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# Introduction and History of the Virology

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Epidemics caused by viruses began when human behavior changed during the **Neolithic period** around 12,000 years ago. From Previously hunter-gatherers to agricultural communities, which allowed viruses to spread rapidly and subsequently to become endemic.

This agricultural revolution included the development of monoculture and presented an opportunity for the rapid spread of many plant viruses such as **potyviruses** that infect potatoes, and other fruits and vegetables, **began about 6,600 years ago.**

**The year 3500 BC:**

Viral diseases known when the human being knew the diseases and began practicing, the first written record of a virus infection, provided by the ancient Egyptian civilization indicated by the photos on the walls of the temples, the stone tablet shows an Egyptian from the 18th dynasty with polio (1580-1350 B.C.) – notice his withered leg and shape of the foot, which are typical of the disease (**Poliomyelitis**).

# The Year 1193 BC

**The Pharaoh Siptah** rules Egypt from 1200-1193 BC when he dies suddenly at the age of about 20.

His mummified body lays undisturbed in his tomb in the Valley of the Kings until 1905 when the tomb was excavated.
The mummy shows that his left leg was withered and his foot was rigidly extended like a horse's hoof - classic paralytic **poliomyelitis**

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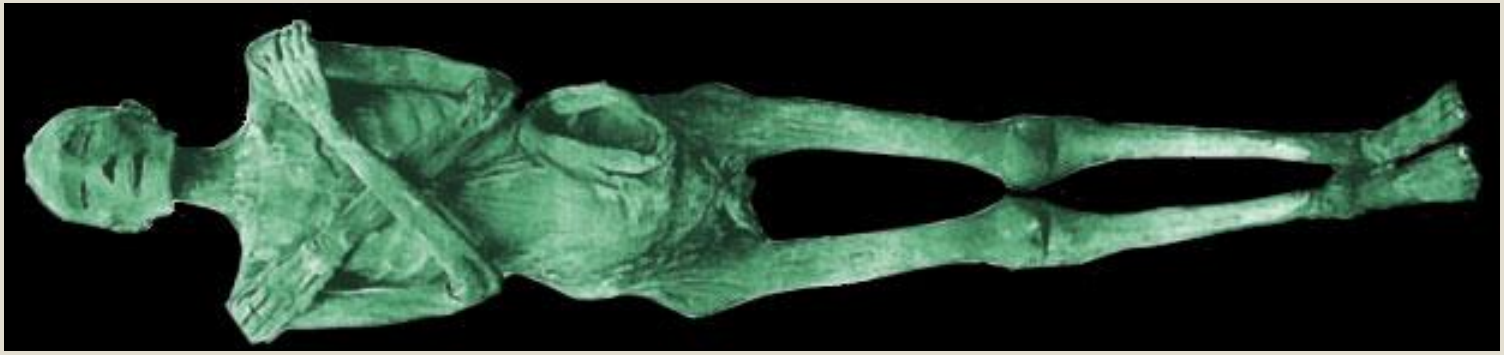
FOOT→

# The Year 1143 BC

**Ramesses V's preserved** mummy shows that he died of **smallpox** at about the age of 35 in 1143 BC.

The pustular lesions on the face of the mummy are very similar to those of more recent patients

However, his head also displays a major wound inflicted either before or shortly after death.



# The Year 1000 BC

Smallpox is endemic in China by 1000BC. In response, the practice of **variolation** is developed.

Recognizing that survivors of smallpox outbreaks are protected from subsequent infection, variolation involves inhalation of the dried crusts from smallpox lesions like snuff, or in later modifications, inoculation of the pus from a lesion into a scratch on the forearm

**Measles** is an old disease, but it was not know until the 10th century that the Persian physician **Muhammad ibn Zakariya al-Razi (865–925)** – known as "Rhazes" – first identified it. Rhazes used the Arabic name hasbah for measles. It has had many other names including rubeola from the Latin word rubeus, "red", and morbilli, "small plague"

Until the 17th century, the term virus was used to refer to all infectious diseases. No distinction was made between bacteria and viruses.

In the 17th century, **Antoni van Leeuwenhoek** invented the light microscope. Now, the term virus was used to describe only those "poisons" that could not be viewed through the microscope.

**Edward Jenner (1749–1823), a British rural physician vaccinated** on 14th May 1796, an 8 year old boy, James Phipps, with material from a cowpox lesion on the hand of a milkmaid, Sarah Nelmes. James, who had never had smallpox.

Small lesion developed at the site of vaccination which healed in 2 weeks.

On 1st July 1796, Jenner challenged the boy by deliberately inoculating him with material from a real case of smallpox !So Jenner developed a smallpox vaccine using milder cowpox viruses.

