Introduction & History of Microbiology

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MMC

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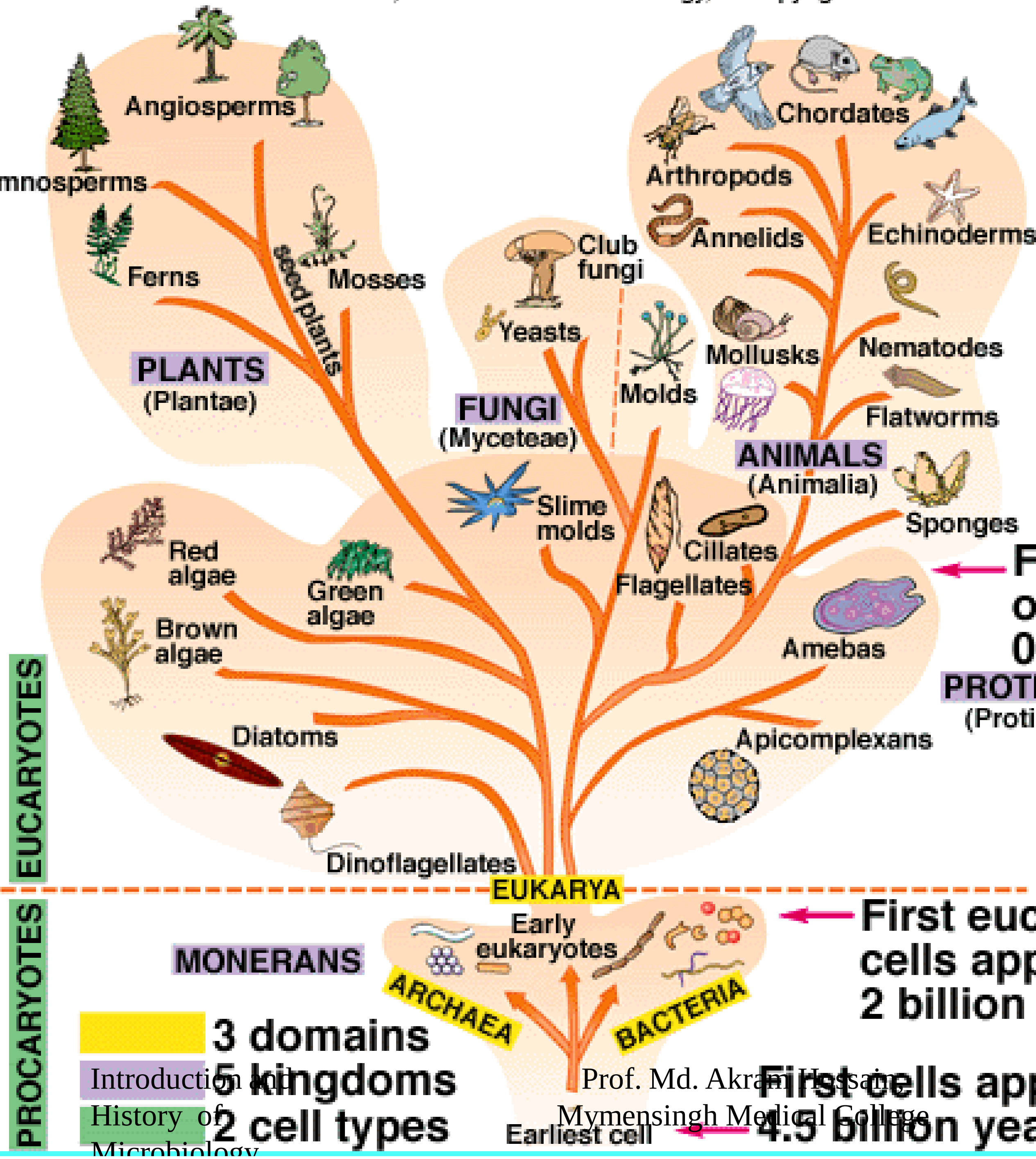
LESSION PLAN

- What is Microbiology? Branches of Microbiology
- History and Time line of Microbiology
- Legends of Microbiology with their contributions.

Family tree of major groups of organisms



First multicellular organisms appear 0.6 billion years ago

First eucaryotic cells appear 2 billion years ago

First cells appear 4.5 billion years ago

What is Microbiology?

- Biology of microscopic organisms.
  - That branch of science that deals with 'microbes'

What is Medical Microbiology?

Branch of medical science that deals with

- the microbes causing disease
- the ways they produce disease
- Diagnosis
- Treatment
- Host response - Immunity
- Prevention

Microorganisms ?

Microbes are the microscopic living entities.

- Virus
- Bacteria
- Fungi
- Protozoa
- Helminths

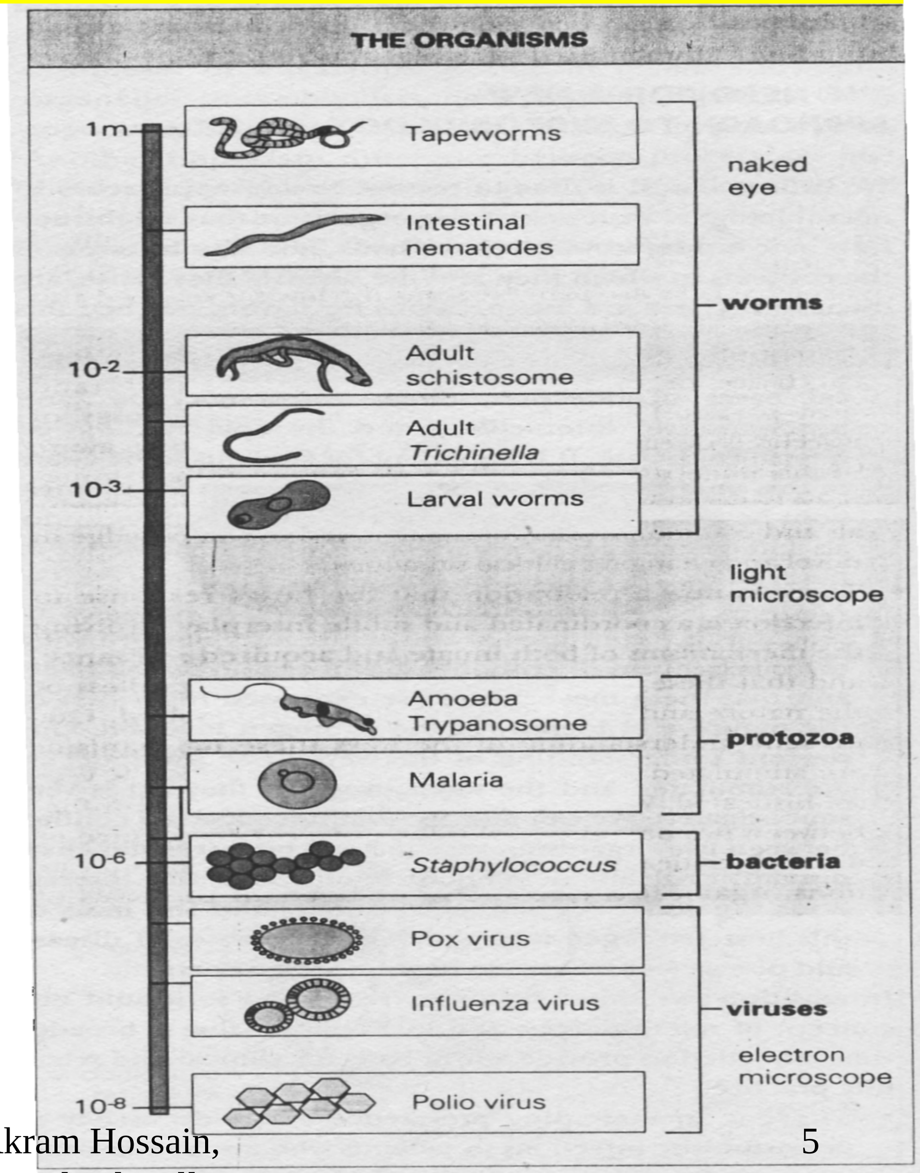


Fig. 1.1 Relative sizes of the organisms covered in this book

Branches of Medical Microbiology

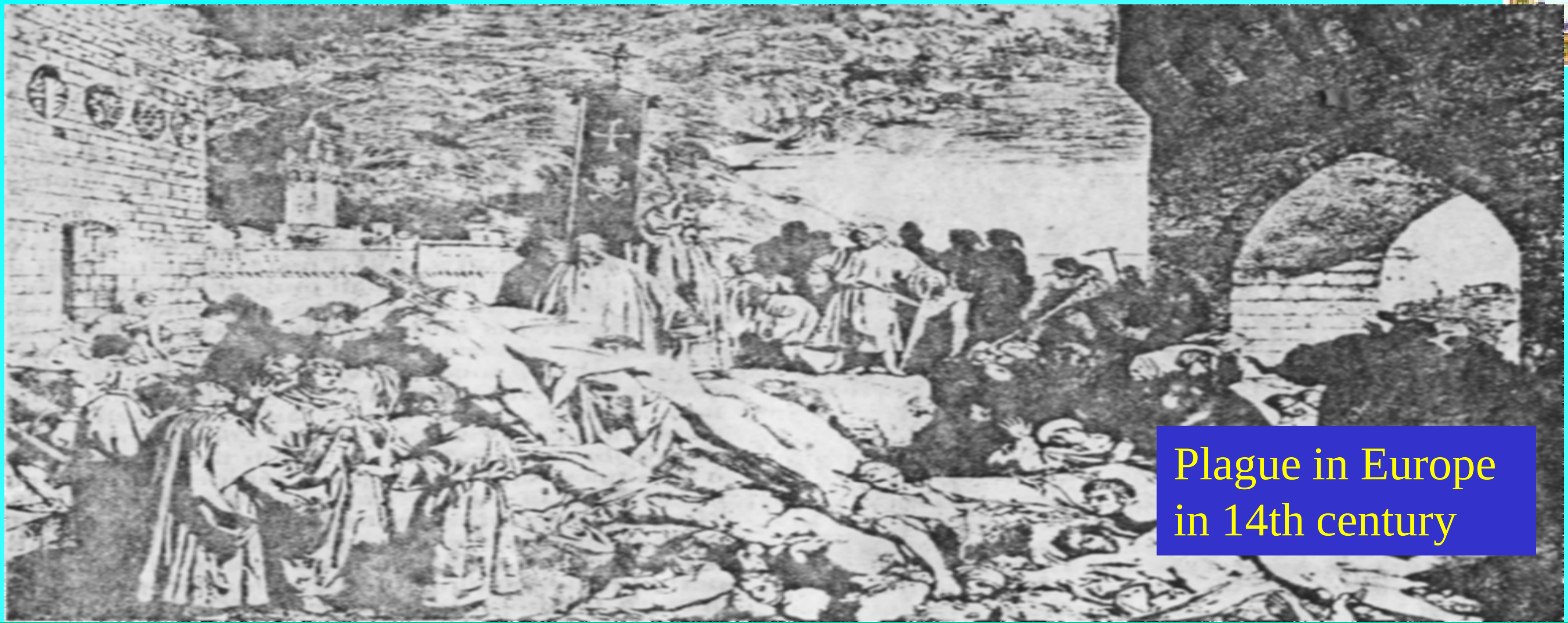
- Bacteriology
- Parasitology
- Mycology
- Virology
- Immunology
- Clinical Microbiology / Infectious Diseases

Microbial diseases in the Past & Present

In Europe -

- Leprosy was prevalent in the 14th century
- Plague in the 15th century
- Syphilis in the 16th century
- Small pox in the 17th and 18th century
- Tuberculosis, measles and scarlet fever in 19th Century
- AIDS in 20th century

Microbial diseases in the past



Plague in Europe in 14th century

Plague- "Black death"

- 542 AD - 1st pandemic killed 100 million (10 crores) people
- 14th Century - "Black death" of Europe killed 25 million (2.5 crores) in Europe
- 1894 - 1896 - killed > 10 million people

Microbial diseases in the past ...

