History of Virology

Class – M.Sc. Biotechnology
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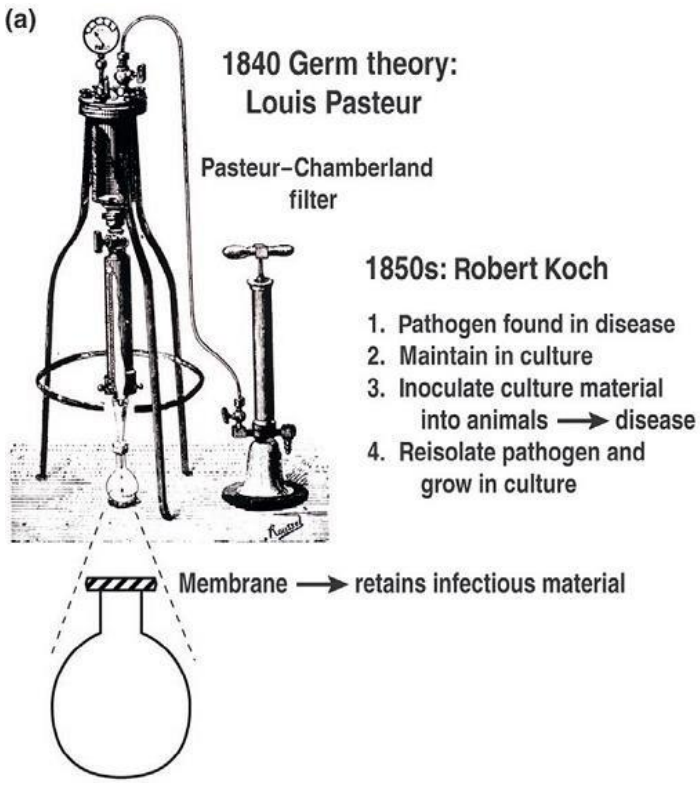
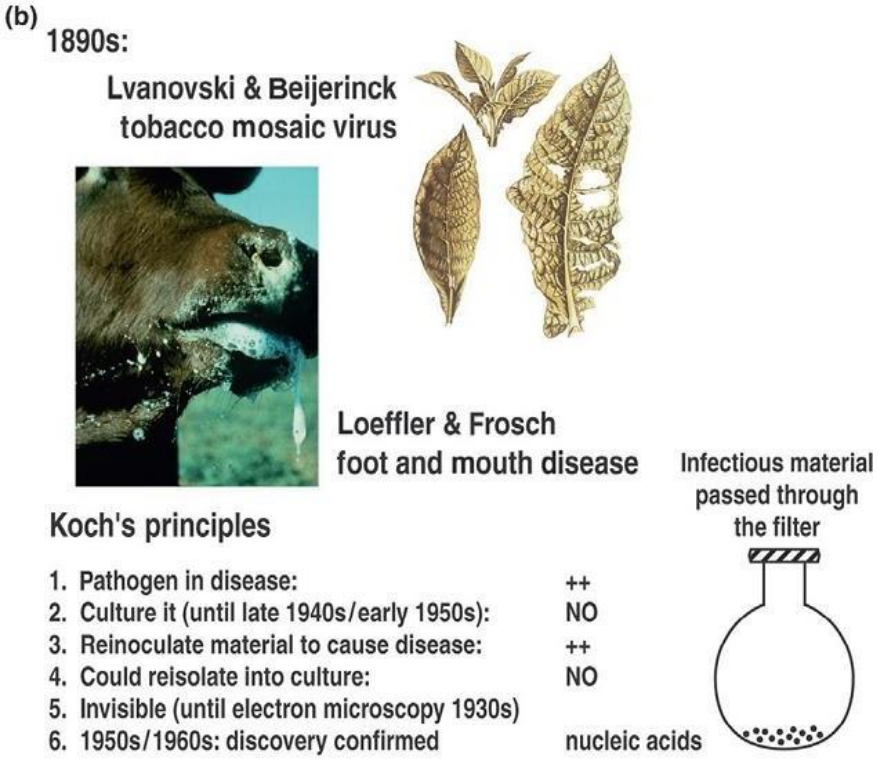
- In earlier times, diseases like rabies, yellow fever, smallpox, etc. were found in human beings, but the relation between these diseases and viruses was not known.
- In those times, microscopes of sufficient power to see viral agents were not invented.
- The cell cultures to grow viruses were unknown
- The probes like antibodies or nucleic acids to mark an infectious agent were not available.
- Furthermore, techniques to concentrate or study nucleic acids and proteins (such as centrifuges and gel electrophoresis) were not available.
- The science of virology emerged after that of bacteriology.
- The identification of viruses as infectious agents followed after work by *Louis Pasteur* and his coworkers in 1800s.
- The laboratory *culturing* process was developed for bacteria, which could be grown on enriched *agar* preparations or *broths*.
- The bacteria were identifiable after their *fixation* on the glass slides, *staining*, and *examination under the microscope*.
- Pasteur's collaborator ***Charles Chamberland*** developed a ***porcelain filter*** with specific pore sizes to remove bacteria from water in 1884.
- After their *collection on filters*, growth on agar and *identification*, specific bacteria could be linked with individual diseases by using *Koch's postulates*.
- When Chamberland made porcelain filter, he had no idea that any kind of infectious agent could pass through it.



