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MOUNTAIN TOP UNIVERSITY

E-Courseware

SCHOOL OF BASIC AND APPLIED SCIENCES

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COURSE GUIDE

COURSE TITLE: INTRODUCTORY VIROLOGY

COURSE CODE: MCB 206

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S. A. IBEMGBO

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COURSE OBJECTIVES

At the end of this course, students should be able to:

Understand the General characteristics of plant, animal and bacterial viruses; viral replication, spread and cytopathic effects.

Comprehend Virus classification, purification and assay.

Describe the Regulation of lytic development and maintenance of the Lysogenic state in bacteriophages lambda, P2 and 14 single stranded DNA and RNA phage; and viroids as pathogens.

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LECTURE 1

GENERAL CHARACTERISTICS OF PLANT, ANIMAL AND BACTERIAL VIRUSES

SCOPE AND CONCEPTS OF VIROLOGY:

The study of viruses is called as virology.

Viruses are simple non-cellular organisms which are made up of genetic materials and protein that can invade living cells. They are very small and they are measured in nanometers. They can only be seen with an electron microscope and can only reproduce by infecting living cells. Their size ranges from 20 nanometers to 250 nanometers.

They are very small submicroscopic infectious particles called virions. All viruses have a nucleocapsid composed of a nucleic acid genome surrounded by a protein capsid. They carry genetic information encoded in their nucleic acid which typically specifies two or more proteins. Some viruses have membranous envelope that lies outside nucleocapsid (Figure 1). The nucleocapsid of the virus can be RNA or DNA, single stranded or double stranded, linear or circular.

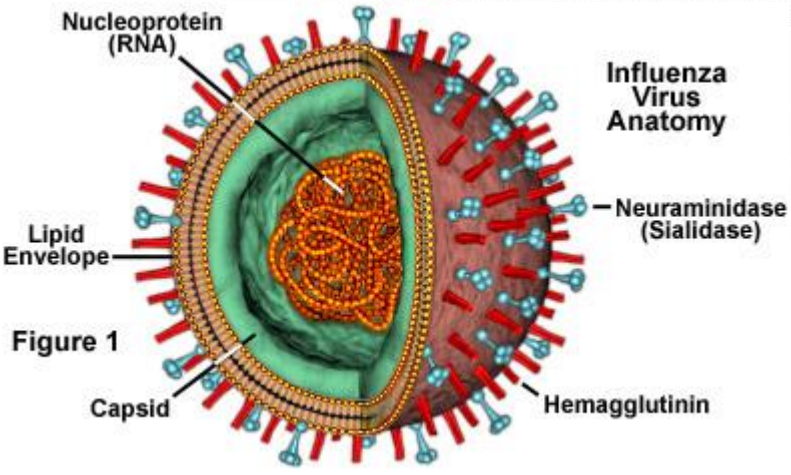

Figure 1. influenza virus

Source: http://micro.magnet.fsu.edu/cells/viruses/influenzavirus.html

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Although each virus has unique aspects of its life cycle, a general pattern of replication is observed. The typical virus life cycle consists of 5 steps.

1. Attachment to the host cell.
2. Entry to the host cell.
3. Synthesis of viral nucleic acid and proteins within the host cell.
4. Self-assembly of virion within the host cell.
5. Release of virion from the host cell.

Viruses are cultured by inoculating a living host such as mouse, rat or a living plant or cell cultures with a virus particle (virion).

Virus purification depends on their large size relative to cell components, high protein content and great stability. Virus concentration may be determined from the virion count or from number of infection unit. They are classified primarily on basis of nucleic acid characteristics, reproductive strategy, capsid symmetry and presence or absence of an envelope.

Viruses can exist in two phases the extracellular and intracellular phases. Virions of extracellular phase possess few if any enzymes and cannot reproduce without a living cell. In the intracellular phase, viruses exist primarily as a replicating nucleic acid that host cell metabolism to synthesize virion components. Eventually complete virus particles are released.

