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## MORPHOLOGY AND GENERAL PROPERTIES OF VIRUSES

### 53.1 INTRODUCTION

Viruses occupy the twilight zone that separates the 'living' from the 'non-living'. They do not have a cellular organization and contain only one type of nucleic acid, either DNA or RNA but never both.

The medical importance of viruses lies in their ability to cause a very large number of human diseases. Viral diseases range from minor ailments like common cold to terrifying diseases like rabies and AIDS.

In this chapter, we shall be discussing the morphology and general properties of viruses.



### OBJECTIVES

After reading this lesson you will be able to:

- explain the concept of viruses, in relation to other microorganisms
- describe the morphological features of viruses
- explain the multiplication of viruses (replication)
- describe the methods of cultivation of viruses
- explain the classification and naming (nomenclature) of viruses

### 53.2 SECTION

#### 53.2.1 Concept of Viruses in relation to other Organisms

Viruses occupy the twilight zone that separates the 'living' from the 'non-living'. They do not have a cellular organization and contain only one type of nucleic



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acid, either DNA or RNA but never both. Viruses are obligate intracellular parasites. They lack the enzymes necessary for protein and nucleic acid synthesis. They are dependent for replication on the synthetic machinery of host cells. They multiply by a complex process and not by binary fission. They are unaffected by antibacterial antibiotics. The differences between viruses and bacteria are shown in Table 53.1.

Viruses cause a wide range of human diseases. They cause infections like common cold, chicken pox, measles, viral encephalitis, rabies and AIDS.

**Table 53.1: Differences between bacteria and viruses**

Properties	Bacteria	Viruses
Cellular organization	Present	Absent
Growth on inanimate media	Yes	No
Binary fission	Yes	No
DNA and RNA	Both are present	Either DNA or RNA
Ribosomes	Present	Absent
Sensitivity to antibacterial antibiotics	Yes	No

**53.2.2 Morphology of Viruses**

**Size:** The extracellular infectious virus particle is called virion. Viruses are much smaller than bacteria. They are too small to be seen under the light microscope. Some large viruses like the poxviruses can be seen under the light microscope when suitably stained.

The viruses range in size from 20 nm to 300 nm. Poxviruses are one of the largest viruses and parvoviruses are one of the smallest viruses. The earliest method of estimating the size of virus particles was by passing them through collodion membrane filters of graded porosity. The average pore diameter of the finest filter that permitted passage of the virion gave an estimate of its size. With the development of the ultracentrifuge, a second method became available. From the rate of sedimentation of the virus in the ultracentrifuge, the particle size could be calculated using Stoke’s law. The third and the most direct method of measuring virus size is electron microscopy. By this method, both the shape and size of virions can be studied.

**Structure, shape and symmetry:** The virion consists essentially of a nucleic acid surrounded by a protein coat, the **capsid**. The capsid with the enclosed nucleic acid is called the **nucleocapsid**. The capsid protects the nucleic acid from harmful agents in the environment. It is composed of a large number of capsomers which form its morphological units. The chemical units of the capsid are polypeptide molecules which are arranged symmetrically. They form a shell around the nucleic acid.



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The capsid shows two kinds of symmetry – icosahedral (cubical) and helical. An icosahedron is a polygon with 12 vertices and 20 facets or sides. Each facet is in the shape of an equilateral triangle. Two types of capsomers are present in the icosahedral capsid. They are the pentagonal capsomers at the vertices (pentons) and the hexagonal capsomers making up the facets (hexons). There are always 12 pentons but the number of hexons varies with the virus group. Examples of viruses with icosahedral symmetry of the capsid are Adenovirus and Herpes Simplex Virus. In the nucleocapsids with helical symmetry, the capsomers and nucleic acid are wound together to form a helical or spiral tube, for example tobacco mosaic virus. All viruses do not show the typical icosahedral or helical symmetry. Some, like the poxviruses, show a complex symmetry.

