# 1 General Features and Classification of Viruses of Medical Importance



## 1.1 Introduction

Viruses are obligate intracellular infectious agents. The term "virus" originates from the Latin word "poison." [1]. Structurally, viruses consist of genetic material, either ribonucleic acid (RNA) or deoxyribonucleic acid (DNA) (but not both), encapsulated within a protein coat called a capsid, and in some cases, an outer lipid envelope. Not all viruses have an envelope. Enveloped viruses are nucleocapsids covered by a lipid bilayer membrane, usually derived from the host cell. In contrast, non-enveloped viruses, also known as naked viruses, lack this lipid bilayer.

The size of viruses typically ranges from 20 to 300 nm in diameter, making them too small to be seen with the naked eye and with an ordinary light microscope [2]. Giant viruses are exceptions; they are large viruses that might be visible under very powerful light microscopes, though details would not be clear [3].

Viruses are incredibly diverse, varying in size, shape, and complexity. They can infect all types of organisms, including animals, plants, and even other microorganisms like bacteria. Despite their simplicity, viruses have profound impacts on health, ecology, and evolution, making them a critical focus of study in microbiology and virology. Figure 1.1 illustrates the hypothetical structure of some viruses of medical importance.

**Examples of giant viruses:**

**Mimivirus:** One of the largest known viruses, measuring around 400 nm in diameter, the mimivirus is large enough to be seen as a speck under a high-resolution light microscope.

While mimivirus is not considered a typical human pathogen, some studies have suggested its presence in patients with pneumonia. However, the role of mimivirus in causing human disease remains unclear and is debated. It may be associated with respiratory infections [4].

**Pandoravirus:** Another giant virus, Pandoravirus, is even larger, measuring around 1 μm (1000 nm). This is well within the resolution range of a light

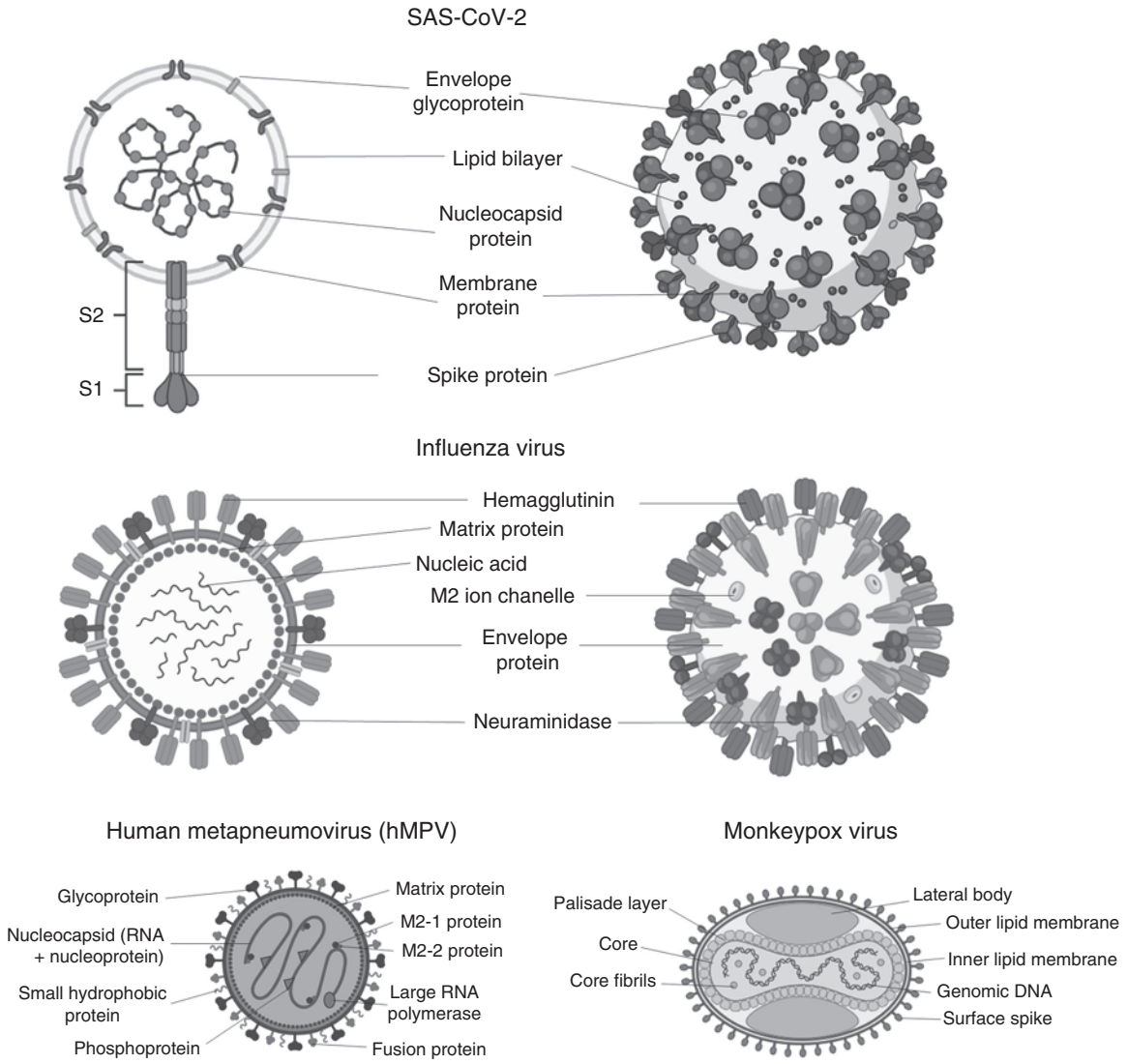


**Figure 1.1** Putative structure of some viruses of medical importance.

*Source:* With permission BioRender.

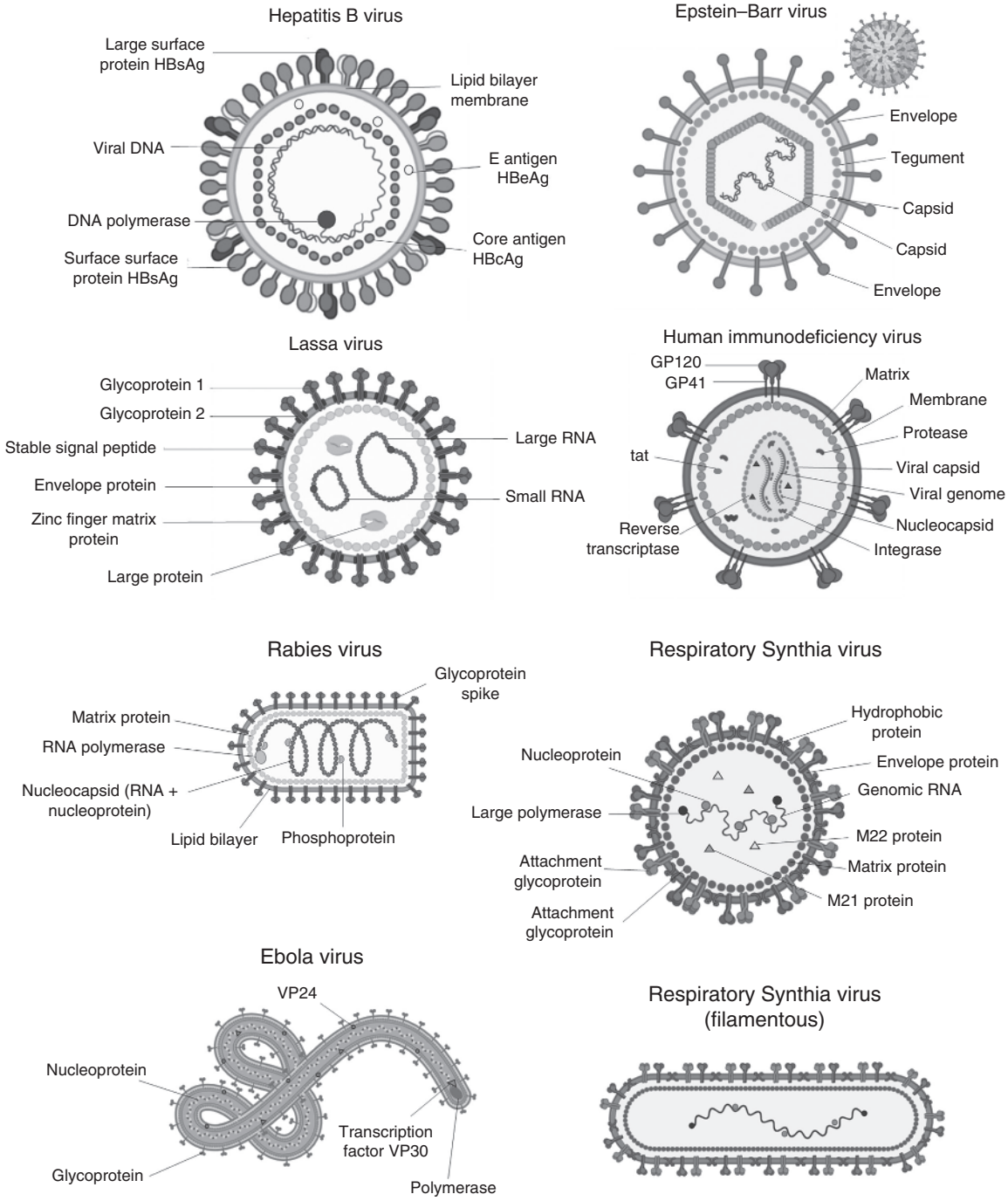


**Figure 1.1** (Continued)

microscope, so it can be seen, although its internal structure would still require an electron microscope for detailed observation [5].

