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Lesson: Virus, Viroids, Mycoplasma and Prions
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Virus, Viroids, Mycoplasma and Prions

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Chapter: Virus, Viroids, Mycoplasma and Prions

Viruses, Prions, Mycoplasma and Viroids

After the discovery by Louis Pasteur and Robert Koch, that the infectious diseases of plants and animals were due to bacteria (minute living organisms or germs), it was expected that the germs for all infectious diseases would be discovered. However bacteriological studies were not able to prove that these small germs are the causative agents of the disease. Russian biologist, Ivanovskyi in 1982 was the first to give the clear evidence of a virus. Studies of tobacco mosaic disease in tobacco plants and hoof-and-mouth disease in cattle pointed to the existence of another type of infectious agent. Mayer (1886) demonstrated that when the juice from tobacco plants infected with the 'mosaic' disease was injected to a healthy plant, it also reproduced the same disease. Even after filtering through the finest bacterial filters, the sap still remained infective, with no evidence of bacteria in the light microscope. Ivanovski concluded that the agents were smaller than the known bacterium, and later they termed this agent as '**Virus**'. Now we know numerous diseases such as – Chicken pox, Influenza, Pneumonia, Polio, Measles, Rabies, Hepatitis, Common Cold and AIDS to name a few, which are caused due to viruses.

The study of viruses is called as '**Virology**'. Viruses (L. virus=poison) are simple, submicroscopic, non-cellular entities, consisting of a proteinaceous covering around central nucleic acid (either DNA or RNA). They are self replicating within the living host, hence they are obligate intracellular parasites. Viruses are smaller than prokaryotic cells ranging from 0.02-0.3 μm.

Virus, Viroids, Mycoplasma and Prions

Smallest virus: Polio virus (28nm)

Largest virus: Small pox virus (200nm)

Value Addition: Facts

- Viruses are obligate parasites
- They are ultra microscopic particles and highly infectious
- Viruses are nucleoproteins
- They become inert chemical when brought outside the host cell.
- Viruses can be easily crystallized
- Viruses are metabolic inert
- Antibiotics have no effect on viruses
- They can undergo mutations
- Viruses do not have any energy producing system

Important Historical Events

E. Jenner	First successful vaccination against small pox.
L. Pasteur	Discovery of rabies as an infectious disease.
A.Meyer	Tobacco mosaic disease was proved to be infectious; probably caused by agents other than bacteria. It was in 1886 that the science of viruses, virology, is considered to have been born.
D. Iwanowski	The causes of tobacco mosaic disease were

	'filterable' through extremely fine pores of Chamberland-Roux filter, the filter capable of retaining bacteria. Iwanowski is considered the discoverer of viruses.
M.W. Beijerinck	A new concept of 'contagium vivum fluidum' i.e. living infectioius fluid was established. He referred the causal agent of tobacco mosaic disease as a 'virus'.
de Herelle	Demonstrated the specific bacteria killing by specific filterable agents and coined the terms '*bacteriophage*' for the latter.
M. Schlesinger	First successful isolation of a virus, the bacteriophage WLL from the bacterium *E. Coli*.
W.M. Stanley	Isolation of a virus. TMV, in its purset crystalline form.
N.W. Pirie and F.C. Bawden	Established that the viruses were made up of proteins and nucleic acids.
M.Delbruck	Discovered mutation in viruses.
Kausche et al.	Electron micrography of TMV
J. Enders	First successful cultivation of a virus (polio) in

	tissue culture.
A. Hershey and M. Chase	Discovery of proteins and nucleic acids to be the non-infective and infective parts of a bacteriophage respectively.
Fraenkel-conrat & Williams	Reconstitution of TMV
Geirer and Charamm	Infectivity of TMV resides in its RNA (its nucleic acid)
A. Issacs and A. Lindemann	Discovery of interferons.
J. Salk and S. Sabine	Discovery of first successful vaccine against polio.
R.L. Sinsheimer	Discovery of bacteriophage X 174 a virus having single-stranded DNA.
R.S. Shafferman & M.E. Morris	Discovery of cyanophages.
H. Temin and D. Baltimore	Discovery of RNA dependent DNA synthesis, a unique phenomenon noted in viruses alone.
Shephered et al.	Cauliflower mosaic virus contains DNA as the

	nucleic acid.
D. Schidolovski and R. Ahmed	Discovery of virus caused cancer in primates.
Harrison et al.	Coined the word 'geminiviruses for plant viruses containing single stranded DNA genome.

Structure of Viruses

A fully assembled infectious virus is called as a "VIRION" (the intact virus unit). The main function of virion is to deliver its DNA or RNA genome into the host cell. Each viral species has a very limited host range. The term 'virus' and 'virion' bear the same connotation and are often interchangeable.

Each virion is composed of two or three parts: (i) the **genetic material** made from either DNA or RNA, (ii) a protein coat, called the **capsid**, (iii) an **envelope** of lipid (Figure 1). A protein coat functions as a shell to protect the viral genome from nucleases. The subunit of capsid is called as '**capsomere'**. The nucleic acid together with the capsid is known as nucleocapsid. Some viruses have membranous envelope that lies outside the nucleocapsid, and are referred as enveloped viruses, while one lacking them are called as naked viruses. In the enveloped viruses, nucleocapsid is surrounded by a lipid bilayer and glycoprotein. Enveloped viruses often exhibit a fringe of glycoprotein spikes called as **peplomers**.