**The year 1886:**

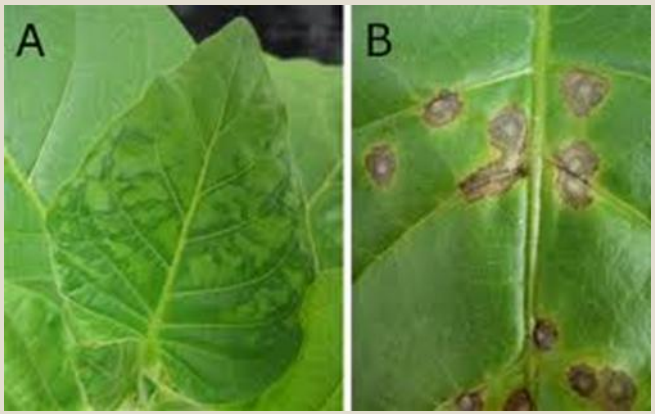
**Louis Pasteur** tested a rabies vaccine. This depended on deliberate, experimental production of the vaccine by serial passage of infectious virus in rabbit spinal cords.
The next vaccines for yellow fever and influenza did not appear until the 1930s.

**Louis Pasteur and Edward Jenner were the first to develop vaccines to protect against viral infections.**


## The birth of virology was by, **Adolf Mayer (1886-1942)**

A German scientist he began his research on diseases of tobacco and, he named the disease tobacco mosaic disease the dark and light spots on infected leaves.

**In one of Mayer's experiments**, he inoculated healthy plants with the juice extracted from diseased plants by grinding up the infected leaves in water. This was the first experimental transmission of a viral disease of plants. He was able to demonstrate that the mosaic disease could spread from plant to plant if the juice of the infected leaves is applied to healthy leaves



**(Dmitri Iwanowski) (1892): Russian scientist** rapidly **repeated Mayer's** observations, demonstrating that the sap of infected plants contained an agent able to transmit the disease to healthy plants, and he added one additional step. He passed the infected sap through a filter that blocked the passage of bacteria, the **Chamberland pasteur filter**, contained pores small enough to retard most bacteria with pore sizes of 0.1 – 1 micron (100 – 1000 nm).

Iwanowski's discovery of the filterable virus. Infected tobacco leaves were crushed and filtered through Chamberland's bacterial filter (b). The cell debris applied to healthy leaves without effect (c), when the clear filtrate was placed on the leaves (d) the leaves shrunken and died. This experiment showed the presence of a "filterable virus" that was smaller than any known bacteria.

This is generally recognized as the beginning of Virology. Unfortunately, neither Iwanowski nor the scientific community fully realize the significance of these results.

**Loeffler and Frosch (1898) passed the first animal virus through a similar filter and discovered the cause of foot-and-mouth disease.**

Walter Reed (1851-1902)

Demonstrated that **yellow fever** was caused by a virus, spread by mosquitoes. During the Spanish-American War & subsequent building of the Panama Canal.

**Karl Landsteiner (1868-1943)** and **Erwin Popper** proved that **poliomyelitis** was caused by a virus. And this viruses could infect **humans as well as animals.**

**Twort in 1911** : British scientist were the first discovered the viruses that attacked the bacteria and later in more detail independently by French scientist d'Herelle, in 1917 who named them **bacteriophage.**

In late 1918, French scientists showed that a "filter-passing virus" could transmit the disease to people and animals, **fulfilling Koch's postulates.**