Viruses are also classified according to the following: host range, size, structure and life cycle.

Host Range: This is determined by the type of appropriate receptors (usually proteins) on the host cell surface. (Bacterial viruses are called bacteriophages because they breakdown bacterial cell wall.

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STRUCTURE OF VIRUSES

A virus consists of nucleic acid (NA) and protein. The NA is the genome of the virus that contains the information necessary for virus multiplication; the protein is arranged around the genome in the form of a shell that is the *capsid*. The shell and the NA make up the *nucleocapsid*. Some virus particles consist of a naked nucleocapsid, while others possess an *envelope* that is acquired from the host as the virus buds out. The complete particle is the *Virion***.**

Size: Smallness and structural simplicity are features of viruses Some are as small as 25µm while some are as large as 300nm. Viruses lack most cellular structures including cytoplasm, ribosomes and a nucleus or a nucleotide.

Structure: Basic structure of a virion is a nucleic acid core surrounded by a protein coat called Capsid.

Nucleic Acid- All cellular organisms store their genetic information in the form of double stranded (ds)DNA. During gene expression, they transcribe their genetic information into RNA. In contrast, various viruses store their genetic information in all forms of nucleic acids; ds DNA, single stranded ss (DNA), dsRNA and ss RNA but each virus uses only a single form. Viruses that use ss DNA convert it into unstable double stranded form only after it enters the host. Viruses that store information in RNA short circuit the flow of information from DNA too RNA to protein

Viral Capsid: The capsid which surrounds the acid core of a virus is made up of subunits capsomeres which in turn are composed of one or more different proteins. Capsids come in 3 basic shapes helical, polyhedral, and complex. The shape depends on how the capsomeres are arranged and how many kinds they are.

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Viral Envelopes: The membrane that enveloped a virus is actually a piece of the host cell's own cytoplasmic membrane. A virion acquires its envelope as it emerges from its host cell. Like the cytoplasmic membranes from which they were derived, viral envelope contains phospholipids and proteins. The phospholipid come from the host cell, but the proteins are encoded in the viral genome. Some of the proteins are glycoproteins (proteins that have sugar molecule attached to it). Enveloped viruses are very sensitive to non-polar solvents such as chloroform and ether because these solvents destroy the virus membrane and their ability to infect. Naked viruses are relatively resistant to non- polar solvents

CHARACTERISTICS OF PLANT, ANIMAL AND BACTERIAL VIRUSES:

PLANT VIRUS: It is a submicroscopic, transmissible intracellular obligate parasite and consists of nucleic acid (either RNA or DNA) which is typically surrounded by a protein coat called capsid. They cannot be grown in artificial media but require living host cell for multiplication. They have both living and non-living properties.

Living characters include their ability to cause disease, reproduce, mutate and have genetic materials. Non living characters are lack of cellular structure, lack of enzymatic activities, respiratory activities and they can be crystalized by physical means.

Structurally, nearly half of the plant viruses may be elongated (rigid rod or flexon threads) and spherical(isometric /polyhedral) and the remaining are cylindrical bacillus.

Examples:

Rigid rod e.g- Tobacco mosaic virus.

Flexons rood e.g Potato virus.

Filamentous rod-eg. Rice Stripe virus.

Isometric rod e.g Cucumber Mosaic virus

Bacilliform rod e.g. Banana Streak virus.

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Important Properties of Plant viruses :

1.They are highly infectious .

2.They are highly resistant to acids , alkalies and salt. e.g tobacco mosaic virus.

3. Virus is resistant to high temperature.e.g Tobaco mosaic virus.

4. Direct Sunlight has no effect on viruses. Tobaco mosaic virus infect healhy plant at 800C , but loses its power between 80oC -90oC .