Virions may be enveloped or nonenveloped. The envelope of viruses is derived from the host cell membrane. This occurs when the virus is released from the host cell by budding. Protein subunits may be present as projecting spikes on the surface of the envelope. They are called **peplomers**. The influenza virus carries two kinds of peplomers: haemagglutinin and neuraminidase. Haemagglutinin is a triangular spike and neuraminidase is mushroom-shaped. Envelope is sensitive to the action of lipid solvents. Envelopes confer chemical, antigenic and biological properties on viruses.

The overall shape of the virus particle varies in different groups of viruses. Most animal viruses are roughly spherical. The rabies virus is bullet shaped. Poxviruses are brick-shaped.

**Chemical properties:** Viruses contain only one type of nucleic acid, either DNA or RNA. Viruses are unique because they carry genetic information on RNA. This property is not seen in any other organism in nature. Viruses also contain protein which makes up the capsid. Enveloped viruses contain lipids derived from the host cell membrane. Most viruses do not have enzymes for the synthesis of viral components or for energy production. Some viruses have enzymes, for example the influenza virus has neuraminidase.

**Resistance:** Viruses are destroyed by heat except a few. They are stable at low temperatures. For long term storage, they are kept at  $-70^{\circ}\text{C}$ . A better method for prolonged storage is lyophilisation or freeze-drying. Viruses are inactivated by sunlight, UV rays and ionising radiation. They are, in general, more resistant than bacteria to chemical disinfectants. Phenolic disinfectants have a weak action on viruses.

### 53.2.3 Multiplication of Viruses

Multiplication of viruses is called viral **replication**. Viruses contain the genetic information for their replication but they lack the enzymes. They depend on host cell machinery for replication. The viral replication cycle can be divided into six



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phases – adsorption, penetration, uncoating, biosynthesis, maturation and release.

**Adsorption:** In this phase, the virus gets attached to the host cell. The host cell should have specific receptors on its surface. These receptors recognize viral surface components. This cell-virus interaction helps the virus to attach to the host cell surface.

**Penetration:** In this phase, the virus enters into the host cell. Bacteria have rigid cell wall. So, viruses which infect bacteria cannot penetrate into the bacterial cell. Only the nucleic acid of the virus enters the bacterial cell. Animal and human cells do not have cell walls. Therefore, whole virus enters the cell. Virus particle may be engulfed by a process called **viropexis**. In case of enveloped viruses, the viral envelope may fuse with the cell membrane of the host cell. Then the nucleocapsid is released into the cytoplasm.

**Uncoating:** This is the process in which the outer layers and capsid of the virus are removed. This mostly occurs by the action of lysosomal enzymes of the host cell. This can also occur by a viral uncoating enzyme. Finally, the viral nucleic acid is released into the cell.

**Biosynthesis:** In this phase, the viral nucleic acid and capsid are synthesised. The enzymes necessary in the various stages of viral synthesis, assembly and release are also synthesised. Certain ‘regulator proteins’ are synthesised. They shut down the normal metabolism of the host cell. They direct the production of viral components. In general, most DNA viruses synthesise their nucleic acid in the host cell nucleus. Exceptions are the poxviruses. They are DNA viruses, but they synthesise all their components in the host cell cytoplasm. Most RNA viruses synthesise all their components in the cytoplasm. Orthomyxoviruses and some paramyxoviruses are exceptions. They synthesise some components in the host cell nucleus. Biosynthesis consists essentially of the following steps:

1. Transcription of messenger RNA (mRNA) from the viral nucleic acid
2. Translation of mRNA into “early proteins” or “non-structural proteins”. They are enzymes responsible for the synthesis of viral components.
3. Replication of viral nucleic acid
4. Synthesis of “late proteins” or “structural proteins”. They are the components of daughter virion capsids.

**Maturation:** This is the assembly of daughter virions following the synthesis of viral nucleic acid and proteins. It can take place in the host cell nucleus or cytoplasm. Herpesviruses and adenoviruses are assembled in the nucleus. Picornaviruses and poxviruses are assembled in the cytoplasm.

**Release:** Viruses which infect bacteria (bacteriophages) are released by lysis of the infected bacterium. Animal viruses are usually released without cell lysis.

