses, but icosahedral viruses tend to be relatively stable, enveloped viruses are heat labile and most pathogenic viruses are inactivated at 55-60°C for 30 min. because their capsid protein is destroyed (an important exception is the hepatitis B virus).

**Cold** - most viruses can be preserved at sub-freezing temperatures; some can withstand lyophilisation and can be stored in the dry state at 4°C or even at room temperature while enveloped viruses tend to lose infectivity after prolonged storage at -90°C.

### pH

Most viruses are stable in the pH range 5-9. Enteroviruses that have to pass through the stomach can withstand low pHs. All viruses are destroyed by alkaline conditions.

### Radiation

UV produces damaging results on double-stranded DNA that can cause inactivation of the virus

x-ray, gamma rays and beta particles inactivate viruses.

### Stabilization by Salts

Magnesium chloride stabilizes polioviruses; magnesium sulphate stabilizes influenza viruses and sodium sulphate stabilizes herpes virus. Important in the preparation of vaccines e.g.. Non-stabilized polio vaccine must be stored at <0°C whereas stabilized vaccine remains potent for weeks at ambient temperature which is an advantage when immunizing in rural areas

### Ether Susceptibility and Lipid Solubility

Enveloped viruses are inactivated by ether whereas non-enveloped ones are not (simple efficient test for the presence of envelopes). Other organic solvents and sodium deoxycholate also destroy the envelope.

### Detergents

Non-ionic detergents solubilize lipid constituents but do not denature the proteins of the capsid. Anionic detergents solubilize the lipid constituents and disrupt the capsids into separated polypeptides

### 50% Glycerol

Many viruses remain alive in 50% glycerol for many years. Vaccinia virus is preserved in 50% glycerol for many years while bacteria are killed.