VIRUSES Chapter 13

I. Properties of Viruses

Virology is the study of viruses and virus-like proteins

A. Nucleic acid enclosed by a protein coat

1. morphology: polygonal, helical or complex
   a. Viruses range in size from 20 to 250 nanometers (nm)
   b. Ordinarily too small to be seen by light microscopy, viruses usually can be detected with electron microscopy

2. Contain DNA or RNA, never both
   Viruses have a unique composition
   a. Some viruses are composed of only one type of nucleic acid, which makes up their genetic code; others, such as Prions, are composed entirely of protein and contain no nucleic acid
   b. Deoxyribonucleic acid (DNA) viruses are composed of DNA
   c. Ribonucleic acid (RNA) viruses are composed of RNA

3. Lack properties of cells such as membranes, ribosomes, enzymes, and ATP synthesizing mechanisms

B. Obligate intracellular parasites

1. Act obligate intracellular parasites, viruses lack the capacity for independent metabolism and reproduce only in living hosts
   a. The hosts that they infect are bacteria, plant cells, animal cells, human cells, and any of the preceding cells in tissue cultures
   b. Viral infection of human cells can cause such diseases as acquired immunodeficiency syndrome (AIDS), chicken pox, hepatitis, and polio

C. Classification

1. Genome structure – DNA or RNA, single-stranded or double-stranded, segmented or a single molecule.
2. Virus particle structure - isometric (icosahedral), helical (rod-shaped), or pleomorphic (irregular in shape)
3. Presence or absence of a viral envelope.
4. The host the virus attacks.

General characteristic

1. Viruses attach to specific receptor sites on host cells
   a. The ability of a virus to infect an organism is determined by the types and presence of receptor sites on host cells
   b. Plant viruses tend to infect only plants and animal viruses tend to infect only animals because of the nature of the receptor sites
   c. Receptor sites are proteins on the surface of cells

2. Once a virus enters a host cell through the receptor site, it takes over the host cell's metabolism and uses the host cell's components to produce more virus particles

a. DNA viruses are produced directly; the host cell builds viral components from the genetic instructions provided by the viral DNA
b. Retro RNA viruses induce production of messenger RNA or transcriptase enzymes, which copy viral RNA back into DNA for use by the host cell

3. Morphology and size:
a. The morphology of viruses is simpler than that of bacteria
(1) The virus particle has a rod-shaped central core composed of nucleic acid
(2) Covering the core is a protein coat called a capsid
(3) An envelope derived from the host cell membrane may protect the viral capsids by camouflaging them with host antigens
(a) Viruses with envelopes tend to be resistant to the host's immune system
(b) Viruses without envelopes are more common in plants

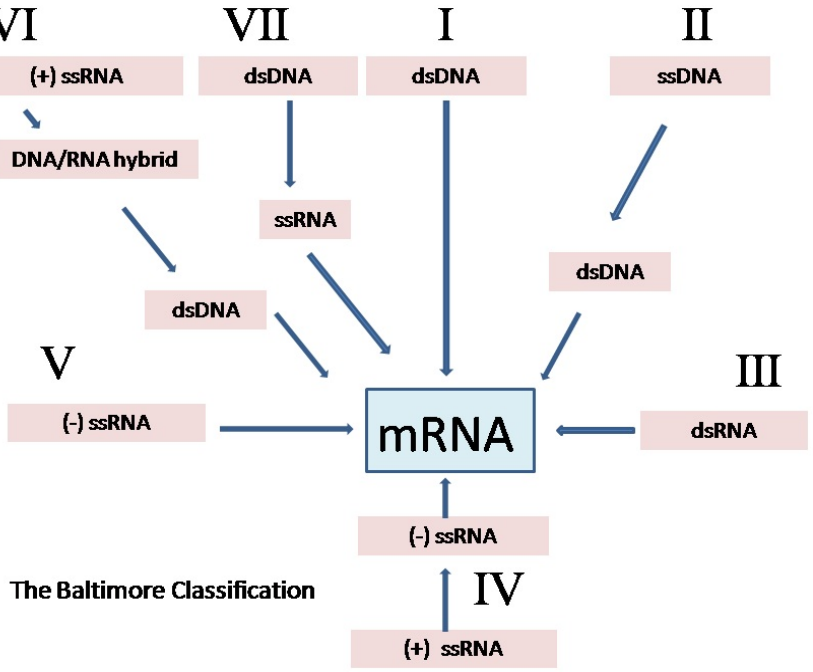
4. Individual virus particles are called virions
a. Virions can be shaped as cubes, spheres, icosahedra (20-sided polygons), or helices
b. They can also occur as complex forms composed of multiple copies of the shapes mentioned above