Currently, there is no conclusive evidence that Pandoravirus infects humans or causes disease. It is primarily studied for its unique genetic characteristics and its interactions with amoebae.

## 1.2 Basic Virus Structure

### 1.2.1 Viral Nucleic Acids

The viral genome consists of nucleic acid, which can be either DNA or RNA, but not both. Unlike cellular organisms or bacterial genomes, viral genomic nucleic acid (RNA or DNA) can be (i) single-stranded or double-stranded, (ii) circular or linear, or (iii) segmented or non-segmented. Segmented means a single virus can have multiple RNA or DNA molecules as part of its genome. Additionally, if a virus is an RNA virus, its genomic RNA can be classified as positive-sense (+RNA), negative-sense (−RNA), or ambisense.

#### *1.2.1.1 RNA Viruses*

**Positive-Sense RNA Viruses** These are viruses whose genetic material functions directly as viral messenger RNA (mRNA), which encodes viral proteins. In other words, the RNA genome can serve as mRNA and be translated by the host's ribosomes to produce viral proteins. Positive-sense RNA viruses make up more than one-third of all known virus genera. Examples include poliovirus, hepatitis C virus (HCV), and coronaviruses such as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

**Negative-Sense RNA Viruses** Negative-sense RNA viruses have genomes that are complementary to mRNA. Before translation can occur, an RNA-dependent RNA polymerase must convert the negative-sense RNA genome into a positive-sense RNA. Examples of negative-sense RNA viruses include the influenza virus, rabies virus, and Ebola virus.

**Ambisense RNA Viruses** Ambisense RNA viruses have genomes that contain both positive- and negative-sense sequences within the same RNA molecule. The viral RNA polymerase must first transcribe the negative-sense portion into positive-sense RNA, while the positive-sense portion can be directly translated. Examples of ambisense RNA viruses include some arenaviruses (e.g., Lassa virus) and bunyaviruses (e.g., Rift Valley fever virus) [6, 7].

#### *1.2.1.2 DNA Viruses*

The genomes of DNA viruses can be either double-stranded (dsDNA) or single-stranded (ssDNA). In general, DNA viruses are more stable and less prone to mutation compared to RNA viruses, providing a higher degree of genetic stability.

**Double-Stranded DNA Viruses** Double-stranded DNA (dsDNA) is the most common type of genome in DNA viruses. The genome can be linear or circular. Examples include adenoviruses (linear dsDNA), herpesviruses (linear dsDNA), poxviruses (linear dsDNA

with covalently closed ends), and papillomaviruses (circular dsDNA).

**Single-Stranded DNA Viruses** Single-stranded DNA (ssDNA) viruses are less common and require conversion into dsDNA for replication and transcription. An example is the parvovirus.

**Partially dsDNA Viruses** Partially dsDNA viruses have circular genomes containing both double-and single-stranded regions. In the case of hepatitis B virus (HBV), one strand is a complete negative-sense strand, while the other is an incomplete positive-sense strand. This "partially" double-stranded genomic structure gives HBV its unique "relaxed" circular DNA structure due to the gap in the positive strand. HBV contains a small portion of RNA (pre-genomic RNA) during certain stages of replication [8].

**Clinical Significance** Most DNA viruses are genetically more stable than RNA viruses. Also, despite their limited coding capacity, RNA viruses evolve rapidly due to lack of proofreading during replication, contributing to their high mutation rates. This rapid evolution presents challenges for vaccine and antiviral drug development, especially in populations with prior exposure.

**Implications of Genetic Stability**

**Evolutionary dynamics**

**DNA viruses:** The genetic stability of DNA viruses can be beneficial for the development of long-lasting vaccines and antiviral therapies.

**RNA viruses:** The high mutation rates of RNA viruses drive rapid evolution, which can complicate the development of effective vaccines and treatments. For example, the rapid genetic changes in influenza viruses necessitate regular updates to the flu vaccine.

**Pathogenicity and host interaction**

**DNA viruses:** Their stable genomes allow for persistent infections and long-term coevolution with their hosts. Examples include herpesviruses and papillomaviruses.

**RNA viruses:** Their genetic variability enables quick adaptation to host defenses and environmental changes, often resulting in acute, rapidly spreading infections. Examples include human immunodeficiency virus (HIV), influenza, and coronaviruses.

**Reason for stability**

**Replication fidelity:** DNA viruses often replicate using host-cell DNA polymerases or their viral DNA polymerases, which have proofreading and error-correcting mechanisms [9]. This ensures higher fidelity during DNA replication, resulting in fewer mutations. In contrast, RNA viruses typically rely on RNA-dependent RNA polymerases (RdRp) for replication, which lack proofreading capabilities. This leads to higher error rates during RNA synthesis and, consequently, higher mutation rates.

**Proofreading mechanisms and error rates:** DNA polymerases have much lower error rates compared to the RNA polymerases used by RNA

viruses. DNA polymerases, particularly those with proofreading activity, have an error rate of approximately $10^{-8}$ to $10^{-11}$ errors per nucleotide. In contrast, RdRp has significantly higher error rates, ranging from approximately $10^{-3}$ to $10^{-6}$ errors per nucleotide [10]. This higher error rate results in greater genetic variability in RNA viruses. The lower mutation rates in DNA viruses contribute to their greater genetic stability, allowing these viruses to maintain genome integrity over time.

## 1.2.2 Virus Capsids and Capsomere Proteins

A capsid is the protein coat that covers, protects, and stabilizes the viral genome. It consists of polypeptide subunits called capsomeres, which form the structural morphology of the virus, giving it a specific shape, such as spherical, rod-like, or conical. Capsid proteins vary phenotypically (in terms of structure and function) and genotypically (in terms of genetics) across different types of viruses. Recent studies have demonstrated that viruses can assume various shapes during different stages of replication. Viral capsids typically exhibit either icosahedral or helical symmetry. Helical capsids can be rigid or flexible, depending on the virus, while icosahedral capsids are generally more rigid [11].

### *1.2.2.1 Helical Symmetry*

Helical symmetry refers to a structural arrangement commonly observed in viruses, where protein subunits, capsomeres, are arranged in a helical structure, creating a rod-like or filamentous shape. This symmetry is primarily found in the nucleocapsids of some viruses, particularly those with single-stranded RNA (ssRNA) genomes, such as influenza and rabies [12].

The helical symmetry of a virus can be mathematically described by the following parameters:

a. **Radius ($r$):** The distance from the center of the helix to the center of a capsomere.
b. **Pitch ($p$):** The vertical distance (along the helix axis) for one complete turn of the helix
c. **Number of capsomeres per turn ($n$):** The number of protein subunits in one complete helical turn.
d. **Axial rise per capsomere ($h$):** The vertical distance between consecutive capsomeres along the helical axis can be calculated as $h = p/n$.
For example
Suppose a helical virus has the following properties: Pitch ($p$) = 5 nm; number of capsomeres per turn ($n$): 13
To find the axial rise per capsomere (h): $h = p/n$
$= 5\,\text{nm}/13 \approx 0.385\,\text{nm}$

### *1.2.2.2 Icosahedral Symmetry*

Icosahedral symmetry is a common and efficient structural form adopted by many viruses to build their capsids. An icosahedron consists of 20 equilateral triangular faces, 12 vertices (where 5 triangular faces meet), and 30 edges (shared between 2 triangular faces) [13]. This symmetry allows for the construction of a stable and closed

shell using a minimal number of distinct protein subunits, optimizing genetic economy. It is common in many DNA viruses and some RNA viruses.

**Triangulation Number (*T*-Number)** The triangulation number ($T$) describes the number of smaller triangular facets into which each of the 20 equilateral triangular faces of the icosahedron is divided. The *T*-number helps to understand the complexity and size of the viral capsid.

Formula:

$$T = h^2 + hk + k^2,$$

where $h$ and $k$ are nonnegative integers.

The *T*-number represents the number of quasi-equivalent positions that the capsomeres can occupy on the icosahedron.