Myxoviruses are released by budding from the cell membrane. The host cell is unaffected. Daughter virions are released into the surrounding medium and may infect other cells. In some viruses (for eg. varicella), transmission occurs directly from cell to cell. In this case, there is very little free virus in the medium. The poliovirus causes cell damage and may be released by cell lysis.

From the stage of penetration till the appearance of mature daughter virions, the virus cannot be demonstrated inside the host cell. During this period, the virus seems to disappear. This is called the “eclipse phase”. The time taken for a single cycle of replication is about 15-30 minutes for bacteriophages. It is about 15-30 hours for animal viruses. A single infected cell may release a large number of progeny virions.



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### 53.2.4 Methods of cultivation of viruses

Viruses are obligate intracellular parasites. They do not grow on culture media used for bacteria. The methods used for cultivation of viruses are:

- 1. Animal inoculation:** Monkeys were used for the isolation of the poliovirus by Landsteiner and Popper in 1909. Infant mice are used for the isolation of coxsackievirus and arboviruses (dengue, chikungunya). Mice may be inoculated by several routes – intracerebral, subcutaneous, intraperitoneal or subcutaneous. Other animals like guinea pigs, rabbits and ferrets are used in some situations.
- 2. Embryonated eggs:** The embryonated hen's egg was first used for the cultivation of viruses by Goodpasture in 1931. This method was further developed by Burnet. Different parts of the egg are used for the cultivation of different viruses. Herpes simplex virus, when inoculated into the chorioallantoic membrane, produces visible lesions called pocks. Inoculation into the amniotic sac is done for the isolation of influenza virus. Yolk sac inoculation is done for the isolation of rabies virus.
- 3. Cell culture:** Probably, the first application of tissue culture in virology was by Steinhardt and colleagues in 1913. They maintained the vaccinia virus in fragments of rabbit cornea. The turning point was the cultivation of poliovirus which was demonstrated by Enders, Weller and Robbins in 1949. They showed that poliovirus, till then considered a strictly neurotropic virus, could be grown in tissue culture of non-neural origin.

**The various types of tissue cultures are described as follows:**

- (i) Organ culture:** Small bits of organs can be maintained in vitro for days and weeks, preserving their original architecture and function. Organ culture is useful for viruses which are highly specialised parasites of certain organs. For example, tracheal ring organ culture is used for the isolation of coronavirus, a respiratory pathogen.



- (ii) **Explant culture:** Fragments of minced tissue can be grown as 'explants' embedded in plasma clots. They may also be cultivated in suspension. Adenoid tissue explant cultures were used for the isolation of adenovirus.
- (iii) **Cell culture:** This is routinely used for growing viruses. Tissues are dissociated into the component cells by the action of enzymes and mechanical shaking. The cells are washed, counted and suspended in a growth medium. The growth medium consists of essential amino acids, glucose, vitamins, salts and a buffer. Antibiotics are added to prevent bacterial contamination. The cell suspension is put into bottles, tubes and petridishes. The cells adhere to the glass or plastic surface, divide and form a confluent monolayer sheet within a week. Cell culture is further classified on the basis of origin, chromosomal characters and the number of generations through which they can be maintained. It is of three types – primary cell culture, diploid cell strain and continuous cell lines. Primary cell cultures are normal cells freshly taken from the body and cultured. They are capable of only limited growth in culture. They cannot be maintained in serial culture. Examples are monkey kidney, human embryonic kidney and chick embryo cell cultures. Diploid cell strains are cells of a single type that retain the original diploid chromosome number and karyotype during serial subcultivation for a limited number of times. After about fifty serial passages, they undergo 'senescence'. Diploid strains developed from human fibroblasts are a good example. Continuous cell lines are cells of a single type, usually derived from cancer cells. They are capable of continuous serial cultivation indefinitely. Hela cell lines are derived from carcinoma of the cervix. Cell culture is used for the isolation of viruses and their cultivation for vaccine production.

