Introduction & History of Microbiology

Professor Md. Akram Hosssain
MMC
Dec 2013
LESSION PLAN

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

Introduction and History of Microbiology

Prof. Md. Akram Hossain,
Mymensingh Medical College
Introduction and History of Microbiology

Prof. Md. Akram Hossain
Mymensingh Medical College
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
Branches of Medical Microbiology

- Bacteriology
- Parasitology
- Mycology
- Virology
- Immunology
- Clinical Microbiology / Infectious Diseases
Introduction and History of Microbiology

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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
- Smallpox in the 17th and 18th century
- Tuberculosis, measles and scarlet fever in the 19th Century
- AIDS in the 20th 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%
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 occur

HBV

- 10 Lakhs people die every year in the world.
- 400 -500 million carriers
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.
<table>
<thead>
<tr>
<th>Disease</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHD</td>
<td>7.2 million</td>
</tr>
<tr>
<td>Cancer</td>
<td>6.3 million</td>
</tr>
<tr>
<td>CVD</td>
<td>4.6 million</td>
</tr>
<tr>
<td>LRTI</td>
<td>3.9 million</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>3.0 million</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2.5 million</td>
</tr>
<tr>
<td>Malaria</td>
<td>2.1 million</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>1.5 million</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>1.2 million</td>
</tr>
</tbody>
</table>
### WHO Report 2002

<table>
<thead>
<tr>
<th>Disease</th>
<th>Death</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>55 million</td>
</tr>
<tr>
<td>Communicable</td>
<td>17.3 million</td>
</tr>
<tr>
<td>Infectious</td>
<td>9.9 million</td>
</tr>
<tr>
<td>CVD</td>
<td>16 million</td>
</tr>
<tr>
<td>Cancers</td>
<td>07 million</td>
</tr>
<tr>
<td>LRTI</td>
<td>3.9 million</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>1.6 million</td>
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<tr>
<td>HIV /AIDS</td>
<td>2.6 million</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>1.2 million</td>
</tr>
<tr>
<td>Measles</td>
<td>0.8 million</td>
</tr>
</tbody>
</table>
**WHO report 1998**

<table>
<thead>
<tr>
<th>Disease Type</th>
<th>Deaths 1997</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total death in 1997</td>
<td>522 million</td>
</tr>
<tr>
<td>Infectious and parasitic disease</td>
<td>173 million</td>
</tr>
<tr>
<td>Coronary vascular diseases</td>
<td>153 million</td>
</tr>
<tr>
<td>Cancers</td>
<td>6.2 million</td>
</tr>
</tbody>
</table>

**Major Infectious Diseases**

<table>
<thead>
<tr>
<th>Disease Type</th>
<th>Deaths 1997</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARI</td>
<td>3.7 million</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>2.9 million</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2.5 million</td>
</tr>
<tr>
<td>HIV /AIDS</td>
<td>2.3 million</td>
</tr>
<tr>
<td>Malaria</td>
<td>2.00 million</td>
</tr>
</tbody>
</table>
Major Microbial diseases in the world

19th Century - in Europe
- Small pox
- Cholera
- Diphtheria
- Leprosy
- Tuberculosis
- Typhoid

20th Century - in Asia, Africa Central & South America
- Diarrhea
- Tuberculosis
- Respiratory infections
- HIV
- Measles
- Malaria
- Filaria
- amoebiasis
- Intestinal helminthiasis

4% of USA people are infected with Giardia
## Disease Prevalence

<table>
<thead>
<tr>
<th>Disease</th>
<th>Prevalence (Lakhs)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Helmintheasis</td>
<td>60.0</td>
<td>11.9</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>59.7</td>
<td>11.8</td>
</tr>
<tr>
<td>Anaemia</td>
<td>48.1</td>
<td>10.0</td>
</tr>
<tr>
<td>Skin disease</td>
<td>45.1</td>
<td>9.0</td>
</tr>
<tr>
<td>PUD</td>
<td>27.1</td>
<td>5.4</td>
</tr>
<tr>
<td>ARI</td>
<td>26.5</td>
<td>5.2</td>
</tr>
<tr>
<td>Malaria</td>
<td>4.3</td>
<td>0.9</td>
</tr>
</tbody>
</table>

**Introduction and History of Microbiology**

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Mymensingh Medical College

17
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
Introduction and History of Microbiology

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Mymensingh Medical College
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.