Examples of *T*-numbers:

***T* = 1:** Simplest form with each triangular face made of a single capsomere. Total of 60 protein subunits (12 vertices × 5 subunits each).

***T* = 3:** Each triangular face is subdivided into three smaller triangles. Total of 180 protein subunits. Example: poliovirus.

***T* = 4:** Each triangular face is subdivided into four smaller triangles. Total of 240 protein subunits. Example: HBV.

***T* = 7:** Each triangular face is subdivided into seven smaller triangles. Total of 420 protein subunits.

**Clinical Applications** Understanding the structural details of icosahedral capsids aids in vaccine development by targeting specific viral proteins and capsid structures. Drugs can be designed to disrupt capsid assembly or stability, inhibiting viral replication. Additionally, in nanotechnology, the icosahedral symmetry of viruses can be used as a model for designing nanomaterials and nanodevices, leveraging the stability and geometric precision of viral capsids.

### *1.2.2.3 Complex Symmetry*

A virus is said to have complex symmetry when the capsid structure combines elements of both icosahedral and helical symmetry. Some viruses, such as poxviruses and bacteriophages, exhibit complex symmetry [14, 15].

- **Function of the capsids**

  **Protection:** The capsid protects the viral genome from degradation by nucleases and harsh environmental conditions.

  **Attachment and entry:** In non-enveloped viruses, capsid proteins often contain receptor-binding sites that facilitate attachment to host cells and entry.

  **Delivery of genetic material:** Once inside the host, the capsid disassembles to release the viral genome for replication.

The **nucleocapsid** and **capsomere** are both structural components of viruses, but they differ in their composition and function:

**Nucleocapsid**

- The nucleocapsid is the combination of a virus's genetic material (either DNA or RNA) and the protein coat that surrounds and protects it [16].

- It serves as a protective layer for the viral genome and aids in the process of infection by ensuring the safe delivery of the genetic material into host cells.
- In some viruses, the nucleocapsid is enclosed by an additional lipid envelope, but in others (non-enveloped viruses), the nucleocapsid is the outermost layer.

**Capsomere**

- A capsomere is a subunit or building block of the capsid, which is the protein shell that surrounds the viral genome.
- Capsomeres are made of protein molecules and self-assemble to form the capsid, which can have various geometric shapes, such as icosahedral or helical.
- The arrangement and number of capsomeres determine the overall shape and symmetry of the viral capsid.

## 1.2.3 Virus Envelope (Membrane) Protein

The virus envelope is a lipid bilayer, embedded with proteins, that surrounds some virus particles. Most enveloped viruses (except poxviruses) acquire their envelope from the host-cell membrane, such as the Golgi apparatus, endoplasmic reticulum (ER), or plasma membrane, during viral maturation or budding [17]. Aside from the viral envelope, which is the last/outer layer of enveloped viruses, some viruses encode glycoprotein projections called spikes or peplomers, which are present on either the outer layer of the viral capsid or envelope [18]. These projections facilitate virus attachment to host cells, entry, and immune evasion. They are crucial for both viral specificity and infectivity.

The membrane (or envelope) of viruses plays a crucial role during three main stages of the viral life cycle: entry into the host cell, assembly of new virions, and release from the host cell.

### *1.2.3.1 Virus Membrane Glycoprotein*

Virus membrane glycoproteins are crucial components of viral envelopes, playing significant roles in the virus's ability to infect host cells (membrane fusion and entry) and evade the immune system. These glycoproteins can be broadly categorized into two structural classes: Class I and Class II glycoproteins.

**Class I Viral Membrane Glycoproteins**

Class I glycoproteins are characterized by their prominent alpha-helical transmembrane domains. They typically undergo significant conformational changes during the process of fusion, shifting from a pre-fusion to a post-fusion state. In their functional form, these glycoproteins often form trimeric structures [19].

Examples of viruses with Class I membrane glycoproteins are

- **Influenza virus:** Influenza hemagglutinin (HA1 and 2) is a glycoprotein. It is responsible for the attachment and subsequent fusion of the influenza virus with the host-cell membrane. However, type II glycoproteins are also found on HA1 [20].

- **Human immunodeficiency virus:** HIV envelope glycoprotein (Env) comprises glycoprotein (gp) 120 and gp41 subunits; this glycoprotein is essential for HIV to attach to and fuse with host cells.

**Class II Viral Membrane Glycoproteins** Class II glycoproteins are characterized by their beta-sheet-rich structures or domains. Unlike Class I glycoproteins, Class II glycoproteins exist as dimers in their pre-fusion state and form a hairpin-like structure upon fusion, facilitating membrane fusion.

Examples of viruses with Class II membrane glycoproteins are

**Dengue virus (DENV):** DENV envelope glycoprotein (E) is a glycoprotein that mediates DENV entry into host cells by binding to receptors and facilitating membrane fusion [21].

**Tick-borne encephalitis virus:** Tick-borne encephalitis virus glycoprotein (E), like DENV glycoprotein, also plays a key role in viral attachment and membrane fusion for viral entry [22, 23].

### *1.2.3.2 Broad Functions of Viral Membrane Glycoproteins*

**Role in Virus Attachment** Viral glycoproteins embedded in the envelope, such as hemagglutinin (HA) in influenza viruses or spike (S) proteins in coronaviruses, recognize and bind to specific receptors on the surface of the host cell. This binding determines the host range and tissue tropism of the virus.

**Role in Virus Entry and Fusion** After attachment, fusion proteins within the viral envelope mediate the merging of the viral envelope with the host-cell membrane. This fusion can occur either directly at the plasma membrane (e.g., HIV) or within endosomes following endocytosis (e.g., influenza virus). Fusion releases the viral nucleocapsid into the host cell's cytoplasm, where viral replication begins.

**Role in Virus Release** Newly formed enveloped virions are released from the host cell either by budding from the plasma membrane or through exocytosis if they bud into intracellular vesicles first. During budding, the viral nucleocapsid associates with the host membrane at the budding site, where viral proteins and glycoproteins are embedded. The envelope wraps around the nucleocapsid, releasing the mature virion. Viral matrix proteins play a key role in linking the nucleocapsid to the envelope, facilitating non-lytic budding.

**Clinical Significance of Viral Membrane Glycoprotein** The presence of a lipid envelope has significant implications for the virus's stability and how it interacts with the environment. The lipid envelope makes viruses more susceptible to disinfectants, particularly those containing alcohol and detergents. These substances can disrupt the lipid bilayer, effectively inactivating the virus outside the body. This property is clinically significant for infection control, as proper hand hygiene and surface disinfection can help prevent the spread of some enveloped viruses.

Enveloped viruses are generally less stable outside the host compared to non-enveloped viruses [24]. They are sensitive to environmental conditions such as heat, desiccation,

and pH changes. This means that, in most cases, enveloped viruses typically require direct transmission routes such as blood, bodily fluids, or close person-to-person contact. Understanding this structure of the virus can aid in developing strategies for controlling outbreaks and implementing preventive measures.

### 1.2.4 Matrix Proteins (in Enveloped Viruses)

Matrix proteins are like the tough scaffolding within an enveloped virus [25]. They lie beneath the envelope and link the envelope with the nucleocapsid, playing a crucial role in the structure and assembly of the virus particle. Their structure can vary depending on the specific virus, but they often have regions that bind to lipids in the envelope and regions that interact with the viral RNA or proteins in the nucleocapsid, helping to anchor the nucleocapsid within the viral membrane and maintain the integrity of the virus [26].

**Function of the virus matrix protein**

In HIV, the matrix protein (MA) plays a crucial role in the assembly and budding of new viral particles.

In influenza viruses, the matrix protein M1 helps maintain the integrity of the viral envelope and interacts with the viral ribonucleoprotein complex (RNP) within the nucleocapsid.

### 1.2.5 Tegument

The tegument is found in some enveloped viruses, specifically in the space between the capsid and the viral envelope. It is prominent in herpesviruses (e.g., herpes simplex virus) [27]. The tegument is composed of various viral proteins, which vary significantly between different viruses. For example, Epstein–Barr virus (EBV) tegument [28] contains proteins like BGLF and viral protein 16 (VP16) (late tegument protein), which are essential for gene expression, immune modulation, and replication. Also, varicella-zoster virus (VZV) has tegument proteins that play crucial roles in virus replication and immune evasion [29]

## 1.3 Classification of Viruses of Medical Importance

Classification of viruses is essential for understanding their biology and epidemiology and for developing strategies to combat viral diseases. In the early days of virology, virus classification was primarily based on characteristics observable under an electron microscope and a few other basic properties, such as morphological characteristics, including shape (symmetry of the capsid), size, and stability under certain conditions [30]. This traditional method provided a limited understanding of viral biology.

As technology advanced, electron microscopy allowed for direct visualization of viruses, providing detailed information about their morphology and size. Molecular techniques, such as nucleic acid sequencing, have since provided a much deeper understanding of viral genetics and phylogeny, leading to more accurate and comprehensive classification systems.