5. Accessory structures (tails, envelopes, spikes, etc.)

D. Incubation periods
1. Incubation periods for viral diseases range from days to years
a. Many infections, such as mumps and chicken pox, incubate for a few days, whereas the human immunodeficiency virus may not produce symptoms for 5 to 10 years
b. Latent, or long-term, infections are possible
(1) These infections are characterized by asymptomatic periods, followed by the reappearance of symptoms of a latent virus

(2) Reactivation results in new viral reproduction

E. Viral types



ICTV classification

The International Committee on Taxonomy of Viruses (ICTV) developed the current classification system and put in place guidelines that put a greater weighting on certain virus properties in order to maintain family uniformity. A universal system for classifying viruses, and a unified taxonomy, has been established since 1966. In determining order, taxonomists should consider the type of nucleic acid present, whether the nucleic acid is single- or double-stranded, and the presence or absence of an envelope. After these three main properties, other characteristics can be considered: the type of host, the capsid shape, immunological properties and the type of disease it causes. The system makes use of a series of ranked taxons. The general structure is as follows:

Order (-virales)

Family (-viridae)

Subfamily (-virinae)

Genus (-virus)

Species (-virus)

The recognition of orders is very recent; to date, only 3 have been named, most families remain unplaced. The committee does not formally distinguish between subspecies, strains, and isolates. In total there are 3 orders, 56 families, 9 subfamilies, 233 genera. ICTV recognizes about 1,550 virus species but about 30,000 virus strains and isolates are being tracked by virologists.

In addition to this classification system, the Nobel Prize-winning biologist David Baltimore devised the Baltimore classification system. The ICTV classification system is used in conjunction with the Baltimore classification system in modern virus classification.

Baltimore Classification
The Baltimore Classification of viruses is based on the method of viral mRNA synthesis

Baltimore classification Group	Contains
I	dsDNA viruses
II	ssDNA viruses
III	dsRNA viruses
IV	(+)ssRNA viruses
V	(-)ssRNA viruses
VI	ssRNA-RT viruses
VII	dsDNA-RT viruses

ss: single-stranded, ds: double stranded
RT: reverse transcribing

The Baltimore classification of viruses is based on the mechanism of mRNA production. All viruses must generate positive strand mRNAs from their genomes, in order to produce proteins and replicate themselves, but different mechanisms are used to achieve this in each virus family. This classification places viruses into seven groups:

• I: Double-stranded DNA (e.g. Adenoviruses, Herpesviruses, Poxviruses)

• II: Single-stranded (+)sense DNA (e.g. Parvoviruses)

• III: Double-stranded RNA (e.g. Reoviruses)

• IV: Single-stranded (+)sense RNA (e.g. Picornaviruses, Togaviruses)

• V: Single-stranded (-)sense RNA (e.g. Orthomyxoviruses, Rhabdoviruses)

• VI: Single-stranded (+)sense RNA with DNA intermediate in life-cycle (e.g. Retroviruses)

• VII: Double-stranded DNA with RNA intermediate (e.g. Hepadnaviruses)

As an example of viral classification, the chicken pox virus, Varicella zoster (VZV), belongs to family Herpesviridae, subfamily Alphaherpesvirinae and genus Varicellovirus. It remains unranked in terms of order. VZV is in Group I of the Baltimore Classification because it is a dsDNA virus that does not use reverse transcriptase.