5. Viruses can be filtered but more effectively through colloidal membrane.

6. The virus can retain power of infection for a long time even out of the living cell.

7. When virus is subjected to a high speed centrifuge, they get sedimented like protein .

8 Viruses increase in number and size within living protoplasm of a cell.

9 They can be transmitted from infected plant to a healthy plant by mechanical and biological means.

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LECTURE 2 - CLASSIFICATION OF VIRUSES

Animal viruses come in many types and they enter the host cell, commandeer and exit the cells in a variety of different ways. Most important characteristics in viral classification are morphology, nature of nucleic acid and genetic relatedness.

Baltimore System Group:

Viruses according to their type of genetic material and it is used to make messenger RNA, (mRNAs), key intermediates in the production of viral proteins and the assembly of new viruses.

Baltimore group classification depends on

1. The molecule it uses as genetic material (DNA or RNA).
2. Whether the genetic material is single or double stranded.
3. The steps the virus uses to make an mRNA.

The Baltimore system divides viruses into seven groups according to the relationship between the virion , the nucleic acid and m RNA transcription (Figure 2).

Note* The RNA within the virion is known as plus (+) or sense strand because it acts as m RNA , whereas the newly synthesized RNA which is complimentary in base sequence to the original infectious strand is called minus (-) or ant sense strand. It acts as template to produce additional (+) strand which may act as m RNA.

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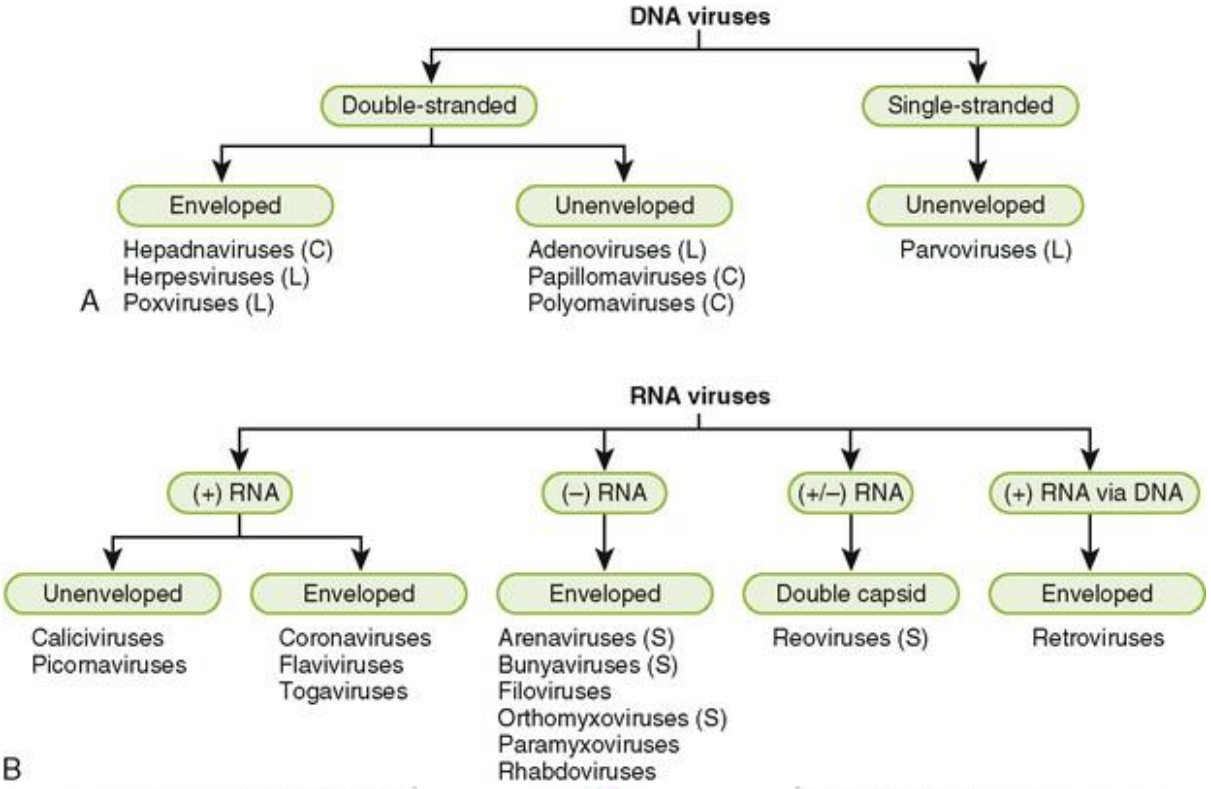

Figure 2: Classification of DNA and RNA viruses

Source: http://www.onlinebiologynotes.com/classification-of-virus/

The Seven groups are as follows.

