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General Characteristics, Structure and Taxonomy of Viruses (6-Dec-2004)

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General

- Viruses are much smaller than prokaryotic or eukaryotic cells.
- Unlike cells, they have a generally simple and static structure.
- They have no metabolic system of their own.
- They depend upon the machinery of the host cell for replication (obligate intracellular parasites).
- They have either DNA or RNA genomes, but lack ribosomes and other factors needed for translation. Thus, they are dependent on the host cells for production of viral proteins.
- Their genomes encode minimal information to ensure the following: 1) genome replication and packaging; 2) production of viral proteins; and 3) subvert cellular functions to allow the production of virions.
- Some viruses (bacteriophages) infect prokaryotic cells, while others infect eukaryotic cells.
- Some viruses destroy cells, producing disease; other persist in infected cells either in a latent or persistent state; and other may cause cellular malignant transformation.

Viral Structure

Viruses are minimally composed of a nucleic acid genome (DNA or RNA) and a protein coat. Many viruses contain an external membrane called an envelope.

- The protein coat, or capsid, of an individual virion (fully assembled virus or virus particle) is composed of multiple copies of one or more types of proteins. These proteins assemble, forming structural units called capsomeres.
- The nucleic acid plus the capsid shell of a virus particle is often called nucleocapsid.
- The simplest viruses are those devoid of envelope with single-stranded DNA or RNA (Fig. 1-1).
- Enveloped viruses contain an external membrane surrounding the nucleocapsid (Fig.1-2). The viral envelope is derived from host cell membranes (nuclear, Golgi apparatus, endoplasmic reticulum or plasma membrane). As such, it is composed by a lipid bilayer, with virus-encoded proteins inserted on it.
- Some viruses, such as bacteriophages, have complex protein tails that are required for attachment and/or penetration of viral DNA into susceptible host cells.

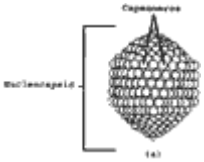

Figure 1.1. Non-enveloped virion with an icosahedral capsid. The nucleic acid is located within the capsid. Illustration is courtesy of A. Wayne Roberts. - To view this image in full size go to the IVIS website at www.ivis.org . -

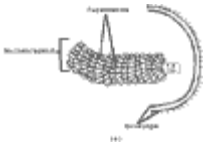

Figure 1.2. Enveloped virion with helical capsid. The nucleic acid is located within the nucleocapsid as indicated the spiral-shaped dotted line. The lines on the outer surface of the envelope represent glycoprotein spikes. Illustration is courtesy of A. Wayne Roberts. - To view this image in full size go to the IVIS website at www.ivis.org . -

Viral Genome

The viral genome consists of either DNA or RNA. Note that a virus does not contain both DNA and RNA simultaneously. The DNA can be single-stranded (ss) (parvoviruses and circoviruses), double-stranded (ds) (polyomaviruses, adenoviruses, herpesviruses), or partially double-stranded (hepadnaviruses). The DNA genome may have their ends covalently linked to each other (circular = polyomavirus, circoviruses) or not linked (linear = adenovirus, herpesvirus, parvoviruses). The genome of poxviruses is ssDNA whose ends are covalently attached to each other.

RNA viral genomes are all linear. The majority of these are single-stranded and a few are double stranded (reoviruses, bornaviruses). Most RNA viruses have their genomes in a single piece (monopartite) while others have it segmented in 10 segments (reoviruses), 7 or 8 segments (orthomyxoviruses), three segments (bunyaviruses) and two segments (arenaviruses). Regarding ssRNAs, there are two major sequence possibilities:

- If the viral ssRNA serve as a message for translation (the same sense of mRNA), it is referred to as positive-sense.
- In contrast, if the viral RNA is antisense (or complementary) to that of mRNA - and thus cannot be translated directly - it is said to be negative-sense.
- In some viruses (*Arenavirus* and *Bunyaviruses*) portions of the RNA genome are transcribed, generating mRNAs, which are then translated. The copy of these mRNAs (complementary, supposedly negative-sense RNAs) may also be translated. This arrangement is unique among viruses and is said to be ambisense.