Influenza

1818 - 1819 - > 20 million died

Rickettsial disease

1818 - 1819 - 15 million infected of which 3 million died

Cholera

1917 -1923 - Six pandemics, 5 from India

1961 - 62,000 cases with a mortality rate of 49.3%

1971 - 1,76,000 cases with a mortality rate of 14.8%

1991 - 5,95,000 cases with a mortality rate of 3.2%

1993 - 2,97,000 cases with a mortality rate of 1.7%

Problem is continuing....

Diarrhea

In the world

- 25 lakhs died in 1996- (7th killer disease) -WHO

In Bangladesh

- 2.6 Lakh children died and 7.6 crores of episodes occur4

HBV

- 10 Lakhs people die every year in the world.
- 400 -500 million carriers

Problem is continuing....

HIV /AIDS

- More than 50 million people are infected with HIV
- More than 16 million people died by the year 2000.
- 13 million children had been orphaned.
- 2.6 million died in 2002

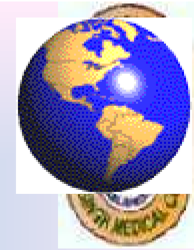
Tuberculosis

- 100 million people are infected by M. tuberculosis / year
- 10 -20 million suffers from Tuberculosis of which 5 million in Bangladesh.
- 2- 3 million people dies.

WHO Report 1997

Disease	Death
CHD	7.2 million
Cancer	6.3 million
CVD	4.6 million
LRTI	3.9 million
Tuberculosis	3.0 million
Diarrhea	2.5 million
Malaria	2.1 million
HIV /AIDS	1.5 million
Hepatitis	1.2 million

WHO Report 2002



Disease	Death
Total	55 million
Communicable	17.3 million
Infectious	9.9 million
CVD	16 million
Cancers	07 million
LRTI	3.9 million
Tuberculosis	1.6 million
Diarrhea	2.2 million
Malaria	1.0 million
HIV /AIDS	2.6 million
Hepatitis	1.2 million
Measles	0.8 million

WHO report 1998

Total death in 1997	-	522 million
Infectious and parasitic disease	-	173 million
Coronary vascular diseases	-	153 million
Cancers	--	6.2 million

Major Infectious Diseases

ARI	- 3.7 million
Tuberculosis	- 2.9 million
Diarrhea	- 2.5 million
HIV /AIDS	-2.3 million
Malaria	-2.00 million

Major Microbial diseases in the the world

19th Century- in Europe

- Small pox
- Cholera
- Diphtheria
- Leprosy
- Tuberculosis
- Typhoid

4% of USA people are infected with Giardia

20th Century- in Asia, Africa Central& South America

- Diarrhea
- Tuberculosis
- Respiratory infections
- HIV
- Measles
- Malaria
- Filaria
- amoebiasis
- Intestinal helminthiasis

MOH& FP of Bangladesh Report 1997

Disease	Prevalence (Lakhs)	%
Helmintheasis	60.0	11.9
Diarrhea	59.7	11.8
Anaemia	48.1	10.0
Skin disease	45.1	9.0
PUD	27.1	5.4
ARI	26.5	5.2
Malaria	4.3	0.9

In One day..

Common cold

1,37,000 adults and 1,64,00 children stay at home because they have Common cold

Diarrheal disease

27,00 Americans become sick due to food posioning.

STD

2,700 Americans discover that they have gonorrhoea and 200 discover that they have syphilis.

Death from Microbial Diseases

- Every year - 5.5 crores die
- Infectious diseases - 1.73 crores (31%)
- Cardiovascular diseases - 1.70 crores (30%)
- others - 2.07 crores
- Among the infectious diseases
  - Resp tract infections - 40 lakhs (95% from LRTI)
  - HIV/AIDS - 26 lakhs
  - GIT infections - 22 lakhs
  - Tuberculosis - 16 lakhs

Pathways of Discovery in Microbiology

- The Historical Roots of Microbiology
- Pasteur and the Defeat of Spontaneous Generation
- Koch, Infectious Disease, and the Rise of Pure
- Culture Microbiology
- Microbial Diversity and the Rise of General
- Microbiology
- The Modern Era of Microbiology

The Historical Roots of Microbiology

- ***Robert Hooke (1635-1703)*** *was the first to describe* microbes Illustrated the fruiting structures of molds
- ***Anton van Leeuwenhoek (1632-1723)*** *was the first to* describe bacteria
- Further progress required development of more powerful microscopes
- ***Ferdinand Cohn (1828-1898)*** *founded the field of*
- bacteriology and discovered bacterial endospores

History of Microbiology

384 -322 BC (2300 years before)

Aristotle and Others - believed that living organisms could develop from non-living materials.

1546 (466 years before)

Hieronymous Fracastorius -Published " On Contagion" First known discussion on contagious infection

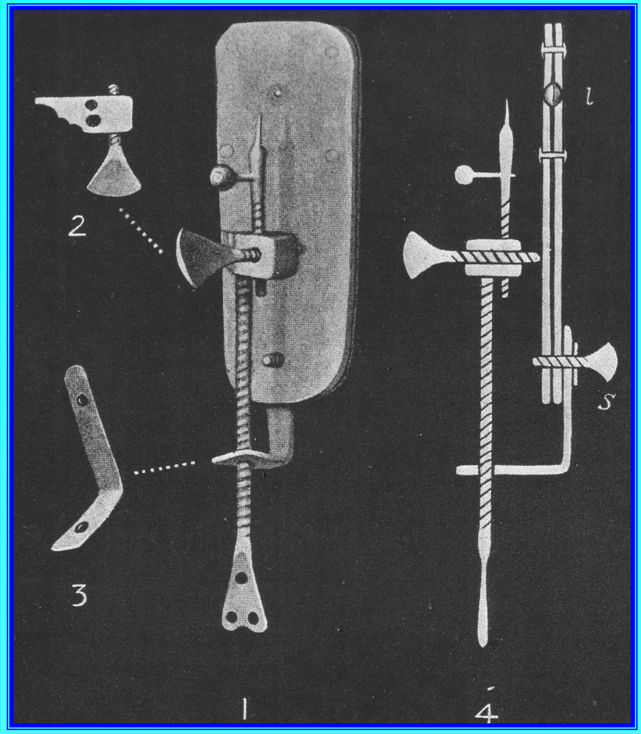
1676 (336 years before)

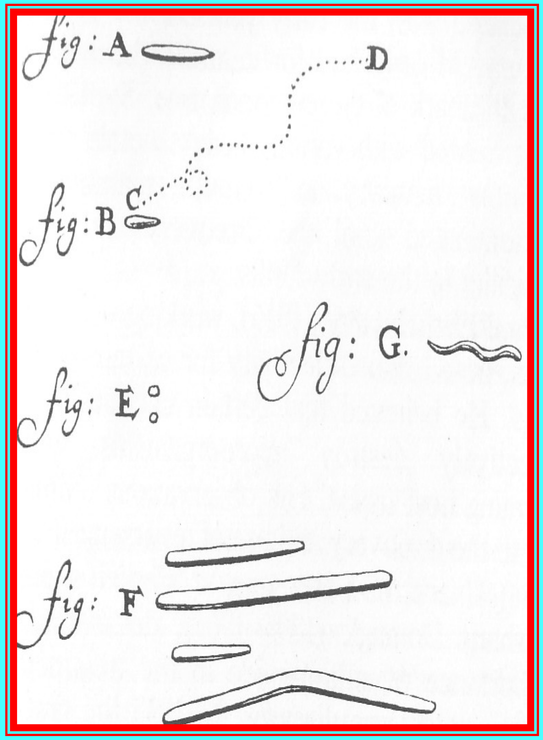
Anton von Leeuwenhoek (1632 -1723) - Invents microscope and observed microbes.

"Where the Telescope ends the microscope begins which of the two has the grander view ?"

Victor Hugo

1676





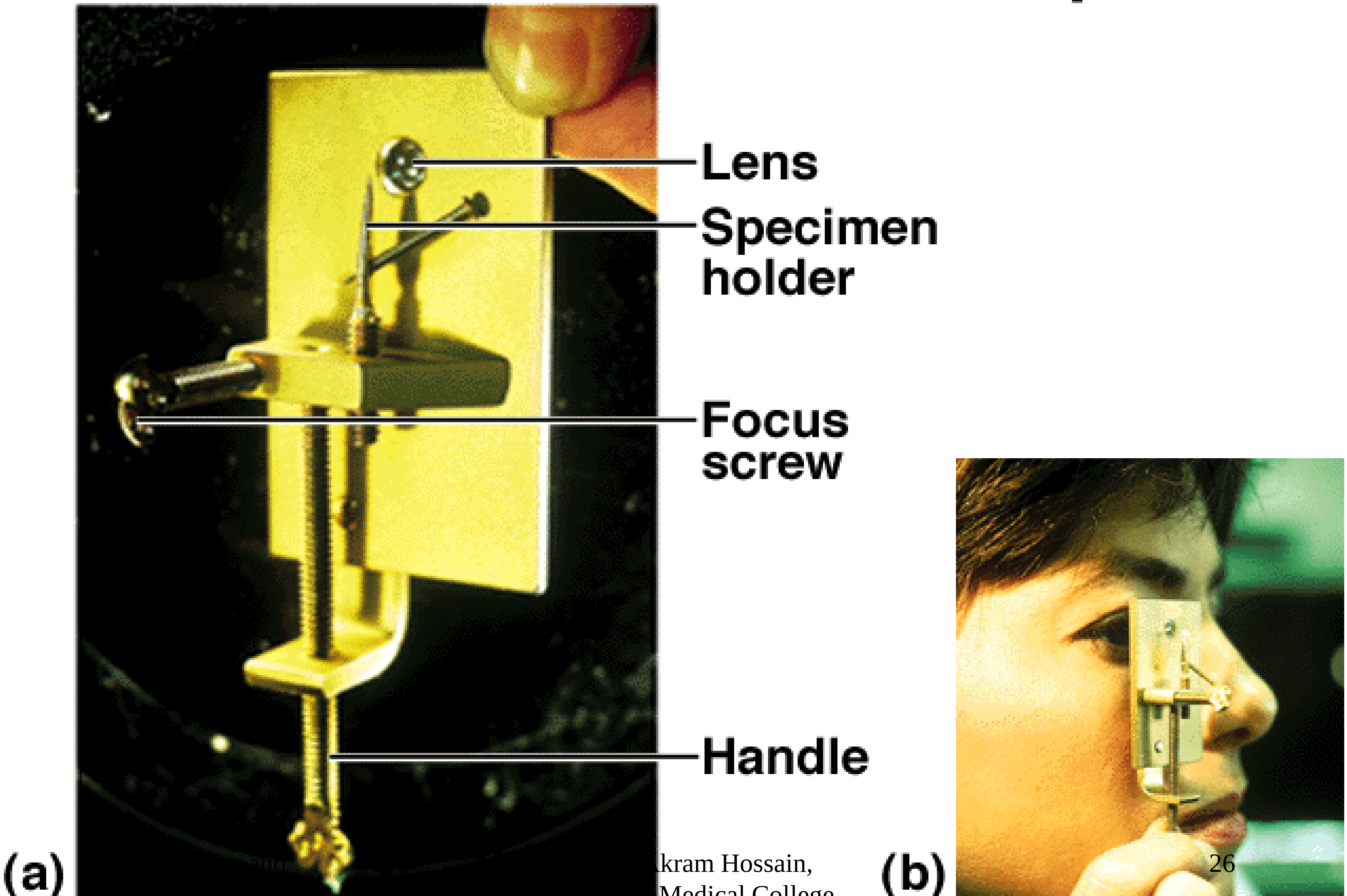
Antony van Leeunhoeck (1632 –1723)

Antony van Leeunhoeck Of Holland discovered Microscope and Observed Bacteria, Yeasts and Protozoa.