**Koch's postulates**

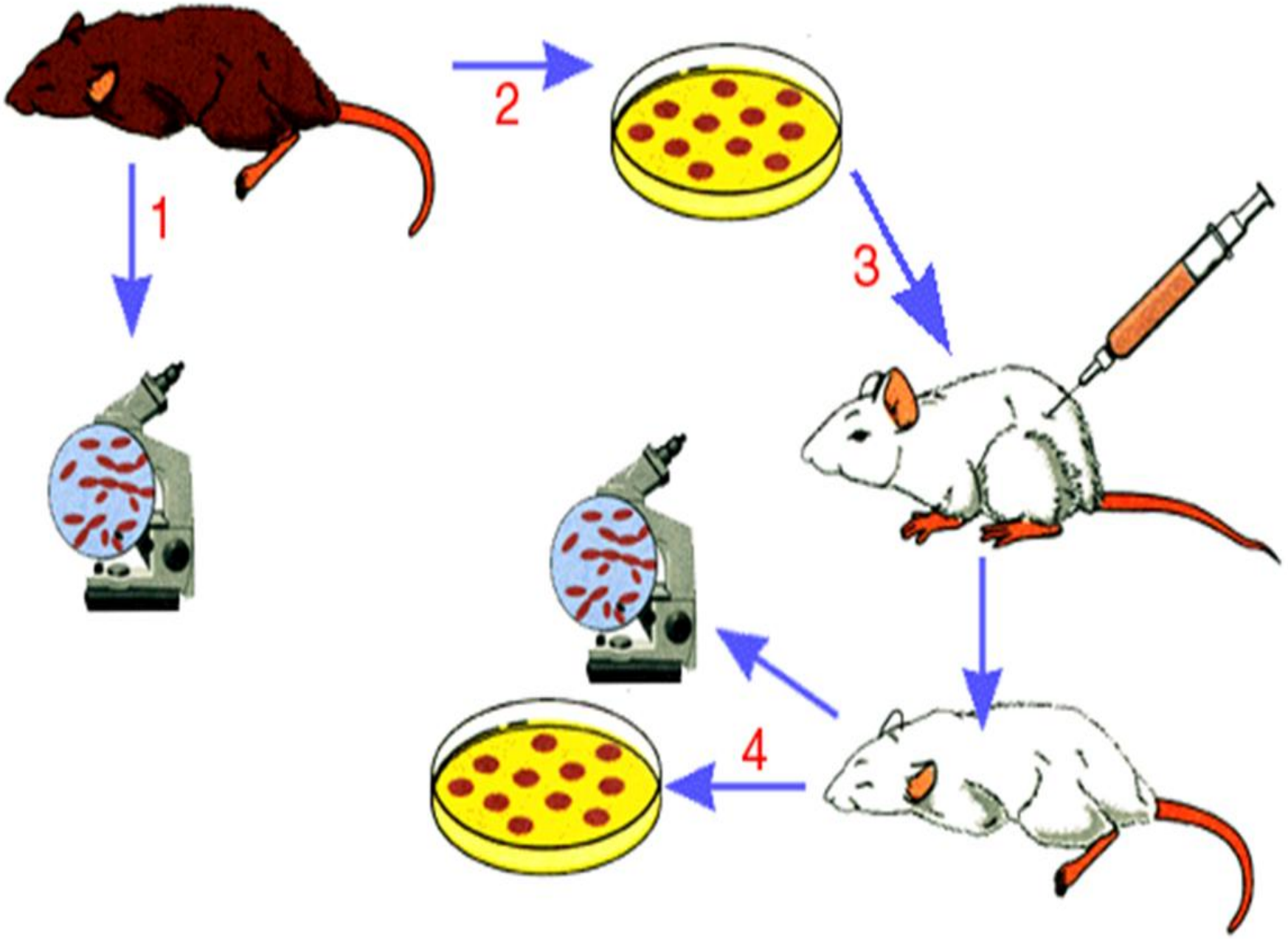
Four criteria that were established by Robert Koch to identify the causative agent of a particular disease, these include:

**1-The microorganism or other pathogen must be present in all cases of the disease**

**2- The pathogen can be isolated from the diseased host and grown in pure culture**

**3- The pathogen from the pure culture must cause the disease when inoculated into a healthy, susceptible laboratory animal**

**4- The pathogen must be reisolated from the new host and shown to be the same as the originally inoculated pathogen**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Until the 1930s most scientists believed that viruses were small bacteria, but following the invention of the electron microscope in 1931 they were shown to be completely different, to a degree that not all scientists were convinced they were anything other than accumulations of toxic proteins.

In 1931 by the German engineers **Ernst Ruska** and **Max Knoll** invention of the **Electron Microscope** (EM) came the first images of viruses.

The situation changed radically when it was discovered that viruses contain genetic material in the form of DNA or RNA. Once they were recognized as distinct biological entities they were soon shown to be the cause of numerous infections of plants, animals and even bacteria.

Max Theiler was the first to propagate yellow fever virus in **chick embryos** and successfully produced an attenuated vaccine - the 17D strain. Theiler's vaccine was so safe and effective that it is still in use today!

This work saved millions of lives and set the model for the production of many subsequent vaccines. For this work, Theiler was awarded the **Nobel Prize in 1951**.

# Avian Influenza

The last pandemic of Influenza virus in the 19th century occurred in 1899 and resulted in the deaths of 250,000 people in Europe.

A new strain of the virus emerged in 1918, and the subsequent pandemic of Spanish flu was one of the worst natural disasters in history.The death toll was enormous; throughout the world around 50 million people died from the infection.

In 1957 another new strain of the virus emerged and caused a pandemic of Asian flu.

The next pandemic occurred when Hong Kong flu emerged in 1968, a new strain of the virus that replaced the 1957 strain.

The most recent pandemic occurred in 2009, involved another strain of Influenza A H1N1, commonly known as "swine flu".

