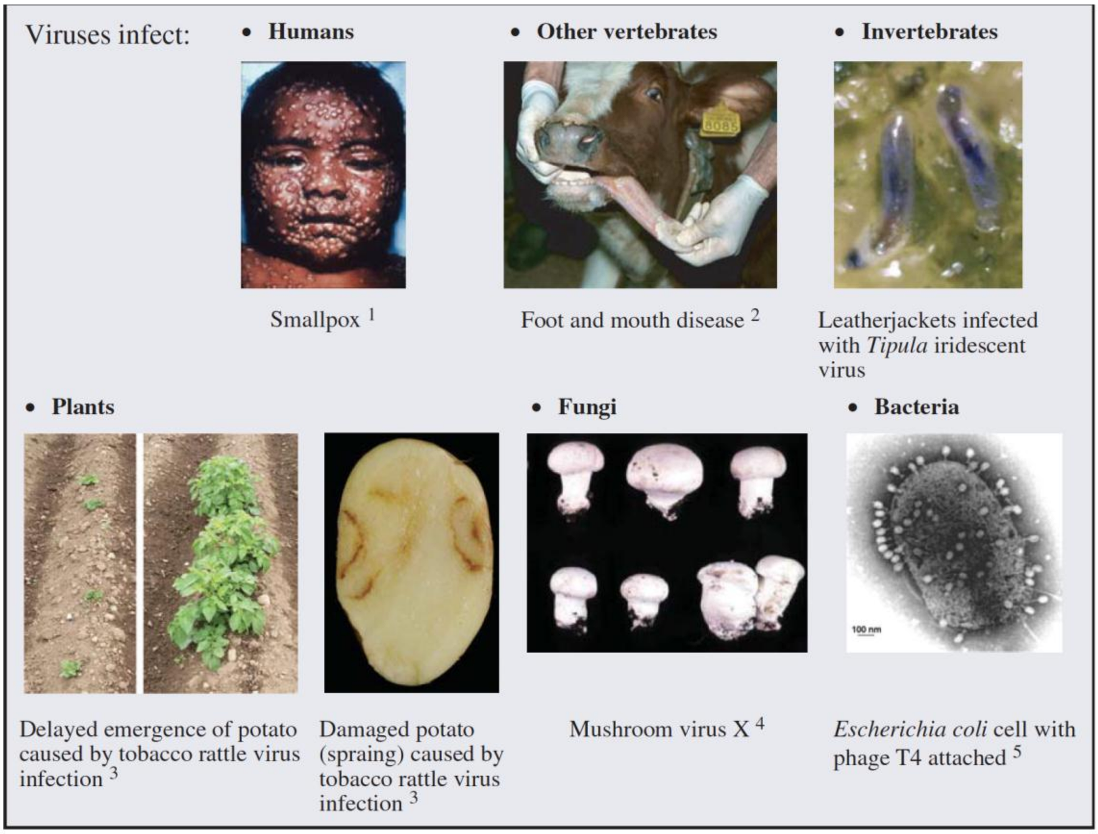
General properties of viruses

المرحله الثالثه /فايروسات
د. انتظار علاوي جعفر / فرع الاحياء المجهريه / كليه الطب / جامعه ذي قار
PhD. M.Sc. Microbiology

Introduction

The viruses are too small to be seen with a light microscope. Their small size allows them to pass through filters that areused to retain back bacteria in contaminated fluids. Hence,they were first described as filterable agents. Viruses, like othermicroorganisms (e.g., bacteria, fungi, and parasites), are theinfectious agents that are associated with disease in humans.

The viruses unlike other infectious agents are **obligate intracellular parasites**, i.e., **they absolutely require living host cells in order to multiply**. In addition, viruses replicate by assembly ofthe individual components rather than by binary fission.



Virology: Principles and Applications John B. Carter and Venetia A. Saunders
© 2007 John Wiley & Sons, Ltd ISBNs: 978-0-470-02386-0 (HB); 978-0-470-02387-7 (PB)

The viruses show the following features:

1. They are filterable agents.
2. They are obligate intracellular parasites.
3. They contain a single type of nucleic acid, i.e., either DNA or RNA, but not both.
4. The virion of the virus particle consists of a nucleic acidgenome packaged into a protein coat (capsid), which itselfis sometimes enclosed by an envelope of lipid, proteins,and carbohydrates known as envelope.
5. They multiply inside the living cells by using the synthesizingmachinery of the host cell.