ANTONY VAN LEEUWENHOEK (1632-1723)

- He was the **first Person**, who invented the microscope and discovered the microbial world.
- He was a draper (Merchant) from Delft, **Holland**. He used to grind lenses and made microscopes as a hobby. The microscopes of Leeuwenhoek could magnify objects **about 200-300 times.**
- With his microscopes, Leeuwenhoek observed a variety of things like **rain water, pond water** and **scrapings from his own teeth**. He saw minute moving objects and called them as "**Little animalcules",** which we now know them as protozoa, yeasts and bacteria.
- He made accurate sketches and communicated his findings to **"Royal Society of London".**
- **Thus, Leeuwenhoek was the first person to discover microscope and the presence of bacteria and spirochetes in mouth**

Leuwenhoek's microscope



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17^{th} – 18^{th} Century

- **Spontaneous generation-** living organisms can develop from nonliving or decomposing matter
- **1688 - Franciso Redi (324 years back)- Italian Physician –** disproved this theory and showed that maggots on decaying meat came from fly eggs.
- **1718- Lady Mary Wortley Montagu (294 yrs back)** Introduction of small pox vaccination by Mary Montague
- **1749 - John Needham (263 years back)** an Irish priest, thought S.G existed because he could boil hay for long time and microbes still arose.
- **1740-1776 La zaro spallanzani (236 years back)** an Italian priest, boiled beef broth for an hour, sealed the flasks and observed no appearance of microorganisms and disproved the theory of spontaneous generation
- ***1774: Joseph Priestley discovers oxygen***
- **1796 –1798. Edward Jenner** (216 yrs back) Discovered Small Pox vaccine in

- **Theodor Schwann**

  German physiologist.

- His many contributions to biology include the
  - development of cell theory,
  - the discovery of Schwann cells in the peripheral nervous system,
  - the discovery and study of pepsin,
  - the discovery of the organic nature of yeast, and
  - the invention of the term metabolism.

(7 December 1810 – 11 January 1882)

- **Francesco Redi** was an Italian physician, naturalist, and poet.
- He is most well known for his series of experiments, published in 1668 as *Experiments on the Generation of Insects*, which is regarded as one of the first steps in refuting "spontaneous generation" - a theory also known as Aristotelian abiogenesis. At the time, prevailing wisdom was that maggots formed naturally from rotting meat.

(February 18, 1626 – March 1, 1697)

Spallanzani was a Catholic who researched the theory about the spontaneous **generation of cellular life in 1768**.

His experiment suggested that microbes move through the air and that they could be killed through boiling.

His work paved the way for later research by Louis Pasteur, who defeated the theory of spontaneous generation.

He also discovered and described animal (mammal) reproduction, showing that it requires both semen and an ovum.

He was the first to perform in vitro fertilization, with frogs, and an artificial insemination, using a dog.

Spallanzani showed that some animals, especially newts, can regenerate some parts of their body if injured or surgically removed.

His great work, however, is the process of digestion., which he proved to be no mere mechanical process of trituration - that is, of grinding up the food - but one of actual chemical solution, taking place primarily in the stomach, by the action of the gastric juice. He also carried out important researches on fertilization in animals (1780).

1729 –1799

1718

I am going to tell you a thing that I am sure will make you wish your self here. The small pox, so fatal and general amongst us, is here entirely harmless by the invention of ingrafting.

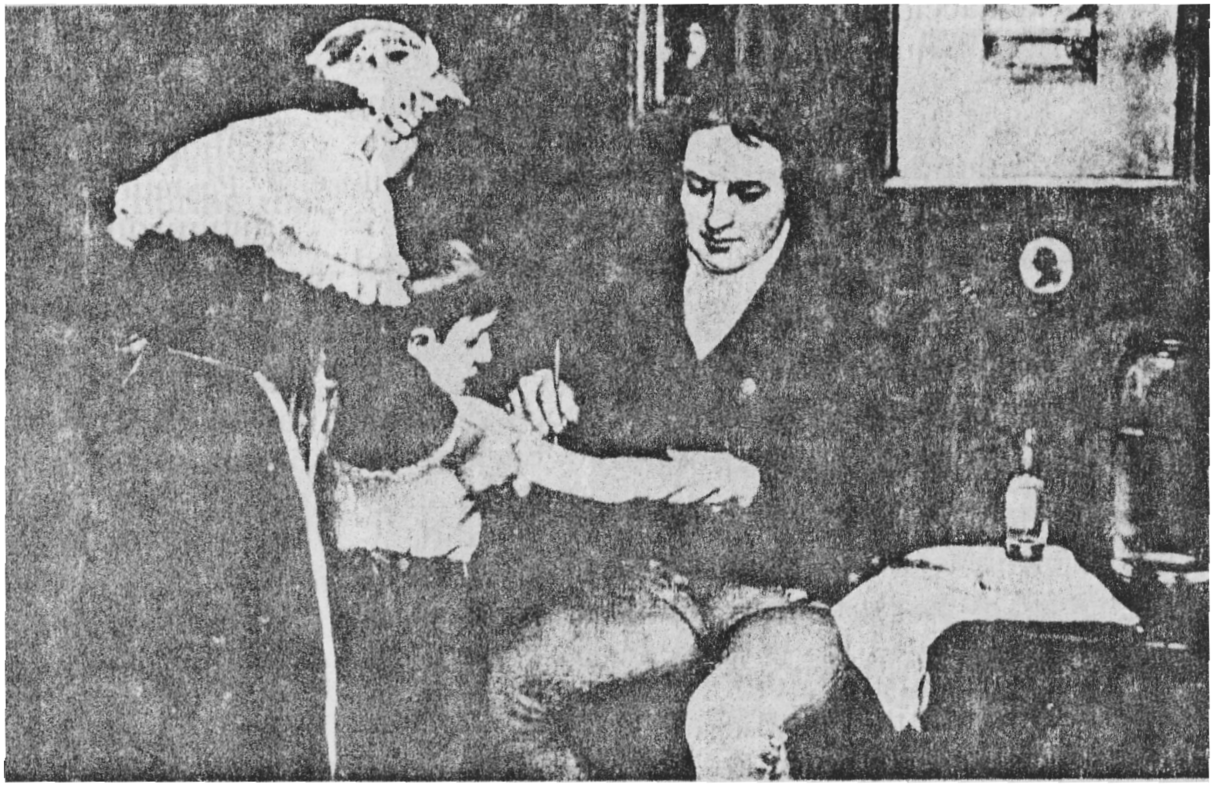
Lady Mary Wortley Montagu

Letter to her family

Introduced vaccination in England in 1718

Lady Mary Wortley Montagu,

Wife of British Ambassador in Turkey



1796 –1798.

Discovered Small Pox vaccine in 1796 –1798.

Edward Jenner (1749 – 1823)

In the Nineteenth century men lost their fear of God and acquired a fear of microbes

Anonymous

19^{th} Century

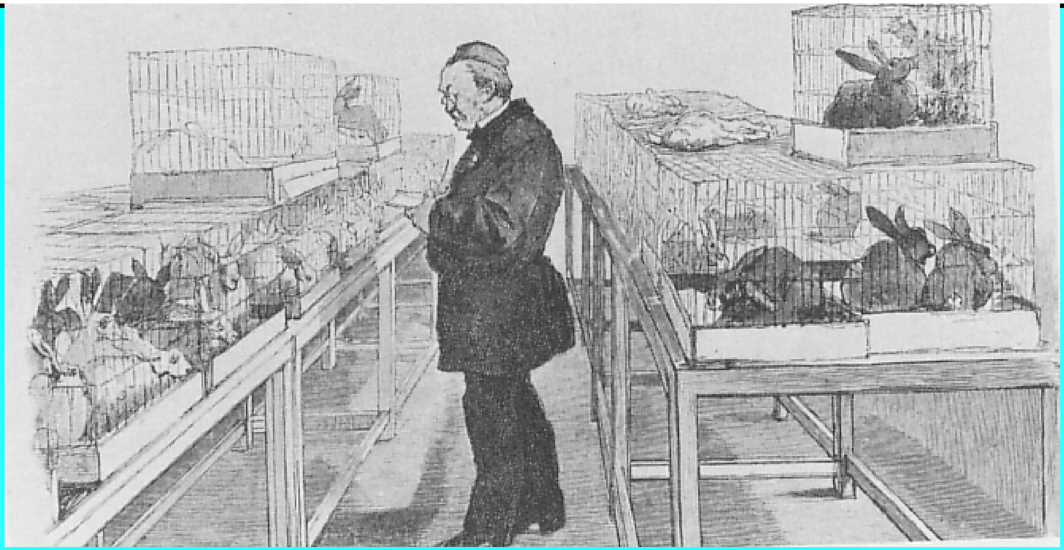
- 1838-39: **Mathias Schleiden and Theodor Schwann** (174 yrs back) independently propose cell theory.
- 1835-1844(about): **Bassi** shows that silkworm disease is caused by a fungus
- 1850 **Ignaz Semmelweis-** Hungarian physician - resident at Viennese hospital. Published The Etiology, Concept and Prophylaxis of Childbirth Fever.
- 1853: **John Snow** showed that cholera is spread by contaminated water
- 1861: **Louis Pasteur -Founder of modern Microbiology** disproves spontaneous generation theory and many other discovery of microbiology
- 1865 : Lister performed first antiseptic operation.

19^{th} Century –Continued-2

- 1866: Mendel publishes laws of heredity
- 1871: Mendeleyev publishes first periodic table
- 1876 – 1883 : **Robert Koch** (136- 129 back) Father of Medical Microbiology discovered pure culture in solid media and many other things**.**
- 1880 : **Paul Ehrlich** discovered synthetic arsenic compound (Salvarson) effective against syphilis also called "magic bullet"
- 1884: **Hans Christian Gram** invents Gram Stain
- 1884 :**Elie Metchnikoff** observes phagocytic cells
- 1888: **Roux and Yersin** show that the symptoms of diphtheria were caused by a toxin
- 1889: **Theobald Smith** shows that ticks can transmit Texas Cattle Fever: first demonstration of a vector

19th Century –Continued-3

- 1890: **Behring and Kitasato** prepare antitoxins for diptheria and tetanus
- 1892: **Ivanowsky** proposes the existence of viruses
- 1894: **David Bruce and wife** discover the cause and vector of sleeping sickness (*Nagana)*
- 1898: **Loeffler and Frosch** isolated the foot and mouth disease virus
- 1899: **Beijerinck** shows that a virus (tobacco mosaic) can cause a disease



1861

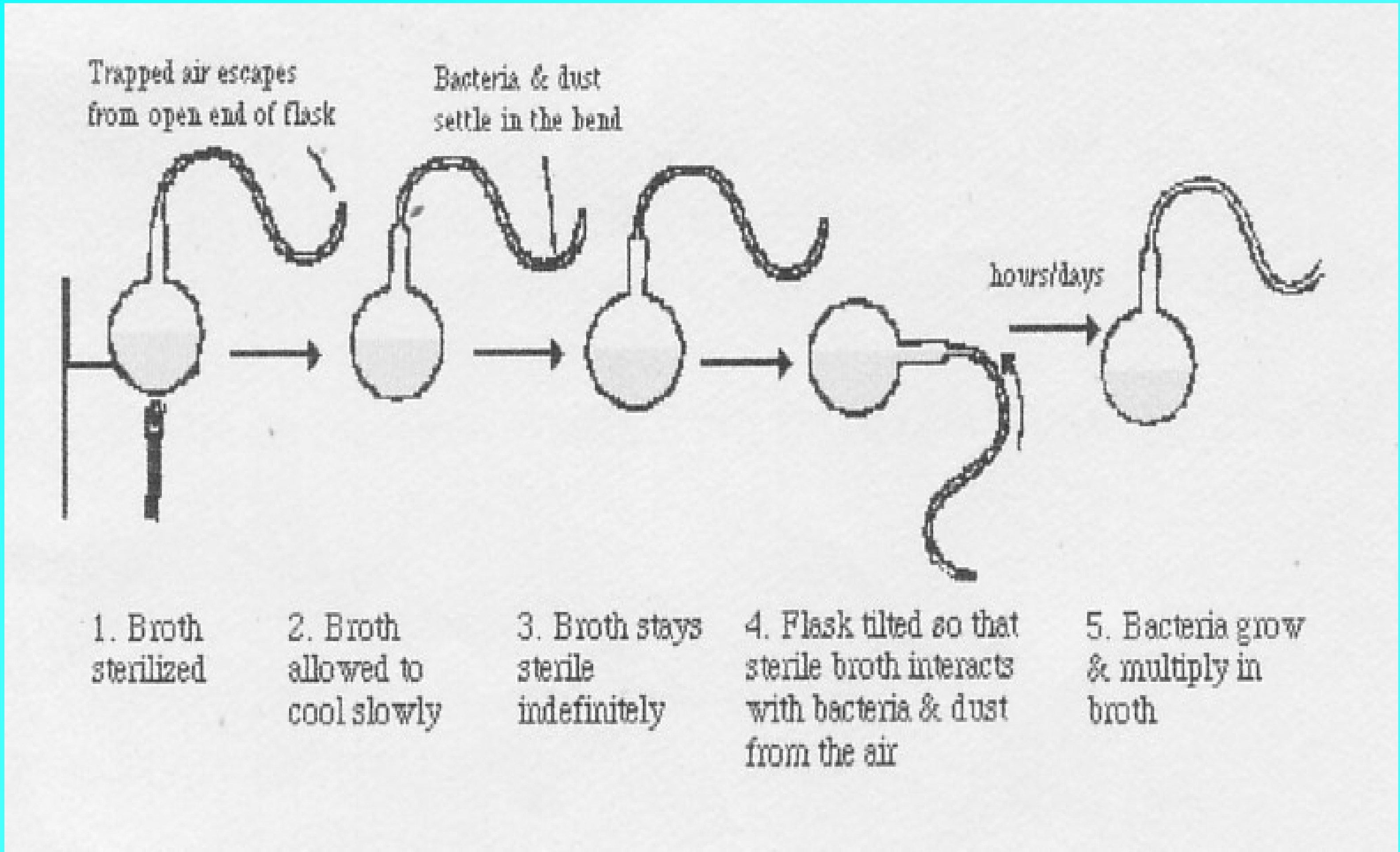
Louis Pasteur (1822 – 1895)

