

Medical microbiology

Virology

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Introduction to virology

Definitions

Virology: the science which deals with study of viruses as causative agents of very important diseases that occurs in human, animals, plants and other living organisms (insects, bacteria,...)

Viruses are the smallest infectious agents (ranging from about 20 to 300 nm in diameter) and contain only one kind of nucleic acid (RNA or DNA) as their genome.

Viruses consist of :

- 1.A nucleic acid genome either DNA or RNA.
- 2.A protein coat (capsid) that enclosed the genome.
- 3.In some cases a lipid membrane (envelope)

Virion:A complete infectious virus particle.

General Properties of Viruses

1. Virus particles are very small in size; they are between 20-500 nm (nanometer) in diameter.
2. Viruses are obligatory intra cellular microorganisms.
3. Multiply inside the cells by replicating their genomes which either DNA or RNA, but not both.

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4. The virus does not contain any organelles (ribosomes, t RNA, metabolic enzymes, etc), but they depend on infected cells to provide all their needed organelles.
5. Virus does not affect with antibiotics.
6. Most viruses sensitive to interferon.
7. Viruses can not grow on artificial media, but only in living cells (specific host, Lab. Animals, chicken embryonated eggs & tissue culture).
8. Some viruses cause latent infection.
9. Viruses can not be seen by simple microscope, but only by Electron microscope (EM).

Classification of viruses

Basis of Classification

The following properties have been used as a basis for the classification of viruses:

1. **Virion morphology**, including size, shape, type of symmetry, presence or absence of peplomers, and presence or absence of membranes.
2. **Virus genome properties**, including type of nucleic acid (DNA or RNA), size of the genome, strand (single or double), whether linear or circular, sense (positive, negative), segments (number, size), nucleotide sequence, percent GC content, and presence of special features (repetitive elements, isomerization, 5'-terminal cap, 5'-terminal covalently linked protein, 3'-terminal poly(A) tract).

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3. **Genome organization and replication**, including gene order, number and position of open reading frames, strategy of replication (patterns of transcription, translation), and cellular sites (accumulation of proteins, virion assembly, virion release).

4. **Virus protein properties**, including number, size, amino acid sequence, modifications (glycosylation, phosphorylation, myristoylation), and functional activities of structural and nonstructural proteins (transcriptase, reverse transcriptase, neuraminidase, fusion activities).

5. **Antigenic properties, particularly reactions to various antisera.**

6. **Physicochemical properties of the virion**, including molecular mass, buoyant density, pH stability, thermal stability, and susceptibility to physical and chemical agents, especially solubilizing agents and detergents.

7. **Biologic properties, including natural host range, mode of transmission, vector relationships.**

Structure of viral nucleic acids:

Genetic information are stored as the following:

1. Double stranded DNA cells (animal, plants, bacteria and some viruses).
2. Single-stranded DNA in other viruses (phage x 174).
3. Single stranded RNA (myxovirus).
4. Double-stranded RNA (reoviruses).

How we can differentiate between DNA and RNA?

- By DNAase or RNAase

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· Between double and single stranded NA; by acridine orange stain, which is yellowish green in double stranded and red orange in single stranded.

Viral shape structure

Nucleocapsid is the arrangement between the viral nucleic acid genome with the capsid, this connection controlled by specific NA genetic information leading to different types of symmetry. Accordingly viruses can be classified into four symmetry structures.

1. Helical symmetry.
2. Cubical symmetry.
3. Binal symmetry.
4. complex symmetry.

viruses can be classified into several families according to the following characters:

A- Characters of viral nucleic acid (N.A):

1. Type of N.A if it is DNA or RNA.
2. Shape of N.A strand if it is ring or straight, single or double strand, segmented or not.
3. Molecular weight (size & diameter of N.A).
4. Replication site of N.A if it is in the cytoplasm or nucleus of infected cells.
5. Presence of transcriptase enzyme.

B- Characters of viral capsid:

1. Shape & size of capsid.
2. Symmetry of capsid with N.A (Helical, Cubical, Binal, Complex).
3. Site of capsid assembly inside the infected cells.

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4. Lipid solvent sensitivity.

5. Number of capsomeres which consisting the capsid.

According to all above characters recently viruses classified into two major groups which are **RNA group & DNA group** as following:

RNA Viruses families:

1. Picornaviridae
2. Orthomyxoviridae
3. Paramyxoviridae
4. Coronaviridae
5. Reoviridae
6. Retroviridae
7. Rhabdoviridae
8. Birnaviridae
9. Bornaviridae
10. Bunyaviridae
11. Togaviridae
12. Astroviridae
13. Arteriviridae
14. Caliciviridae
15. Flaviviridae

DNA Viruses families:

1. Parvoviridae
2. **Anelloviridae** (No specific disease associations have been proven).
3. **Polyomaviridae**
4. Papillomaviridae
5. Adenoviridae

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6. Hepadenaviride
7. Herpesviridae
8. Poxviridae

Atypical Virus Like Particles

There are four exceptions to the typical virus as described previously:

Defective viruses Composed of viral nucleic acid and proteins, but cannot replicate without a helper virus.