Prof. Md. Akram Hossain,
Mymensingh Medical College
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

- Lens
- Specimen holder
- Focus screw
- Handle

(a) [Image of microscope parts]
(b) [Image of person using microscope]
17th – 18th Century

- **Spontaneous generation** - living organisms can develop from nonliving or decomposing matter

- **1688** - **Francisco 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).
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
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
19th 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.
19th 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 (Salvarsan) 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
• 1890: Behring and Kitasato prepare antitoxins for diphtheria 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
Louis Pasteur (1822 – 1895)
French, is the Founder of Modern Microbiology

Important contributions
- Disproves spontaneous generation theory
- showed that yeasts converted sugar to ethanol and CO2 (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
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
• 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
Robert Koch (1843 –1910), German

1876 - 1892

Father of Medical Microbiology

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

Koch’s phenomenon

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Koch’s phenomenon

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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
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Joseph Lister (1827 – 1912) Scottish Surgeon

Discovered aseptic surgery by using carbolic acid.
Paul Ehrlich discovered synthetic arsenic compound (Salvarsan) effective against syphilis also called “magic bullet” in 1880.
discovered phagocytic phenomenon in 1883.

Elie Metchnikoff (1845 – 1916)
1890.

Discovered Humoral immunity by Antibody in 1890.

Emil Adolf von Behring (1854-1917)

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20th century discoveries
20th century - 1

- 1900: **Walter Reed** shows that mosquitos are the vector for yellow fever
- 1905: **Schaudinn and Hoffman** show that *Treponema pallidum* causes syphilis
- 1908: **Paul Ehrich** develops first chemotherapeutic 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.
- 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)

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• 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.
• 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.

Max Theiler (1899 – 1972) was American virologist. He was awarded the Nobel Prize in 1951 for vaccine against yellow fever.
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.

Baron Florey OM FRS (1898 – 21 1968)
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 Helicobacter
- 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.
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 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.
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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.
Introduction and History of Microbiology

Prof. Md. Akram Hossain,
Mymensingh Medical College
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.
• 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.
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.
• 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 *Helicobacter*

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)
Sir Alexander Fleming of Scotland discovered penicillin in 1929.
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.
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 in 1963

Dr. Kazi Abul Mansur, Bangladesh
1979

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

The Only Microbial Disease Ever Completely Defeated
Introduction and History of Microbiology

Prof. Md. Akram Hossain,
Mymensingh Medical College
Success and scopes of Microbiology

• Diagnosis
  • Infectious
  • Autoimmune
  • Other diseases

• Treatment
  • Infectious,
  • Autoimmune
  • Some cancers

• Eradication of disease

• Prevention of disease

• Organ transplantation

• Medical legal applications

• Food and Pharmaceutical Industry

• Agriculture

• Molecular biology

• Genetic engineering

• Biotechnology
### Table 1.1 Some Important Events in the Development of Microbiology