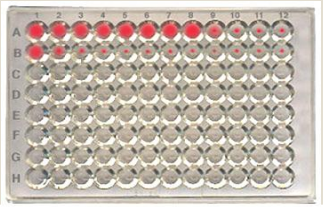
The strain of Influenza A virus subtype H1N1 that killed up to 50 million people during the Spanish flu pandemic in 1918 was reconstructed in 2005. Sequence information was pieced together from preserved tissue samples of flu victims; viable virus was then synthesized from this sequence.

The 2009 flu pandemic involved another strain of Influenza A H1N1, commonly known as "swine flu".

**In 1931** it was shown that **influenza virus** could be grown in **fertilized chicken eggs**, a method that is still used today to produce vaccines.

In 1941, **George Hirst** discovered that adding influenza virus particles to red blood cells caused them to **agglutinate** or stick together forming a lattice, a phenomenon called **hemagglutination**.

Hemagglutination provided a convenient method of diagnosing influenza in the laboratory.



**John Enders**, **Thomas Weller** (1915–) and **Frederick Robbins** (1916–) were able to grow **poliovirus** in vitro using **human tissue culture**. (Nobel Prize, 1954) This development led to the isolation of many new viruses in **tissue culture**.

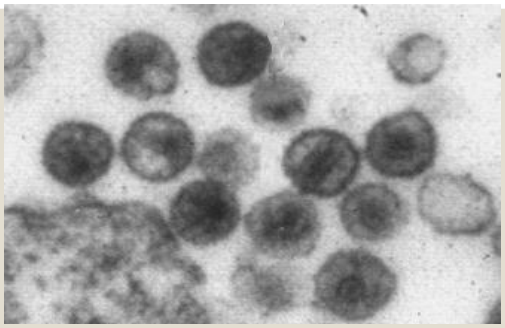
**What is TC?**

**lick Isaacs and Jean Lindemann (1957):** Discovered the interferon. Although the initial hopes for interferons as broad spectrum antiviral agents equivalent to antibiotics have faded, interferons were the first cytokines to be studied in detail.

**Baruch Blumberg** discovers **hepatitis B virus (HBV)**. (Nobel Prize, 1976) Blumberg went on to develop the first vaccine against the HBV, considered by some to be the first vaccine against cancer because of the strong association of hepatitis B with liver cancer.

**In 1965, Howard Temin and David Baltimore**
Described the first retrovirus: an RNA-virus that was able to insert its genome in the form of DNA into the host's genome.
Reverse transcriptase, the key enzyme that retroviruses use to translate their RNA into DNA, was first described in 1970.
The first retrovirus infecting humans was identified by **Robert Gallo in 1974**. Later it was found that reverse transcriptase is not specific to retroviruses; retrotransposons which code for reverse transcriptase are abundant in the genomes of all eukaryotes.
About 10-40% of the human genome derives from such retrotransposons.

The discovery of **reverse transcription** established a pathway for genetic information flow from RNA to DNA, refuting the so-call "central dogma" of molecular biology.



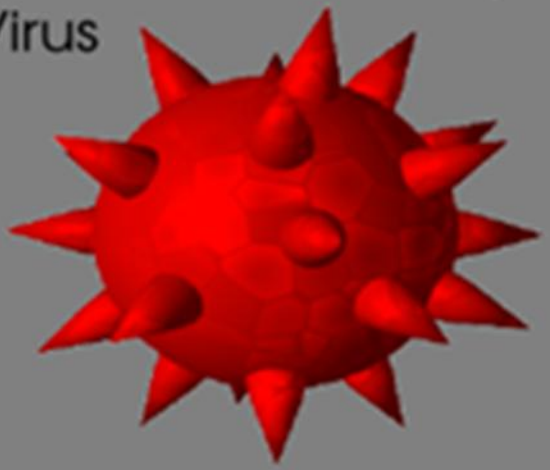
The first cases of **AIDS** were reported in **1981**, and **HIV(**human immunodeficiency virus )**,** the retrovirus causing it, was identified in 1983 by **Robert Gallo** and **Luc Montagnier**. Tests detecting HIV infection by detecting the presence of HIV antibody were developed. Subsequent tremendous research efforts turned HIV into the best studied virus.

In only two years since the start of the AIDS epidemic the agent responsible has been identified.

HIV-1 is one of the most significant viruses to have emerged in the last quarter of the 20th century and over 70 million individuals have been infected by the virus. By 2011, an estimated 35 million had died from AIDS, making it one of the most destructive epidemics in recorded history.

# HIV & AIDS

**HIV**: Human Immunodeficiency Virus



HIV is a virus which attacks immune system in humans.

**AIDS**: Acquired Immune Deficiency Syndrome

AIDS is a medical condition (immune system is too weak to fight infections).