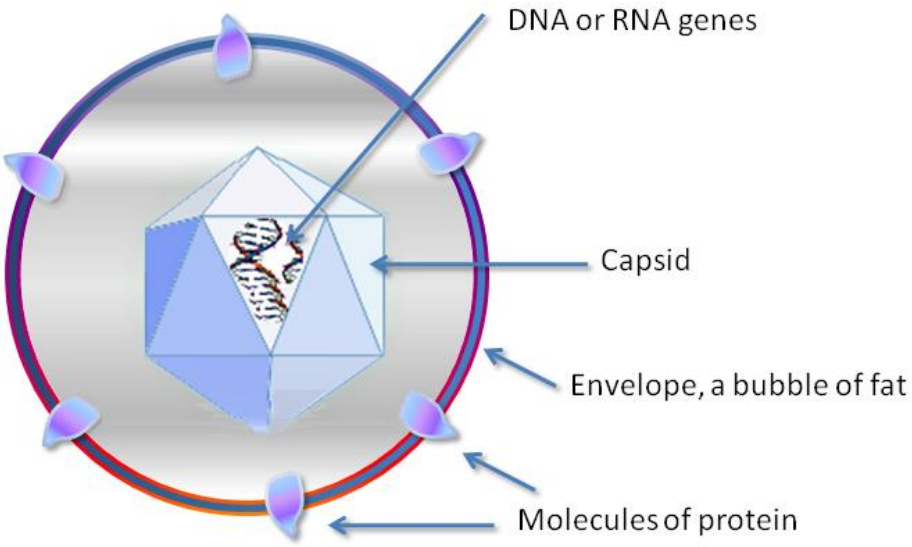


Figure 1: Structure of a Typical Virus

Source: http://www.en.wikipedia.org

Viruses exhibit different shapes and symmetry (Table 1). The symmetry refers to the way in which the capsomeres are arranged in the virus capsid. Accordingly following are the four categories:

Shapes of Virues	Polyhedral viruses	Helical viruses	Complex viruses	Enveloped viruses
	They are also called **icosahedral** viruses because of their symmetry.These viruses are composed of polyhedral protein	The nucleic acid genome in these viruses, is wound inside a cylindrical protein capsid with helical symmetry.	These viruses are composed of various proteins that functions to protect the genome, attach to cells, and introduce the nucleic acid	These viruses are surrounded by a membrane made up of glycoproteins that seek out cells to infect. E.g.: Influenza

	shells. E.g.: Poliovirus, herpes simplex virus	E.g.: TMV and M13	inside. E E.g.: Vacinia virus	and HIV

Table 1: Shapes and Symmetry in viruses.

Viral genomes are smaller in size. The genome of the virus may consist of DNA or RNA, which may be single stranded (ss) or double stranded (ds), linear or circular.

Viruses containing Double-stranded DNA (ds-DNA)

Viruses containing double-stranded DNA are called as "**Caulimoviruses**"

Smallpox (variola)	Herpesviruses	Adenoviruses
Vaccinia	Mirabilis Mosaic Virus (MMV)	Cauliflower Mosaic Virus (CaMV)

Viruses containing Single-stranded DNA (ss-DNA)

Viruses containing single-stranded DNA are called as "**Geminiviruses**"

Bacteriophage Phi X 174	M13
Bean Golden Mosaic Virus (BGMV)	Beat Curly Top Virus (BCTV)

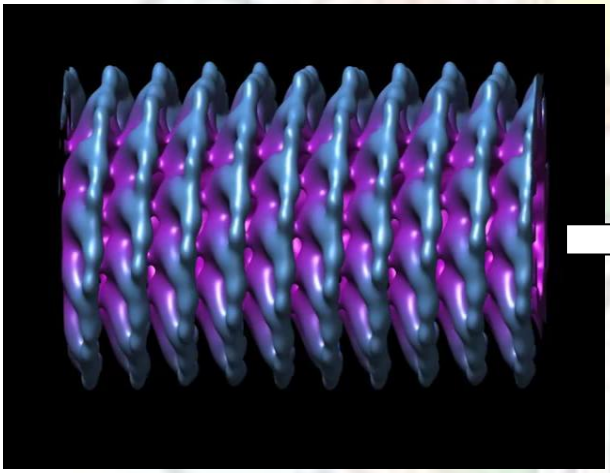
Viruses containing Double-stranded RNA (ds-RNA)

Wound Tumor Virus (WTV)	Rice Dwarf Virus (RDV)
Rotavirus	Reovirus

Viruses containing Single-stranded RNA (ss-RNA)

Tobacco Mosaic Virus (TMV)	Potato Virus X (PVX)
Influenza Virus	Poliomyelitis Virus

Value Addition



Ebola virus disease (EVD)

Ebolaviruses contain single-stranded, non-infectious RNA genomes.

Ebolavirus genomes contain seven genes

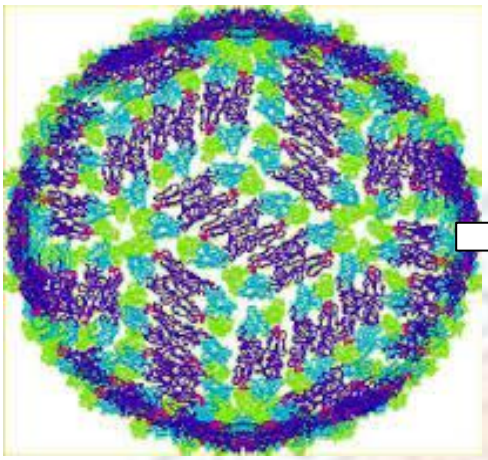
EBOV is thought to infect humans through contact with mucous membranes or through skin breaks

Source: http://www.commons.wikimedia.org

Cyanophages

- Cyanophage is a virus that attacks blue green algae (Cyanobacteria).
- These contain double stranded DNA as its genome.
- Safferman and Morris in 1963 reported a virus infecting Lyngbya, Phormidium and Plectonema and named it as LPP-I.
- Cyanophages body consists of an icosahedral head and a long helical tail.