French, is the Founder of **Modern Microbiology**

Important contributions

- Disproves spontaneous generation theroy
- showed that yeasts converted sugar to ethanol and CO_2 (1857)
- showed that sugar could be converted to lactic acid by certain animalcules (1857)
- showed that microorganisms were required to cause food spoilage
- showed that beer and wine were turned to vinegar in presence of microbes
- invented pasteurization
- Culture technique in liquid media
- Disease production by microbes
- Causative agents of Anthrax, Rabies
- Live attenuated vaccine, ARV

“No more shall spontaneous generation rear its ugly head !”
Louis Pasteur



Germ Theory of Louis Pasteur
Swan neck experiment

Final blow to theory of spontaneous generation

- **John Tyndall (1877)**
  - demonstrated that dust carries microorganisms
  - showed that if dust was absent, nutrient broths remained sterile, even if directly exposed to air
  - also provided evidence for the existence of exceptionally heat-resistant forms of bacteria

Recognition of the Relationship between Microorganisms and Disease

- Agostini Bassi (1835)
  - □showed that a disease of silkworms was caused by a fungus
- M. J. Berkeley (ca. 1845)
  - demonstrated that the Great Potato Blight of Ireland was caused by a fungus
- Heinrich de Bary (1853)
  - showed that smut and rust fungi caused cereal crop diseases

Other evidence

- **Lister & Semmelweis** - aseptic techniques in medicine
- **Ignaz Philipp Semmelweis**
  - Autopsies and disease (puerperal fever)
  - Nervous breakdown
- **Joseph Lister**
  - provided indirect evidence that microorganisms were the causal agents of disease
  - developed a system of surgery designed to prevent microorganisms from entering wounds
- Spray phenol in the instruments and over the wounds
- his patients had fewer postoperative infections

The Role of Microorganisms in Disease

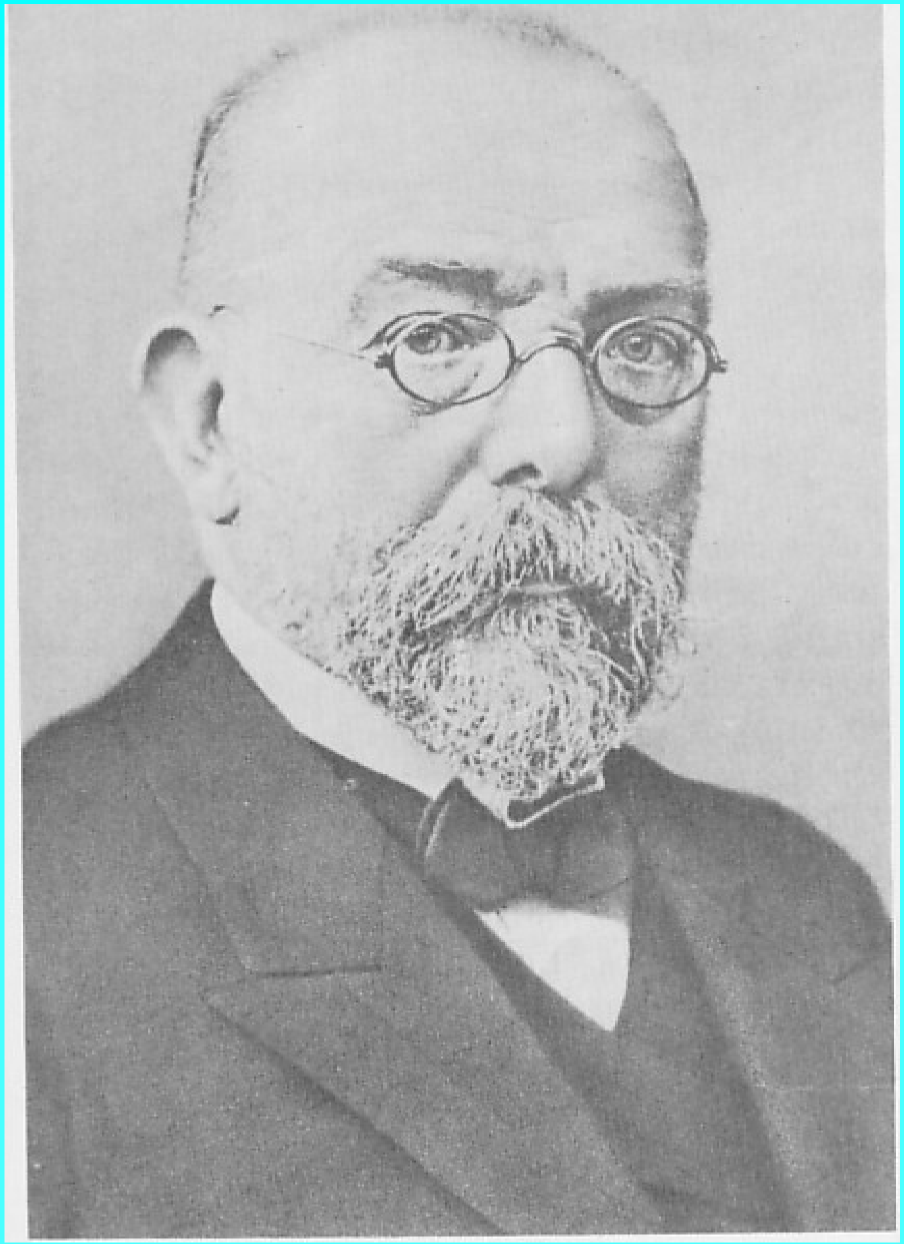
- was not immediately obvious
- establishing connection depended on
- development of techniques for studying
- microbes
- once established, led to study of host
- defenses - immunology

More evidence…

Louis Pasteur
showed that the pébrine disease of silkworms was caused by a protozoan

Final Proof….

- **Robert Koch (1880s)**
  - established the relationship between Bacillus anthracis and anthrax
  - used criteria developed by his teacher Jacob Henle (1809-1895)
  - these criteria now known as Koch’s postulates
    - still used today to establish the link between a particular microorganism and a particular disease



1876 - 1892

Father of Medical Microbiology

- Pure culture in solid media
- Koch's pastulates
- Koch's phenomenon
- Isolated
    - B. anthracis
    - M. tuberculosis
    - Cholera bacilli

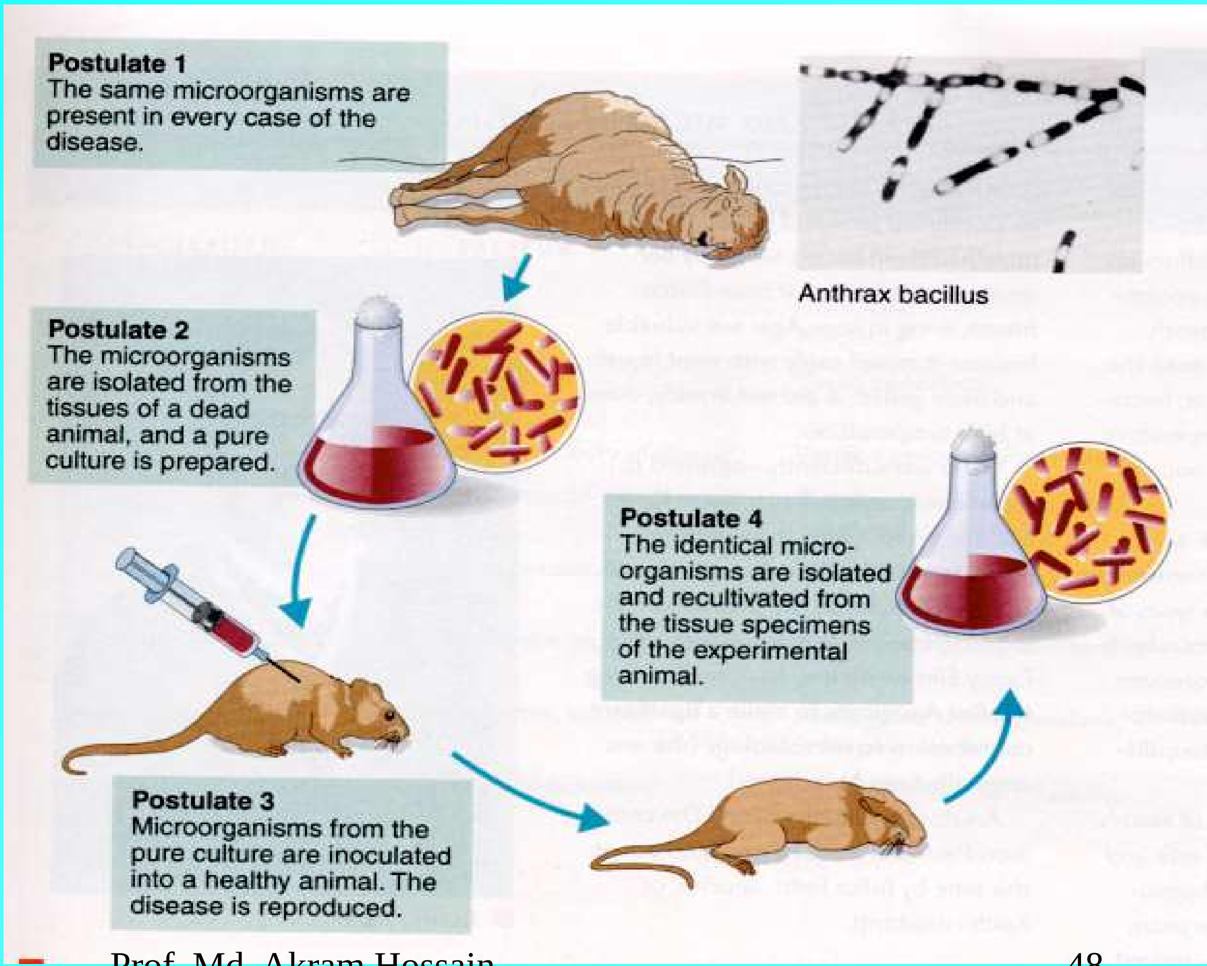
Robert Koch (1843 –1910), German

The Development of Techniques for Studying Microbial Pathogens

- Koch’s work led to discovery or
- development of:
  - Agar (with the help of Fannie and Walter Hesse)
- Petri dish (Richard Petri)
  - nutrient broth and nutrient agar
- methods for isolating microorganisms- pure
  - culture
  - anthrax
  - TB
- cholera