The genes contained within the genome may encode anywhere from a few (*Polyomavirus*, 6 - 7 genes, 5000 nucleotides in length) to greater than 70 – 100 different gene products (Herpesviridae, 60 to 120 genes, 120,000 - 220,000 nucleotide bases pairs in length).

In general, RNA virus genomes are smaller, with a 30,000 nucleotide maximum size as seen in the *Coronavirus*. One hypothesis for this is that the viral RNA polymerases are more error prone compared with viral DNA polymerases. Thus, replication fidelity may limit size. In contrast, DNA virus genomes can reach up to 300,000 nucleotides as seen in some species of Herpesviridae.

The Capsid

The function of the capsid is to protect the viral genome during its transfer from cell to cell. Capsids are made up of multiples copies of one single protein or by association of several different proteins. Capsids made up of multiple copies of a single protein provide a good example of economy, since a single gene can encode the products needed to encapsidate the whole genome.

- The capsid of a virus can take on a variety of geometric shapes that are characteristic of the various viral families. These include:
    - Icosahedral naked (picornaviruses, polyomaviruses); or enveloped (herpesviruses). This geometric shape has several triangular faces and corners (see Fig. 1-1); the number of faces and corners may vary according to the number and type of association among structural proteins/units.
    - Helical structure, naked (tobacco mosaic virus) or enveloped (rabies virus), (see Fig. 1-1 and Fig. 1-2).
    - Complex, which are mixtures of arrangements (e.g., bacteriophage, poxviruses).
- Viruses vary in size from circoviruses at 17 - 22 nm in diameter to poxviruses approaching 300 nm. The latter viruses are brick to ovoid in shape and large enough to be seen under the light microscope, unlike the other viruses that require an electron microscope to be visualized.
- In visualizing the structure of a virus, several techniques have been used. X-ray crystallography is a means of determining the physical structure, dimensions of the individual proteins and components of the virus. The obtained information is then used to "build" the overall structure of the virus particle. Electron microscopy is used to generate information about the overall shape of the virus; it is also used with diagnostic purposes through detection of virus

particles in clinical specimens. Methods for visualizing virions are described in detail in Chapter 2.

Five Basic Structural Forms

Based upon basic morphology, as indicated above, there are five different basic structural forms of viruses. These forms are listed below with examples:

- Naked icosahedral - adenoviruses and picornaviruses.
- Naked helical - tobacco mosaic virus; no known human or animal viruses have this structure.
- Enveloped icosahedral - togaviruses and flaviviruses.
- Enveloped helical - rhabdoviruses and paramyxoviruses.
- Complex - bacteriophages and poxviruses.

Viral Envelopes

The viral envelope, characteristic of some virus families, is derived from membranes of the host cell by budding, which occurs during the release of the virions from the cell. This membrane is mainly a piece of the plasma membrane; however, it may be part of the Golgi Apparatus, endoplasmic reticulum or the nuclear membrane, depending upon the virus and the cellular compartment where the replication takes place. Regardless of origin, the envelope is composed by a lipid bilayer - of cellular origin - and associated proteins. The proteins associated with the lipid bilayer are largely of viral origin (virus-encoded) and are mainly glycoproteins. The number of viral proteins in the envelope may vary from one up to more than ten, depending on the virus. Virus envelope glycoproteins perform several functions, including the initial attachment of the virion to the target cell, penetration, fusion, and cell-to-cell spread, amongst others. The attachment of a virion to the cellular surface requires the envelope to be intact and the glycoproteins in their native conformation. Antiviral drugs that are directed against the envelope proteins can decrease the ability of the virus to attach and initiate infection, thereby decreasing infectivity.