Value Addition



Dengue Fever Virus

Dengue fever virus (DENV) is an RNA virus of family flaviviridae.

Dengue virus is transmitted by *Aedes* mosquitoes.

Dengue can also be transmitted via infected blood products and through organ donation.

Source: http://www.viraldiseasesd.wikispaces.com

Mycophages

- M. Holling first gave evidence of viruses in cultivated diseased mushroom (Mushroom Die-back Disease), thus establishing the fact that fungi are also attacked by viruses. Such viruses are called as Mycophages or fungal viruses.
- Majority of the known Mycophages are typically isodiametric.
- The most outstanding feature of Mycophages is possession of the segmented and double stranded ribonucleic acid (ds-RNA) usually with 1-8segments.
- The double stranded RNA segments are separately enclosed into identical capsids. This feature of Mycophages differentiates them from plant and animal ds-RNA viruses in which the genetic material segments are all enclosed in a single virion.

Retro Viruses

- Retro viruses are single stranded RNA containing animal viruses.
- Retroviruses are named for an enzyme known as reverse transcriptase, which were discovered by Howard Temin and David Baltimore independently.
- These replicate through DNA intermediates, via a process of reverse transcription, in presence of reverse transcriptase enzyme.
- Retroviruses cause tumour growth and certain cancers in animals and are also associated with slow infections.
- HIV (Human Immunodeficiency Virus) is a famous example of retro virus causing AIDS (acquired Immune Deficiency Syndrome) (Figure 2).

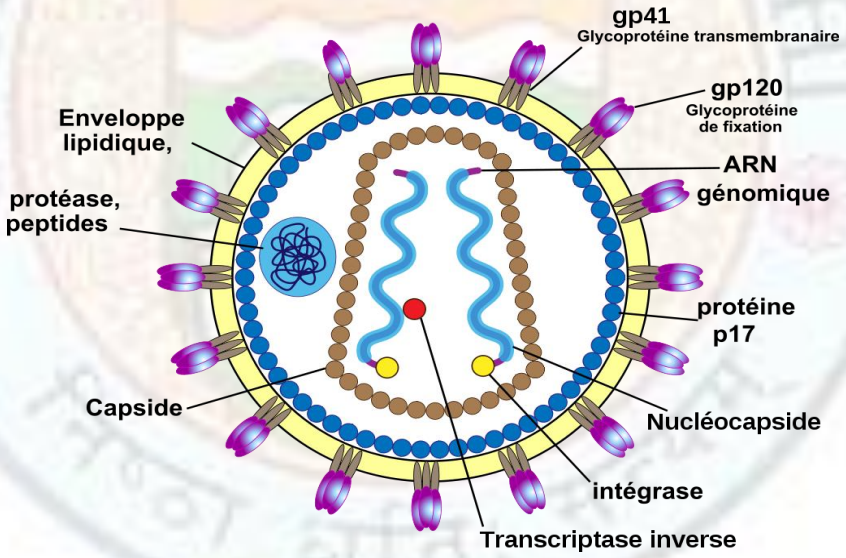


Figure 2: Structure of HIV

Source: http://www.commons.wikimedia.org

Tobacco Mosaic Virus (TMV)

- W.M.Stanley in 1935 first time isolated TMV in its crystalline form and was awarded Noble prize. This was the first isolation of a virus.

- TMV is a simple rod shaped helical virus (Figure 3).
- It consists of a single stranded RNA (5.6%) enveloped by a protein coat (94.4%)
- R.Franklin calculated 2130 capsomeres in a complete helical rod of TMV.
- TMV penetrates and enter the host cell in toto.

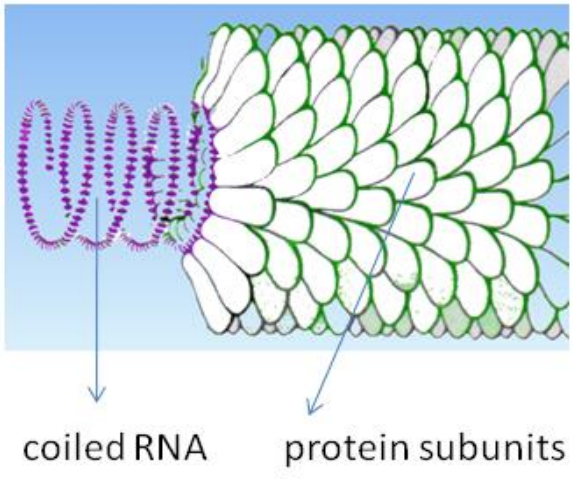
	
Tobacco mosaic virus symptoms on tobacco Source: http://www.en.wikipedia.org	Structure of Tobacco mosaic virus Source: http://www.commons.wikimedia.org

Figure 3: Showing TMV symptoms and structure

Bacteriophages

- Bacteriophages are the viruses which infect bacteria. They are commonly called as "phages" or "coliphages"
- The credit for making this discovery goes to E.Twort and de.Herelle.