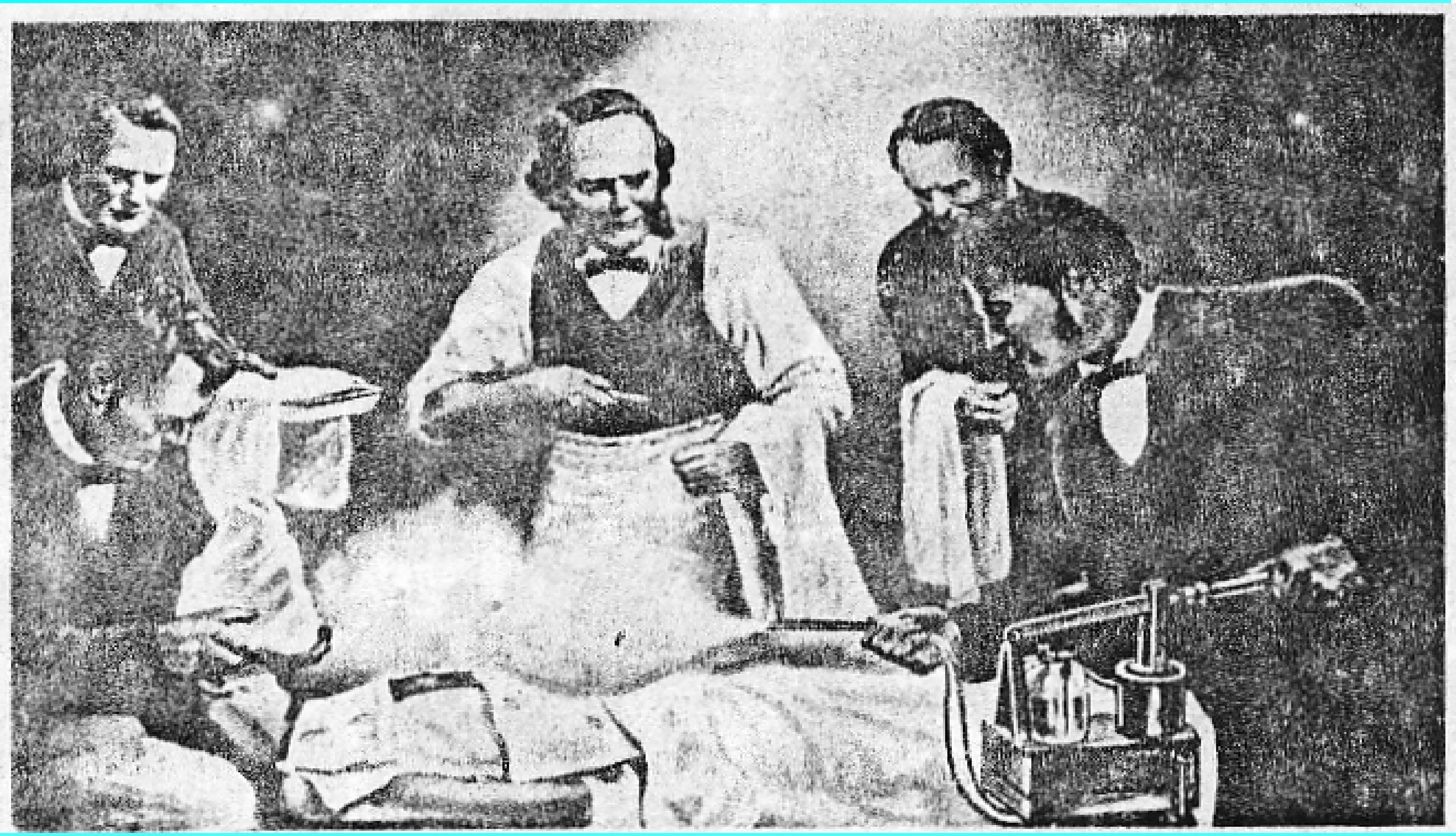
Koch's Postulates

Postulates
Were originally
outline by Jakob Henle
in 1940



Fannie and Walter Hesse

1877



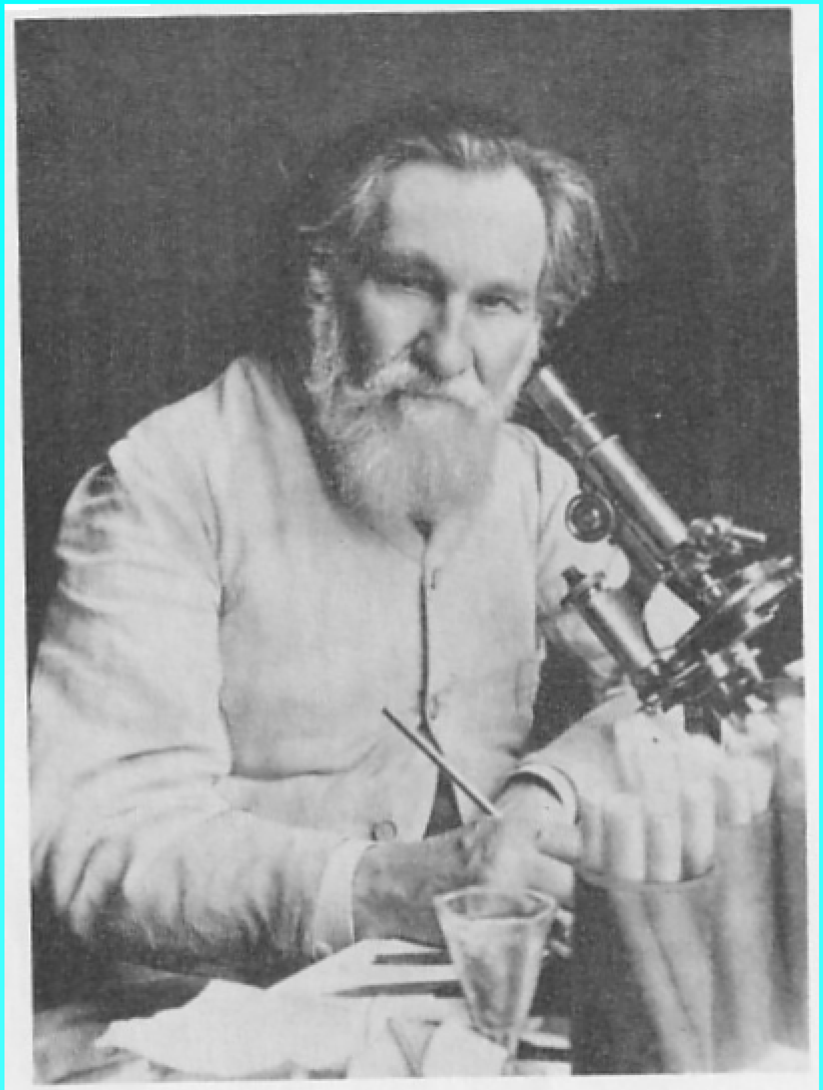
Joseph Lister (1827 – 1912)Scottish Surgeon

Discovered aseptic surgery by using carbolic acid.

1880.

Paul Ehrlich discovered synthetic arsenic compound (Salvarson) effective against syphilis also called "magic bullet" in 1880.

Paul Ehrlich (1854 – 1915)



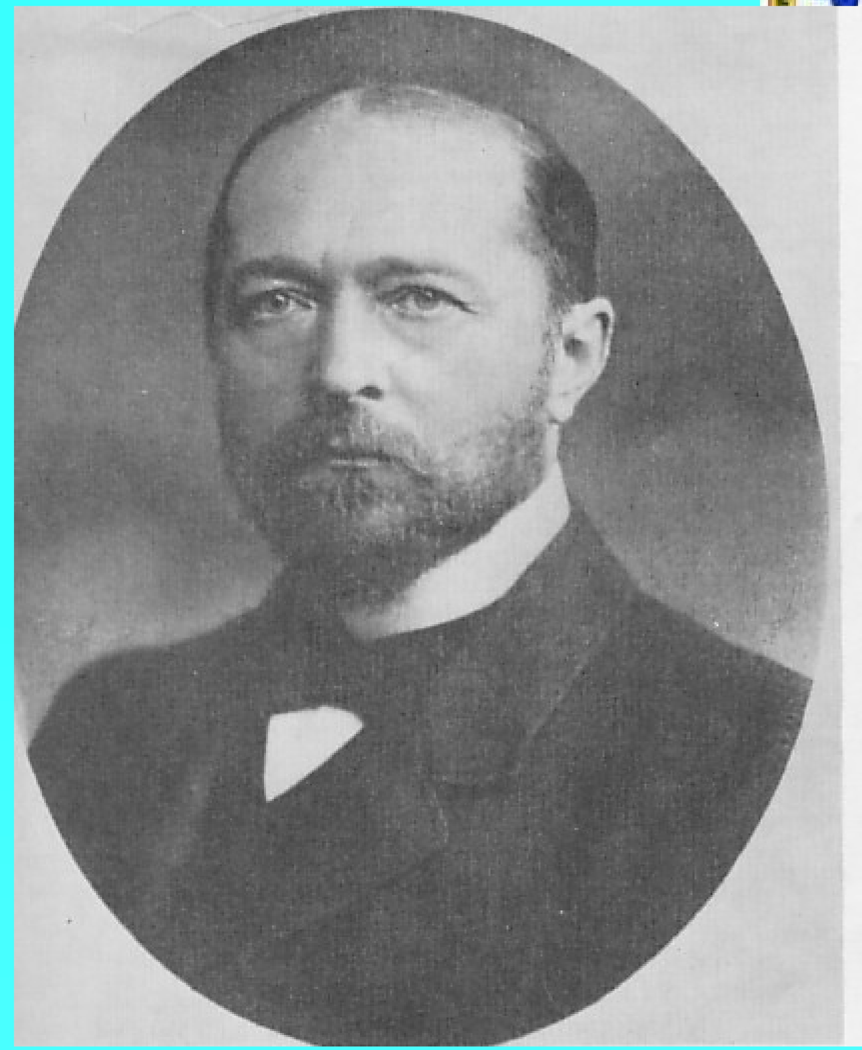
Elie Metchnikoff (1845 – 1916)

1883

discovered phagocytic phenomenon in 1883.

1890.

Discovered Humoral immunity by Antibody in 1890.



Emil Adolf von Behring (1854-1917)

20^{th} century discoveries

20^{th} century -1

- 1900: **Walter Reed** shows that mosquitos are the vector for yellow fever
- 1905: **Schaudinn and Hoffman** show that *Treponema pallidum causes syphillis*
- 1908: **Paul Ehrich** develops first chemotheraputic drug (Compound 606)
- 1911: **Peyton Rous** shows that a virus can cause cancer
- 1929: **Alexander Fleming** discovers penicillin
- 1935: **Stanley** - tobacco mosaic virus
- 1938 : **Max Theiller** (Noble prize in 1945) - Successful vaccination against yellow fever
- 1941: **Howard Florey** develops penicillin into a drug and treats first patient

Fritz Richard Schaudinn was a German zoologist

One of Founder of Protozoology

- the causative agent of **syphilis in 1905 with Hoffman**
- **amoebic dysentery** and
- **sleeping sickness, malaria**
- **human hookworm infection**

Schaudinn died during his journey back to Germany from an International Medicine Meeting in Lisbon, when he underwent an urgent surgery aboard due to gastrointestinal amebian abscesses. **Such amebian infection had probably been voluntarily acquired when he did research on amoebas**

Fritz Richard Schaudinn 1871-1906

- Erich Hoffmann (April 25, 1868 – May 8, 1959) was a German dermatologist
- Hoffmann is remembered for his research performed with zoologist Fritz Schaudinn (1871-1906) at the Charité Clinic in Berlin.
- In 1905 Schaudinn and Hoffmann discovered the bacterium that was responsible for **syphilis**, Treponema pallidum.
- The organism was removed from a papula in the vulva of a patient with secondary syphilis.