Class 1 (double stranded DNA viruses):

The mRNA is synthesized on a dsDNA genome template (+dsDNA→ (+)m RNA) which occurs in a cell. Examples are Pox viruses: Vaccinia virus. Herpes Viruses : Herpes simplex virus Types 1 and 2. Epstein Barr virus.

2. Class 2. (+) ssDNA viruses: Here in such viruses, an intermediate DNA is synthesized before the synthesis of m RNA transcript +ssDNA → +m RNA . The m RNA has the same polarity as the DNA. E.g Parvo viruses.

3. Class 3 (+) ssRNA viruses : The RNA has similar polarity as the m RNA e.g Picorna viruses e.g Poilo virus.

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4. Class 4 (-) ssRNA viruses: Here the virion RNA is complementary to m RNA . Two types are found in this class. Rhabdoviruses e.g. Mumps Measles. Orthomyxo-viruses e.g Human Influenza.

5. Class 5. dsRNA viruses : All the viruses of this class have segemental genome. The dsRNA acts as template and asymmetrically synthesize (+) m RNA. e.g Reoviruses.

6. Class 6 . (+) ssRNA-RT viruses.

In these viruses (+) ssRNA directs the syntheses of (-)DNA which in turn acts as template for the transcription of m RNA . Virion RNA and m RNA are of the same polarity. Retroviruses are examples such as Mouse Leukemia viruses, HIV.

7 . Class 7. dsDNA –RT viruses.. This group consist of DNA containing hepatitis B viruses.

Within each of these groups, many characteristics are used to classify the viruses into families, genera and species. Typically a combination of characters are used and some of the most important are :

1. Particle morphology:- The shape and size of particles as seen

   under electron microscope.
2. Genome properties :- This include the number of genome components and the translation strategy.
3. Biological properties:- This may include the type of host and the mode of transmission.
4. Serological properties:- This uses the relatedness of vrion proteins.

The International committee on Taxonomy of viruses (ICTV) devised and implemented several rules on the naming and classification of viruses since 1990. They oversee till now ,the naming and placement of viral classification starts at the level of order and follows as stated with the taxon suffixes given in Italics.

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Order-(virales)→family (-viridae)-subfamily (virinae)→Genus(-virus) →Species (-virus). This system of nomenclature differs from other taxonomic codes on many points. A minor point is that names of orders and families are italicized. Most importantly, species names generally take the form of (disease virus). ICTV nomenclature is used to classify animal viruses into families and genera. But plant viruses are not like that, but group names derived from prototype virus are used by plant virologist.

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LECTURE 3 - VIRAL REPLICATION:

Outside the host cell, viruses exit only in the form of virions which cannot replicate. To replicate, a virus must infect a host cell. To do so, the virion attaches itself to the cell by a process called adsorption. Then the viral genome enters the host cell by a process called penetration. During penetration, some types of viruses open and disassemble, so that only the nucleic acid enters the host cell. The process of removing the capsid and envelope is called un-coating. In other cases, the entire virion is taken into the host cell and un-coating later. After un-coating, the viral nucleic acid directs the host cell to make viral component nucleic acid and protein. Intact new virions re-appear only as these components are re-assembled in the process of maturation. Soon afterwards, the virus particles exit the infected cell during the process of release, often but not always the cell is killed (Figure 3).

