LECTURE-1

Introduction: Viruses and their Importance

Virus: is infectious particle containing one type of nucleic acid and surrounded by protein coat. The viral particle has ability to replicate only in living host cell, and cause disease.

Virus infect all cellular life form: **eukaryotes** (vertebrate animals, invertebrate animals, plant, fungi) and **prokaryotes** (bacteria and archaea).

As a science, virology evolved later than bacteriology because comparatively large size of bacteria made them visible even with simple microscope. the physical nature of viruses was not fully revealed until the invention of the electron microscope (EM), the infections they caused have been known and feared since the dawn of history.

The Latin word virus means "poisonous fluid", and this is just what seemed to the first virologists.

In the latter part of nineteenth century, Iwanowski in Russia and Beijerinck in Holland both showed that a plant infection, Tobacco mosaic, could be transmitted by extracts that had been passed through a chamber and filter, and hence could not contain bacteria. Soon, afterwards, Foot-and-mouth disease of cattle was also transmitted by bacteria-free filtrates, and it came to be realized that living agents, smaller than any known bacteria but capable of multiplying, could cause a wide range of diseases in plants and animals.

Viruses infect:

- **Humans**

Smallpox [1]

- **Other vertebrates**

Foot and mouth disease [2]

- **Invertebrates**

Leatherjackets infected with *Tipula* iridescent virus

- **Plants**

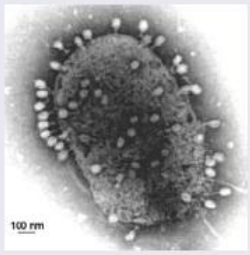
Delayed emergence of potato caused by tobacco rattle virus infection [3]

Damaged potato (spraing) caused by tobacco rattle virus infection [3]

- **Fungi**

Mushroom virus X [4]

- **Bacteria**



Escherichia coli cell with phage T4 attached [5]

Nature of viruses

Viruses have the following characteristics :

1. They are small particles:

Bacteria are measured in terms of the micrometer (µm), which is 10^{-6} of a meter. For viruses, we use the nanometer (nm) as the unit, which is a thousand times smaller (10^{-9} of a meter). Virus range from about 20 nm to 150 nm in diameter.

2. Viruses have genes:

They possess only one type of nucleic acid, either DNA or RNA but never both. Whereas the genome of cells are composed of double-stranded DNA, there are four possibilities for a virus genome:

- double-stranded DNA (dsDNA)
- single-stranded DNA (ssDNA).
- double-stranded RNA (dsRNA).
- single-stranded RNA (ssRNA).

The genome is enclosed in a protein coat known as a capsid.
(genome + capsid + other components in many cases= virion).

3. Viruses are parasites:

They are totally dependent on living cells for replication and existence. Viruses differ from cells in the way in which they multiply. A new cell is always formed directly from a pre-existing cell, but a new virion is never formed directly from a pre-existing virion. New virions are formed by a process of replication, which takes place inside a host cell and involves the synthesis of components followed by their assembly into virions. Viruses are therefore parasites of cells, and are dependent on their hosts for most of their requirements, including:

• building-blocks such as amino acids and nucleosides;

• protein-synthesizing machinery (ribosomes);

• energy, in the form of adenosine triphosphate.

A virus modifies the intracellular environment of its host in order to enhance the efficiency of the replication process. Modifications might include production of new membranous structures, reduced expression of cell genes or enhancement of a cell process.

General properties of viruses:

Viruses are unlike any other forms of organisms. They are different from other infectious organisms in the following specific properties:

1. Viruses possession of only one type of nucleic acid , either DNA or RNA , but never both.
2. Viruses are not considered as cell because they do not have a cellular composition and inert metabolically. They lack cellular organelles such as: nucleus, cytoplasm, mitochondria, ribosome, Golgi apparatus, and endoplasmic reticulum (they have no metabolic system of their own).

3. Viruses are not capable of independent replication ,but they replicate only within living host cell, therefore they are known as obligate intracellular parasites.
   - Viruses inside living host cell are active, whereas outside living cells are inactive (inert). Therefore viruses fall at linked between living and nonliving things.
   - Viruses cannot grow on inanimate culture media (non-living), but grow in tissue cultures (living cells).

4. Their genomes encode minimal information to ensure the following:
   a- genome replication and packaging.
   b- production of viral proteins.
   c- subvert cellular functions to allow the production of virions.

5. Viruses cannot replicate by binary fission or mitosis ,but they replicate by complex process .
   - The viruses produce many copies of their nucleic acid and proteins, and then re-assemble into multiple new viruses (progeny viruses).
   - One virus can replicate to produce hundreds of progeny viruses , whereas other organisms , one cell divides to produce only two daughter cells.
6. All viruses are pathogenic, and the viruses infect all types of organisms in nature (such as animals, plants, fungi, bacteria).
7. Viruses cannot seen by light microscope (therefore the viruses termed as submicroscopic agents), but they can seen by electronic microscope.
8. Viruses are unaffected by antibiotic agents but sensitive to antiviral chemotherapy agents and interferon.