## 1.3.1 Traditional Classification

### *1.3.1.1 Classification Based on Physicochemical Properties*

In this type of classification system, viruses can be classified based on susceptibility to physical or chemical agents (especially ether and detergents), pH stability, thermal stability, solvent stability, cation stability, radiation stability, and buoyant density.

This system of classification is particularly valuable in laboratory research, biosafety, epidemiological surveillance, sterilization protocols, vaccine development, and public health interventions.

a. **Classification based on susceptibility to solvents (e.g., ether, chloroform, and detergents):** Enveloped viruses are generally sensitive to lipid solvents like ether or detergents, which disrupt the viral envelope, leading to inactivation [31]. In contrast, non-enveloped viruses are more resistant [32]. This feature is used to differentiate between these two structural types.
b. **Classification based on pH stability:** Viruses can be classified as acid-stable or acid-labile. That is, some viruses are stable over a wide pH range, while others are inactivated outside narrow pH limits. For example, enteric viruses like picornaviruses, such as poliovirus, are stable in acidic conditions (up to pH 3.0), allowing survival in the stomach [33]. However, rhinovirus is not acid-stable [34]. This characteristic is relevant for understanding oral transmission routes.
c. **Classification based on thermal stability:** This refers to how resistant a virus is to heat. Thermally stable viruses (e.g., hepatitis A and E) can withstand pasteurization-like conditions, whereas others are easily inactivated by mild heat [35]. Exposure to heat at 70–72 °C for 2 minutes substantially lowers the level of infectious virus, though it typically does not achieve a reduction greater than 4 $\log_{10}$ [36]. This property also influences sterilization and vaccine storage protocols.
d. **Classification based on radiation stability:** Most viruses are sensitive to ultraviolet exposure because of the pyrimidine dimer (thymidine) [37]. However, since only DNA and not RNA contains thymidine, DNA viruses are more sensitive to ultraviolet or ionizing radiation than RNA viruses [38]. Ultraviolet radiation, in particular, is used to disinfect surfaces and air in hospital and laboratory settings.
e. **Classification based on cation sensitivity:** Certain viruses require specific ions (e.g., $Mg^{2+}$ or $Ca^{2+}$) to maintain structural stability or facilitate infectivity. Removing these ions or altering ionic strength can destabilize the virion or affect its ability to infect host cells [39].
f. **Classification based on buoyant density:** Viruses have characteristic buoyant densities in gradient centrifugation media (e.g., cesium chloride). This property is widely used in virus purification and identification techniques.

g. **Classification based on desiccation resistance:** Resistance to drying can vary. For example, non-enveloped viruses such as adenoviruses and enteroviruses are more resistant to desiccation, allowing survival on surfaces for extended periods [40].
h. **Classification based on sensitivity to oxidizing agents and disinfectants:** Some viruses, particularly non-enveloped ones, can survive exposure to alcohols or chlorine-based disinfectants, while enveloped viruses are more readily inactivated [41].

### *1.3.1.2 Classification Based on Viral Pathogenesis*

This involves categorizing viruses according to their ability or affinity to infect specific cells, tissues, or organs, a concept known as "tropism." Classifying viruses based on tissue tropism provides insights into their pathogenicity, clinical manifestations, and epidemiology. These viruses are named based on the part of the body they primarily infect. However, it is important to note that while a virus may have a primary site of infection, it is not exclusively limited to causing symptoms at that site. Following are examples of virus classification based on viral pathogenesis:

**Respiratory Viruses** These are viruses that primarily infect the respiratory tract, including the nasal passages, throat, trachea, and lungs. Viruses in this category are referred to as respiratory viruses because they predominantly cause clinical symptoms and tissue damage in the respiratory system. Their classification under this nomenclature is based on their tropism for respiratory epithelium, and this tropism is often mediated by specific cellular receptors and cofactors found abundantly on respiratory epithelial cells. These molecular interactions are essential for viral attachment, entry, and replication, which in turn drive their tissue specificity and disease profile.

**Examples include**

- **Influenza viruses:** Cause respiratory infections, ranging from mild colds to severe pneumonia. Influenza viruses bind to sialic acid residues on glycoproteins of respiratory epithelial cells via their HA proteins, leading to infection of the upper and lower respiratory tract [42].
- **Rhinoviruses:** Major cause of the common cold, infecting the upper respiratory tract. Rhinoviruses target intercellular adhesion molecule-1 (ICAM-1) on nasal mucosa epithelial cells, explaining their restriction to the upper respiratory tract and association with the common cold [43].
- **Respiratory syncytial virus (RSV):** Causes bronchiolitis and pneumonia majorly in infants young children and high-risk adults. RSV uses nucleolin, CX3C chemokine receptor 1, and heparan sulfate proteoglycans (HSPGs) for entry into airway epithelial cells, contributing to bronchiolitis in infants [44, 45].
- **Coronaviruses:** SARS-CoV-2. It uses the angiotensin-converting enzyme 2 (ACE2) receptor, which is expressed in the nasal epithelium, trachea, and alveolar cells, accounting for both mild upper respiratory tract infections and severe lower respiratory tract involvement [46].

- **Human metapneumovirus (hMPV):** hMPV primarily infects respiratory epithelial cells and uses multiple cellular components for entry [47]. Although the exact primary receptor is not fully defined, studies have shown that hMPV binds to HSPGs on the surface of epithelial cells, initiating attachment. In addition, integrins (particularly αVβ1) have been implicated as co-receptors or facilitators of viral entry [48]. These receptor interactions contribute to the virus's tropism for the upper and lower respiratory tract, especially in infants, the elderly, and immunocompromised individuals.

The naming convention, therefore, is not only based on clinical presentation but also reflects virological behavior and host–pathogen interaction. Respiratory viruses may belong to different families (e.g., *Orthomyxoviridae*, *Coronaviridae*, *Paramyxoviridae*), but their shared tissue targeting unifies their classification under this pathogenesis-based nomenclature.

**Gastrointestinal Viruses** These viruses are grouped under this nomenclature based on their predominant site of infection – gastrointestinal (GI) tract, which includes the stomach, intestines, and associated mucosa. They are referred to as GI or enteric viruses because their clinical manifestations, diarrhea, vomiting, abdominal cramps, and dehydration, result directly from viral replication and damage to intestinal epithelial cells. Their ability to survive harsh gastric conditions, such as low pH and digestive enzymes, is critical to their infectivity and shapes their classification. In particular, they are highly adapted to infect enterocytes (intestinal epithelial cells), and this tropism is mediated by specific cellular receptors and glycans that facilitate attachment, entry, and replication.

**Examples**

- **Rotaviruses:** One of the leading causes of severe diarrhea in infants and young children globally [49]. Rotavirus targets mature enterocytes in the small intestine. Entry is facilitated by interactions with cell surface glycans, including sialic acid, integrins (α2β1, αVβ3), and heat shock cognate protein 70 (hsc70) [50]. The VP4 and VP7 outer capsid proteins mediate these receptor interactions [51].
- **Noroviruses:** Cause acute gastroenteritis, commonly leading to outbreaks of foodborne illness [52]. They are known for causing acute gastroenteritis in all age groups and are often associated with outbreaks. Noroviruses bind to histo-blood group antigens (HBGAs) expressed on the surface of gut epithelial cells [53]. The variation in HBGA expression among individuals partly explains susceptibility differences.
- **Enteroviruses:** Include coxsackieviruses and echoviruses. They are capable of systemic spread, and initial replication occurs in the oropharynx and intestinal mucosa. Receptors include poliovirus receptor PVR (CD155) for poliovirus and CAR for group B coxsackieviruses [54].

- **Astrovirus:** Infects intestinal epithelial cells, especially in children. The exact receptor remains unclear, but evidence suggests that entry may involve cell surface carbohydrates, and the virus can resist gastric acidity, aiding fecal–oral transmission.

**Hepatotropic Viruses** Hepatotropic viruses are classified based on their specific affinity for liver tissue. They cause inflammation of the liver (hepatitis) as the primary pathological outcome. The term hepatotropic reflects their tissue tropism – that is, their capacity to target and replicate within hepatocytes (liver cells). This classification is distinct and clinically relevant due to the unique disease course, modes of transmission, and long-term complications associated with liver-specific viral infections. These viruses, despite belonging to different families, share a common pathogenesis – hepatocellular injury, which may result from direct viral cytotoxicity, immune-mediated damage, or chronic inflammation that predisposes the host to fibrosis, cirrhosis, and even hepatocellular carcinoma (HCC).

**Examples**

- **Hepatitis A virus (HAV):** Causes acute hepatitis, primarily transmitted through ingestion of contaminated food and water. Humans are the only known reservoir [55].
- **HBV:** Can cause both acute and chronic hepatitis, leading to liver cirrhosis and HCC.
- **HCV:** Often leads to chronic hepatitis, with a high risk of progressing to cirrhosis and liver cancer.