6. They replicate by the assembly of the individual components and do not replicate by division, such as binaryfission.
7. They have a few or no enzymes for their own metabolism. They always use host cell machinery to produce their components, such as viral messenger RNA (mRNA),protein, and identical copies of the genome.

The differences between bacteria and viruses are summarizedin **Table -1**. The viruses affect a wide range of hosts. There areviruses that infect invertebrates, vertebrates, plants, protists, fungi,and even bacteria. In medical microbiology, we are concernedmainly with viruses that infect either humans or bacteria. Theviruses that infect bacteria are known as bacteriophages or phages.

Table -1 Comparison of bacteria, rickettsiae, chlamydiae, and viruses

Character Character	Typical bacteria	Rickettsiae	Chlamydiae	Viruses
Intracellular parasite	No	Yes	Yes	Yes
Cellular organization	Yes	Yes	Yes	No
Plasma membrane	Yes	Yes	Yes	No
Replication by binary fission	Yes	Yes	Yes	No
Growth on inanimate media	Yes	No	No	No
Pass through bacteriological filters	No	No	Yes	Yes
Possess both DNA and RNA	Yes	Yes	Yes	No
ATP-generating metabolism	Yes	Yes	No	No
Ribosome	Yes	Yes	Yes	No
Sensitive to antibiotics	Yes	Yes	Yes	No
Sensitive to interferon	No	No	Yes	Yes

Morphology of Viruses

The extracellular, infectious viral particle is called the virion:

- It is a complete, fully developed infectious viral particle composed of nucleic acid surrounded by a protein coat. The latter protects it from the environment and is a vehicle of transmission from one host to another. The viruses are classified on the basis of differences in structure of these coats.
- The virion may be **enveloped** by being surrounded by a membrane or may be **nonenveloped**, without being surrounded by a membrane.
- The virion may also contain essential or accessory enzymes or other proteins.

Size

The clinically important viruses vary widely in their size (Fig. 50-1). They range from as small as 20-nm viruses (picornaviruses)to as large as 300-nm viruses (poxvirus). Passingthe viruses through collodion membrane filter with differentpore sizes was the earliest method of determining the size of the virus. Subsequently, ultracentrifugation method was usedto determine the size of the viruses by calculating from therate of sedimentation of virus in the ultracentrifuge. Electronmicroscopy is the most recent method for determining the sizeas well as the shape of the virus.

Structure and Symmetry of Virus

Viral structure

The virion consists of a nucleic acid core, the genome , surrounded by a protein coat, the capsid (Fig. 50-2). The capsid together with the enclosed nucleic acid is known as the nucleocapsid .Some viruses are surrounded by envelopes.

The capsid

The nucleic acid of a virus is surrounded by a protein coat called the **capsid**. Each capsid is composed of a large number ofprotein subunits (polypeptides) called capsomeres, which formits morphological units. The polypeptide molecules composingthe capsomeres are of a single type in some viruses, while inother viruses several types may be present. The arrangement ofcapsomeres is characteristic of a particular type of virus.

Functions of capsid

- Symmetrically arranged polypeptide molecules of capsidform an impenetrable shell around the nucleic acid core.
- The capsid facilitates entry of viral genome into the hostcells by adsorbing readily to cell surfaces.
- The capsid of the virus protects its nucleic acid from theactivity of nuclease enzymes in biological fluids and therebyfacilitates attachment of virus to target cells in the host

The structure of the viral capsid is best demonstrated by X-raycrystallography or electron microscopy. On the basis of capsidstructure, the viruses can be classified into different morphologicaltypes as follows:

Helical viruses: The helical viruses appear rod-like and may be rigid or flexible. The viral genome is found within hollow cylindricalcapsid that has a helical structure. The examples of helicalviruses include rabies virus, Ebola hemorrhagic virus, etc.

Polyhedral viruses: The polyhedral viruses appear as manysidedviruses. The viruses consist of capsids in the shape ofan icosahedron. It is a regular polyhedron with 20 triangularfaces. The capsomere of each face forms an equilateral triangle.Adenovirus is an example of polyhedral virus in the shape oficosahedron.