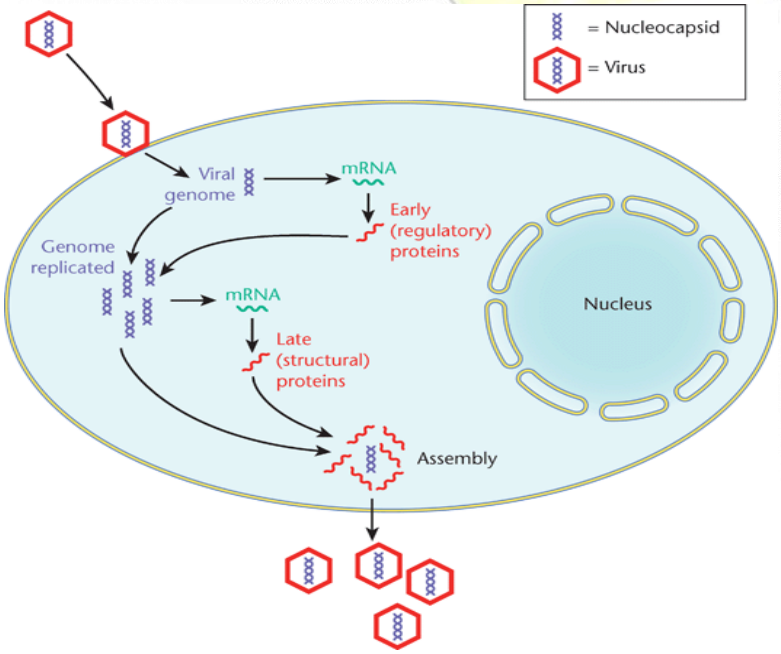

Figure 3: life cycle of a typical virus

Source: http://www.els.net/WileyCDA/ElsArticle/refId-a0000438.html

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VIRUS PURIFICATION.

Purification makes use of several virus properties. Viruses that are very large relative to proteins, are often more stable than normal cell components and have surface proteins.

Techniques useful for isolation of viruses are:

1. Differential and density gradient centrifugation.
2. Precipitation of viruses.
3. Denaturation of contaminants.
4. Enzymatic digestion of host cell constituents.

Differential and density gradient centrifugation are often used in the initial purification steps to separate virus particles from host cells. Infected cells are first disrupted in a buffer to produce an aqueous suspension or homogenate density of cell component and viruses. Viruses can then be isolated by differential centrifugation . This is a centrifugation of a suspension at various speed to separate particles of different sizes. Additional means of purification of a virus can be achieved by gradient centrifugation. Viruses can also be separated from other particles based on very small differences in density. Gradient can also be used to separate viruses based on differences in their sedimentation rate.

CYTOCIDAL INFECTIONS AND CELL DAMAGE

An infection that results in cell death is a cytocidal infection. Microscopic and macroscopic degenerative changes or abnormalities in host cells and tissues are referred to as cytopathic effects.

Mechanisms of host cell damage are described, but more than one can take place to cause cell damage.

1. Many viruses can inhibit host DNA, RNA and protein synthesis. (Such Cytocidal viruses include Picorna viruses, Herpes viruses and Adeno viruses).

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2. Cell endosomes may be damaged, resulting in the release of hydrolyte enzymes and cell destruction.
3. Virus infection can drastically alter plasma membranes through the insertion of virus specific proteins, so that infected cells are attacked by the immune system of host. When infected by viruses such as herpes viruses and measles viruses, as many as 50 to 100 cells may fuse into one abnormal giant multinucleated cell called a syncytium . HIV appears to destroy CD4+ T helper cells at least through its effects on the plasma membrane.
4. High concentration of proteins from several viruses (e.g mump virus and influenza virus can have a direct toxic effect on cells and the organisms.
5. Intracellular structures called inclusion bodies are formed during many virus infections. These may result from the clustering of subunits or virions within the nucleus or cytoplasm.
6. Chromosomal distruptions can result from infections by herpes viruses and others.
7. The host cell may not be directly destroyed, but transformed into a malignant cell.

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