- The body of the typical bacteriophage (T-phage) consists of head and tail. Head being hexagonal in appearance and the tail cylindrical (Figure 4).
- Bacteriophage resembles with living organisms in having DNA as the genome.
- The proteinaceous body of the bacteriophage remains outside and the nucleic acid enters the host cell at the time of infection.
- Lambda phage is also a type of bacteriophage and its name was coined by A.Lwoff.

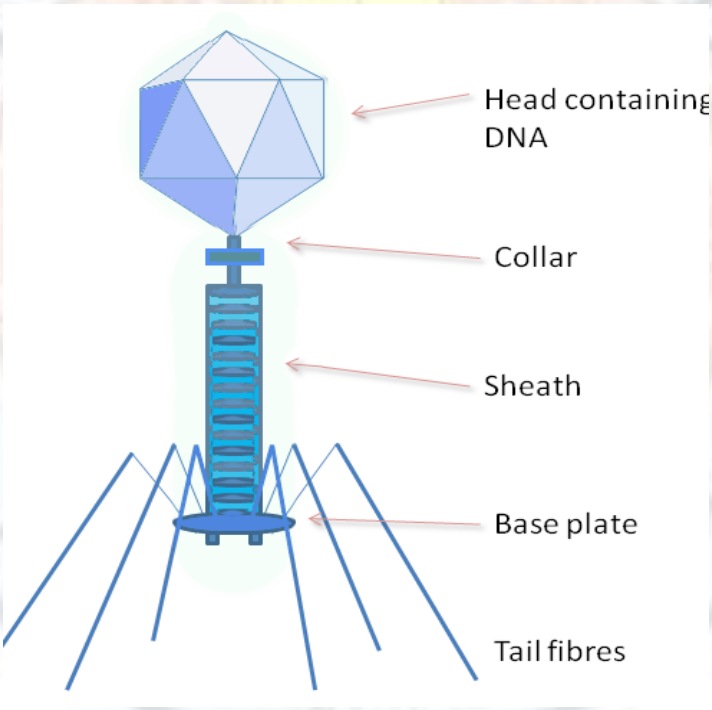


Figure 4: Structure of a Bacteriophage

Source: http://www.commons.wikimedia.org

Viral Reproduction (Bacteriophage)

In the **lytic cycle,** (considered as main cycle in viral replication), once the viral DNA enters the cell it transcribes itself into the host cell's messenger RNAs, resulting in the destruction the host cell's DNA and the virus takes over the cell's metabolic activities. Viruses that only use lytic cycle are called **virulent viruses**. The lytic cycle comprises of six-stage. The first stage is the "penetration" in which the virus injects its own nucleic acid into a host cell. In some viruses this genetic material is circular and mimics a bacterial plasmid. The cell's replication and translation mechanism is overtaken by the virus. The bacterial cell wall is dissolved by specialized viral proteins. Due to high internal osmotic pressure (water pressure) the cell bursts. Resulting in the release of progeny virions into the surrounding environment, which can go on to infect other cells (Table 2).

Lysogeny, or the **lysogenic cycle**, is one of the cycles of viral reproduction. In Lysogeny integration of the viral DNA into the bacterial chromosome takes place, to produce the prophage (genetic material of the bacteriophage), leading to a formation of a circular replicon in the bacterium's cytoplasm. With the reproduction of bacterium, the prophage is copied and is present in each of the daughter cells. The daughter cells continue to replicate with the prophage present or the prophage can exit the bacterial chromosome to start the lytic cycle. In this condition the virus genome lives and replicates normally as the host's DNA replicates. The lysogenic virus (called as temperate phage) can remain in this state for several replications, until it excises itself from the host DNA and undergoes a lytic cycle (Figure 5). A cell that contains a prophage is known as a **Lysogen**.