Enveloped viruses: The helical and polyhedral viruses when covered by envelope are called as enveloped helical or envelopedpolyhedral viruses, respectively. Influenza virus is an exampleof enveloped helical virus, and herpes simplex virus is an exampleof enveloped polyhedral virus.

Complex viruses: Some viruses, such as viruses of bacteria (e.g., bacteriophages), have complicated structures and arecalled complex viruses. The detailed structure and function ofbacteriophages are described in Chapter 54.

The envelope

In some viruses, the capsid is covered by an envelope, such viruses are called enveloped viruses. **All of the negative-stranded RNA viruses are enveloped**. The viruses that lack envelope are**called nonenveloped or naked viruses**. Properties of the envelopedand naked viruses are summarized in Tables 50-2 and50-3, respectively.
The virion envelope usually consists of lipids, proteins, and glycoproteins. It has a membrane structure similar to cellularmembrane of the host cell. The viral envelope does not containany cellular proteins, even though viruses are released fromthe host cell by an extrusion process that coats the virus witha layer of host cell plasma membrane that becomes the viralenvelope. In most cases, the envelope contains proteins that aredetermined and encoded by viral nucleic acid. The lipid componentof

the envelope is usually of host cell origin.Depending on the virus, the envelopes of the viruses may ormay not be covered by spikes. The spikes are glycoprotein-likeprojections on the outer surface of the envelope. Most spikesact as **viral attachment protein (VAP)**.

■ The VAP that binds to red blood cells is called hemagglutinin. The ability of certain viruses, such as influenza virusto agglutinate red blood cells is due to the presence of thesehemagglutinins. The process is called hemagglutination andit forms the basis of hemagglutination inhibition test usedin the viral serology.

■ The VAPs in some viruses perform different functions, such as neuraminidase activity of influenza virus, fusion glycoproteinof paramyxovirus and C3b receptor associated withherpes simplex virus.The structural components of envelope remain biologicallyactive only in aqueous solutions and are readily destroyed bydrying or on treatment with acids, detergents, and solvents,such as ether, leading to inactivation of virus. They are rapidlykilled in stomach due to sensitivity of enveloped componentsto gastric acidity. Therefore, most of the enveloped viruses areusually transmitted through body fluids, such as blood, respiratorydroplets, tissue exudates, etc.

Viral symmetry

Three types of symmetry are observed depending on the arrangement of the capsid around the nucleic acid core(genome). These are

(a) icosahedral (cubical)

(b) helical

(c) complex symmetry.

Icosahedral symmetry: Two types of capsomeres constitute the icosahedral capsule. They are the pentagonal capsomeres orthe vertices (pentons) and hexagonal capsomeres making up thefacets (hexons) (Fig. 50-3). There are always 12 pentons, but thenumber of hexons varies with the virus group.Each penton has fivefold symmetry (pentamer or pentagon)in the shape of an equilateral triangle. This pentamer symmetryis found in simple viruses, such as the picornaviruses and parvoviruses.In picornaviruses, each pentamer is made up of fiveprotomers, each of which is composed of three subunits of fourdifferent proteins.The hexamer symmetry is usually found in large capsidvirions, such as herpesviruses and adenoviruses. Hexons aremade up of certain structurally distinct capsomeres betweenthe pentons at the vertices. The presence of hexon extends theicosahedral and is called an icosadeltahedral. The adenovirusnucleocapsid has 12 pentons and 240 hexons, whereas theherpesvirus nucleocapsid has 12 pentons and 150 hexonssurroundedby an envelope.