Table: Comparison of medical important organisms.

Characteristic	Virus	Bacteria	Fungi	Protozoa
Cells	No	Yes	Yes	Yes
Diameter (μm)	0.02- 0.3	1-5	3-10 (yeast)	15-25 (trophozoites)
Nucleic acid	Either DNA or RNA	Both	Both	Both
Type of nucleus	none	prokaryotic	Eukaryotic	Eukaryotic
Mitochondria	Absent	Absent	Present	Present
Ribosome	Absent	70s	80s	80s
Nature of outer surface	Capsid (protein) and lipoprotein envelop	Rigid cell wall contains peptidoglycan	Rigid wall with chitin	Flexible membrane
Motility	None	Some	No	Most
Method of replication	Complex	Binary fission	Budding or mitosis	Mitosis
ATP	Absent	Present	Present	Present

Origin of Viruses

There are three major theories that have been advanced for the origin of viruses:

1- Viruses originated in the primordial soup co-evolved with more complex life forms. **(Coevolution)**

2- The evolved from free-living organisms that invaded other life forms and gradually lost functions. **(Retrograde evolution)**

3- Viruses are "escaped" pieces of nucleic acid no longer under control by the cell- also termed the escaped gene theory. **(Escaped gene theory)**

The great variety of viruses present in the living world affirms that they originated independently many, many times during evolution. Viruses also originated from other viral types through mutation.

Reasons for studying viruses

1. Some viruses cause disease

Viruses are important agents of many human diseases, ranging from the trivial (e.g. common colds) to the lethal (e.g. rabies), and viruses also play roles in the development of several types of cancer. As well as causing individuals to suffer, virus diseases can also affect the well-being of societies. Smallpox had a great impact in the past and AIDS is having a great impact today. There is therefore a requirement to understand the nature of viruses, how they replicate and how they cause disease. This knowledge permits the development of effective means for prevention, diagnosis and treatment of virus diseases through the production of vaccines, diagnostic reagents and techniques, and antiviral drugs. These medical

applications therefore constitute major aspects of the science of virology. Veterinary virology and plant virology are also important because of the economic impact of the many viruses that cause disease in domestic animals and crop plants: foot and mouth disease virus and rice yellow mottle virus are just two examples. Another area where viruses can cause economic damage is in the dairy industry, where phages can infect the lactic acid bacteria that are responsible for the fermentations that produce cheese, yogurt and other milk products.

2. Some viruses are useful

Some viruses are studied because they have useful current or potential applications.

• ***Phage typing of bacteria.***

Some groups of bacteria, such as some *Salmonella* species, are classified into strains on the basis of the spectrum of phages to which they are susceptible. Identification of the phage types of bacterial isolates can provide useful epidemiological information during outbreaks of disease caused by these bacteria.

• ***Sources of enzymes.***

A number of enzymes used in molecular biology are virus enzymes. Examples include reverse transcriptase from retroviruses and RNA polymerases from phages.

• ***Pesticides.***

Some insect pests are controlled with baculoviruses and myxomavirus has been control rabbits.

• ***Anti-bacterial agents.***

In the mid-20th century phages were used to treat some bacterial infections of humans. Interest waned with the discovery of antibiotics, but has been renewed with the emergence of antibiotic-resistant strains of bacteria.

• ***Anti-cancer agents.***

Genetically modified strains of viruses, such as herpes simplex virus and vaccinia virus, are being investigated for treatment of cancers. These strains have been modified so that they are able to infect and destroy specific tumor cells, but are unable to infect normal cells.

• ***Gene vectors for protein production.***

Viruses such as certain baculoviruses and adenoviruses are used as vectors to take genes into animal cells growing in culture. This technology can be used to insert into cells genes encoding useful proteins, such as vaccine components, and the cells can then be used for mass production of the proteins.

• ***Gene vectors for treatment of genetic diseases.***

Children with severe combined immunodeficiency (baby in the bubble syndrome) have been successfully treated using retroviruses as vectors to introduce into their stem cells a non-mutated copy of the mutated gene responsible for the disease.

3. Virus studies have contributed to knowledge

Much of the basic knowledge of molecular biology, cell biology and cancer has been derived from studies with viruses. Here are a few examples.

• A famous experiment carried by Alfred Hershey and Martha Chase, and published in 1952, used phage T2 and *E. coli* to provide strong evidence that genes are composed of DNA.

• The first enhancers to be characterized were in genes of simian virus 40 (SV40).

• The first transcription factor to be characterized was the transplantation (T) antigen of SV40.

• The first nuclear localization signal of a protein was identified in the T antigen of SV40.

• Introns were discovered during studies of adenovirus transcription.
• The role of the cap structure at the 5 end of eukaryotic messenger RNA was discovered during studies with vaccinia virus and a reovirus.

• The first internal ribosomal entry site to be discovered was found in the RNA of poliovirus.

• The first RNA pseudoknot to be discovered was that in the genome of turnip yellow mosaic virus.