# Rabies

Is an often fatal disease caused by the infection of mammals with rabies virus.

*rabies* is a Sanskrit word (*rabhas*) that dates from 3000 BC,which means "madness" or "rage", and the disease has been known for over 4000.

In France during the time of Louis Pasteur (1822–1895) there were only a few hundred rabies infections in humans each year.

Pasteur showed that when the dried spinal cords from dogs that had died from rabies were crushed and injected into healthy dogs they did not become infected. He repeated the experiment several times on the same dog with tissue that had been dried for fewer and fewer days, until the dog survived even after injections of fresh rabies-infected spinal tissue. Pasteur had immunized the dog against rabies, as he later did with 50 more.

As humans have changed their behaviour during history, so have viruses. In ancient times the human population was too small for pandemics to occur and, in the case of some viruses, too small for them to survive.

**In the 20th and 21st century** increasing population densities, revolutionary changes in agriculture and farming methods, and high speed travel have contributed to the spread of new viruses and the re-appearance of old ones. Like smallpox, some viral diseases might be conquered, but new ones, such as **severe acute respiratory syndrome** (SARS), will continue to emerge.

The first attempts at gene therapy involving viral vectors began in the early 1980s, when retroviruses were developed that could **insert a foreign gene into the host's genome**. They contained **the foreign gene but did not contain the viral genome** and therefore could not reproduce. Tests in mice were followed by tests in humans, beginning in 1989. The first human studies attempted to correct the genetic disease severe combined immunodeficiency (SCID), but clinical success was limited. In the period from 1990 to 1995, gene therapy was tried on several other diseases and with different viral vectors, but it became clear that the initially high expectations were overstated. In 1999 a further setback occurred when 18-year-old **Jesse Gelsinger** died in a **gene therapy** trial. He suffered a severe immune response after having received an adenovirus vector.

Success in the gene therapy of two cases of X-linked SCID was reported in 2000.

Gene therapy is an experimental technique that uses genes to treat or prevent disease. In the future, this technique may allow doctors to treat a disorder by **inserting a gene into a patient’s cells instead of using drugs or surgery**.

Replacing a mutated gene that causes disease with a healthy copy of the gene.

Virology: Is the science that deals with discovery, isolation , identification, characterization, pathogenecity, pathogenesis and classification of viruses.

**Virus:**

Is an infectious agent which is obligate intracellular parasite require a hosts to cause damage. They contain only one type of functional nucleic acid either RNA or DNA.

Viruses are not organisms, and contain no functional ribosome's, mitocondria or other cellular organelles. The virus was capable to replication only within the living cells such as bacteria, animals or plants by using the synthesizing machinery of the cell cause the synthesis of specialized structures that can transfer viral nucleic acid to other cells.

Viruses are generally made up of two parts, the outer protein shell (called a capsid) and the genetic information inside. Generally the morphology of a virus can be one of two structures, that of a **sphere or that of a tube**.

**What is a virus?**

Viruses are uniquely different from the many uni-cellular micro-organisms you have studied so far. **Protozoa**, **yeasts**, **bacteria**, **mycoplasmas**, **rikettsiae** and **chlamydiae** are all living organisms with the following features in common:

They are all **cells**

They store their **genetic information** as **DNA**

Within their cell, they contain all the **organelles** necessary for producing energy and **synthesizing proteins, carbohydrates**, cell wall structures etc.

Replicate by means of **binary fission**

Viruses,

- Small size
- Filtrable agents
- Obligate intracellular parasites, Can not make energy or proteins, independently of a host cell.

Viral genome

# RNA or DNA, Never both !!!!!!

Viruses have a **naked** capsid or **envelope** with attached proteins

Do not replicate by division=binary fusion

Viral components are produced in the host cell and assembled.

Viruses do not have the genetic capability to multiply by division.

All replication and infection restricted to N.A core.

The virus are non-living entities out the body inert and inside the body are obligatory.

## Are Viruses living or non living?

Viruses being the simplest and most primitive, it is difficult to assign to them any rank in the living kingdom. It is also not easy to define the features viruses within the accepted frame work of living beings. Hence it is better to regard them as an intermediate stage between living and non living. Some of the characters of living as well as non living exhibited by viruses are as follows:-

## characters of living beings

1 .Viruses have genetic material (DNA or RNA)
2.They mutate
3.They can grow
4.They can be transmitted from one host to another
5.They are capable of multiplication within a host
6.They react to heat, radiation and chemicals
9.They are able to infect and cause disease to living beings.
10. The DNA and proteins of viruses are similar in composition and structure to those of higher organisms.