<table>
<thead>
<tr>
<th>Date</th>
<th>Microbiological History</th>
<th>Other Historical Events</th>
</tr>
</thead>
<tbody>
<tr>
<td>1546</td>
<td>Fracastoro suggests that invisible organisms cause disease</td>
<td>Publication of Copernicus’s work on the heliocentric solar system (1543)</td>
</tr>
<tr>
<td>1590–1608</td>
<td>Jansen develops first useful compound microscope</td>
<td>Shakespeare’s <em>Hamlet</em> (1600–1601)</td>
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<tr>
<td>1676</td>
<td>Leeuwenhoek discovers “animalcules”</td>
<td>J. S. Bach and Handel born (1685)</td>
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<tr>
<td>1688</td>
<td>Redi publishes work on spontaneous generation of maggots</td>
<td>Isaac Newton publishes the <em>Principia</em> (1687)</td>
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<tr>
<td>1765–1776</td>
<td>Spallanzani attacks spontaneous generation</td>
<td>Linnaeus’s <em>Systema Naturae</em> (1735)</td>
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<tr>
<td>1786</td>
<td>Müller produces first classification of bacteria</td>
<td>Mozart born (1756)</td>
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<tr>
<td>1798</td>
<td>Jenner introduces cowpox vaccination for smallpox</td>
<td>French Revolution (1789)</td>
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<tr>
<td>1838–1839</td>
<td>Schwann and Schleiden, the Cell Theory</td>
<td>Beethoven’s first symphony (1800)</td>
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<tr>
<td>1835–1844</td>
<td>Bassi discovers that silkworm disease is caused by a fungus and proposes that many diseases are microbial in origin</td>
<td>The battle of Waterloo and the defeat of Napoleon (1815)</td>
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<td>1847–1850</td>
<td>Semmelweis shows that childbed fever is transmitted by physicians and introduces the use of antiseptics to prevent the disease</td>
<td>Faraday demonstrates the principle of an electric motor (1821)</td>
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<td>1849</td>
<td>Snow studies the epidemiology of a cholera epidemic in London</td>
<td>England issues first postage stamp (1840)</td>
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<td>1857</td>
<td>Pasteur shows that lactic acid fermentation is due to a microorganism</td>
<td>Marx’s <em>Communist Manifesto</em> (1848)</td>
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<td>1858</td>
<td>Virchow states that all cells come from cells</td>
<td>Velocity of light first measured by Fizeau (1849)</td>
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<td>1861</td>
<td>Pasteur shows that microorganisms do not arise by spontaneous generation</td>
<td>Clausius states the first and second laws of thermodynamics (1850)</td>
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<td>1867</td>
<td>Lister publishes his work on antiseptic surgery</td>
<td>Graham distinguishes between colloids and crystalloids</td>
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<td>1869</td>
<td>Miescher discovers nucleic acids</td>
<td>Melville’s <em>Moby Dick</em> (1851)</td>
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<td>Otis installs first safe elevator (1854)</td>
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<td>Bunsen introduces the use of the gas burner (1855)</td>
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<td>Darwin’s <em>On the Origin of Species</em> (1859)</td>
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<td>American Civil War (1861–1865)</td>
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<td></td>
<td>Mendel publishes his genetics experiments (1865)</td>
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<td>Cross-Atlantic cable laid (1865)</td>
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<td></td>
<td>Dostoevski’s <em>Crime and Punishment</em> (1866)</td>
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<td></td>
<td>Franco-German War (1870–1871)</td>
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<thead>
<tr>
<th>Date</th>
<th>Microbiological History</th>
<th>Other Historical Events</th>
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<tr>
<td>1876–1877</td>
<td>Koch demonstrates that anthrax is caused by <em>Bacillus anthracis</em></td>
<td>Bell invents telephone (1876)</td>
</tr>
<tr>
<td>1880</td>
<td>Laveran discovers <em>Plasmodium</em>, the cause of malaria</td>
<td>Edison’s first light bulb (1879)</td>
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<tr>
<td>1881</td>
<td>Koch cultures bacteria on gelatin</td>
<td>Ives produces first color photograph (1881)</td>
</tr>
<tr>
<td>1882</td>
<td>Pasteur develops anthrax vaccine</td>
<td>First central electric power station constructed by Edison</td>
</tr>
<tr>
<td>1884</td>