Erich Hoffmann (April 25, 1868 – May 8, 1959)

- He was involved in the discovery of the role of viruses in the transmission of certain types of cancer. In 1966 he was awarded a Nobel Prize in Physiology or Medicine for his work. (50 years later—this may be a record for the time between a discovery and a Nobel Prize).
- As a pathologist he made his seminal observation, that a malignant tumor (specifically, a sarcoma) growing on a domestic chicken could be transferred to another fowl simply by exposing the healthy bird to a cell-free filtrate, in 1911.
- This finding, that cancer could be transmitted by a virus (now known as the **Rous sarcoma virus, a retrovirus**), was widely discredited by most of the field's experts at that time.
- Since he was a relative newcomer, it was several years before anyone even tried to replicate his prescient results.

(Francis) Peyton Rous FRS 1879 – 1970

- Wendell Meredith Stanley (16 August 1904 – 15 June 1971) was an **American biochemist, virologist and Nobel laureate.**
- Stanley's work contributed to on **lepracidal compounds, diphenyl stereochemistry and the chemistry of the sterols**.
- His researches on the virus causing the **mosaic disease in tobacco plants** led to the isolation of a nucleoprotein which displayed tobacco mosaic virus activity.
- Stanley was awarded the Nobel Prize in Chemistry for 1946

Wendell Meredith Stanley (16 August 1904 – 15 June 1971)

Max Theiler (1899 – 1972) was American virologist.

He was awarded the Nobel Prize in 1951 for vaccine against yellow fever.

- In 1926 they disproved Hideyo Noguchi's hypothesis that yellow fever was caused by the bacterium Leptospira icteroides, and in 1928 (the year after the disease was identified conclusively as a virus), they showed that the African and South American viruses are immunologically identical
- In the course of this research Theiler himself contracted yellow fever but survived and developed immunity.
- After passing the yellow fever virus through laboratory mice, Theiler found that the weakened virus conferred immunity on Rhesus monkeys. However, it was only in 1937, after the particularly virulent Asibi strain from West Africa had gone through more than a hundred subcultures, that Theiler and his colleague Hugh Smith announced the development of the 17-D vaccine.
- Between 1940 and 1947 the Rockefeller Foundation produced more than **28 million doses of the vaccine** and finally ended yellow fever as a major disease. For this work Theiler received the 1951 Nobel Prize in Physiology or Medicine.

Baron Florey OM FRS (1898 – 21 1968)

Howard Walter Florey, was an Australian pharmacologist and pathologist who shared the Nobel Prize in Physiology or Medicine in 1945 with Sir Ernst Boris Chain and Sir Alexander Fleming for his role in the making of penicillin.

Florey's discoveries are estimated to have saved over **6 million lives**,

Sir Robert Menzies, Australia's longest-serving Prime Minister, said that "in terms of world well-being, Florey was the most important man ever born in Australia

20th century -2

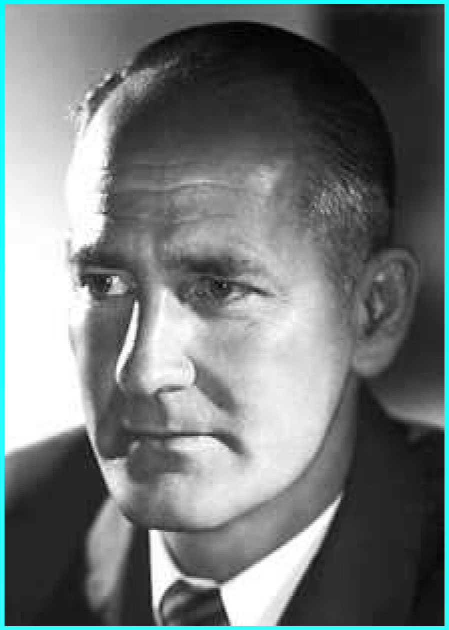
- 1940: Electron Microscope by Ruska
- 1941 : **George Beadle & E. Tatum** -(Noble prize in 1958) - " one gene one enzyme concept")
- 1944: **Avery, MacLeod, and McCarty** show that DNA is the genetic material
- 1953: **Watson & Crick -**propose DNA structure
- 1967 : **Sir Frank Mac Farlane Burnet** –Immunological tolerance
- 1973: **Cohen , Boyer, Chang, and Helling** clone DNA
- 1977: World Health Organization eradicates smallpox
- 1983 : **Luc Montaigner and Robert Gallo** - HIV as causative agent of AIDS. **L.W Riley & Colleagues** - *E.coli O:157* as CA of HUS.
- 1984 : Barry J Marshall -Campylobacter pylori from PUD later named as Helicobatcer
- 1996: **Bishop and Varmus** discover oncogenes
- 1995: First complete genetic sequence of a bacterium is published

Ernst August Friedrich Ruska (25 December 1906 – 27 May 1988 was a German physicist who won the Nobel Prize in Physics in 1986 for his work in electron optics, including the design of the first electron microscope.

After leaving Siemens in 1955, Ruska served as director of the Institute for Electron Microscopy of the Fritz Haber Institute until 1974. Concurrently, he served at the institute and as professor at the Technical University of Berlin from 1957 until his retirement in 1974.

In 1986, he was awarded half of the Nobel Prize in Physics for his many achievements in electron optics; Gerd Binnig and Heinrich Rohrer won a quarter each for their design of the scanning tunneling microscope. He died in West Berlin in 1988.

Ernst Ruska
(1906-1988)



George Wells Beadle (1903 – 1989)

George Wells Beadle (October 22, 1903 – June 9, 1989) was an American scientist in the field of genetics, and Nobel Prize in Physiology or Medicine Nobel laureate who with Edward Lawrie Tatum discovered the role of genes in regulating biochemical events within cells.

Beadle and Tatum's key experiments involved exposing the bread mold Neurospora crassa to x-rays, causing mutations.

In a series of experiments, they showed that these mutations caused changes in specific enzymes involved in metabolic pathways. These experiments led them to propose a direct link between genes and enzymatic reactions, known as the "one gene, one enzyme" hypothesis

Electron microscope

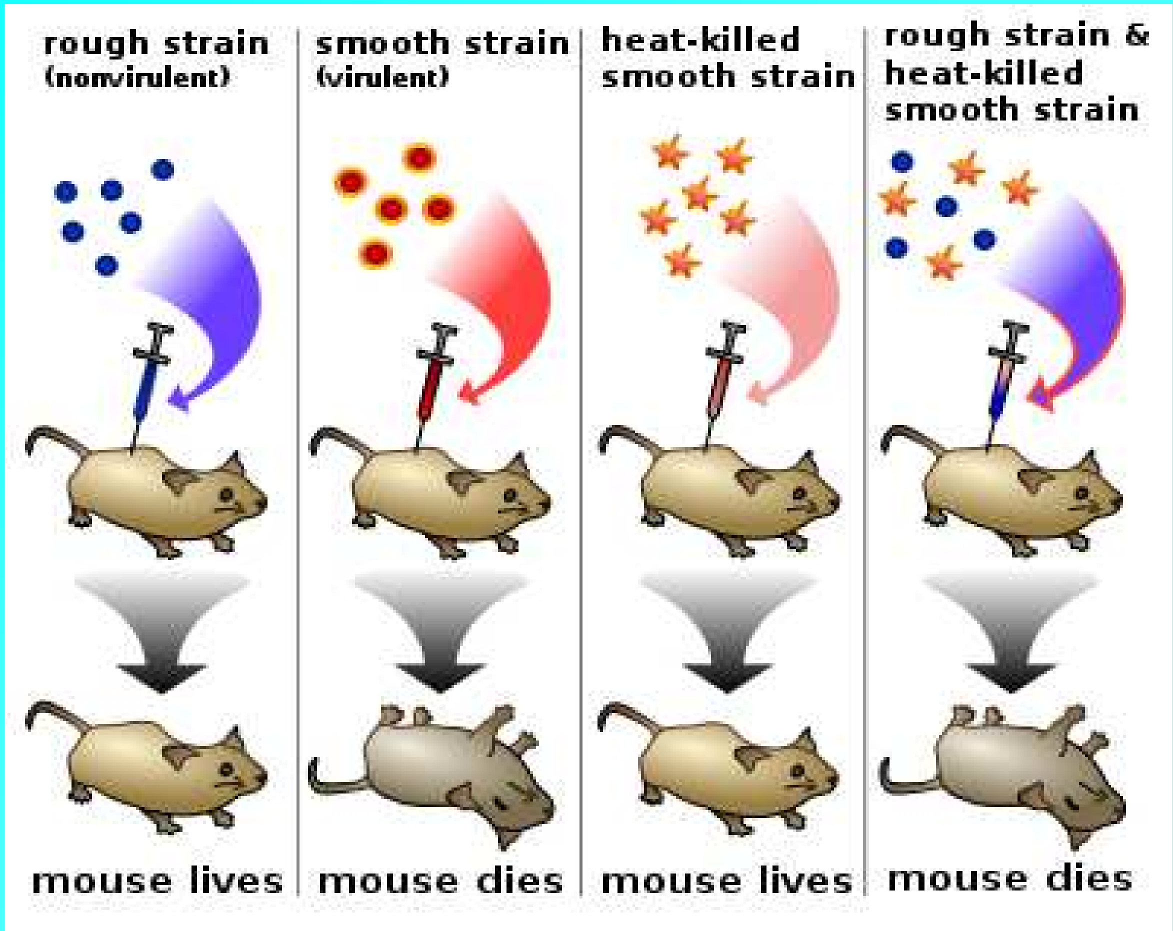
Edward Lawrie Tatum (December 14, 1909 – November 5, 1975) was an American geneticist.

He shared half of the Nobel Prize in Physiology or Medicine in 1958 with George Wells Beadle for showing that genes control individual steps in metabolism.

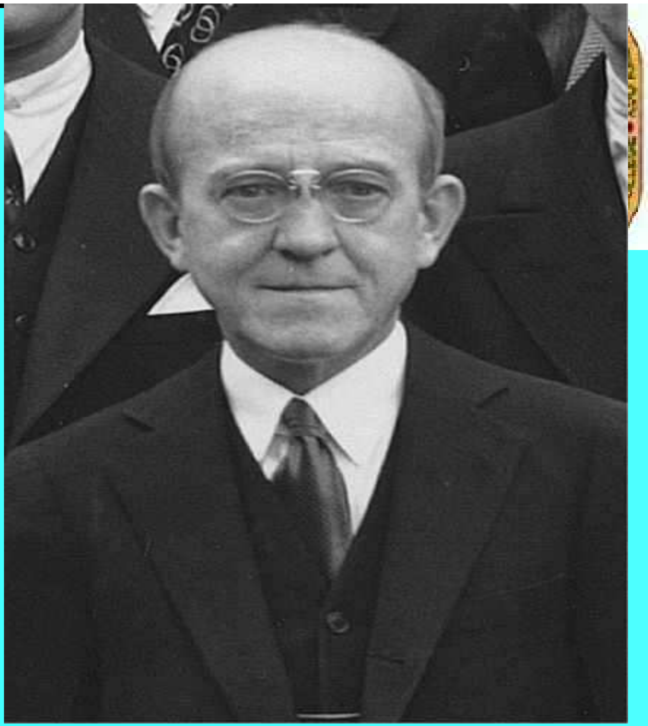
Beadle and Tatum's key experiments involved exposing the bread mold Neurospora crassa to x-rays, causing mutations. In a series of experiments, they showed that these mutations caused changes in specific enzymes involved in metabolic pathways.

These experiments, published in 1941, led them to propose a direct link between genes and enzymatic reactions, known as the "one gene, one enzyme" hypothesis.