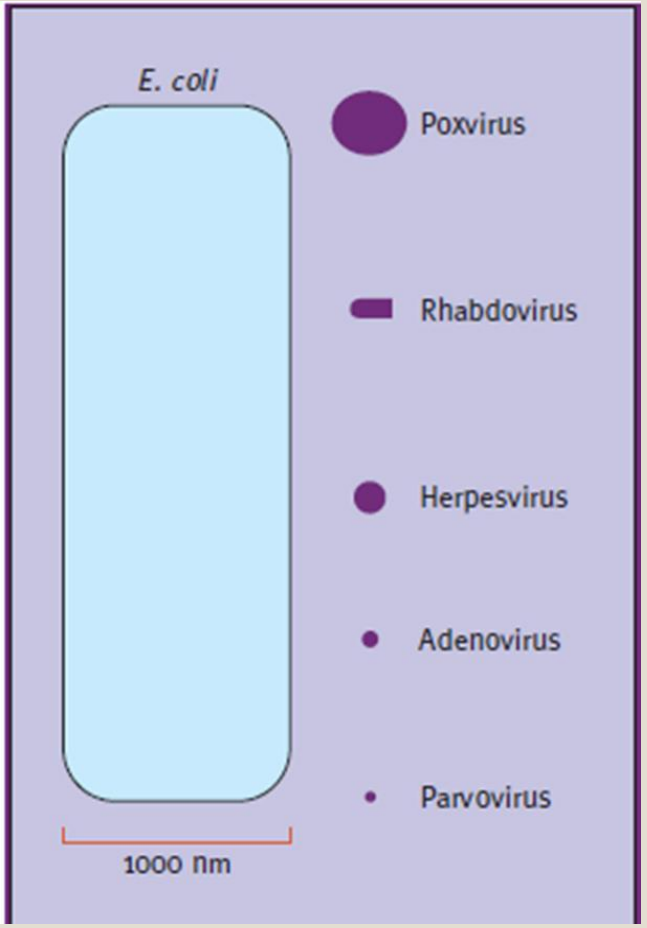
## Characters of non living:

1.They can be crystallized like an ordinary chemical and stored in a bottle or test tube indefinitely.
2.Outside the host viruses are inert.
3.There is no cell wall, membrane or cytoplasm.
4.There are no cell organelles and there is no metabolism.

## Size of Viruses

Clinically important viruses Range from **18-20(nm) such as, Parvoviruses** to **300 nm (poxviruses).**

Range from small and simple (parvoviruses and picornaviruses) **to** Large and complex viruses (pox viruses and herpesviruses).

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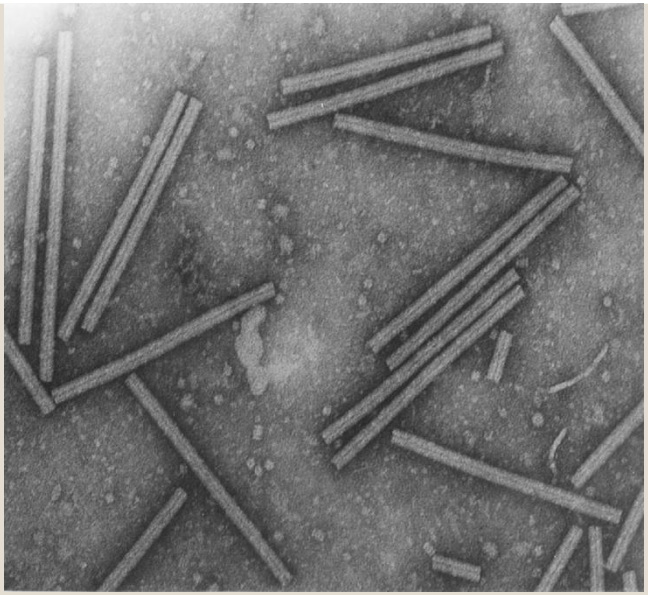
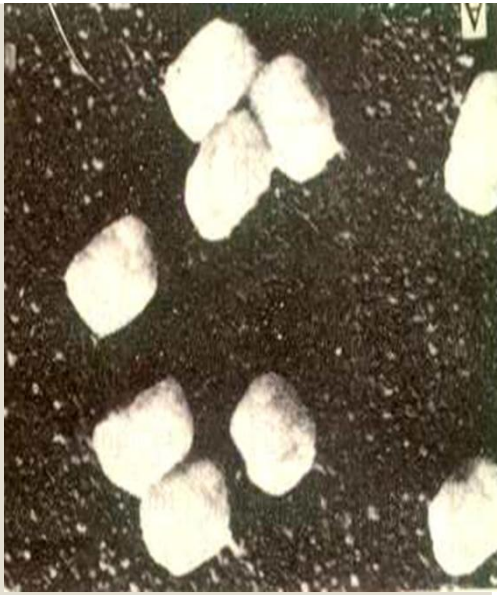
## Shape of Viruses