Viruses in cell cultures can be detected by various methods like cytopathic effect, special staining techniques and detection of viral nucleic acid by molecular techniques like polymerase chain reaction (PCR). Cytopathic effect is the morphological change in the cultured cells which is produced by the virus growing in those cells. These changes can be seen by microscopic examination of the cell cultures. The cytopathic effects (CPE) produced by different groups of viruses are characteristic and help in the presumptive identification of virus isolates. For example, measles virus produces syncytium formation; adenovirus produces large granular clumps resembling bunches of grapes; enteroviruses produce crenation of cells and degeneration of the entire cell sheet.

### 53.2.5 Classification and naming of viruses

Till about 1950 little was known of the basic properties of viruses. They were named haphazardly, based on the diseases they caused or on the place of their isolation. They were grouped according to affinity to different systems or organs





of the body (tropism). So, human viruses were classified as dermatropic, that is those producing skin lesions (smallpox, chickenpox, measles), neurotropic, that is those affecting the nervous system (poliomyelitis, rabies), pneumotropic, that is those affecting the respiratory tract (influenza, common cold) and viscerotropic, that is those affecting visceral organs (hepatitis). Bawden (1941) made the pioneering suggestion that viral nomenclature and classification should be based on the properties of viruses and not upon host responses. From the early 1950s, viruses began to be classified into groups based on their physiochemical and structural features. Nomenclature and classification are now the official responsibility of the International Committee on Taxonomy of Viruses (ICTV).

Viruses are classified into two main divisions based on the type of nucleic acid they possess: riboviruses contain RNA and deoxyriboviruses contain DNA. Further classification is based on other properties like strandedness of nucleic acid, symmetry of nucleic acid, presence of envelope, size and shape of virion and number of capsomeres.

**DNA viruses:** A few medically important families of DNA viruses are - Herpesviridae, Adenoviridae, Hepadnaviridae, Parvoviridae and Papillomaviridae.

The Herpesviridae family consists of enveloped double-stranded DNA viruses having an icosahedral capsid. Examples of this family are herpes simplex virus and varicella zoster virus. Herpes simplex virus causes skin lesions like herpes labialis. It can also cause viral encephalitis. Parvoviridae consists of non-enveloped single-stranded DNA viruses, for example Parvovirus B19. The Hepadnaviridae family includes Hepatitis B virus which is a partially double-stranded DNA virus. Papillomaviridae family includes human papilloma virus which is responsible for causing skin warts.

**RNA viruses:** Some medically important families of RNA viruses are - Picornaviridae, Orthomyxoviridae and Paramyxoviridae, Flaviviridae, Rhabdoviridae and Retroviridae. Members of the family Picornaviridae are small (20-30 nm), non-enveloped, icosahedral viruses with single-stranded RNA genome. Examples include poliovirus and coxsackievirus. The viruses included in Orthomyxoviridae are enveloped viruses carrying haemagglutinin and neuraminidase peplomers on the envelope. The genome consists of single-stranded RNA in several (eight) pieces. Thus, they have a segmented genome. An example of this family is influenza virus. Flaviviridae consists of enveloped single-stranded RNA viruses. Examples include yellow fever virus, Japanese encephalitis virus and dengue virus. The members of Retroviridae family are enveloped RNA viruses which have a special enzyme called 'reverse transcriptase'. This enzyme is an RNA dependent DNA polymerase. It is required in the synthesis of DNA from RNA. An example of the Retroviridae family is Human Immunodeficiency Virus (HIV) which causes AIDS (acquired immunodeficiency syndrome).

## MODULE

Microbiology



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### Morphology and General properties of Viruses

Based on the mechanism of replication, Baltimore (1970) categorised viruses into seven categories. This is called the Baltimore classification.