**Neurotropic Viruses** These are viruses that primarily infect the nervous system, including the brain and spinal cord. They are grouped because they share the ability to breach the blood–brain barrier, infect neurons or glial cells, and often cause encephalitis, meningitis, neuropathy, or paralysis.

**Examples**

- **Rabies virus:** Causes fatal encephalitis, primarily transmitted through animal bites. It particularly causes acute viral encephalitis. Its transmission via animal bites underscores its distinct neuroinvasive pathogenesis
- **Poliovirus:** Infects motor neurons, leading to poliomyelitis and potential paralysis. Poliovirus infects and destroys anterior horn motor neurons, leading to poliomyelitis and flaccid paralysis. Despite initial replication in the gut, its severe outcome defines its nomenclature placement.
- **Herpes simplex virus (HSV):** Can cause encephalitis and meningitis, along with peripheral nervous system infections like cold sores and genital herpes. Both HSV-1 and HSV-2 exhibit neurotropism, establishing latency in sensory ganglia and occasionally causing encephalitis, meningitis, or radiculopathy. Their ability to persist and reactivate in neural tissues contributes to their inclusion in this group.

**Lymphotropic Viruses** These are viruses that primarily infect the lymphatic system, including lymph nodes and immune cells,

specifically targeting T lymphocytes or B lymphocytes.

**Examples**

- **EBV:** Causes infectious mononucleosis and is associated with certain cancers like Burkitt's lymphoma [56].
- **Human T-lymphotropic virus (HTLV):** Associated with adult T-cell leukemia or lymphoma. Although generally asymptomatic, a few (3–5%) develop adult T-cell leukemia [57].
- **Human immunodeficiency virus (HIV):** Infects T-helper cells, leading to acquired immunodeficiency syndrome (AIDS).

**Clinically relevant**

- Classifying viruses based on the site of infection or disease presentation (e.g., respiratory, enteric, neurotropic) is highly practical for clinical diagnosis and patient management. It helps healthcare professionals quickly associate symptoms with likely viral agents and guides appropriate testing and treatment.
- This system provides an intuitive and organ-specific framework that is easy to understand and use across disciplines, including medicine, nursing, epidemiology, and public health. Terms like hepatotropic, neurotropic, or dermatotropic viruses immediately signal the type of disease involved.
- Since the classification is tied to disease outcomes and transmission routes, it aids in targeted surveillance, outbreak response, and vaccine deployment. For instance, respiratory viruses can be managed with airborne precautions, while enteric viruses prompt sanitation measures.
- This system supports early outbreak detection based on clinical syndromes, especially where laboratory confirmation is delayed or unavailable. If multiple patients present with meningitis, a neurotropic virus is suspected, prompting faster action.

**Overlaps and ambiguity**

- Many viruses do not restrict themselves to one organ system. For example, enteroviruses may initially infect the GI tract but later affect the nervous system. This can create confusion in classification and may lead to mislabeling or oversimplification.
- This system does not reflect evolutionary relationships or molecular structure, which are important for understanding virus biology, mutation patterns, and vaccine design. It may group unrelated viruses that happen to affect the same organ.
- In molecular virology and advanced research, pathogenesis-based classification is insufficient. Researchers often require more granular, genetic-based classifications (e.g., Baltimore classification or International Committee on Taxonomy of Viruses [ICTV] taxonomy) to understand replication strategies and genome characteristics.
- The same virus can cause different diseases in different hosts or under different conditions. For instance,

cytomegalovirus (CMV) may be asymptomatic in healthy individuals but neurotropic or hepatotropic in immunocompromised patients, complicating classification.
- Viruses that cause secondary, asymptomatic or mild infections may be under-recognized in pathogenesis-based systems, even if they are epidemiologically significant (e.g., certain blood-borne viruses or emerging zoonoses).

### 1.3.1.3 Classification Based on Serological Properties

Serological classification of viruses is based on their antigenic properties, specifically how they react to specific antibodies. This method is crucial for understanding virus epidemiology, vaccine development, and diagnosis. Viruses are classified into serotypes and serogroups based on the differences and similarities in their surface antigens (proteins or glycoproteins on the viral envelope or capsid) that are recognized by the immune system.

**Virus Serotypes** Serotypes are distinct variations within a species of viruses that elicit a specific immune response. Different serotypes of the same virus can cause different immune reactions, as this could lead to type-specific immunity [58].

**Examples**
- **DENV:** There are four serotypes (DENV-1, DENV-2, DENV-3, and DENV-4) [59]. Infection with one serotype provides lifelong immunity to that serotype but not to the others [60].
- **Poliovirus:** There are three serotypes (PV1, PV2, and PV3), each requiring a specific immune response (minimal heterotypic immunity) [61].

**Virus Serogroups** A serogroup is a broader classification that includes multiple serotypes sharing common antigenic properties, specifically those that the immune system recognizes.

**Examples:**
- **Enteroviruses:** Include multiple serogroups such as coxsackieviruses and echoviruses, each with numerous serotypes.
- **Orthomyxoviruses:** Influenza A viruses are categorized into different serogroups based on the HA and neuraminidase (NA) proteins, leading to different subtypes like H1N1 and H3N2.

### 1.3.1.4 Classification Based on Vector Relationship

Viruses can be classified based on how they are transmitted through vectors. Usually, these viruses are transmitted among animals without ever infecting humans. Humans become incidentally infected by certain arthropods, rodents, and, in some cases, by direct contact with the infected animal.

**Arthropod-Borne Viruses**
- They are classified as arboviruses. This group of viruses is transmitted through blood-sucking arthropods (especially insects and ticks) [62]. The virus can penetrate and replicate in an insect's gut and salivary

gland, where it can be transmitted to another host when bitten. In some instances, the insect is generally unarmed or has no obvious disease. Birds are usually reservoir hosts for some arbovirus. Other reservoir hosts include rodents and nonhuman primates like monkeys. However, there is a high possibility of human-to-human transmission. Examples are listed in Table 1.1.

**Rodent-Borne Viruses** They are classified as roboviruses [63]. They belong to the *Arenaviridae* and *Hantaviridae* virus families. Rodent-borne viruses are primarily transmitted to humans through contact with rodents or their body fluids, including urine, feces, and saliva. These viruses often have significant implications for human health, causing a range of diseases [63].

Rodents, especially the most diverse order of mammals, serve as reservoirs and vectors for virus transmission. It is rare for reservoir hosts to become chronically infected and overtly diseased. Many robovirus diseases are extremely lethal and contagious and can be acquired in both urban and especially in rural areas among poor people who depend on farming for survival.

**Table 1.1** Arboviruses of medical importance based on vector relationship in tropical countries.

| Vector type | Virus | Disease |
|---|---|---|
| Mosquito-borne viruses | Dengue virus (DENV) | Dengue fever, dengue hemorrhagic fever |
| | Zika virus | Zika fever, congenital Zika syndrome |
| | Chikungunya virus | Chikungunya fever |
| | West Nile virus (WNV) | West Nile fever, a neuroinvasive disease |
| | Yellow fever virus | Yellow fever |
| | Japanese encephalitis virus (JEV) | Japanese encephalitis |
| | Rift Valley fever virus (RVFV) | Rift Valley fever |
| Tick-borne viruses | Tick-borne encephalitis virus (TBEV) | Tick-borne encephalitis |
| | Crimean–Congo hemorrhagic fever virus (CCHFV) | Crimean–Congo hemorrhagic fever |
| | Powassan virus | Powassan encephalitis |
| Sandfly-borne viruses | Toscana virus | Meningoencephalitis |
| | Sandfly fever Sicilian virus | Sandfly fever |
| | Sandfly fever Naples virus | Sandfly fever |

Examples are Lassa virus, common in West Africa, transmitted by a multimammate rat (*Mastomys natalensis*) [64]. Transmission of this disease is from rodents through direct handling or contact with infected rodent droppings, saliva, or urine. Other examples are listed in Table 1.2.

Except for the possibility of human-to-human transmission, the distribution of robovirus and arbovirus diseases is generally restricted to the areas inhabited by the vectors or reservoirs.

## 1.3.2 Baltimore Classification

The Baltimore classification system was developed in 1971 by David Baltimore [65]. It is the most widely used method for classifying viruses. It groups viruses into seven classes based on three key characteristics [66]: (i) Type of nucleic acid – DNA or RNA; (ii) number of strands – single-stranded (ss) or double-stranded (ds); (iii) sense of the RNA genome (for RNA viruses only) – positive-sense (+ssRNA) or negative-sense (−ssRNA). See Table 1.3.