<td>Koch discovers tubercle bacillus, <em>Mycobacterium tuberculosis</em></td>
<td>Mark Twain’s <em>The Adventures of Huckleberry Finn</em> (1884)</td>
</tr>
<tr>
<td>1885</td>
<td>Koch’s postulates first published</td>
<td>First motor vehicles developed by Daimler (1885–1886)</td>
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<tr>
<td>1886</td>
<td>Metchnikoff describes phagocytosis</td>
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<tr>
<td>1887</td>
<td>Autoclave developed</td>
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<tr>
<td>1889</td>
<td>Gram stain developed</td>
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<tr>
<td>1887–1890</td>
<td>Pasteur develops rabies vaccine</td>
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<tr>
<td>1889</td>
<td>Escherich discovers <em>Escherichia coli</em>, a cause of diarrhea</td>
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<tr>
<td>1886</td>
<td>Fraenkel discovers <em>Streptococcus pneumoniae</em>, a cause of pneumonia</td>
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<tr>
<td>1887</td>
<td>Petri dish (plate) developed by Richard Petri</td>
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<tr>
<td>1887–1890</td>
<td>Winogradsky studies sulfur and nitrifying bacteria</td>
<td>Hertz discovers radio waves (1888)</td>
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<tr>
<td>1889</td>
<td>Beijerinck isolates root nodule bacteria</td>
<td>Eastman makes box camera (1888)</td>
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<tr>
<td>1890</td>
<td>Von Behring prepares antitoxins for diphtheria and tetanus</td>
<td>First zipper patented (1895)</td>
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<tr>
<td>1892</td>
<td>Ivanowsky provides evidence for virus causation of tobacco mosaic disease</td>
<td>Röntgen discovers X rays (1895)</td>
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<tr>
<td>1894</td>
<td>Kitasato and Yersin discover <em>Yersinia pestis</em>, the cause of plague</td>
<td>Thomson discovers the electron (1897)</td>
</tr>
<tr>
<td>1895</td>
<td>Bordet discovers complement</td>
<td>Spanish-American War (1898)</td>
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<tr>
<td>1896</td>
<td>Van Ermengem discovers <em>Clostridium botulinum</em>, the cause of botulism</td>
<td>Planck develops the quantum theory (1900)</td>
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<tr>
<td>1897</td>
<td>Buchner prepares extract of yeast that ferments</td>
<td>First electric typewriter (1901)</td>
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<tr>
<td>1899</td>
<td>Ross shows that malaria parasite is carried by the mosquito</td>
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<tr>
<td>1900</td>
<td>Beijerinck proves that a virus particle causes the tobacco mosaic disease</td>
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<tr>
<td>1902</td>
<td>Reed proves that yellow fever is transmitted by the mosquito</td>
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<tr>
<td>1902</td>
<td>Landsteiner discovers blood groups</td>
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<tr>
<td>1903</td>
<td>Wright and others discover antibodies in the blood of immunized animals</td>
<td>First powered aircraft (1903)</td>
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<tr>
<td>1905</td>
<td>Schaudinn and Hoffmann show <em>Treponema pallidum</em> causes syphilis</td>
<td>Einstein’s special theory of relativity (1905)</td>
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<tr>
<td>1906</td>
<td>Wassermann develops complement fixation test for syphilis</td>
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<tr>
<td>1909</td>
<td>Ricketts shows that Rocky Mountain spotted fever is transmitted by ticks and caused by a microbe (<em>Rickettsia rickettsii</em>)</td>
<td>First model T Ford (1908)</td>
</tr>
<tr>
<td>1910</td>
<td>Ehrlich develops chemotherapeutic agent for syphilis</td>
<td>Peary and Hensen reach North Pole (1909)</td>
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<tr>
<td>1911</td>
<td>Rous discovers a virus that causes cancer in chickens</td>
<td>Rutherford presents his theory of the atom (1911)</td>
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<tr>
<td>1915–1917</td>
<td>D’Herelle and Twort discover bacterial viruses</td>
<td>Picasso and cubism (1912)</td>
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<tr>
<td>1921</td>
<td>Fleming discovers lysozyme</td>
<td>Lindberg’s transatlantic flight (1927)</td>
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<tr>
<td>1923</td>
<td>First edition of <em>Bergey’s Manual</em></td>
<td>Stock market crash (1929)</td>
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<tr>
<td>1928</td>
<td>Griffith discovers bacterial transformation</td>
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<tr>