II. DNA Viruses

A. General information

1. DNA viruses, which have only deoxyribonucleic acid in their core, typically occur as icosahedral forms

2. After inserting their DNA into the host DNA, the viruses are duplicated during replication, translation, and transcription (see Chapter 13 for more information on DNA replication, translation, and transcription)

3. Cell cultures allow microbiologists to grow these viruses for study
   a. Research with DNA viruses has led to advances in genetics, gene therapy, vaccination and prevention of disease, and cancer treatment
   b. Vaccines to combat hepatitis B, for instance, are produced by recombinant-gene technology

4. DNA viruses often form cellular masses known as inclusion bodies, which are helpful in identification

B. Means of identification

1. DNA viruses can be identified by the signs and symptoms of the diseases that they cause

2. If the virus forms inclusion bodies in host cells, these inclusions may be seen when the organism is examined under a microscope

3. Another means of identification are the **specific antibodies** produced in response to viral antigens; these antibodies can be measured in the blood
   (a) Serological: Western blot test

4. Growing of Virus
   a. Egg or cell line culture

5. Nucleic Acid reproduction (molecular methods) to identify by
   a. RFLP (restriction fragment length polymorphism)
   b. PCR (polymerase chain reaction)

6. Electron microscope

C. Taxonomic classification: Adenovirus

1. This group of viruses infects mammals and birds through airborne and fecaloral transmission
2. Adenoviruses affect the upper respiratory tract, intestinal tract, and conjunctivae
3. This virus affects liver cells, causing fever, malaise, jaundice, and (occasionally) death h
4. It is unrelated to any other known human virus

III. Bacteriophages

A. Fine structure
   1. Capsid (head), {sheath, tail fiber, baseplate, pin} = Tail

B. Detection and quantification (see lab 15)

C. Life cycle of a lytic phage

1. Molecular events during **5 distinct stages**:
   a. 1- attachment; 2 - penetration; 3 - biosynthesis 4 - maturation 5 - release
2. **Eclipse** period
   a. The period of time is when viral multiplication is complete, yet, infective virions are not present.
3. **Burst time**
   a. averages 20 - 40 minutes
   b. the number of phage particles released from a single cell is referred to burst size
      Ranging from 50 to 200 particles

D. Life cycle of a lysogenic phage

Lysogeny is a state of cell chromosome where a bacteriophage genome has been inserted into the bacterial chromosome by nonreciprocal recombination occurring between the phage chromosome and the bacterial chromosome. This insertion occurs at specific locations in each of chromosomes where there in homology of sequences in the two chromosomes.

Lysogenic conversion is the state of a cell that shows new properties like ability to form cytotoxins. The *tox* gene, coding for a toxic protein affecting eukaryotic cells, is on the phage genome that is expressed in the bacterium without causing lysis of the bacterial cell and production of more phage. The *tox* gene that is located in a corynephage chromosome codes for diphtheria toxin that kills susceptible human cells. When this phage chromosome becomes inserted into chromosome of the bacterium Corynebacterium diphtheriae, human infection with this microbe leads to formation and release of diphtheria toxin in the human host producing symptoms of diphtheria.

1. Molecular events during replication

a. Lysogenic phages are also called temperate phages
   (1) may also induce lyitic cycle,
   (2) are also capable of incorporating into the host DNA (inserted phage DNA is called a **prophage**)
b. In lysogeny, the phage remains latent or inactive.
   (1) Host cells are known as ***lysogenic*** cells.

2. Formation of prophage
   a. 1 - **Penetration;**
      2 - Original linear phage DNA **forms a circle**;
      3 - circular DNA **becomes part of the circular bacterial DNA** (the lysogenic cycle);
      4 - Prophage genes are **repressed** by two repressor proteins products of the prophage virus

3. Relationship to **specialized (restricted) transduction**
   a. When host cell replicates ---- prophage DNA is replicated but prophage remains silent
   b. Spontaneous event or UV light or certain chemicals causes phage to pop out of host DNA becoming active
      (1) Lytic cycle initiated

4. Important results of lysogeny
   First, the lysogenic cell is immune to reinfection by the same phage virus **but** the cell is not immune to other virion attacks.

   Second, Phage conversion: The host cell may exhibit new properties.