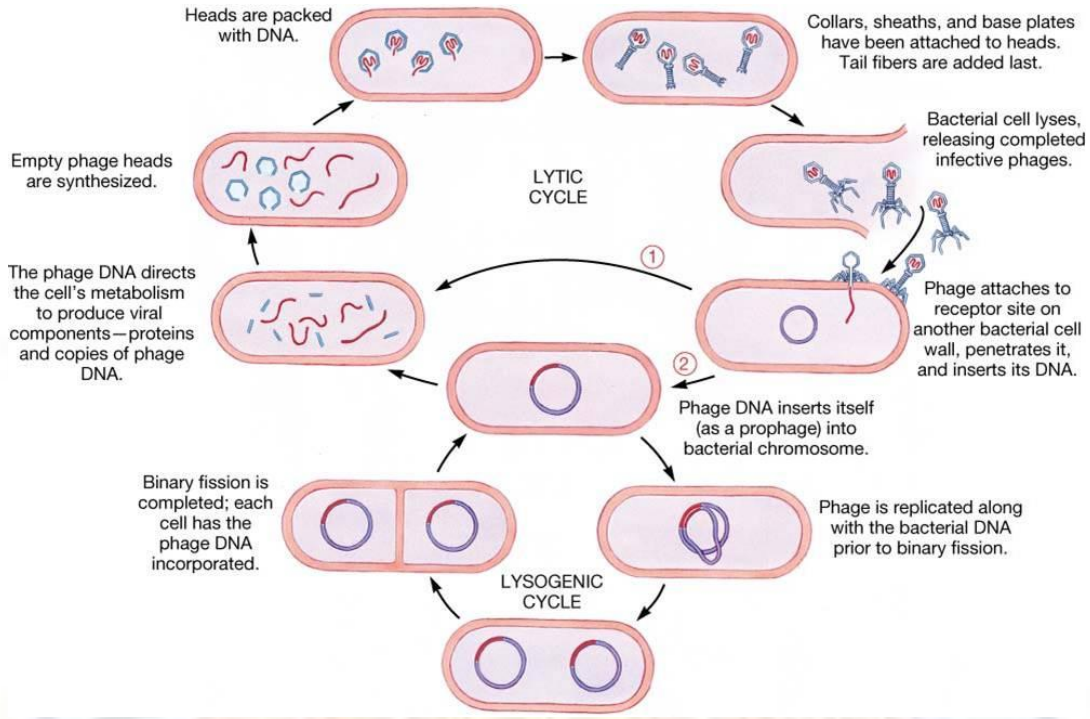


Figure 5: Diagrammatic representation of Lytic and Lysogenic Cycle

Source: http://www.biowikikoons.wikispaces.com

Lytic Cycle	Lysogenic Cycle
Cell DNA destroyed by Viral DNA, takes over the functions and destroys the cell.	Viral DNA merges with Cell DNA and the cell is not destroyed.
Virus replicates and produces progeny.	Virus does not produce progeny.
There are symptoms of viral infection.	There are no symptoms of viral infection.
Viruses that only use lytic cycle are called **virulent viruses**.	The lysogenic virus are called as **temperate phage**

Table 2: Differences between Lytic and Lysogenic Cycles

Viroids

These represents a novel class of subviral entities that cause diseases and are the smallest/ simplest known agents of infectious diseases. Viriods is just a small fragment of RNA and is not encapsidated i.e. it exists as "naked nucleic acid (RNA)" and lack protein coat. They are also known by the names "naked viruses", metaviruses" or pathogen. The size of the RNA ranges from 240-600 nucleotides, which is approximately one-tenth the size of the smaller viruses.

The first Viroids were discovered by T.O. Diener. He found that the Potato Spindle Tuber Disease was caused by Potato Spindle Tuber Viriod (PSTV), which is a small circular RNA, lacking a protein coat. Hence this disease is credited as the first plant disease. Diener named the pathogen a **viroid** other important diseases are: Chrysanthemum Stunt Disease, Citrus Exocortis Disease, tomato Bunchy Top Disease etc. The evidence for animal diseases caused by viroids is not as strong as for plants. Few diseases, thought to be caused by viroid, are **Kuru** disease in humans, **Encephalopathy** disease in Mink and **Creutzfeldt-Jacob** disease in humans. The viriods replicate in and the progeny remains limited to the nucleus of the infected host cell. It is possibly because of their susceptibility to nuclease enzymes. Viroids are transmitted, most probably, always in association with piece of nuclei or chromatin. Their independent transmission is not observed.

A brief comparison between virus and viroids is given below in Table 3:

Features	Virus	Viroid
Nucleic Acid	DNA or RNA (ss or ds)	RNA (ss)
Protein	Present	Absent
Capsid	Present	Absent

Host	Bacteria, animal and plants	Absent

Table 3: Comparison between virus and viroid

Mycoplasma

Mycoplasmas are typical prokaryotes and are the smallest and simplest self reproducing microorganisms. They are capable of autonomous growth and reproduction. It is genus of bacteria lacking a cell wall, hence placed in a separate class Mollicutes. Formerly mycoplasmas were called as **Pleuropneumonia-like organisms (PPLO)** (Figure 6). Absence of a cell wall makes them resistant against many common antibiotics, which target cell wall synthesis. But Mycoplasma is bounded by a triple-layered unit membrane. Nowak first proposed the term "Mycoplasma" to replace PPLO.

Mycoplasma are pleomorphic (vary in shape) and mostly non-motile and do not produce spores. They multiply by binary fission. They can be saprophytic or parasitic and usually facultative anaerobes. Some species are pathogenic in humans, e.g. *M. pneumoniae*, causes pneumonia and other respiratory disorders.