- **Spherical**
- Rod-shaped
- Brick-shaped
- Tadpole-shaped
- Bullet-shaped
- Filament

Spherical

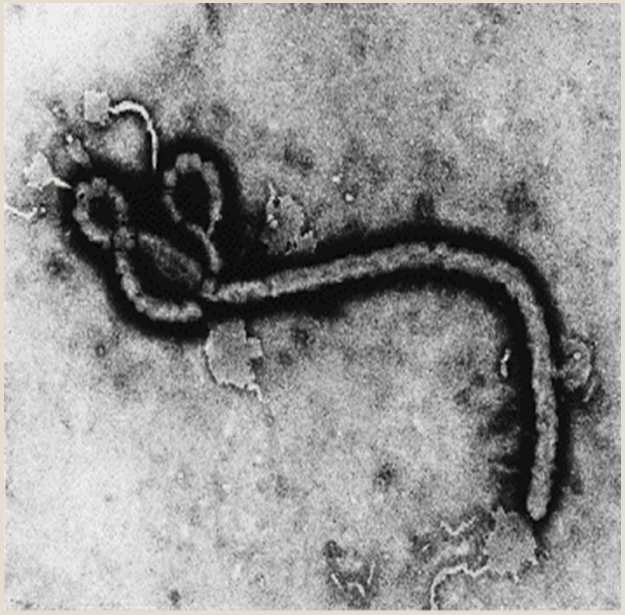


Rod-shaped

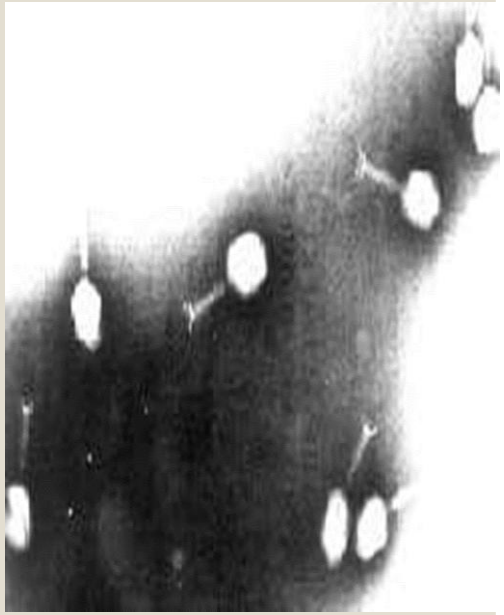


Brick-shaped

Bullet-shaped

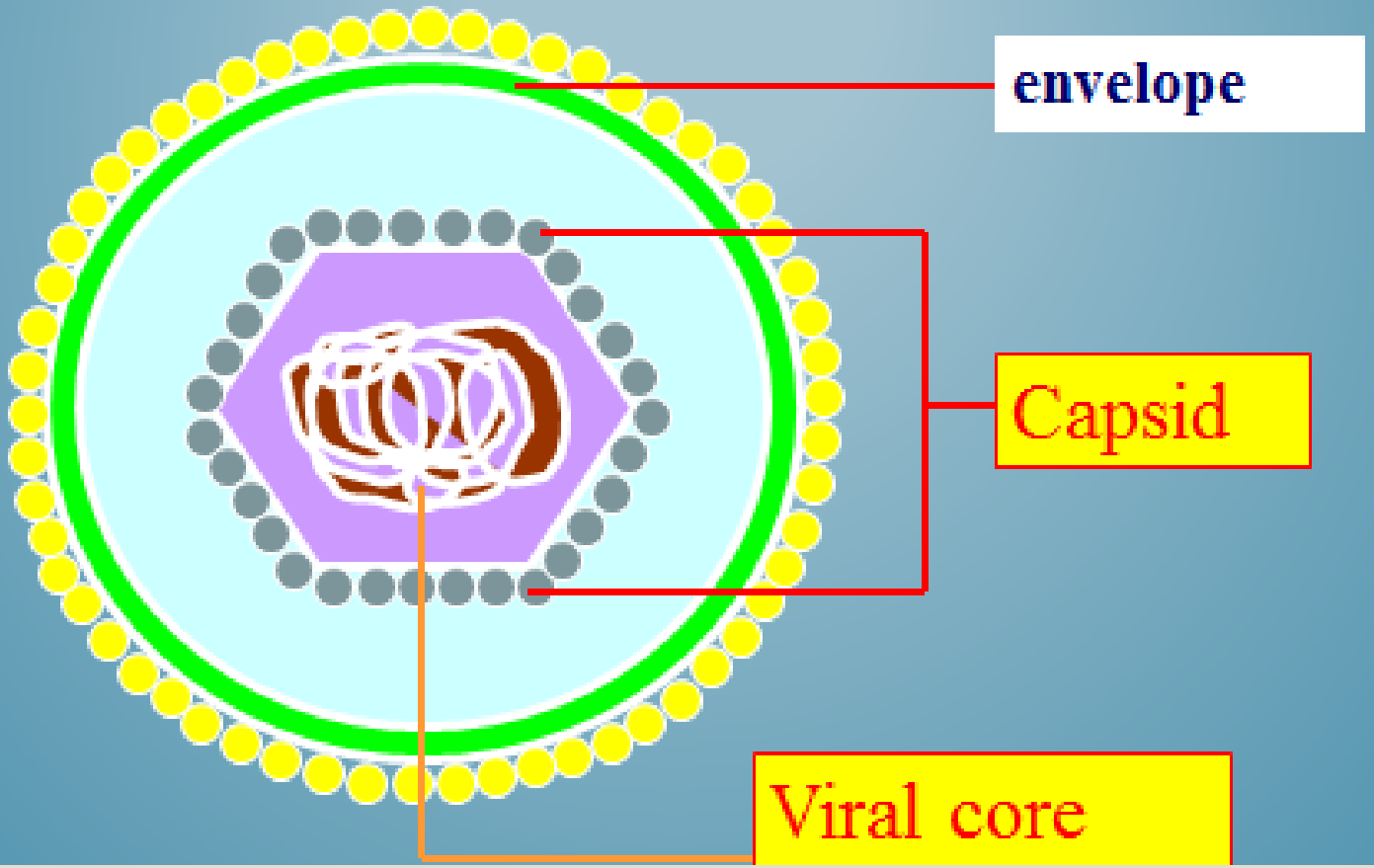


Filament



Tadpole-shaped

# VIRION



**Virions**: Are complete virus particle and is made up of from( 10-15%) nucleic acid and from( 50-90%) percent protein. The general purpose of the proteins is to protect the genetic information, they have ability to induce the diseases condition in animals, plants and human.

**Viroid**: Contain RNA only. They are small (less than 400 nucleotides), single stranded, circular RNAs. The RNAs are not packaged, do not appear to code for any proteins, and so far have only been shown to be associated with plant disease such as Bean mosaic virus, Wound tumor virus, Potato yellow dwarf virus.

**Prions:**

Are protein particles do not contain nucleic acid. Prions contain a single protein called **PrP,** Prion PrP leads to induce certain diseases associated with nervous system, such as the mad cow disease or bovine spongiform encephalitis(BSE), Scrapie in sheep, CWD – chronic wasting disease in deer. Prions Present in nervous tissue, and transmitted by Surgical instruments and Consumption of infected meat/ nervous tissue.

# The Differences between Viruses and Unicellular microorganisms

| | Property | Bacteria | Rickettsiae | Mycoplasmas | Chlamydiae | Viruses |
|---|---|---|---|---|---|---|
| 1- | >300nm diameter | + | + | ± | ± | - |
| 2- | Growth on nonliving media | + | - | + | - | - |