**Table 1.2** Rodent-borne viruses of medical importance.

| Virus family | Virus name | Disease(s) | Primary rodent host(s) |
|---|---|---|---|
| *Hantaviridae* | Sin Nombre virus* | Hantavirus pulmonary syndrome (HPS) | Deer mouse (*Peromyscus maniculatus*) |
| | Hantaan virus* | Hantavirus pulmonary syndrome (HPS) (common in the Americans) and Hemorrhagic fever with renal syndrome (HFRS) (common in Asia) | Striped field mouse (*Apodemus agrarius*) |
| | Puumala virus* | HFRS | Bank vole (*Myodes glareolus*) |
| | Seoul virus** | HFRS | Norway rat (*Rattus norvegicus*) |
| *Arenaviridae* | Lassa virus* | Lassa fever | Multimammate rat (*Mastomys natalensis*) |
| | Junin virus | Argentine hemorrhagic fever (AHF) | Drylands vesper mouse (*Calomys musculinus*) |
| | Machupo virus | Bolivian hemorrhagic fever (BHF) | Large vesper mouse (*Calomys callosus*) |
| | Lymphocytic choriomeningitis virus (LCMV) | Lymphocytic choriomeningitis (LCM) | House mouse (*Mus musculus*) |

* Highlights reported case(s) in tropical countries.
** Reported possible emerging zoonotic risk in tropical countries.

**Table 1.3** Baltimore classification of viruses.

| Class | Nucleic acid | Replication strategy | Examples |
|---|---|---|---|
| Class I | Double-stranded DNA (dsDNA) | Replicate using host DNA polymerase | Herpesviruses, adenoviruses, poxviruses |
| Class II | Single-stranded DNA (ssDNA) | Replicate by converting to double-stranded DNA first | Parvoviruses |
| Class III | Double-stranded RNA (dsRNA) | Replicate using an RNA-dependent RNA polymerase | Rotaviruses |
| Class IV | Single-stranded RNA (ssRNA, positive-sense) | Directly serves as mRNA for protein synthesis | Picornaviruses, coronaviruses |
| Class V | Single-stranded RNA (ssRNA, negative-sense) | Replicate via an RNA-dependent RNA polymerase | Influenza viruses, rabies virus |
| Class VI | ssRNA with reverse transcription | Convert RNA to DNA via reverse transcriptase, then integrate into host DNA | Retroviruses (e.g., HIV) |
| Class VII | dsDNA with reverse transcription | Replicate via an RNA intermediate and reverse transcription | Hepadnaviruses (e.g., HBV) |

Source: Adapted from [65].

### 1.3.3 Classification Based on Genomic Organization and Molecular Processes

The classification of viruses based on genomic organization and molecular processes is also a more common approach that provides deeper insights into viral biology, replication mechanisms, and evolutionary relationships. This method involves analyzing the structure and function of the viral genome as well as the molecular processes involved in virus replication, transcription, and translation. See Tables 1.4 and 1.5.

### 1.3.4 International Committee on Taxonomy of Viruses (ICTV) Classification of Viruses

The ICTV was established in 1966, and it is the generally accepted form of virus classification [67]. The ICTV develops and maintains a universal system for naming and categorizing viruses based on a combination of genetic, structural, and biological properties and evolutionary relationships [67]. In this system of classification, viruses are classified in hierarchical order related

**Table 1.4** Classification of viruses based on genomic organization and molecular processes.

| Properties | Classification |
|---|---|
| Type of viral genome | DNA or RNA |
| Number of strands | Single-stranded (ss), double-stranded (ds), or partially double-stranded |
| Size of the viral genome | Large-genome DNA viruses or small-genome DNA viruses |
| Genome segment | Segmented or non-segmented |
| Genome sense | Positive-sense RNA viruses, negative-sense RNA viruses, or RNA ambisense |
| Open reading frame | Number and position of open reading frame(s) |
| Other features | Guanine + cytosine (G+C) contents, 5′ terminal cap, 3′terminal poly (A) tail |

**Table 1.5** Morphological classification of viruses.

| Morphological properties | Classification | Examples |
|---|---|---|
| Membrane (envelope) | Enveloped viruses | DNA envelope viruses. Examples include herpesviruses, hepadnaviruses (now split into two separate families: *Papillomaviridae* [which includes human papillomaviruses, or HPV] and *Polyomaviridae*) |
| | | RNA enveloped virus. Examples include filovirus, paramyxoviruses, rhabdovirus, and coronaviruses |
| | Naked or non-enveloped viruses | DNA non-enveloped viruses, e.g., adenoviruses, papovavirus |
| | | RNA non-enveloped virus e.g., picornaviruses, hepatitis A virus |
| Capsid structure (viral symmetry) | Icosahedral | Non-enveloped icosahedral: poliovirus, hepatitis A virus. |
| | | Enveloped virus Icosahedral: Yellow fever virus, HIV-1, herpes simplex viruses |
| | Helical | Enveloped virus: measles virus, mumps virus |
| | | Non-enveloped virus: tobacco mosaic virus |
| Complex structure | Combination of icosahedral and helical capsid | Poxviruses |

to the classification system of other cellular organisms – binomial nomenclature. The latest update on viral nomenclature can be found at `https://ictv.global`. This classification is based on the following:

- **Morphology**: Includes the shape of the virus particle, the presence of an envelope, and the symmetry of the capsid.
- **Genetic material**: Includes the type of nucleic acid (DNA or RNA) and its structure (single or double-stranded, segmented, etc.).
- **Host range**: Considers the types of organisms that the virus can infect.
- **Phylogenetics**: Considers the evolutionary relationships between viruses.

According to ICTV, virus classification starts from the most diverse realm and continues to a more specific nomenclature – species. This universally accepted classification of viruses employs hierarchical levels (suffix in brackets) from Realm (*-viria*), Subrealm (*-vira*), Kingdom (*-virae*), Subkingdom (*-virites*), Phylum (*-viricota*), Subphylum (*-viricota*), Class (*-viricete*), Subclass (*-viricetidae*), Order (*-virales*), Suborder (*-virineae*), Family (*-viridae*), Subfamily (*-virinae*), Genus (*-virus*), Subgenus (*-virus*), and to species (Tables 1.6 and 1.7).

**Table 1.6** Classification of viruses of medical importance based on ICTV classification.

| Families | Examples | Common name | Clinical observations/ disease/symptoms |
|---|---|---|---|
| **RNA viruses** | | | |
| *Flaviviridae* | Flaviviruses | Yellow fever virus | Severe hemorrhagic fever |
| | Hepatitis C viruses | | |
| *Picornaviridae* | Enteroviruses | Poliovirus | |
| | Hepatoviruses | Hepatitis A virus | |
| *Caliciviridae* | Caliciviruses | | Gastroenteritis |
| *Matonaviridae* | Rubiviruses | Rubella virus | Maculopapular rash, often misdiagnosed as measles or scarlet fever |
| *Togaviridae* | Alphaviruses | Chikungunya virus | Rash, arthritis |
| | | O'nyong'nyong virus | Rash, arthritis |
| | | Igbo-Ora virus | |
| *Astroviridae* | Mamastroviruses | | Infantile gastrointestinal infection |

(*Continued*)

**Table 1.6** (Continued)

| Families | Examples | Common name | Clinical observations/ disease/symptoms |
|---|---|---|---|
| *Reoviridae* | Rotaviruses | Rotavirus 1 | Gastroenteritis, vomiting, and fever |
| *Orthomyxoviridae* | Influenza A and B viruses | Human influenza virus | Respiratory infection, common cold and flu |
| *Paramyxoviridae* | Rubulaviruses | Newcastle disease and mumps virus | Respiratory infections and mumps |
| | Measles viruses | Measles virus | Measles |
| *Filoviridae* | Filovirus | Ebola virus | Severe hemorrhagic fever |
| | | Marburg virus | Severe hemorrhagic fever |
| *Coronaviridae* | Coronaviruses | Severe acute respiratory syndrome (SARS) | Respiratory infections and common cold |
| | | Coronavirus disease 2019 (COVID-19) | Respiratory infections and common cold |
| | | Middle East respiratory syndrome coronavirus (MERS-CoV) | Respiratory infections and common cold |
| *Arenaviridae* | Arenaviruses | Lassa virus | Severe hemorrhagic fever |
| *Rhabdoviridae* | Lyssaviruses | Rabies virus | Encephalitis |
| | | Mokola virus | Fever, convulsion |
| | Vesiculoviruses | | Flu-like symptoms |
| *Retroviridae* | Retroviruses | Human T-lymphocyte virus 1 | |
| | Lentiviruses | Human immunodeficiency virus (HIV) 1 and 2 | AIDS |
| *Hantaviridae* | Orthohantaviruses | Hantavirus | Hantavirus hemorrhagic fever with renal syndrome |
| *Phlenuiviridae* | Phleboviruses | Rift Valley fever phlebovirus | Fever, headaches, liver complications |
| **DNA viruses** | | | |
| *Poxviridae* | Molluscipoxviruses | Molluscum contagiosum virus | Skin disease |
| | Orthopoxviruses | Variola (smallpox) virus* | Fever, headache, fatigue |