Table 50-2

Component	Properties	Biological functions
Membrane	Environmentally labile; disrupted by acid,detergents, drying, and heat	Must stay wet
Lipids	Modifies cell membrane during replication	Cannot survive in the gastrointestinal tract
Proteins	Released by budding and cell lysis	Spreads in large droplets, secretions, organ transplants, and blood transfusion
Glycoprotein		Does not need to kill the

		cell to spread
		May need antibody-and cell-mediated immune response for protection and control
		Elicits hypersensitivity and inflammation to cause immunopathogensis

Table 50-3

component	Properties	Biological functions
protien	Environmentally stable to temperature, acid, proteases, detergents, and dying	Can be spread easily through fomites, from hand to hand, by dust, and by small droplets
	Is released from cell by lysis	Can dry out and retain infectivity
		Can survive the adverse conditions of the gut
		Can be resistant to detergents and poor sewage treatment
		Antibody may be sufficient for immunoprotection

Figure

Helical symmetry: The nucleic acid and the capsomeres are wound together to form a spherical or spiral tube. The viruseswith helical structure usually appear as rods and their capsomeresself-assemble on the RNA genome into rods extending tothe length of the genome. These capsomeres cover and protectthe RNA. The tubular nucleocapsid structure may be rigid asin tobacco mosaic virus, but may be pliable and may be coiledon itself in case of some other animal viruses. Helical nucleocapsidsare usually demonstrated within the envelope of mostnegative-stranded RNA viruses.

Complex symmetry: Some viruses may not exhibit either icosahedral or helical symmetry but instead may exhibit a complexsymmetry. For example, poxvirus showsa complex symmetry.

Shape

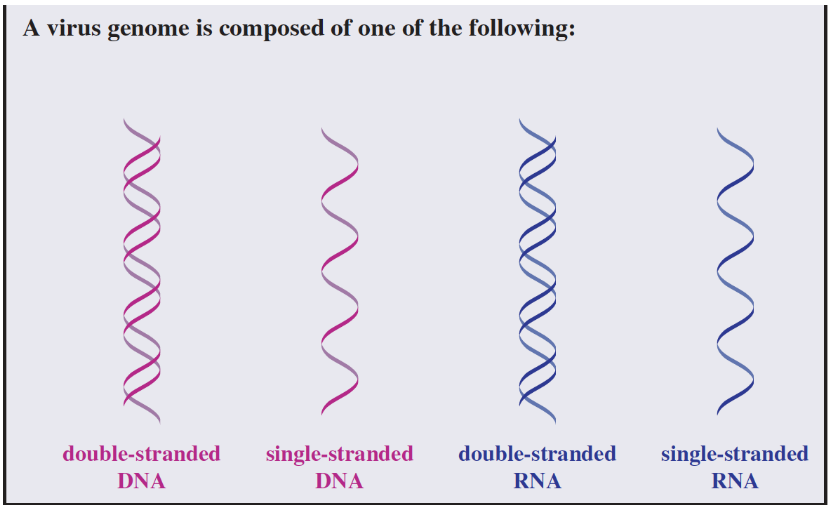
Most of the enveloped viruses are round or pleomorphic with exception of poxvirus and rhabdovirus. Rhabdovirus is a bulletshapedvirus, whereas poxvirus is brick shaped.

Viral Nucleic Acid, Proteins, and Lipids

Viral nucleic acid

The genome of the virus consists of either DNA or RNA but never both (Fig. 50-4). The DNA can be single stranded or double stranded. Depending on the virus, the DNA can be linear or circular. The RNA can be either positive sense (_) like mRNA or negative sense (_), double stranded (_ /_), or ambiguous (containing _ and _ regions of RNA attached to it). In some RNA viruses, such as the influenza virus, the

RNA genome is in several separate segments, each segment encoding an individual gene.The total amount of nucleic acid may vary from a fewthousand nucleotides to as many as 250,000 nucleotides



Viral proteins and lipids

Viruses contain proteins, which constitute capsids. The viral protein protects the nucleic acid as well as determines theantigenic specificity of the virus. In addition, the envelopedviruses contain lipids, which are derived from the host cellmembrane.

Susceptibility to Physical and ChemicalAgents

Disinfectants

The viruses are usually more resistant than bacteria to chemical disinfectants. Most viruses are relatively resistant to phenol.The oxidizing agents, such as hydrogen peroxide, potassiumpermanganate, hypochlorite, and organic iodine compounds,are most active antiviral disinfectants. Formaldehyde and_ -propiolactone are also active virucidal agents, which arecommonly used for preparation of killed viral vaccines.The chlorination of drinking water is useful for killingmost of the common viruses with exception of hepatitisA and polioviruses. These two viruses are relatively resistant tochlorination.

Temperature

Most of the viruses with few exceptions are highly heat labile. They are inactivated within seconds at 56°C, within minutes at37°C, and within days at 4°C.