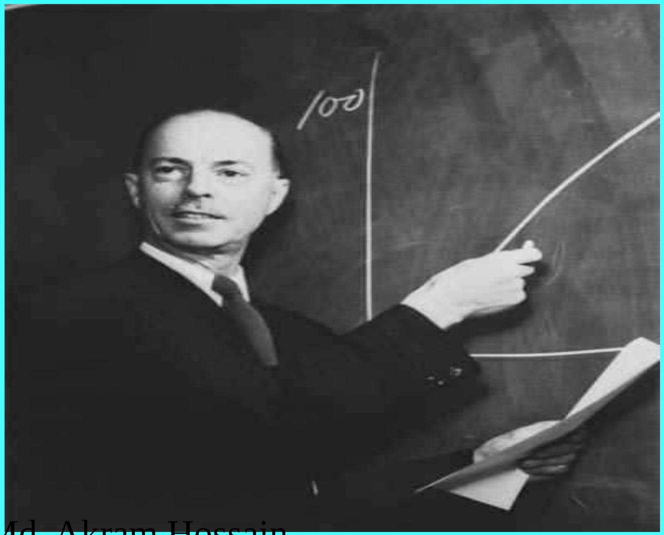
- The Avery–MacLeod–McCarty experiment was an experimental demonstration, reported in 1944 by Oswald Avery, Colin MacLeod, and Maclyn McCarty, that DNA is the substance that causes bacterial transformation.
- It was the culmination of research in the 1930s and early 1940s at the Rockefeller Institute for Medical Research to purify and characterize the "transforming principle" responsible for the transformation phenomenon first described in Griffith's experiment of 1928: killed Streptococcus pneumoniae of the virulent strain type III-S, when injected along with living but non-virulent type II-R pneumococci, resulted in a deadly infection of type III-S pneumococci.
- In their paper "Studies on the Chemical Nature of the Substance Inducing Transformation of Pneumococcal Types: Induction of Transformation by a Deoxyribonucleic Acid Fraction Isolated from Pneumococcus Type III", published in the February 1944 issue of the Journal of Experimental Medicine,
- Avery and his colleagues suggest that DNA, rather than protein as widely believed at the time, may be the hereditary material of bacteria, and could be analogous to genes and/or viruses in higher organisms.


rough strain
(nonvirulent)
smooth strain
(virulent)
heat-killed
smooth strain
rough strain &
heat-killed
smooth strain
mouse lives
mouse dies
mouse lives
mouse dies

Maclyn McCarty (with Watson and Crick)



Oswald Avery



Colin MacLeod

Experimental work

- Pneumococcus is characterized by smooth colonies and has a polysaccharide capsule that induces antibody formation; the different types are classified according to their immunological specificity.
- The purification procedure consisted of first killing the bacteria with heat and extracting the saline-soluble components. Next, the protein was precipitated out using chloroform and the polysaccharide capsules were hydrolyzed with an enzyme. An immunological precipitation caused by type-specific antibodies was used to verify the complete destruction of the capsules. Then, the active portion was precipitated out by alcohol fractionation, resulting in fibrous strands that could be removed with a stirring rod.
- Chemical analysis showed that the proportions of carbon, hydrogen, nitrogen, and phosphorus in this active portion were consistent with the chemical composition of DNA. To show that it was DNA rather than some small amount of RNA, protein, or some other cell component that was responsible for transformation, Avery and his colleagues used a number of biochemical tests. They found that trypsin, chymotrypsin and ribonuclease (enzymes that break apart proteins or RNA) did not affect it, but an enzyme preparation of "deoxyribonucleodepolymerase" (a crude preparation, obtainable from a number of animal sources, that could break down DNA) destroyed the extract's transforming power.
- Followup work in response to criticism and challenges included the purification and crystallization, by Moses Kunitz in 1948, of a DNA depolymerase (deoxyribonuclease I), and precise work by Rollin Hotchkiss showing that virtually all the detected nitrogen in the purified DNA came from glycine, a breakdown product of the nucleotide base adenine, and that undetected protein contamination was at most 0.02% by Hotchkiss's estimation

• Reception and legacy

- The experimental findings of the Avery–MacLeod–McCarty experiment were quickly confirmed, and extended to other hereditary characteristics besides polysaccharide capsules. However, there was considerable reluctance to accept the conclusion that DNA was the genetic material. According to Phoebus Levene's influential "tetranucleotide hypothesis", DNA consisted of repeating units of the four nucleotide bases and had little biological specificity. DNA was therefore thought to be the structural component of chromosomes, whereas the genes were thought likely to be made of the protein component of chromosomes. This line of thinking was reinforced by the 1935 crystallization of tobacco mosaic virus by Wendell Stanley, and the parallels among viruses, genes, and enzymes; many biologists thought genes might be a sort of "super-enzyme", and viruses were shown according to Stanley to be proteins and to share the property of autocatalysis with many enzymes.

• Reception and legacy…

- . Furthermore, few biologists thought that genetics could be applied to bacteria, since they lacked chromosomes and sexual reproduction. In particular, many of the geneticists known informally as the phage group, which would become influential in the new discipline of molecular biology in the 1950s, were dismissive of DNA as the genetic material (and were inclined to avoid the "messy" biochemical approaches of Avery and his colleagues). Some biologists, including fellow Rockefeller Institute Fellow Alfred Mirsky, challenged Avery's finding that the transforming principle was pure DNA, suggesting that protein contaminants were instead responsible. Although transformation occurred in some kinds of bacteria, it could not be replicated in other bacteria (nor in any higher organisms), and its significance seemed limited primarily to medicine

Reception and legacy…

- Scientists looking back on the Avery–MacLeod–McCarty experiment have disagreed about just how influential it was in the 1940s and early 1950s. Gunther Stent suggested that it was largely ignored, and only celebrated afterwards—similarly to Gregor Mendel's work decades before the rise of genetics. Others, such as Joshua Lederberg and Leslie C. Dunn, attest to its early significance and cite the experiment as the beginning of molecular genetics.
- A few microbiologists and geneticists had taken an interest in the physical and chemical nature of genes before 1944, but the Avery–MacLeod–McCarty experiment brought renewed and wider interest in the subject. While the original publication did not mention genetics specifically, Avery as well as many of the geneticists who read the paper were aware of the genetic implications—that Avery may have isolated the gene itself as pure DNA. Biochemist Erwin Chargaff, geneticist H. J. Muller and others praised the result as establishing the biological specificity of DNA and as having important implications for genetics if DNA played a similar role in higher organisms. In 1945, the Royal Society awarded Avery the Copley Medal, in part for his work on bacterial transformation.

Reception and legacy…

- Between 1944 and 1954, the paper was cited at least 239 times (with citations spread evenly though those years), mostly in papers on microbiology, immunochemistry, and biochemistry. In addition to the follow-up work by McCarty and others at the Rockefeller Institute in response to Mirsky's criticisms, the experiment spurred considerable work in microbiology, where it shed new light on the analogies between bacterial heredity and the genetics of sexually-reproducing organisms.
- French microbiologist André Boivin claimed to extend Avery's bacterial transformation findings to Escherichia coli,[20] although this could not be confirmed by other researchers.
- In 1946, however, Joshua Lederberg and Edward Tatum demonstrated bacterial conjugation in E. coli and showed that genetics could apply to bacteria, even if Avery's specific method of transformation was not general.
- Avery's work also may have played a role in the continuation of X-ray crystallography studies of DNA by Maurice Wilkins, who faced pressure from his funders to make whole cells, rather than biological molecules, the subject of his research.

Despite the significant number of citations to the paper and positive responses it received in the years following publication, Avery's work was largely neglected by much of the scientific community. Although received positively by many scientists, the experiment did not seriously affect mainstream genetics research, in part because it made little difference for classical genetics experiments in which genes were defined by their behavior in breeding experiments rather than their chemical makeup. H. J. Muller, while interested, was focused more on physical rather than chemical studies of the gene, as were most of the members of the phage group. Avery's work was also neglected by the Nobel Foundation, which later expressed public regret for failing to award Avery a Nobel Prize

Reception and legacy…

- By the time of the 1952 Hershey–Chase experiment, geneticists were more inclined to consider DNA as the genetic material, and Alfred Hershey was an influential member of the phage group.Erwin Chargaff had shown that the base composition of DNA varies by species (contrary to the tetranucleotide hypothesis),
- and in 1952 Rollin Hotchkiss published his experimental evidence both confirming Chargaff's work and demonstrating the absence of protein in Avery's transforming principle. Furthermore, the field of bacterial genetics was quickly becoming established, and biologists were more inclined to think of heredity in the same terms for bacteria and higher organisms.
- After Hershey and Chase used radioactive isotopes to show that it was primarily DNA, rather than protein, that entered bacteria upon infection with bacteriophage,[it was soon widely accepted that DNA was the material. Despite the much less precise experimental results (they found a not-insignificant amount of protein entering the cells as well as DNA), the Hershey–Chase experiment was not subject to the same degree of challenge.
- Its influence was boosted by the growing network of the phage group and, the following year, by the publicity surrounding the DNA structure proposed by Watson and Crick (Watson was also a member of the phage group). Only in retrospect, however, did either experiment definitively prove that DNA is the genetic material

1983

•**Luc Montaigner and Robert Gallo** - HIV as causative agent of AIDS.

•**L.W Riley & Colleagues** - *E.coli O:157* as CA of HUS.

1984

Barry Marshall -*Campylobacter pylori* from PUD later named as *Helicobatcer*

1985

Robert Gallo, Dani Bolognesi, Sam Broder - AZT as anti HIV drug

1900

Walter Reed - Yellow fever- caused by a virus (1st human viral disease)

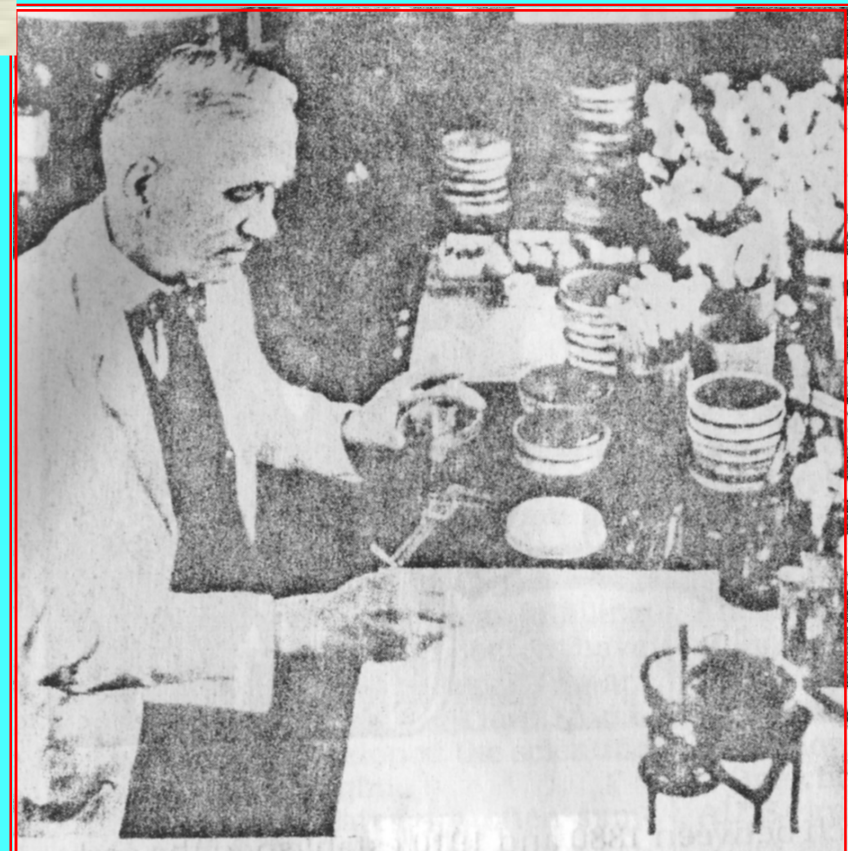
Chance favors the prepared mind
Louis Pasteur

1929.

1929

Alexander Fleming publishes the first paper describing **penicillin and its effect on gram positive microorganisms**. This finding is unique since it is a rare example of bacterial lysis and not just microbial antagonism brought on by the mold

Sir Alexander flemming of Scotland discovered penicillin in 1929.



Sir Alexander flemming (1881- 1955)

1934

1934

- Ladislaus Laszolo Marton - First use of electron microscope 200 -300,000x

(1937 - first electronic monograph of bacteria.)

- Alice Evans - Typing of bacteriophage.

To be your best self

To change your world, you must change yourself.
To blame and complain will only make matters worse.
Whatever you care about, is your responsibility.
What you see in others, shows you yourself.
See the best in others, and you will be your best.
Give to others, and you give to yourself.
Appreciate beauty, and you will be beautiful.
Admire creativity, and you will be creative.
Love, and you will be loved.
Seek to understand, and you will be understood.
Listen, and your voice will be heard.
Teach, and you will learn.
Show your best face to the mirror,
and you'll be happy with the face looking back at you.