      Example: Corynebacterium diphtheriae (causes diphtheria) The organism can produce toxin only when it carries a temperate phage, prophage carries the gene coding for the toxin

   Third, ***Specialized transduction***: Transfer of bacterial DNA from previous to new host. Bacterial DNA is packaged along with prophage DNA in the same capsid.
      (1) Bacteriophage λ picks up the *gal* gene for galactose carrying it to galactose negative cell

IV. Animal Viruses

A. **Replication of animal viruses**
   1. Multiplication of animal virus follow the basic patter that of bacteriophage with several differences
      a. mechanism of cellular penetration
      b. Synthesis and assembly of new viral components differs
         (1) Animal viruses have different enzymes not found in phages

B. **Cultivation**
   1 - **Attachment** to receptor site on cell membrane
      a. Animal virus do not contain appendages like tail fibers
      b. Attachment sites of virus may include spikes: *Influenzaviurs*
      c. Gene variation between animals results in variability of susceptibility of animal host

2. **Penetration** 3 methods of viral penetration into eukaryotic host cell
   a. **endocytosis**: folding of the cell membrane inward engulfing enveloped virus
      1) Enveloped virus uncoats within cytoplasm of host release nucleic acid
   b. **Fusion**: Envelope of Enveloped viruses fuse with host plasma membrane
      (1) releasing capsid into cell's cytoplasm HIV works in this manner
   c. **Direct penetration** of nucleic acid into cytoplasm through membrane of host without capsid entering the cytoplasm

3. **Uncoating**
   a. Viral nucleic acid separates from its protein coat.

   b. Enzymes degrade the proteins of the viral capsid releasing the virus nucleic acid
      Poliovirus works in this manner

C. **Replication & Maturation**

Biosynthesis of Nucleic Acid

Virus uses the host system to make new nucleic acid

Proteins and capsid are synthesized in cytoplasm.

Proteins migrate into nucleus and are assembled into active virus.

Released from host cell

DNA viruses

Transcription and translation using host enzymes

Exception is Poxviruses - All component synthesized in cytoplasm. Poxviruses use their own transcriptase enzyme

D. Importance: Interactions with host cells

1. **Active infections** caused by DNA viruses include hepatitis, infectious monomucleosis, Burkitt's lymphoma, chicken pox, and small pox.

2. **Latent infections** caused by DNA viruses include genital herpes and pharyngitis cause by adenovruses

3. **Oncogenic** (cancer-causing) and potentially oncogenic DNA viruses are common; such viruses cause cancer of the liver and genitourinary tract, as well as lymphoma and papilloma.

4. **Prions**: infectious protein particles:
   a. the gene of PrP^{c} is located on chromosome 20 in the humans. PrP^{c} produced by cells is secreted to the cell surface. This type of disease runs in the family line.

   b. PrP^{sc} is reacts with PrP^{c} on the cell surface converting the PrP^{c} to PrP^{sc}

   c. PrP^{sc} is taken in by endocytosis and accumulates in the lysome.

V. RNA Viruses

A. General information

1. RNA viruses, which have only ribonucleic acid in their core, occur as cubic, icosahedral, helical, and spherical forms
2. They contain transcriptase enzymes that copy viral RNA back into DNA; the DNA can then be used for viral replication
3. These viruses often form cellular inclusions that are useful in identification
4. Non-retro RNA viruses replicate within the cytoplasm of the host
   a. Positive (+) strand RNA synthesize negative (-) strand RNA
      1) -RNA templates for further synthesis of +RNA
      1) +RNA acts as $_{m}$RNA templating the protein synthesis

B. Means of identification

1. RNA viruses can be identified by the signs and symptoms of the diseases that they cause
2. Host cell inclusion bodies may be formed and can be seen during microscopic examination
3. Electron microscopy also is useful for identifying RNA viruse
4. Specific antibodies produced to viral antigens can be measured in the blood
5. Cell cultures permit growth of these viruses for study

C. Importance

1. Active infection caused by RNA viruses includes various diseases of plants, animals, and humans; human diseases include colds, encephalitis, mumps, and measles
2. Latent infections are also possible
3. Oncogenic or potentially oncogenic viruses are common; RNA viruses produce many types of leukemia