■ The viruses such as influenza, measles, and mumps are very labile and may survive outside the host only for a few hours.

■ Other viruses, such as polio and hepatitis A, are relatively much stable and may survive for many days, weeks, or evenmonths in the environment

■ Viruses, such as hepatitis B, show resistance to heating at 60°C for 60 minutes; slow viruses, such as scrapie virus, areresistant to autoclaving at 121°C for 15 minutes.The viruses are stable at low temperature. They can be stored by freezing at _35°C or _70°C. Lyophilization or freeze-drying isuseful for long-term storage of the viruses. The poliovirus is anexception, as it does not withstand freeze-drying.

pH

The viruses usually remain viable in a pH range of 5–9, but aresensitive to extremes of acidity and alkalinity. Rhinoviruses arevery susceptible to acidic pH, while enteroviruses are highlyresistant.

Lipid solvents

Ether, chloroform, and detergents are active against enveloped viruses but are not active against nonenveloped, nakedviruses.

Radiations

The viruses are readily inactivated by sunlight, ultraviolet (UV)radiations, and ionizing radiations.

Replication of Viruses

The replication of viruses in the host cell depends upon the synthesis mechanism of the host cell for manufacture of differentviral components. The genetic information for viral multiplicationis present in the viral nucleic acid. Multiplication ofviruses follows the basic pattern of bacteriophage multiplication,but has several important differences (Box 50-1).The multiplication of viruses, both DNA- and RNAcontainingviruses, is divided into six phases as follows:(i) attachment, (ii) penetration, (iii) uncoating, (iv) biosynthesis,(v) maturation, and (vi) release (Fig. 50-5).

Attachment

Attachment or adsorption is the first event in the infectionof the cell by a virus. The viruses have attachment sites thatattach to the complementary receptor sites on the host cellsurface. These receptor proteins in the virus are distributedon surface of the virus. These receptor proteins vary from onevirus to another (Table 50-4). For example, in influenza virusthese receptor proteins are the spikes present on the surfaceof the envelope, whereas in adenovirus these receptor proteinsare small fibers present at the corner of the icosahedron.The attachment sites of the virus bind specifically tothe complementary receptors on the surface of the host(Table 50-5). These receptor sites on the cell vary depending onthe nature of the virus:

■ Rabies virus binds specifically to the acetylcholine receptors found on neural cells

■ HIV-1 binds specifically to the CD4, a 60-kDa glycoproteinon the surface of mature T lymphocytes.

■ Influenza virus binds specifically to sialic acid residue of glycoprotein receptor sites on the surface of respiratoryepithelium.Susceptibility of the host to virus infection, therefore, dependsupon the presence or absence of receptors on the cell surface.

Steps in viral replication

1. Recognition of the target cell.
2. Attachment of the virus particle to the cell surface.
3. Penetration into the host cells.
4. Uncoating of the virus of its outer layers and capsid.
5. Biosynthesis
    - Transcription of mRNA from viral nucleic acid.
    - Translation of mRNA into “early proteins.”
    - Replication of viral nucleic acid.
    - Synthesis of late proteins.
6. Assembly of virus in the nucleus or cytoplasm.
7. Budding of enveloped viruses.
8. **Release of virus.**

<u>DNA Viruses</u>

These belong to the following families (Table 50-6):

Adenoviridae: The members of the family Adenoviridaeare medium-sized viruses measuring 20–90 nm in size. Theseviruses are nonenveloped, icosahedral viruses with 252 capsomeres.They are so named because they were first isolatedfrom adenoids. These viruses are mostly associated with acute respiratory diseases.

Poxviridae: These are large-sized, brick-shaped viruses measuring 300 _ 240_ 100_ in size. They have a complex structurewith a core containing a single linear molecule of doublestranded DNA genome. The pox (pox : pus-filled lesions) virusesare associated with skin lesions. The viral components are synthesizedand assembled in the cytoplasm of infected host cells.

Herpesviridae: These are medium-sized icosahedral nucleocapsidviruses (100 nm) containing 162 capsomeres. They areenveloped viruses containing linear, double-stranded DNA.They are named after spreading (herpetic) appearance of coldsores. The viruses multiply in the nucleus of the host cells.