| 3- | Binary fission | + | + | + | + | - |
| 4- | DNA and RNA | + | + | + | + | - |
| 5- | NA infectious | - | - | - | - | +[a] |
| 6- | Ribosomes | + | + | + | + | - |
| 7- | Metabolism | + | + | + | + | - |
| | Sensitive to interferon | - | - | - | - | + |
| 8- | Sensitivity to antibiotic | + | + | + | + | -[b] |

## Legends

+ positive, - negative, NA=Nucleic Acid,

a-Some among both DNA and RNA viruses

b-The antibiotic rifampicin inhibits poxvirus replication

## General characteristic of virus:

1. Very small agent can not seen ordinary (ranging from about 20 nm to about 300 nm in diameter),whereas a bacterial cell like a staphylococcus might be 1000nm in diameter, the largest of the human pathogenic viruses, the poxviruses, measure only 300nm and the smallest, the poliovirus, is only 20nm in diameter. Are mostly, therefore, beyond the limit of resolution of the light microscope and have to be visualized with the electron microscope.
2. They contain one type of nucleic acid either RNA or DNA.
3. They multiply by replication of their nucleic acid comparing with other microorganism which replicated by binary fission.
4. May be surrounded by a lipid-containing membrane called envelope.
5. They don't carry enzyme .
6. They don't growth on synthetic media but grow in living cell.
7. They can pass through the filters that don't allow bacteria to do so.
8. There are no ribosomes and organelles inside the virus.
9. Antibiotic have not affected on viruses, whereas viruses sensitive to interferon.
10. Some viruses can caused latent infection.
11. The nucleic acid of some viruses can caused infection