**Table 1.6** (Continued)

| Families | Examples | Common name | Clinical observations/ disease/symptoms |
|---|---|---|---|
| *Adenoviridae* | Mastadenoviruses | Human adenovirus | Respiratory and gastrointestinal infection. Keratoconjunctivitis |
| *Papillomaviridae* | Papillomaviruses | Human papillomavirus | Warts or papilloma, precancerous lesions |
| *Polyomaviridae* | Polyomavirus | Polyomavirus hominis 1 (BK virus) | Nephropathy |
| | | Human polyomavirus 2 (JK virus) | Progressive multifocal leukoencephalopathy |
| *Parvoviridae* | Erythroparvoviruses | Human parvovirus B19 | *Erythema infectiosum* (fifth disease), arthritis, and arthralgia |
| | Dependoparvoviruses | Adeno-associated virus | |
| *Hepadnaviridae* | *Orthohepadnaviruses* | Hepatitis B | Liver cirrhosis, hepatocellular carcinoma |
| *Herpesviridae* | Varicelloviruses | Varicella-zoster virus (chickenpox) | Shingles and fever |
| | Cytomegaloviruses | Human cytomegalovirus | Cytomegalic inclusion disease and cerebral calcification |
| | Lymphocryptoviruses | Epstein–Barr virus | Swollen glands in the neck, fever, and rash |
| | Simplex viruses | Herpes simplex virus 1 and 2 | Mucosal ulcers, encephalitis, skin vesicles, and meningitis |
| | Roseola viruses | Roseola infantum (sixth disease) | Febrile seizures, fever, and rash |
| | Rhadinoviruses | Kaposi's sarcoma-associated herpesvirus | Kaposi's sarcoma, cancer (common in AIDS patients), and primary effusion lymphoma |

* Eradicated worldwide.

**Table 1.7** List of viruses of medical importance and the disease(s) they cause.

| Virus name | Family | Diseases |
|---|---|---|
| Human immunodeficiency virus (HIV) | *Retroviridae* | Acquired immunodeficiency syndrome (AIDS) |
| Hepatitis B virus (HBV) | *Hepadnaviridae* | Hepatitis B, liver cirrhosis, hepatocellular carcinoma |
| Hepatitis C virus (HCV) | *Flaviviridae* | Hepatitis C, liver cirrhosis, hepatocellular carcinoma |
| Influenza virus | *Orthomyxoviridae* | Influenza (flu) |
| Measles virus | *Paramyxoviridae* | Measles |
| Mumps virus | *Paramyxoviridae* | Mumps |
| Rubella virus | *Togaviridae* | Rubella (German measles) |
| Human papillomavirus (HPV) | *Papillomaviridae* | Cervical cancer, genital warts |
| Varicella-zoster virus (VZV) | *Herpesviridae* | Chickenpox, shingles |
| Epstein–Barr virus (EBV) | *Herpesviridae* | Infectious mononucleosis, Burkitt's lymphoma |
| Herpes simplex virus (HSV) | *Herpesviridae* | Herpes simplex (cold sores, genital herpes) |
| Cytomegalovirus (CMV) | *Herpesviridae* | Retinitis, pneumonia, encephalitis, and gastrointestinal disease. |
| Zika virus | *Flaviviridae* | Zika fever, congenital Zika syndrome |
| Dengue virus (DENV) | *Flaviviridae* | Dengue fever |
| Severe acute respiratory syndrome coronavirus (SARS-CoV) | *Coronaviridae* | Severe acute respiratory syndrome (SARS) |
| Middle East respiratory syndrome coronavirus (MERS-CoV) | *Coronaviridae* | Middle East respiratory syndrome (MERS) |
| SARS-CoV-2 | *Coronaviridae* | Coronavirus disease 2019 (COVID-19) |
| Norovirus | *Caliciviridae* | Acute gastroenteritis |
| Rotavirus | *Reoviridae* | Severe diarrhea in infants and young children |
| Rhinovirus | *Picornaviridae* | Common cold |
| Enterovirus | *Picornaviridae* | Hand, foot, and mouth disease, poliomyelitis |
| Rabies virus | *Rhabdoviridae* | Rabies |

**Table 1.7** (Continued)

| Virus name | Family | Diseases |
|---|---|---|
| Ebola virus | *Filoviridae* | Ebola virus disease |
| Marburg virus | *Filoviridae* | Marburg virus disease |
| Human T-cell leukemia virus (HTLV) | *Retroviridae* | Adult T-cell leukemia/lymphoma |
| Human parainfluenza virus (HPIV) | *Paramyxoviridae* | Parainfluenza |
| Respiratory syncytial virus (RSV) | *Paramyxoviridae* | Respiratory syncytial virus infection |
| Hantavirus | *Hantaviridae* | Hantavirus pulmonary syndrome, hemorrhagic fever with renal syndrome |
| Lassa virus | *Arenaviridae* | Lassa fever |
| Chikungunya virus | *Togaviridae* | Chikungunya fever |
| Yellow Fever virus | *Flaviviridae* | Yellow fever |
| West Nile virus | *Flaviviridae* | West Nile fever |
| Hepatitis A virus (HAV) | *Picornaviridae* | Hepatitis A |
| Hepatitis E virus (HEV) | *Hepeviridae* | Hepatitis E |
| Human T-lymphotropic virus 1 (HTLV-1) | *Retroviridae* | Adult T-cell leukemia/lymphoma |
| Human T-lymphotropic virus 2 (HTLV-2) | *Retroviridae* | HTLV-2 associated myelopathy |
| Human parvovirus B19 | *Parvoviridae* | Fifth disease (erythema infectiosum) |
| Human herpesvirus 6 (HHV-6) | *Herpesviridae* | Roseola infantum (sixth disease) |
| Human herpesvirus 7 (HHV-7) | *Herpesviridae* | Roseola-like symptoms |
| Human herpesvirus 8 (HHV-8) | *Herpesviridae* | Kaposi's sarcoma |
| John Cunningham virus (JC Virus) or human polyomavirus 2 | *Polyomaviridae* | Progressive multifocal leukoencephalopathy (PML) |
| BK Virus | *Polyomaviridae* | Nephropathy |
| Simian virus 40 (SV40) | *Polyomaviridae* | Potentially linked to certain cancers |
| Coxsackievirus | *Picornaviridae* | Hand, foot, and mouth disease, myocarditis |
| Echovirus | *Picornaviridae* | Aseptic meningitis, myocarditis |
| Rhinovirus | *Picornaviridae* | Common cold |

(*Continued*)

**Table 1.7** (Continued)

| Virus name | Family | Diseases |
|---|---|---|
| SARS-CoV | *Coronaviridae* | Severe acute respiratory syndrome (SARS) |
| MERS-CoV | *Coronaviridae* | Middle East respiratory syndrome (MERS) |
| SARS-CoV-2 | *Coronaviridae* | COVID-19 |
| Crimean–Congo hemorrhagic fever virus | *Nairoviridae* | Crimean–Congo hemorrhagic fever |
| Sin Nombre virus | *Hantaviridae* | Hantavirus pulmonary syndrome |
| Rift Valley fever virus | *Bunyaviridae* | Rift Valley fever |
| Toscana virus | *Bunyaviridae* | Toscana virus infection |
| Nipah virus | *Paramyxoviridae* | Nipah virus infection |
| Hendra virus | *Paramyxoviridae* | Hendra virus infection |
| Ross river virus | *Togaviridae* | Ross River fever |
| Eastern equine encephalitis virus | *Togaviridae* | Eastern equine encephalitis |
| Western equine encephalitis virus | *Togaviridae* | Western equine encephalitis |
| Venezuelan equine encephalitis virus | *Togaviridae* | Venezuelan equine encephalitis |
| La Crosse virus | *Bunyaviridae* | La Crosse encephalitis |
| Powassan virus | *Flaviviridae* | Powassan virus disease |
| Human metapneumovirus (hMPV) | *Paramyxoviridae* | Respiratory tract infections |
| Human bocavirus | *Parvoviridae* | Respiratory tract infections |
| Astrovirus | *Astroviridae* | Gastroenteritis |
| Sapovirus | *Caliciviridae* | Gastroenteritis |
| Colorado tick fever virus | *Reoviridae* | Colorado tick fever |
| Toscana virus | *Bunyaviridae* | Toscana virus infection |
| Monkeypox virus | *Poxviridae* | Monkeypox |
| Molluscum contagiosum virus | *Poxviridae* | Molluscum contagiosum |

Note: The list is inexcusable.