D. Taxonomic classification: Arenavirus

1. This class of viruses infects rodents, primates, and humans through airborne transmission and vector bites
2. Arenaviruses affect the central nervous system, blood, lungs, and kidneys
3. Examples include lymphocytic choriomeningitis virus, Lassa fever virus, and South American hemorrhagic fever virus

E. Taxonomic classification: Bunyavirus

1. These viruses infect mammals and humans through bites from mosquitoes and flies
2. Bunya viruses affect the central nervous system and cause febrile illnesses
3. California virus (a cause of encephalitis) is a bunyavirus

F. Taxonomic classification: Coronavirus

1. These viruses are so named because, under an electron microscope, they resemble a corona or crown
3. Coronaviruses affect the upper respiratory tract in adults and the lower respiratory tract in children
4. Viral strains that cause the common cold belong to this group

G. Taxonomic classification: Influenzavirus

1. The influenzaviruses infect birds, mammals, and humans through airborne transmission
2. This virus causes an acute infection of the respiratory tract
3. Three major strains of influenzavirus have been identified-types A, B, and C

H. Taxonomic classification: Mosaic viruses

1. Mosaic viruses infect plants through airborne transmission or via vectors
2. The virus infection causes hyperplastic lesions on the stems, leaves, and fruit of the plant
3. Tobacco mosaic virus, the cause of tobacco mosaic disease, results in significant economic loss to farmers
4. Because these viruses infect only plants, they provide microbiologists with a safe means of studying viral structure and reproduction

I. Taxonomic classification: Paramyxovirus

1. Paramyxovirus, a subgroup of the myxoviruses, infects birds and humans through airborne and person-to-person transmission
2. The virus particles affect the salivary glands, gonads, skin and mucous membranes, lungs, lymph nodes, central nervous system, and internal organs
3. Paramxyoviruses cause mumps, measles, and rubeola; respiratory syncytial virus (a chief cause of infection in infants); and Newcastle disease

J. Taxonomic classification: Picornavirus

1. These viruses infect many animals, as well as humans, by airborne and oral transmission
2. They affect the respiratory tract, intestinal tract, and nervous system and cause generalized disease
3. Picornaviruses comprise the enteroviruses and the rhinoviruses
   a. Rhinoviruses are the primary cause of the common cold
   b. Other picornaviruses include coxsackieviruses A and B (the cause of fever, meningitis, encephalitis, and paralysis); echoviruses (the cause of acute gastrointestinal disease); and poliovirus types 1, 2, and 3 (the cause of polio)

K. Taxonomic classification: Reovirus

1. Reoviruses, formerly classified as a subgroup of the echo viruses, infect mammals and humans by oral transmission or through tick bites
2. The intestinal tract and central nervous system are affected by these viruses
3. Reoviruses include rotavirus (which accounts for up to 50% of acute gastroenteritis in children younger than age 2) and bivirus (the cause of Colorado tick fever)

L. Taxonomic classification: Retrovirus

1. Retroviruses infect animals and humans through transmission of blood and other body fluids
2. These viruses, which affect white blood cells, the nervous system, the lymphatic system, and internal organs, cause decreased immunity to other infections and cancer
3. Included in this group of viruses are the human T-lymphotropic viruses I and II (the cause of human leukemias) and the human immunodeficiency virus (the cause of AIDS)

M. Taxonomic classification: Rhabdo virus

1. Animals and humans can be infected by these viruses through the bites of infected individuals
2. Rhabdo viruses affect the central nervous system and cause paralysis and convulsions
3. Examples of rhabdo viruses are the rabies virus (the cause of rabies in animals and humans), the Marburg virus (the cause of Marburg disease), and the Ebola virus (the cause of severe hemorrhagic fever)

N. Taxonomic classification: Togavirus

1. Togaviruses are so named because they have envelopes, or "togas"
2. This subgroup of the arboviruses infects animals and humans via transmission from individuals

or mosquitoes

3. These viruses affect the skin, mucous membranes, nervous system, and internal organs, causing inflammation, fever, rash, or encephalitis

4. Togaviruses comprise the German measles, or rubella, virus and numerous viruses carried from animals to humans by mosquitoes and ticks