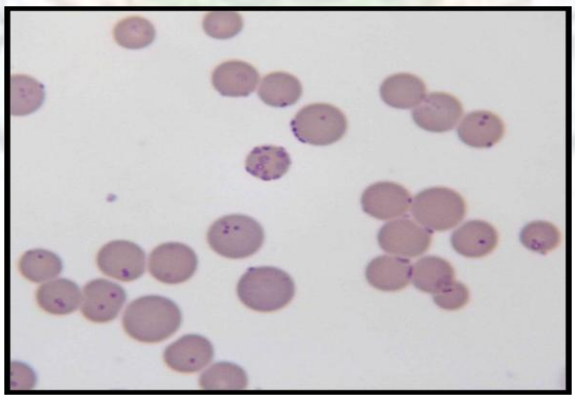
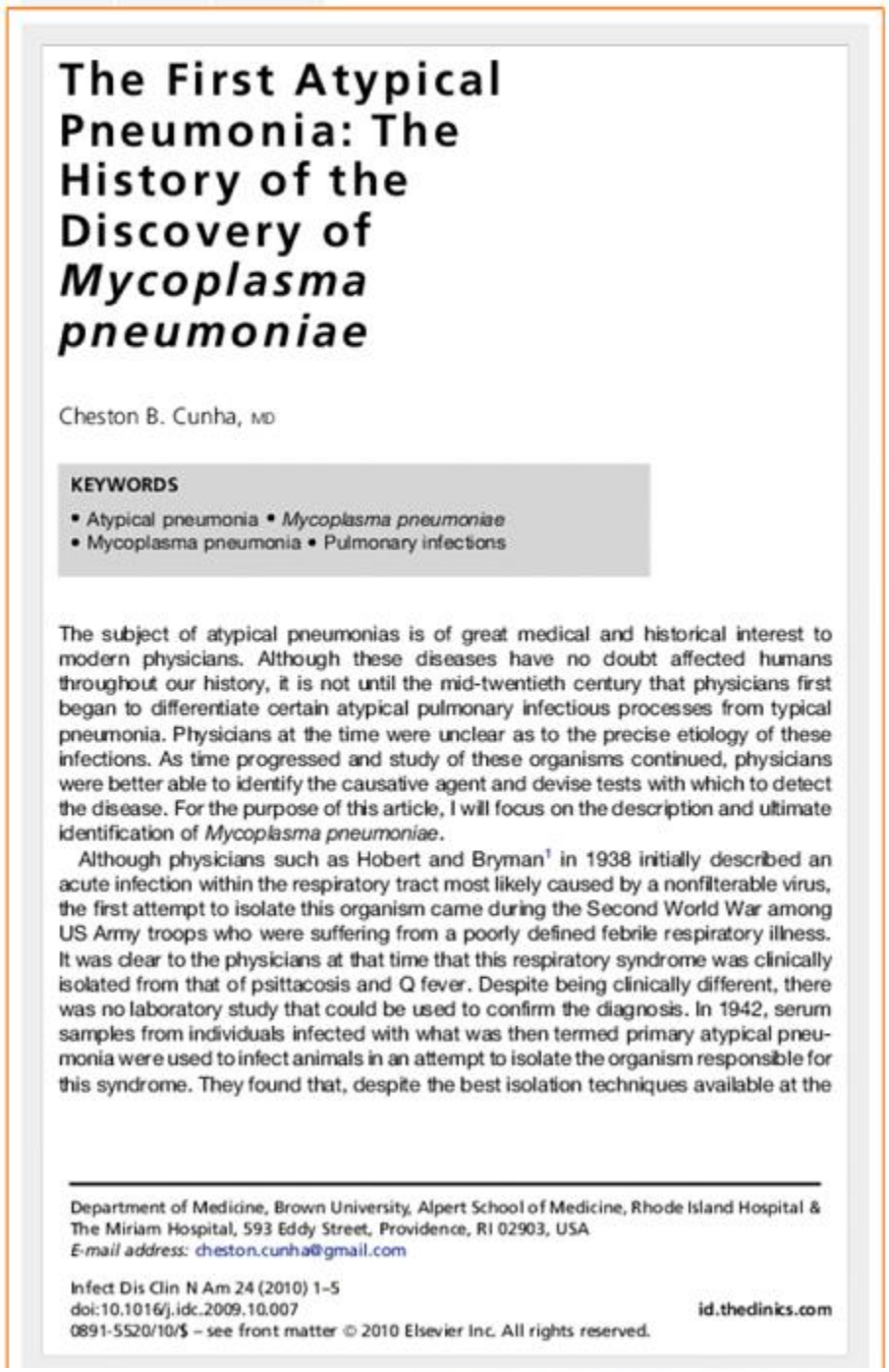


Figure 6: *M. haemofelis* (Wright-Geiemsa Staining 100X)

Source: http://www.en.wikipedia.org

In 1960s, some plant diseases were found to be caused by such microorganisms which resemble mycoplasmas in their morphology and characteristics but differ from Mycoplasmas in not satisfying "Koch's postulates", the pathogenecity test of a pathogen. Due to this, these microbes have been named "Mycoplasma-like Organism (MLOs).

The smallest viable Mycoplasma cell known is that of Mycoplasma hominis H39 which is about 0.33 micrometer.



The First Atypical Pneumonia: The History of the Discovery of *Mycoplasma pneumoniae*

Cheston B. Cunha, MD

KEYWORDS

- Atypical pneumonia • *Mycoplasma pneumoniae*
- Mycoplasma pneumonia • Pulmonary infections

The subject of atypical pneumonias is of great medical and historical interest to modern physicians. Although these diseases have no doubt affected humans throughout our history, it is not until the mid-twentieth century that physicians first began to differentiate certain atypical pulmonary infectious processes from typical pneumonia. Physicians at the time were unclear as to the precise etiology of these infections. As time progressed and study of these organisms continued, physicians were better able to identify the causative agent and devise tests with which to detect the disease. For the purpose of this article, I will focus on the description and ultimate identification of *Mycoplasma pneumoniae*.

Although physicians such as Hobert and Bryman[1] in 1938 initially described an acute infection within the respiratory tract most likely caused by a nonfilterable virus, the first attempt to isolate this organism came during the Second World War among US Army troops who were suffering from a poorly defined febrile respiratory illness. It was clear to the physicians at that time that this respiratory syndrome was clinically isolated from that of psittacosis and Q fever. Despite being clinically different, there was no laboratory study that could be used to confirm the diagnosis. In 1942, serum samples from individuals infected with what was then termed primary atypical pneumonia were used to infect animals in an attempt to isolate the organism responsible for this syndrome. They found that, despite the best isolation techniques available at the