## 1.4 How Will Newly Identified Viruses Be Named?

Naming newly identified viruses involves a systematic process overseen by the ICTV. The goal is to ensure that the naming is standardized, informative, and avoids confusion. Here is a step-by-step overview of how newly identified viruses are named:

1. **Initial identification and characterization**
   **Detection:** New viruses are typically identified through research involving clinical samples, environmental samples, or laboratory investigations.
   **Characterization:** Scientists characterize the virus based on its genetic material, structure, replication mechanism, and pathogenic properties. Specifically, by determining whether it is DNA or RNA, its symmetry, the presence of an envelope, and other biological properties. If unknown, the information, such as the origin of the virus (animal or human origin) and the host range (types of cells or organisms the virus can infect), must be determined. Also, information regarding the disease association or any observed disease or symptoms linked to the virus must be determined or reported.
2. **Preliminary classification**
   Once sufficient virological data have been gathered – including genetic, structural, and biological characteristics – a preliminary classification is typically established for provisional scientific communication and further study. At this stage, the virus may be tentatively assigned to an existing family based on its key features or classified into a new family if it represents a novel group. Within that family, the virus is further placed into an appropriate genus, or a new genus may be proposed if required. The species designation follows, informed by a combination of sequence identity, host range, replication strategy, and pathogenicity.
3. **Submission to ICTV**
   **Proposal:** Following this initial classification, researchers proceed with a formal submission to the ICTV. This involves preparing a comprehensive proposal that outlines the proposed taxonomic placement, supported by detailed genomic sequences, structural characteristics, and relevant biological or pathological data.
   **Review:** The ICTV evaluates these proposals through peer review before ratifying any official changes to virus taxonomy. ICTV may set up specialized committees that review these proposals. This process involves peer review and may include consultation with other experts in virology.
4. **Naming convention**
   **Virus family and genus:** Names for new viruses are generally chosen based on established conventions. Families often have names that reflect shared properties, while genera are named to reflect more specific relationships.

**Species names:** New species names usually reflect the disease they cause or other relevant characteristics. The names are chosen to be descriptive and avoid overlap with existing names.

**Virus names:** The specific name of the virus itself can be derived from the disease it causes or distinctive features of the virus. Recently, naming viruses based solely on their place of discovery is no longer acceptable. The current approach emphasizes more descriptive, systematic, and sometimes neutral names.

5. **Reasons for changing previous naming practices**

**Avoiding stigmatization**

Naming viruses after geographic locations can sometimes lead to stigma or blame. For example, the early names of viruses such as the "Spanish flu" or "Wuhan coronavirus" can unfairly associate the disease with a specific region or population, potentially causing social or economic issues.

**Scientific precision**

Modern naming practices aim to reflect the virus's biological and genetic characteristics more accurately. This helps in better understanding and communicating about the virus's nature, replication, and classification.

**Globalization and spread**

Viruses can spread rapidly across the globe, making it less relevant to name them after a specific location. For instance, the name "Wuhan coronavirus" is unacceptable. The virus quickly became a pandemic infection, and the name was updated to "SARS-CoV-2" to reflect its relationship to SARS.

Also, in classifying viruses, it is important to avoid people's names to prevent any unintended offense or confusion. Similarly, avoiding the names of animals or food sources is important to prevent unnecessary concern or negativity toward certain animals or food items.

6. **Approval and publication**

**Approval:** The ICTV's executive committee reviews and approves the proposed names. This step ensures that the name follows the taxonomic rules and does not conflict with existing names.

**Publication:** Once approved, the names are published in the scientific literature and official ICTV resources. This includes databases, taxonomic lists, and other reference materials.

7. **Ongoing updates:**

As more information becomes available, the classification and naming of viruses may be updated. This ensures that the names remain accurate and relevant to the virus's characteristics and relationships.

## 1.5 Study Questions

### Case Study Questions

**1.1** A 30-year-old female patient presents with symptoms of fever, headache, and rash. Laboratory tests reveal the presence of a virus with a single-stranded RNA

genome and a lipid envelope. Based on this structural information:

**(a)** What type of virus is most likely causing the infection?

**(b)** Explain how the presence of a viral envelope might influence the virus's susceptibility to disinfectants and environmental conditions.

**1.2** A 24-month-old female is diagnosed with a severe respiratory infection. Electron microscopy reveals the presence of spike proteins, and molecular studies reveal an RNA genome. Considering the basic structure of this virus:

**(a)** What kind of virus can this be, and why?

**(b)** How could this impact public health since it is an RNA virus?

**(c)** What implications does the virus's RNA genome have for its replication strategy and potential treatments?

**1.3** A healthcare worker is accidentally exposed to a blood sample spilled on the bench from a patient previously diagnosed to be infected with a viral infection while working on a laboratory bench. The virus is known to have a helical capsid structure and an RNA genome. Based on the virus structure:

**(a)** What precautions should be taken to prevent further exposure or infection?

**(b)** Discuss the role of the helical capsid in the virus's ability to infect host cells.

**(c)** How might the RNA genome affect the mutation rate and the development of antiviral resistance?

**1.4** A 32-year-old European man presents with symptoms of fever, myalgia, severe headache, and abdominal pain. A few days later, he develops jaundice, and his laboratory tests show elevated liver enzymes. This is his first time traveling to a tropical region where mosquitoes are prevalent. Considering viral pathogenesis, which class of viruses is most likely responsible for his symptoms, and what is the significance of understanding the pathogenesis of this viral class?

**1.5** A 45-year-old woman presents with a persistent cough, chest pain, and shortness of breath. Imaging shows bilateral lung infiltrates. Laboratory results confirm a positive test for a virus with an RNA genome. Considering the classification based on viral pathogenesis, which class of virus is likely responsible, and why is it important to classify this virus based on the disease it causes?

**1.6** A 5-year-old child presents to the emergency department with a high fever, severe cough, and difficulty breathing. The child's condition rapidly deteriorated and was admitted to the intensive care unit. A respiratory sample was taken, and laboratory results revealed the presence of a virus with a single-stranded, negative-sense RNA genome. To which Baltimore group does this virus belong? What could be a potential virus responsible?

**1.7** A research laboratory was studying a newly discovered virus that causes hemorrhagic fever syndrome in humans. Initial genetic analysis shows that the virus has a single-stranded, positive-sense RNA genome. How would this virus be categorized? What is an example of a known virus in this group, and how does its classification inform the strategies for vaccine development?

## Objectives

**1.1 Which of the following is a characteristic of enveloped viruses?**
- (a) Increased resistance to environmental stress
- (b) Sensitivity to detergents and alcohol-based disinfectants
- (c) Replication exclusively in the nucleus
- (d) Presence of a helical capsid

**1.2 What structural component of a virus determines its shape?**
- (a) Lipid envelope
- (b) Nucleic acid type
- (c) Capsid
- (d) Spike proteins

**1.3 Which of the following statements about RNA viruses is true?**
- (a) They are always enveloped
- (b) They have a lower mutation rate compared to DNA viruses
- (c) They typically replicate in the host cell's cytoplasm
- (d) They have a double-stranded RNA genome

**1.4 In which way does the presence of a viral envelope affect the mode of transmission of a virus?**
- (a) Increases resistance to desiccation
- (b) Enhances transmission via the fecal–oral route
- (c) Requires close contact or fluid exchange for transmission
- (d) None of the above

**1.5 Which part of a virus is primarily responsible for its ability to attach and enter a host cell?**
- (a) Nucleic acid
- (b) Capsid
- (c) Envelope glycoproteins
- (d) Matrix proteins

**1.6 The presence of a double-stranded DNA genome is a characteristic of which virus family?**
- (a) *Flaviviridae*
- (b) *Herpesviridae*
- (c) *Picornaviridae*
- (d) *Retroviridae*

**1.7 Which of the following is a major reason why RNA viruses tend to have higher mutation rates than DNA viruses?**
- (a) RNA viruses replicate faster
- (b) RNA-dependent RNA polymerases lack proofreading ability
- (c) RNA viruses are more complex
- (d) RNA viruses infect more host species

**1.8 Which of the following virus families is primarily transmitted by arthropod vectors?**
- (a) *Herpesviridae*
- (b) *Papillomaviridae*
- (c) *Flaviviridae*
- (d) *Adenoviridae*

**1.9 What type of vector is commonly associated with the transmission of viruses in the *Togaviridae* family?**
- (a) Mosquitoes
- (b) Ticks
- (c) Fleas
- (d) Lice

**1.10 Which of the following is a key factor in the pathogenesis of viral infections?**
- (a) The virus's ability to evade the immune system
- (b) The host's blood type

(c) The ambient temperature
(d) The availability of antibiotics

**1.11 Which mechanism is commonly used by viruses to spread from one host cell to another within a host?**
(a) Direct cell-to-cell contact
(b) Humoral immunity
(c) Phagocytosis
(d) Extracellular matrix degradation

## References


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