The process of budding, and thus acquisition of the envelope by the newly formed virions, may or may not result in death of the host cell. If many virions are released simultaneously, the integrity of the host cell membrane may be compromised enough to lead to death of the cell. Alternatively, the release of virions may be slow and consistent resulting in chronic shedding and persistent infections. Indeed, unlike the non-enveloped viruses, which are released from the cell mainly through cell lysis and consequently death, egress of enveloped viruses is often compatible with cell survival. Therefore, budding provides a means of viral egress without leading to cell death.

Viral Proteins

There are two basic types of virus-encoded proteins: structural and non-structural. The structural proteins are those that are part of the physical structure of the virion (capsid, envelope), while nonstructural proteins are produced inside infected cells and play roles in different steps of viral replication. The number of proteins encoded by viral genomes varies greatly, from as few as two proteins to over hundreds.

Structural proteins are typically those that compose the capsid and package the nucleic acid genome. In some enveloped viruses, there is a protein layer between the capsid and the envelope (the tegument). The proteins that make up the tegument are also structural. External structural proteins of the capsid or envelope are ligands, which interact with receptors on the surface of target cells. Some of these proteins (glycoproteins) are processed in the lumen of the rough endoplasmic reticulum, where oligosaccharides are attached to the polypeptide chain. They are then sent to the Golgi apparatus, to secretory vesicles, and ultimately fuse with the plasma membrane where they are present on the surface of the infected cell. This is especially important for enveloped viruses. Envelope glycoproteins play roles in mediating interactions between the virions and cells (attachment, penetration, fusion, cell-to-cell spread) and are major targets for neutralizing antibodies.

Nonstructural proteins are primarily, but not exclusively, enzymes, such as those associated with the processes of genome transcription, replication and protein processing. An example of a nonstructural protein is reverse transcriptase of retroviruses, which makes a DNA copy of a RNA template. This step is an important feature of retroviruses whose RNA needs to be converted to DNA in order to be incorporated into the host chromosome. Some viruses encode several non-structural proteins that play diverse accessory roles in the regulation of viral and cellular gene expression, regulation of different steps of the viral cycle, counteraction of host defenses, cell transformation, *et cetera*.

Other Viral Components

Lipids - The lipids of viruses are derived from the cellular membranes of the host cell. These are composed mainly of phospholipids (50 - 60%) and the remainder is cholesterol. As a result of being derived from host cell membranes, the composition of lipids varies. The lipid bilayer of the host membranes surrounding the virion of enveloped viruses also possesses viral proteins and glycoproteins, such as the characteristic spikes of some enveloped viruses. The overall lipid

composition of enveloped viruses is approximately 20 - 35% dry weight. The remainder is divided between the nucleic acid and protein portions.

Carbohydrates - The carbohydrates of viruses occur as oligosaccharide side chains of glycoproteins, glycolipids, and mucopolysaccharides. The composition of the carbohydrates corresponds to that of the host cell. However, the glycoproteins typically have an *N*– or *O*- glycosidic linkage. Viral carbohydrates are mainly found in the envelope. Some of the larger, more complex viruses contain internal glycoproteins or glycosylated capsid proteins.

Viral Taxonomy - Viruses constitute a large and heterogeneous group. They are classified in hierarchical taxonomic categories based on many features. The classification is dynamic in that new viruses are continuously being discovered and more information is accumulating about viruses already known. The classification and nomenclature used in this book was current at the time of writing. The latest changes appear in reports of the International Committee on the Taxonomy of Viruses (ICTV), seventh edition ().

The basic viral hierarchical classification scheme is: Order - Family - Subfamily - Genus - Species - Strain / Type. A number of viral characteristics, referred to below, define each of these taxonomic categories. Orders have the suffix -*virales*, families contain the suffix -*viridae*, while genera contain the suffix -*virus*. A virus species constitutes a replicating lineage that occupies an ecological niche, for example, a particular disease.

Viruses are placed in families on the basis of many features. A basic characteristic is nucleic acid type (DNA or RNA) and morphology, that is, the virion size, shape, and the presence or absence of an envelope. The host range and immunological properties (serotypes) of the virus are also used. Physical and physicochemical properties such as molecular mass, buoyant density, thermal inactivation, pH stability, and sensitivity to various solvents are used in classification.