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doi:10.1016/j.idc.2009.10.007
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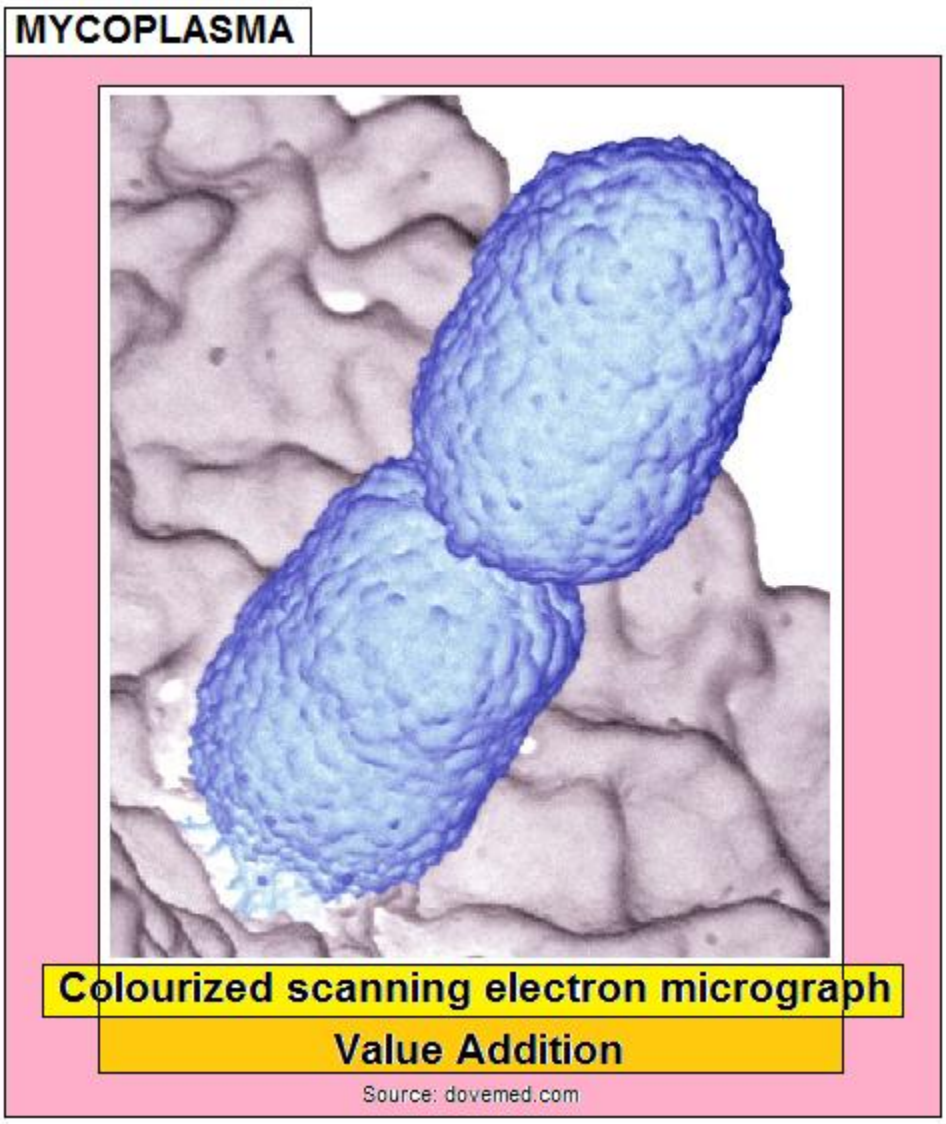
Value Addition: Screenshot of article by Cheston B. Cunha on history of discovery of *Mycoplasma*

Virus, Viroids, Mycoplasma and Prions



Value Addition

Koch's postulates:

- Presence of disease causing organisms in abundance in host suffering from the disease and absent in healthy organisms.
- The disease causing organism must be isolated from a diseased organism and grown in pure culture.
- The same must cause disease when introduced into a healthy organism again.
- On isolation it should be same as the native agent.

Prions

Prions are proteinous infectious particles that lack nucleic acid. Thus, it is entirely different entity from bacteria, fungus or virus. Stanley B. Prusiner, coined the term "*prion"* In 1982.

As Prions are misfolded protein molecules, hence not considered as living organisms, which may propagate by transferring a misfolded protein state. These are extremely stable and gather in infected tissue, causing tissue damage and cell death.

Prions are composed of an uncharacteristic pathogenic isoform of the prion protein (PrP) in mammals. PrP found in infectious material has a various structure. The normal form of the protein is called **PrP^{C}**, whereas **PrP^{Sc}** is the infectious (the C is for 'cellular' PrP, while the Sc for 'scrapie'). The mammalian prions cause Scrapie and other neurogenerative diseases, e.g. mad cow disease, Creutzfeldt-Jakob disease, kuru, fatal familial insomnia, and an anomalous form of genetic dementia. All known prion diseases, collectively called **Transmissible Spongiform Encephalopathies (TSEs)** (Figure 7), are untreatable and deadly. **Bovine Spongiform Encephalopathies also called as Mad cow disease** is a famous example of prions disease. No plant disease caused by prions is known.