<td>1929</td>
<td>Fleming discovers penicillin</td>
<td>Hitler becomes chancellor of Germany (1933)</td>
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<tr>
<td>1931</td>
<td>Van Niel shows that photosynthetic bacteria use reduced compounds as electron donors without producing oxygen</td>
<td>Krebs discovers the citric acid cycle (1937)</td>
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<tr>
<td>1933</td>
<td>Ruska develops first transmission electron microscope</td>
<td>World War II begins (1939)</td>
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<tr>
<td>1935</td>
<td>Stanley crystallizes the tobacco mosaic virus</td>
<td>The insecticide DDT introduced (1944)</td>
</tr>
<tr>
<td>1937</td>
<td>Domagk discovers sulfa drugs</td>
<td>Atomic bombs dropped on Hiroshima and Nagasaki (1945)</td>
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<tr>
<td>1941</td>
<td>Chatton divides living organisms into procaryotes and eucaryotes</td>
<td>United Nations formed (1945)</td>
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<td>1944</td>
<td>Avery shows that DNA carries information during transformation</td>
<td>First electronic computer (1946)</td>
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<td>1946</td>
<td>Waksman discovers streptomycin</td>
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<td>1949</td>
<td>Lederberg and Tatum describe bacterial conjugation</td>
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<td></td>
<td>Enders, Weller, and Robbins grow poliovirus in human tissue cultures</td>
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<tr>
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<tr>
<td>1950</td>
<td>Lwoff induces lysogenic bacteriophages</td>
<td>Korean War begins (1950)</td>
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<tr>
<td>1952</td>
<td>Hershey and Chase show that bacteriophages inject DNA into host cells</td>
<td>First hydrogen bomb exploded (1952)</td>
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<td>Zinder and Lederberg discover generalized transduction</td>
<td>Stalin dies (1952)</td>
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<td>1953</td>
<td>Phase-contrast microscope developed</td>
<td>First commercial transistorized product (1952)</td>
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<td>Medawar discovers immune tolerance</td>
<td>U.S. Supreme Court rules against segregated schools (1954)</td>
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<tr>
<td>1955</td>
<td>Jacob and Wollman discover the F factor is a plasmid</td>
<td>Montgomery bus boycott (1955)</td>
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<tr>
<td>1959</td>
<td>Yalow develops the radioimmunoassay technique</td>
<td>Sputnik launched by Soviet Union (1957)</td>
</tr>
<tr>
<td>1961</td>
<td>Jacob and Monod propose the operon model of gene regulation</td>
<td>Birth control pill (1960)</td>
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<tr>
<td>1961–1966</td>
<td>Nirenberg, Khorana, and others elucidate the genetic code</td>
<td>First humans in space (1961)</td>
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<tr>
<td>1961</td>
<td>Porter proposes the basic structure for immunoglobulin G</td>
<td>Cuban missile crisis (1962)</td>
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<tr>
<td>1962</td>
<td>First quinolone antimicrobial (nalidixic acid) synthesized</td>
<td>Nuclear test ban treaty (1963)</td>
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<td>Civil Rights March on Washington (1963)</td>
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<tr>
<td>1970</td>
<td>Discovery of restriction endonucleases by Arber and Smith</td>
<td>President Kennedy assassinated (1963)</td>
</tr>
<tr>
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<td>Discovery of reverse transcriptase in retroviruses by Temin and Baltimore</td>
<td>Arab-Israeli War (1967)</td>
</tr>
<tr>
<td>1973</td>
<td>Ames develops a bacterial assay for the detection of mutagens</td>
<td>Martin Luther King assassination (1968)</td>
</tr>
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<td></td>
<td>Cohen, Boyer, Chang, and Helling use plasmid vectors to clone genes in bacteria</td>
<td>Neil Armstrong walks on the moon (1969)</td>
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<tr>
<td>1975</td>
<td>Kohler and Milstein develop technique for the production of monoclonal antibodies</td>
<td>Salt I Treaty (1972)</td>
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<tr>
<td></td>
<td>Lyme disease discovered</td>
<td>Vietnam War ends (1973)</td>
</tr>
<tr>
<td>1977</td>
<td>Recognition of archaea as a distinct microbial group by Woese and Fox</td>
<td>President Nixon resigns because of Watergate cover-up (1974)</td>
</tr>
</tbody>
</table>

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