- Researchers soon realized that some filtrates (materials that passed through the filters) remained infectious even after the bacteria were filtered out.
- In 1898, *Dmitri Losifovich Ivanovski* (Ivanovski, 1899), in Russia, and *Martinus Beijerinck* (Beijerinck, 1899), in the Netherlands, *demonstrated* that the *material responsible for* a disease of *tobacco plants*, instead of being retained, *passed through the then smallest pore-sized filter* used in *the Pasteur–Chamberland apparatus without losing infectivity.*
- Thus, the material at the bottom of the filter-containing flask was smaller than bacteria and proved to remain infective when transferred to an uninfected recipient (plant) of the type from which it was first retrieved.
- Ivanovsky and Beijerinck identified the first virus (a plant virus) and named it tobacco mosaic virus.
- Almost at the same time, Friedrich Loeffler and Paul Frosch (Loeffler and Frosch, 1898), in Germany, utilizing a similar approach, concluded that the agent causing *foot-and-mouth disease of cattle* also passed through porcelain filters and induced symptoms of disease when inoculated back into healthy cattle.



- These observations, highly controversial at the time, provided the ***basis*** for defining ***viruses as subcellular*** entities that caused distinct forms of tissue destruction, which became hallmarks of specific diseases.
- The *term 'virus'* had been used earlier to refer to *poisons* and to *infectious agents in general*.
- ***Beijerinck*** used the term to refer to specific pathogenic (disease-causing) molecules incorporated into cells.
- He also believed that *these molecules could borrow the existing metabolic and replicative mechanisms of the infected cells (host cells) for their own use.*
- Further progress in virology required development of techniques for isolating, propagating, and analyzing viruses.
- Visualization of viruses was made possible after the discovery of electron microscopy in the mid-1930s.
- But, culturing of living cells necessary for viral replication was not possible until the late 1940s to early 1950s.

1900	J. Carroll, J. Lazear, A. Agramonte, W. Reed, C. Finlay, W. Gorgas	First human virus: yellow fever virus, first use of consent form for human clinical investigation, identify mosquito as a transmitting agent, control of virus by elimination of mosquito breeding sites
1915	F. Twort	Discovery of bacteriophages
1917	F. d'Herelle	Bacteriophages, plaque assay
1923–28	A. Carrel, H. Maitland, M. Maitland	Tissue culture of embryo explants and first tissue culture cultivation of virus: Rous virus, vaccinia virus
1928	R. Lancefield, E. Lennette, others	Beginning of viral disease diagnosis
1931	A. Woodruff, E. Goodpasture	Use of embryonated hen's eggs as a host for viruses

- 1935: The American scientist ***Wendell Stanley*** *crystallized tobacco mosaic virus*, showing that an agent with properties of a living organism also *behaved as a chemical substance*. The crystals consisted of protein and ribonucleic acid (RNA). The nucleic acid was soon shown to be important in the infectivity of viruses.
- Viruses were *first observed with an electron microscope in 1939*.
- From that time both chemical and microscopic studies were used to investigate viruses.

- By 1952 the American biologists ***Alfred Hershey*** and ***Martha Chase*** had demonstrated that the genetic material of some viruses is another nucleic acid, deoxyribonucleic acid (DNA).
- In 1953 the American postdoctoral student ***James Watson*** and the English biophysicist ***Francis Crick*** determined the *structure of DNA*.
- The stage was set for rapid advances in understanding how DNA functions as genetic material both in viruses and in cellular organisms.
- Since the 1950s hundreds of viruses have been isolated and characterized.
- Although much remains to be learned about viruses, tremendous progress has been made in understanding their structure and how they function.

- **Peter Medawar**, awarded the Nobel Prize in Medicine and Physiology in **1960**, **defined viruses as a piece of nucleic acid surrounded by bad news**.