The normal form, **PrP^{C},** is converted into **PrP^{sc}** through a process whereby a portion of its α-helical and coil-structure is refolded into a β-sheet. This structural transistion is accompained by profound changes in the physiochemical properties of the **PrP. PrP^{C}** is sensitive to proteases whereas

PrP^{sc} is proteases resistant. High content of β-sheets in **PrP^{sc}** results in the formation of amyloid structure that is absent from the **PrP^{C} form.**

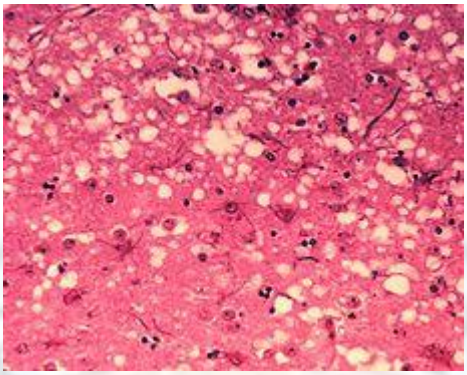


Figure 7: Prion-affected tissue sections showing microscopic "holes", causing "spongy" tissue appearance

Source: https://en.wikipedia.org/wiki/File:Histology_bse.jpg

SUMMARY

- Viruses are intracellular parasites that replicate only after infecting specific host cells.
- Individual viral particles are called as virions; generally contain either RNA or a DNA, surrounded by multiple copies of coat proteins, forming the nucleocapsid, which in many animal viruses is surrounded by a phospholipid bilayer, or envelope.
- Cyanophages (ds DNA) is a virus that attacks blue green algae (Cyanobacteria).
- Viruses attaching fungi are called as Mycophages or fungal viruses (ds RNA).
- Tobacco Mosaic Virus (TMV) containing ss-RNA, causes Tobacco Mosaic Diseases (TMD).

- bacterial viruses are known as bacteriophages.
- Viroids are subviral entities. Smallest known agents of infectious diseases. Viriods is just a small fragment of RNA and is not encapsidated
- Mycoplasmas are smallest self reproducing organism, lacking a cell wall. Earlier known as Pleuropneumonia-like organisms (PPLO).
- Prions are proteinous infectious particles that lack nucleic acid.
- Bovine Spongiform Encephalopathies also called as Mad cow disease is a famous example of prions disease.

Exercise/ Practice

1. Which of these characteristics of living things is exhibited by a virus?

   a) heredity b) metabolism
   c) response to stimulus d) interaction with the environment.

2. Which of the following would be the best definition of reverse transcription?

   a) making a protein off of a DNA template
   b) making a DNA using an RNA molecule as a template
   c) making polysaccharides out of monosaccharides
   d) none of these

3. A capsid is ___.

   a) the lipid/protein membrane surrounding a virus

b) the nucleic adic core of a virus
c) the enzymes associated with a bacteriophage
d) the proteins that surround a typical virus

4. When a virus is in the lytic cycle, which of these will occur?

a) Viral DNA becomes incorporated into the host DNA
b) Host cell produces many new viruses before it breaks apart
c) The viral DNA replicates and is separated by the cell's spindle apparatus
d) Antiviral defenses of the cell expel the viral DNA

5. When a virus is in the lysogenic cycle, which of these will occur?

a) Viral DNA becomes incorporated into the host DNA
b) Host cell produces many new viruses before it breaks apart
c) The viral DNA replicates and is separated by the cell's spindle apparatus
d) Antiviral defenses of the cell expel the viral DNA

6. Differentiate between the following:

   a. Virus and Viroid
   b. Lytic and Lysogenic cycle
   c. Cyanophage and Bacteriophage

7. Write short notes on:

   a. Prions
   b. Mycoplasma

8. Fill in the blanks:

   a. First isolation of a virus was done by……
   b. Viruses grow and multiply within the …….
   c. Wound tumor virus (WTV) has …….as genetic material.
   d. Bacteriophage are the viruses which infect ……..
   e. Interferon produces within the infected cells against……
   f. HIV stands for……..
   g. Koch’s postulates are related to……
   h. TMV is a simple …….. shaped ……. Virus.

i. Viruses are …….. parasites
j. Kuru disease in humans is caused by…….

Glossary

Bacteriophage: A virus that infects bacteria

Capsid: The protein coat that protects a virus and houses its genetic material

Dengue virus: A flavivirus, existing as four antigenically related but distinct types, that causes both the classic and hemorrhagic form of Dengue.

Enveloped virus: A virus having an outer lipoprotein bilayer acquired by budding through the host cell membrane.

Icosahedron: The shape of some capsids that resembles 20-sided dice

Human Immunodeficiency Virus (HIV): A retrovirus that causes Acquired Immunodeficiency Syndrome (AIDS)

Virus, Viroids, Mycoplasma and Prions

Mycoplasm: Smallest and simplest self reproducing microorganisms, typically a prokaryote

Prion: An infectious protein responsible for diseases like kuru and mad cow disease. Prions are able to cause disease and infect without DNA or RNA genomes

Prophage: The genome of a bacteriophage that integrates into the bacterial genome

Reverse transcriptase: A retrovirus enzyme that converts RNA into DNA

Retrovirus: A virus that replicates by converting its RNA genome into a DNA genome that integrates into the host's genome

Temperate phage: A bacteriophage that is capable of entering a lysogenic cycle

Lysogenic cycle: A type of replication in certain viruses that infect bacteria (bacteriophages) where the bacteriophage integrates into the bacterial genome

Lysis: The bursting of a cell, usually through overproduction of viral particles

Lytic cycle: A type of bacteriophage replication where they replicate in a bacterium until they lyse the cell

Viroid: A single-stranded RNA plant pathogen that is different from viruses in that it does not have a protein coat or envelope

Virology: The study of viruses

Virus: an extremely small infectious agent that can only replicate inside of living cells

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http://www.ucmp.berkeley.edu/alllife/virus.html

Virus, Viroids, Mycoplasma and Prions