To be your best self

The good you find in others, is in you too. The faults you find in others, are your faults as well. After all, to recognize something you must know it.

The possibilities you see in others, are possible for you as well. The beauty you see around you, is your beauty.

The world around you is a reflection, a mirror showing you the person you are.

To be your best self

Appreciate beauty, and you will be beautiful.
Admire creativity, and you will be creative.

Love, and you will be loved.
Seek to understand, and you will be understood.
Listen, and your voice will be heard.

Teach, and you will learn.

Show your best face to the mirror,

and you'll be happy with the face looking back at you.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1958

1958

WHO declares Crusade against small pox globally which finally begins in 1967 and eradicated in 1977.

Discovered
- Important media (Monsurs media)
- transport technique for V. cholera in1963

Dr. Kazi Abul Mansur, Bangladesh

1979

1979

Small pox was declared officially eradicated, last natural case seen in Somalia in 1977.

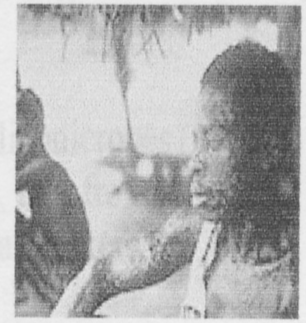
The Only Microbial Disease Ever Completely Defeated

Success and scopes of Microbiology

- Diagnosis
  - Infectious
  - autoimmune
  - other diseases
- Treatment
  - Infectious,
  - autoimmune
  - some cancers
- Eradication of disease
- Prevention of disease
- Organ transplantation
- Medico-legal applications

1979

Smallpox (*variola*) is declared officially eliminated; last natural case seen in Somalia in 1977. Small quantities remain held under tightly controlled conditions in the U.S. and former U.S.S.R. **THE ONLY MICROBIAL DISEASE EVER COMPLETELY DEFEATED.**



- Food and Pharmaceutical Industry
- Agriculture

- Molecular biology
- Genetic engineering
- Biotechnology

Table 1.1 Some Important Events in the Development of Microbiology

Date	Microbiological History	Other Historical Events
1546	Fracastoro suggests that invisible organisms cause disease	Publication of Copernicus's work on the heliocentric solar system (1543)
1590–1608	Jansen develops first useful compound microscope	Shakespeare's *Hamlet* (1600–1601)
1676	Leeuwenhoek discovers "animalcules"	J. S. Bach and Handel born (1685)
1688	Redi publishes work on spontaneous generation of maggots	Isaac Newton publishes the *Principia* (1687)
		Linnaeus's *Systema Naturae* (1735)
		Mozart born (1756)
1765–1776	Spallanzani attacks spontaneous generation	
1786	Müller produces first classification of bacteria	French Revolution (1789)
1798	Jenner introduces cowpox vaccination for smallpox	Beethoven's first symphony (1800)
		The battle of Waterloo and the defeat of Napoleon (1815)
		Faraday demonstrates the principle of an electric motor (1821)
1838–1839	Schwann and Schleiden, the Cell Theory	England issues first postage stamp (1840)
1835–1844	Bassi discovers that silkworm disease is caused by a fungus and proposes that many diseases are microbial in origin	Marx's *Communist Manifesto* (1848)
1847–1850	Semmelweis shows that childbed fever is transmitted by physicians and introduces the use of antiseptics to prevent the disease	Velocity of light first measured by Fizeau (1849)
		Clausius states the first and second laws of thermodynamics (1850)
1849	Snow studies the epidemiology of a cholera epidemic in London	Graham distinguishes between colloids and crystalloids
		Melville's *Moby Dick* (1851)
		Otis installs first safe elevator (1854)
		Bunsen introduces the use of the gas burner (1855)
1857	Pasteur shows that lactic acid fermentation is due to a microorganism	
1858	Virchow states that all cells come from cells	Darwin's *On the Origin of Species* (1859)
1861	Pasteur shows that microorganisms do not arise by spontaneous generation	American Civil War (1861–1865)
		Mendel publishes his genetics experiments (1865)
		Cross-Atlantic cable laid (1865)
1867	Lister publishes his work on antiseptic surgery	Dostoevski's *Crime and Punishment* (1866)
1869	Miescher discovers nucleic acids	Franco-German War (1870–1871)

continued...

Table 1.1 Some Important Events in the Development of Microbiology

Date	Microbiological History	Other Historical Events
1876–1877	Koch demonstrates that anthrax is caused by *Bacillus anthracis*	Bell invents telephone (1876)
		Edison's first light bulb (1879)
1880	Laveran discovers *Plasmodium*, the cause of malaria	
1881	Koch cultures bacteria on gelatin	Ives produces first color photograph (1881)
	Pasteur develops anthrax vaccine	
1882	Koch discovers tubercle bacillus, *Mycobacterium tuberculosis*	First central electric power station constructed by Edison (1882)
1884	Koch's postulates first published	Mark Twain's *The Adventures of Huckleberry Finn* (1884)
	Metchnikoff describes phagocytosis	
	Autoclave developed	
	Gram stain developed	
1885	Pasteur develops rabies vaccine	First motor vehicles developed by Daimler (1885–1886)
	Escherich discovers *Escherichia coli*, a cause of diarrhea	
1886	Fraenkel discovers *Streptococcus pneumoniae*, a cause of pneumonia	
1887	Petri dish (plate) developed by Richard Petri	
1887–1890	Winogradsky studies sulfur and nitrifying bacteria	Hertz discovers radio waves (1888)
1889	Beijerinck isolates root nodule bacteria	Eastman makes box camera (1888)
1890	Von Behring prepares antitoxins for diphtheria and tetanus	
1892	Ivanowsky provides evidence for virus causation of tobacco mosaic disease	First zipper patented (1895)
1894	Kitasato and Yersin discover *Yersinia pestis*, the cause of plague	
1895	Bordet discovers complement	Röntgen discovers X rays (1895)
1896	Van Ermengem discovers *Clostridium botulinum*, the cause of botulism	
1897	Buchner prepares extract of yeast that ferments	Thomson discovers the electron (1897)
	Ross shows that malaria parasite is carried by the mosquito	Spanish-American War (1898)
1899	Beijerinck proves that a virus particle causes the tobacco mosaic disease	
1900	Reed proves that yellow fever is transmitted by the mosquito	Planck develops the quantum theory (1900)
1902	Landsteiner discovers blood groups	First electric typewriter (1901)

continued...

Table 1.1 Some Important Events in the Development of Microbiology

Date	Microbiological History	Other Historical Events
1903	Wright and others discover antibodies in the blood of immunized animals	First powered aircraft (1903)
1905	Schaudinn and Hoffmann show *Treponema pallidum* causes syphilis	Einstein's special theory of relativity (1905)
1906	Wassermann develops complement fixation test for syphilis	
1909	Ricketts shows that Rocky Mountain spotted fever is transmitted by ticks and caused by a microbe (*Rickettsia rickettsii*)	First model T Ford (1908) Peary and Hensen reach North Pole (1909)
1910	Ehrlich develops chemotherapeutic agent for syphilis	Rutherford presents his theory of the atom (1911)
1911	Rous discovers a virus that causes cancer in chickens	Picasso and cubism (1912) World War I begins (1914)
1915–1917	D'Herelle and Twort discover bacterial viruses	Einstein's general theory of relativity (1916) Russian Revolution (1917)
1921	Fleming discovers lysozyme	
1923	First edition of *Bergey's Manual*	Lindberg's transatlantic flight (1927)
1928	Griffith discovers bacterial transformation	
1929	Fleming discovers penicillin	Stock market crash (1929)
1931	Van Niel shows that photosynthetic bacteria use reduced compounds as electron donors without producing oxygen	
1933	Ruska develops first transmission electron microscope	Hitler becomes chancellor of Germany (1933)
1935	Stanley crystallizes the tobacco mosaic virus Domagk discovers sulfa drugs	
1937	Chatton divides living organisms into procaryotes and eucaryotes	Krebs discovers the citric acid cycle (1937) World War II begins (1939)
1941	Beadle and Tatum, one-gene-one-enzyme hypothesis	
1944	Avery shows that DNA carries information during transformation Waksman discovers streptomycin	The insecticide DDT introduced (1944) Atomic bombs dropped on Hiroshima and Nagasaki (1945)
1946	Lederberg and Tatum describe bacterial conjugation	United Nations formed (1945) First electronic computer (1946)
1949	Enders, Weller, and Robbins grow poliovirus in human tissue cultures	

continued...

Table 1.1 Some Important Events in the Development of Microbiology

Date	Microbiological History	Other Historical Events
1950	Lwoff induces lysogenic bacteriophages	Korean War begins (1950)
1952	Hershey and Chase show that bacteriophages inject DNA into host cells	First hydrogen bomb exploded (1952) Stalin dies (1952)
	Zinder and Lederberg discover generalized transduction	First commercial transistorized product (1952)
1953	Phase-contrast microscope developed	U.S. Supreme Court rules against segregated schools (1954)
	Medawar discovers immune tolerance	
	Watson and Crick propose the double helix structure for DNA	
1955	Jacob and Wollman discover the F factor is a plasmid	Montgomery bus boycott (1955)
	Jerne and Burnet propose the clonal selection theory	Sputnik launched by Soviet Union (1957)
1959	Yalow develops the radioimmunoassay technique	Birth control pill (1960)
1961	Jacob and Monod propose the operon model of gene regulation	First humans in space (1961)
1961–1966	Nirenberg, Khorana, and others elucidate the genetic code	Cuban missile crisis (1962) Nuclear test ban treaty (1963)
1962	Porter proposes the basic structure for immunoglobulin G	Civil Rights March on Washington (1963)
	First quinolone antimicrobial (nalidixic acid) synthesized	President Kennedy assassinated (1963) Arab-Israeli War (1967) Martin Luther King assassination (1968) Neil Armstrong walks on the moon (1969)
1970	Discovery of restriction endonucleases by Arber and Smith	
	Discovery of reverse transcriptase in retroviruses by Temin and Baltimore	
1973	Ames develops a bacterial assay for the detection of mutagens	Salt I Treaty (1972)
	Cohen, Boyer, Chang, and Helling use plasmid vectors to clone genes in bacteria	Vietnam War ends (1973)
1975	Kohler and Milstein develop technique for the production of monoclonal antibodies	President Nixon resigns because of Watergate cover-up (1974)
	Lyme disease discovered	
1977	Recognition of archaea as a distinct microbial group by Woese and Fox	Panama Canal Treaty (1977)

continued...

Table 1.1 Some Important Events in the Development of Microbiology

Date	Microbiological History	Other Historical Events
	Gilbert and Sanger develop techniques for DNA sequencing	
1979	Insulin synthesized using recombinant DNA techniques	Hostages seized in Iran (1978)
	Smallpox declared officially eliminated	Three Mile Island disaster (1979)
1980	Development of the scanning tunneling microscope	Home computers marketed (1980)
1982	Recombinant hepatitis B vaccine developed	AIDS first recognized (1981)
1982–1983	Discovery of catalytic RNA by Cech and Altman	First artificial heart implanted (1982)
1983–1984	The human immunodeficiency virus isolated and identified by Gallo and Montagnier	Meter redefined in terms of distance light travels (1983)
	The polymerase chain reaction developed by Mullis	
1986	First vaccine (hepatitis B vaccine) produced by genetic engineering approved for human use	Gorbachev becomes Communist party general secretary (1985) Berlin Wall falls (1989)
1990	First human gene-therapy testing begun	Persian Gulf War with Iraq begins (1990)
		Soviet Union collapse; Boris Yeltsin comes to power (1991)
1992	First human trials of antisense therapy	
1995	Chickenpox vaccine approved for U.S. use	
	Haemophilus influenzae genome sequenced	
1996	*Methanococcus jannaschii* genome sequenced	Water found on the moon (1998)
	Yeast genome sequenced	
1997	Discovery of *Thiomargarita namibiensis*, the largest known bacterium	
	Escherichia coli genome sequenced	
2000	Discovery that *Vibrio cholerae* has two separate chromosomes	