Whether the RNA or DNA is single or double stranded, the organization of the genome and the presence of particular genes comprise important aspects of the current taxonomy of viruses. All of the former are used to place a virus into a particular order or family. For example, the order Mononegavirales encompasses those viruses possessing a negative sense, single stranded RNA genome. Lastly, classification is based upon macromolecules produced (structural proteins and enzymes), antigenic properties and biological properties (e.g., accumulation of virions in cells, infectivity, hemagglutination).

The viral families are listed in the Table of Contents under various categories of their nucleic acid. The families are discussed in the book in the order in which they appear in the Contents.

Table 1.1 provides basic information on each of the major taxonomic categories of viruses.

Table 1.1. Classification and Some Basic Characteristics of Vertebrate Viruses

Single-Stranded DNA Viruses

Family	Capsid Symmetry Virion Size (nm)	Subfamily	Genus	Representative Species
Circoviridae	Icosahedral; 17-25		*Circovirus*	Beak and feather disease virus
			Gyrovirus	Chicken anemia virus
Parvoviridae	Icosahedral; 18-26	Parvovirinae	*Parvovirus*	Canine & feline parvovirus
			Erythrovirus	B19 virus
			Dependovirus	Adeno-associated virus 2
			ADMV-like viruses	Aleutian mink disease virus
			BPV-like viruses	Bovine parvovirus

Double-Stranded DNA Viruses				
Family	**Capsid Symmetry Virion Size (nm)**	**Subfamily**	**Genus**	**Representative Species**
Poxviridae	Complex; 140-260 by 220-450	Chordopoxvirinae	*Orthopoxvirus*	Vaccinia virus
			Parapoxvirus	Orf virus
			Avipoxvirus	Fowlpox virus
			Capripoxvirus	Sheeppox virus
			Leporipoxvirus	Myxoma virus
			Suipoxvirus	Swinepox virus
			Molluscipoxvirus	Molluscum contagiosum virus
			Yatapoxvirus	Yaba monkey tumor virus
Herpesviridae	Icosahedral; 120-200	Alphaherpesvirinae	*Simplexvirus*	Human herpesvirus 1
			Varicellovirus	Human herpesvirus 3
			Marek's disease-like viruses	Gallid herpesvirus 2
			Infectious laryngo-tracheitis-like viruses	Gallid herpesvirus 1
		Betaherpesvirinae	*Cytomegalovirus*	Human herpesvirus 5
			Muromegalovirus	Murid cytomegalovirus 1
			Roseolovirus	Human herpesvirus 6
		Gammaherpesvirinae	*Lymphocryptovirus*	Epstein-Barr virus
			Rhadinovirus	Ovine herpesvirus 2
Polyomaviridae	Icosahedral; 40-45		*Polyomavirus*	SV 40 virus
Papillomaviridae	Icosahedral; 52-55		*Papillomavirus*	Bovine papillomavirus 1
Adenoviridae	Icosahedral; 80-110		*Mastadenovirus*	Bovine adenovirus
			Aviadenovirus	Fowl adenovirus A
			Atadenovirus	Ovine adenovirus D
			Siadenovirus	Turkey haemorrhagic enteritis virus
Asfarviridae	Complex; 175-215		*Asfivirus*	African swine fever virus
Iridoviridae	Icosahedral; 125-300		*Ranavirus*	Frog virus 3
			Lymphocystisvirus	Lymphocystis disease virus 1

DNA and RNA Reverse Transcribing Viruses				
Family	**Capsid Symmetry Virion Size (nm)**	**Subfamily**	**Genus**	**Representative Species**
Hepadnaviridae	Icosahedral; 42-47		*Orthohepadnavirus*	Hepatitis B virus
			Avihepadnavirus	Duck hepatitis B virus
Retroviridae	Icosahedral; 80-100		*Alpharetrovirus*	Avian leukosis virus
			Betaretrovirus	Ovine pulmonary adenocarcinoma virus
			Gammaretrovirus	Feline leukemia virus
			Deltaretrovirus	Bovine leukemia virus
			Epsilonretrovirus	Walleye dermal sarcoma virus
			Lentivirus	Feline immunodeficiency virus
			Spumavirus	Bovine foamy virus