Pseudoviruses Contain host DNA instead of viral DNA ,its infect the host cell but don't replicate.

Viriods Consist of a single molecule of circular single strand RNA with no protein coat or envelope. They replicate and causes several diseases in plant but not in human

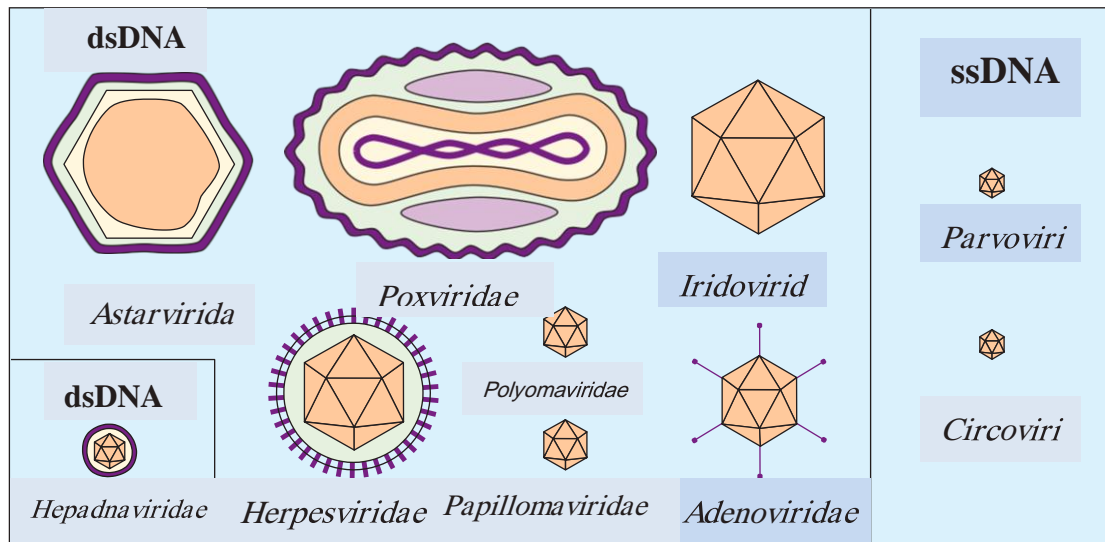
Prions Smallest known infectious particles, composed only protein .This protein has ability to causes fatal disease called spongiform encephalopathy slowly progressive diseases include :
scrapie disease in sheep, Bovine spongiform encephalopathy in cattle and kuru disease in human

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DNA viruses:

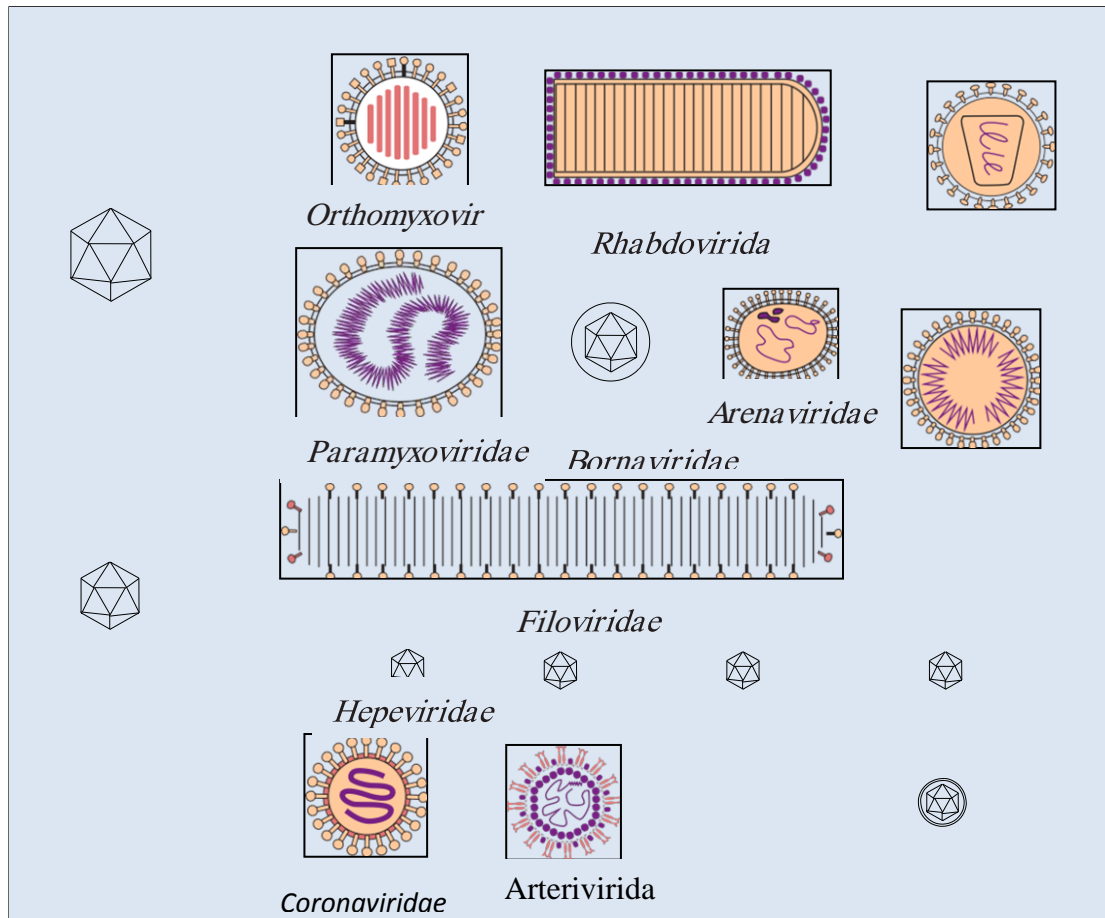


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RNA viruses:



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Pathogenesis

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Viral pathogenesis is the process that occurs when a virus infects a cell and causes cellular changes.

Disease pathogenesis is a subset of events during an infection that results in disease manifestation in the host.

Steps in Viral Pathogenesis

Specific steps involved in viral pathogenesis are the following: viral entry into the host, primary viral replication, viral spread, cellular injury, host immune response, viral clearance or establishment of persistent infection, and viral shedding.

A. Entry and Primary Replication

Most viral infections are initiated when viruses attach and enter cells of one of the body surfaces—skin, respiratory tract, gastrointestinal tract, urogenital tract, or conjunctiva.

B. Viral Spread and Cell Tropism

Some viruses, such as influenza viruses (respiratory infections) and noroviruses (gastrointestinal infections), **produce disease at the portal of entry and typically do not spread systematically**. Others can spread to distant sites (eg, cytomegalovirus [CMV], HIV, rabies virus) and cause additional disease manifestations . **Mechanisms of viral spread vary,**

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but the most common route is via the bloodstream or lymphatics. The presence of virus in the blood is called **viremia**.

Virions may be free in the plasma (eg, enteroviruses, togaviruses) or associated with particular cell types (eg, measles virus) . Viruses may multiply within those cells (eg, Epstein-Barr virus [EBV] is lymphotropic.

C. Cell Injury and Clinical Illness

Destruction of virus-infected cells in the target tissues and physiologic alterations produced in the host by the **tissue injury** are partly responsible for the development of disease.

Some tissues, such as intestinal epithelium, can rapidly regenerate and withstand extensive damage better than others, such as the brain.

D. Recovery from Infection

Following a viral infection, the host will succumb, recover, or establish a chronic infection. Recovery mechanisms include both innate and adaptive immune responses. Interferon (IFN) and other cytokines and possibly other host defense factors are involved. The relative importance of each component differs with the virus and the disease.

E. Virus Shedding

The last stage in pathogenesis is the shedding of infectious virus into the environment. This is a necessary step to maintain a viral infection in

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populations of hosts. Shedding usually occurs from the body surfaces involved in viral entry.

Viral Virulence

Virulence refers **to the capacity of a virus to cause disease in an infected host**. It is a quantitative statement of the degree or extent of pathogenesis. In general, a **virulent** virus causes significant disease, whereas an **avirulent** or **attenuated** virus causes no or reduced disease, respectively.

Virulence depends on

- Dose
- Virus strain (genetics)
- Inoculation route - portal of entry
- Host factors - eg. Age SV in adult neurons goes persistent but is lytic in young

Measuring Viral Virulence

Virulence can be quantified in a number of ways. One approach is to determine **the concentration of virus** that causes **death or disease in 50% of the infected animals**. This parameter is called the **50% lethal dose (LD50)**, the **50% paralytic dose (PD50)**, or the **50% infectious dose (ID50)**, depending on the parameter that is measured.

Other measurements of virulence include :

- mean time to death or appearance of symptoms
- measurement of fever or weight loss.

Virus-induced tissue damage can be measured directly by :

- examining histological sections or the blood.

The safety of live attenuated poliovirus vaccine is determined by assessing the extent of pathological lesions in the central nervous system in experimentally inoculated monkeys.

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- The reduction in blood concentration of CD4+ lymphocytes caused by human immunodeficiency virus type 1 infection is another example.

Indirect measures of virulence include assays for liver enzymes (alanine or aspartate amino-transferases) that are released into the blood as a result of virus-induced liver damage.

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