Papovaviridae: These are small (40–55 nm) viruses containing double-stranded DNA with 72 capsomeres. They arenonenveloped viruses. They replicate in the nucleus of hostcell along with host cell chromosome. This may cause hostcells to proliferate, resulting in a tumor. Papovaviruses are acronyms to papillomas (warts), polyomas (tumors), and vacuolation (cytoplasmic vacuolationproduced by some of theseviruses).

Hepadnaviridae: Hepadnaviridae (hepa : liver; dna : DNA core) are so named because they cause hepatitis and contain DNA asgenome. These viruses differ from other DNA viruses by synthesizing their DNA by copying RNA using reverse transcriptase. Human hepatitis B virus, an important virus associated withhuman disease, is included in this family.

RNA Viruses

These belong to the following families (Table 50-7):

Togaviridae: These viruses include arboviruses and alphaviruses. Most of these viruses multiply in arthropods as well as in vertebrates. Togaviridae (toga: envelope) are enveloped viruses containing single-stranded RNA genome. These viruses are small spherical viruses measuring 40–70 nm in size.

Rhabdoviridae: Rhabdoviruses (rhabdo: rod) are bullet-shaped viruses. They are enveloped, measure 130–300 _ 20 nm in size, and contain a single-stranded RNA.

Reoviridae: They are icosahedral, nonenveloped viruses measuring 60–80 nm in size. They contain double-layered capsid enclosing 10–12 segments of double-stranded RNA. Their name is derived from the first letters of respiratory, enteric, and orphan. When first discovered, the viruses were not associated with any diseases, hence were called orphan viruses. These viruses are now known to cause respiratory and intestinal infections.

Retroviridae: Retroviruses (re: reverse, tr: transcriptase) viruses are so named because characteristically they possess the enzyme, reverse transcriptase RNA-dependent DNA polymerase. They are icosahedral, enveloped viruses measuring 100 nm in size. Many of these viruses are associated with tumors in infected hosts. One of the genera, Lentivirus includes the subspecies HIV-1 and HIV-2, thecausative agents of aquiredimmunideficiency syndrome(AIDS).

Picornaviridae: Picornaviruses (pico: small) are the smallest viruses, measuring 20–30 nm in size. They are nonenveloped,icosahedral viruses with single-stranded RNA genome.These include three genera (Enterovirus, Rhinovirus, andHepatovirus) of medical importance.

Orthomyxoviridae: These are medium-sized (80–120 nm)viruses. They are spherical and elongated, enveloped virusesconsisting of single-stranded but segmented (eight segments)RNA genome. Influenza virus is the only virus of medicalimportance belonging to this group.

Paramyxoviridae: These are pleomorphic, enveloped virusesmeasuring 150 nm in size. They contain nonsegmented,single-stranded, linear RNA. Three genera have been described:Paramyxovirus, Morbillivirus, and Pneumovirus.

Bunyaviridae: These are enveloped, spherical viruses measuring 90–100 nm in size. The genera of medical importance includeBunyavirus, Hantavirus, Uukuvirus, Phlebovirus, and Nairovirus.

Arenaviridae: They are spherical, pleomorphic viruses withvariable sizes (50–300 nm). They contain electron-dense, chromosome-like particles giving a sandy appearance; hence they are named arenaviruses (arena: sand).

Calciviridae: These are naked nonenveloped viruses. They are small and spherical, and measure 35–39 nm in size. They show32 cup-shaped depressions arranged in symmetry.

Filoviridae: They are long filamentous, enveloped viruses withvariable sizes. They contain single-stranded RNA genome. TheMarburg and Ebola virus are the viruses of medical importance.

Prions

Prions are infectious particles, which can transmit a disease. These prions are composed chiefly a protein without any detectablenucleic acid. Unlike conventional viruses, the prions apparently have no virion structure or genomes and evoke no immune response in the infected host. These are extremely resistant to inactivation by heat, disinfectants, and radiation.

The prions are causative agents of slow viral infections, such as subacute spongiform encephalopathy. After long incubation period of years, they produce a progressive disease that causes damage to the central nervous system, leading to subacute spongiform encephalopathy. The detailed description of prions and slow virus diseases is provided in Chapter 69.