Double Stranded RNA Viruses				
Family	**Capsid Symmetry Virion Size (nm)**	**Subfamily**	**Genus**	**Representative Species**
Reoviridae	Icosahedral; 60-80		*Orthoreovirus*	Mammalian orthoreovirus
			Obivirus	Blue tongue virus
			Rotavirus	Rotavirus A
			Coltivirus	Colorado tick fever virus
			Aquareovirus	Aquareovirus A
Birnaviridae	Icosahedral; 60-70		*Aquabirnavirus*	Infectious pancreatic necrosis virus
			Avibirnavirus	Infectious bursal disease virus

Single Stranded, Negative Sense RNA Viruses				
Family	**Capsid Symmetry Virion Size (nm)**	**Subfamily**	**Genus**	**Representative Species**
Paramyxoviridae	Helical; 150-200 by 1000-10,000	Paramyxovirinae	*Respirovirus*	Bovine influenza virus 3
			Rubulavirus	Porcine rubulavirus; mumps virus
			Morbillivirus	Canine distemper virus; measles virus
			Henipavirus	Hendra virus
			Avulavirus	Newcastle disease virus
		Pneumovirinae	*Pneumovirus*	Bovine respiratory syncytial virus
			Metapneumovirus	Avian pneumovirus

Single Stranded, Negative Sense RNA Viruses				
Family	**Capsid Symmetry Virion Size (nm)**	**Subfamily**	**Genus**	**Representative Species**
Rhabdoviridae	Helical; 45-100 by 100-430		*Vesiculovirus*	Vesicular stomatitis Indiana virus
			Lyssavirus	Rabies virus
			Ephemerovirus	Bovine ephemeral fever virus
			Novirhabdovirus	Infectious haematopoietic necrosis virus
Orthomyxoviridae	Helical; 80-129 by up to 2000		*Influenzavirus A*	Influenza A virus
			Influenzavirus B	Influenza B virus
			Influenzavirus C	Influenza C virus
			Thogotovirus	Thogoto virus
			Isavirus	Infectious salmon anemia virus
Bunyaviridae	Helical; 80-100		*Orthobunyavirus*	Akabane virus
			Hantavirus	Hantaan virus
			Nairovirus	Nairobi sheep disease virus
			Phlebovirus	Rift Valley fever virus
Bornaviridae	Icosahedral; 100-130		*Bornavirus*	Borna disease virus
Arenaviridae	Helical; 50-300		*Arenavirus*	Lymphocytic choriomeningitis virus
			Deltavirus	Human hepatitis D virus
Filoviridae	Helical; 80 by 1400		*Marburg-like viruses*	Marburg virus
			Ebola-like viruses	Ebola virus

Single Stranded, Positive Sense RNA Viruses				
Family	**Capsid symmetry Virion size (nm)**	**Subfamily**	**Genus**	**Representative species**
Picornaviridae	Icosahedral; 22-30		*Enterovirus*	Polio virus
			Rhinovirus	Human rhinovirus A
			Cardiovirus	Encephalomyo-carditis virus
			Aphthovirus	Foot-&-mouth disease virus
			Hepatovirus	Hepatitis A virus
			Parechovirus	Human parechovirus
			Erbovirus	Equine rhinitis B virus
			Kobuvirus	Aichi virus
			Teschovirus	Porcine teschovirus
Calciviridae	Icosahedral; 35-39		*Lagovirus*	Rabbit hemorrhagic disease virus
			Norovirus	Norwalk virus
			Sapovirus	Swine calicivirus
			Vesivirus	Swine vesicular exanthema virus
Astroviridae	Icosahedral; 27-30		*Mamastrovirus*	Human astrovirus
			Avastrovirus	Turkey astrovirus
Coronaviridae	Helical; 60-220		*Coronavirus*	Infectious bronchitis virus
			Torovirus	Equine torovirus
Arteriviridae	Icosahedral; 40-60		*Arterivirus*	Equine arteritis virus
Togaviridae	Icosahedral; 70		*Alphavirus*	Sindbis virus
			Rubivirus	Rubella virus
Flaviviridae	Icosahedral; 40-60		*Flavivirus*	Yellow fever virus
			Pestivirus	Bovine viral diarrhea virus 1
			Hepacivirus	Hepatitis C virus
Nodaviridae	Icosahedral; 29-32		*Betanodavirus*	Striped jack nervous necrosis virus