#### INTEXT QUESTIONS 53.1

1. The genetic material in viruses is:  
A. DNA only  
B. RNA only  
C. Either DNA or RNA  
D. Both DNA and RNA
2. Protein subunits presenting as projecting spikes on the surface of the envelope are called:  
A. Capsomeres  
B. Capsid  
C. Nuceocapsid  
D. Peplomers
3. Which of the following is the correct sequence of viral replication?  
A. Penetration, uncoating, adsorption, biosynthesis, maturation and release  
B. Adsorption, penetration, uncoating, biosynthesis, maturation and release  
C. Biosynthesis, penetration, uncoating, adsorption, maturation and release  
D. Adsorption, biosynthesis, maturation, uncoating, penetration and release
4. Methods used for viral cultivation are:  
A. Cell culture  
B. Animal inoculation  
C. Embryonated eggs  
D. All of the above
5. Baltimore classified viruses on the basis of:  
A. Diseases caused by them  
B. Structure  
C. Replication mechanism  
D. Physiochemical properties



#### WHAT YOU HAVE LEARNT

- Viruses do not strictly fall into the category of unicellular organisms because they do not have a cellular organisation.
- Viruses are obligate intracellular parasites which contain only one type of nucleic acid (DNA or RNA). They are dependent on the synthetic machinery of the host cell for replication.
- The extracellular infectious virus particle is called the virion. The viruses are smaller than bacteria ranging in size from 20-300 nanometers.



## Morphology and General properties of Viruses

- The virion consists of a central nucleic acid core surrounded by a protein coat called capsid. Nucleocapsid consists of the capsid enclosing the nucleic acid core.
- The capsid protects the nucleic acid from inactivation and is made up of a large number of capsomeres.
- The capsid may have icosahedral, complex or helical symmetry.
- The virions may be enveloped or non-enveloped. The envelope is a lipoprotein. Protein subunits which occur as projecting spikes on the envelope surface are called peplomers as seen in influenza virus (haemagglutinin and neuraminidase).
- Enveloped viruses are susceptible to organic solvents. The envelope helps the virus in attachment to the host cell surface.
- Most animal viruses are roughly spherical; some are irregular and pleomorphic. Some have distinctive shapes like bullets (rabies) and bricks (poxviruses).
- Most viruses are inactivated by heat, in seconds at 56°C. Viruses are inactivated if stored for several days at 4 °C, but survive storage at -70 °C. Viruses are inactivated by sunlight, ultraviolet rays and ionising radiation. Viruses are easily destroyed by chemical disinfectants like chlorine, hydrogen peroxide and hypochlorite.
- Viral multiplication consists of six sequential phases – adsorption, penetration, uncoating, biosynthesis, maturation and release from the host cell.
- Cultivation of viruses is important for the diagnosis of viral infections and the production of vaccines. Viruses can be cultivated by animal inoculation, inoculation into embryonated eggs and tissue culture. Tissue culture consists of organ culture, explants culture and cell culture. Cell culture is further classified into primary cell culture, diploid cell strains and continuous cell lines. This classification is based on the origin of cells, their chromosomal characters and the number of generations through which they can be maintained.
- Viruses in cell cultures can be identified by cytopathic effects (CPE), special staining techniques and molecular techniques like PCR.
- Viruses were previously classified on the basis of their affinity towards different systems or organs. Recently, they have been classified on the basis of their physiochemical properties and structure. The International Committee on Taxonomy of Viruses (ICTV) is responsible for the classification and naming of viruses.
- Viruses are broadly classified into DNA and RNA viruses.
- Baltimore (1970) classified viruses on the basis of their replication mechanisms.

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## Morphology and General properties of Viruses



### TERMINAL QUESTIONS

1. Describe the differences between bacteria and viruses.
2. Describe the morphology of viruses under the following headings – structure, shape and symmetry.
3. Describe the methods of viral cultivation.
4. Describe the various types of tissue cultures with suitable examples.
5. Define Cytopathic effect (CPE). Give suitable examples of viruses showing CPE.
6. Enumerate three DNA viruses and three RNA viruses along with the disease caused by each one of these
7. Give stepwise detailed description of viral replication.



### ANSWERS TO INTEXT QUESTIONS

#### 53.1

1. C. Either DNA or RNA
2. D. Peplomers
3. B. Adsorption, penetration, uncoating, biosynthesis, maturation and release
4. D. all of the above
5. C. Replication mechanism