Atypical Particles Associated with Infections

Defective Viruses - Defective viruses are those virus particles whose genome lacks a specific gene or genes due to either mutation or deletion. As a result, defective viruses are not capable of undergoing a productive life cycle in cells. However, if the cell infected with the defective virus is co-infected with a "helper virus", the gene product lacking in the defective one is complemented by the helper and defective virus can replicate. Interestingly, for some viruses, during infection a greater quantity of defective virions is produced than infectious virions (as much as 100:1). The production of defective particles is a characteristic of some virus species and is believed to moderate the severity of the infection/disease in *vivo*. Virusoids, discussed later in this section, are examples of defective viruses.

Pseudovirions - Pseudovirions may be produced during viral replication when the host genome is fragmented. As a result of

this process, host DNA fragments are incorporated into the capsid instead of viral DNA. Thus, pseudovirions possess the viral capsid to which antibodies may bind and facilitate attachment and penetration into a host cell, but they cannot replicate once they have gained access to a host cell, as they have none of the essential viral genes for the process.

Prions - Although not viral, prions are proteinaceous infectious particles associated with transmissible spongiform encephalopathies (TSE) of humans and animals. TSEs include the Creutzfeldt-Jacob disease of humans, scrapie of sheep and bovine spongiform encephalopathy. Prions and the TSEs of animals are discussed in detail in Chapter 29. At postmortem, the brain has large vacuoles in the cortex and cerebellum regions an thus prion diseases are called "spongiform encephalopathies". Closer examination of brain tissue reveals the accumulation of prion-protein associated fibrils and amyloid plaques. These diseases are characterized by loss of motor control, dementia, paralysis, wasting and eventually death. Details of pathogenesis are largely unknown.

Viroids - Viroids are naked, low-molecular weight nucleic acids that are extremely resistant to heat, ultraviolet, and ionizing radiation. These particles are composed exclusively of a single piece of circular, single stranded RNA that has some double-stranded regions. Viroids mainly cause plant diseases, such as potato spindle tuber disease.

Virusoids - Virusoids (also called satellite RNAs) are similar to viroids in that they are naked, low-molecular weight nucleic acids that are extremely resistant to heat and ultraviolet and ionizing radiation. However, they depend on a helper virus for replication. Virusoids replicate in cytoplasm via a RNA dependent RNA polymerase.

Novel Virus Family - Mimiviridae
Mimiviridae is a family of viruses that contains one member, Mimivirus. The name Mimivirus is derived from "mimicking microbe". It was discovered in 1992 inside a protozoan and is the largest virus known to date, about 400 nm in diameter. The capsid is icosahedral in shape, the virion lacks an envelope, and has a circular dsDNA genome, which is 1.2 Mb in length and contains 1,260 genes. The Mimivirus genome sequence was published in 2004.

Glossary
Bacteriophage: A virus that infects prokaryotic cells and has many of the attributes of animal and plant viruses. It requires a living bacterium to carryout its reproductive cycle.

Budding: In this process enveloped viruses acquire their envelope. It is preceded by insertion of virus-specific glycoproteins into host cell membranes. Budding occurs most frequently at the plasma membrane and confers infectivity.

Mucopolysaccharide: A class of polysaccharides (glycosamineglycans) such as heparin, hyaluronic acid and chondroitin sulfate that bind water to form thick gelatinous, mucoid material.

Oligosaccharide: A sugar that contains a known small number of monosaccharide units.