History and importance of medical microbiology

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Medical Microbiology

- Medical microbiology is a subset of microbiology that deals with microorganisms (including viruses, bacteria, fungi, and parasites) colonizing or infecting humans.
- Through examination of their phenotypic features (e.g., shape, structure, reproduction, physiology, and metabolism, etc.), medical microbiology aims to identify microorganisms of interest, diagnose associated infectious diseases, determine their pathogenic mechanisms, treat and prevent their recurrence.
- **Antony van Leeuwenhoek** was regarded as "**father of microbiology**" for being the first person to observe microorganisms with a self-made light microscope in 1676.
- Although Fracastoro and a few others had suggested that invisible organisms produced disease, most believed that disease was due to causes such as supernatural forces, poisonous vapors called miasmas, and imbalances between the four humors thought to be present in the body.
- The idea that an imbalance between the four humors (blood, phlegm, yellow bile [choler], and black bile [melancholy]) led to disease had been widely accepted since the time of the Greek physician Galen (129–199).
- Robert Koch was credited for establishing the discipline of medical microbiology in 1876–84, with the formulation of germ theory, isolation of bacteria in pure culture, and development of Koch's postulates.
- Nonetheless, contributions by others have significantly enhanced the capability and extended the utility of medical microbiology.

Recognition of the Relationship between Microorganisms and Disease

- Support for the germ theory of disease began to accumulate in the early nineteenth century.
- Agostino Bassi (1773–1856) first showed a microorganism could cause disease when he demonstrated in 1835 that a silkworm disease was due to a fungal infection.
- He also suggested that many diseases were due to microbial infections.
- In 1845 **M. J. Berkeley** proved that the great Potato Blight of Ireland was caused by a fungus.
- Following his successes with the study of fermentation, **Pasteur** was asked by the French government to investigate the pébrine disease of silkworms that was disrupting the silk industry.
- After several years of work, he showed that the disease was due to a protozoan parasite.
- The disease was controlled by raising caterpillars from eggs produced by healthy moths.

Scientific Developments

Contributions of Louis Pasteur

- "Father of modern microbiology", "Father of medical microbiology",

1. Coined the term microbiology
2. Proposed germ theory of disease
3. Disapproved theory of spontaneous generation
4. Developed sterilization techniques
5. Developed methods and techniques for cultivation of microorganisms
6. Studies on pebrine (silk worm disease), anthrax, chicken cholera and hydrophobia
7. Pasteurization
8. Coined the term vaccine
9. Discovery of attenuation and chicken cholera vaccine
10. Developed live attenuated anthrax vaccine
11. Developed rabies vaccine
12. Noticed Pneumococci

...Recognition of the Relationship between Microorganisms and Disease

- **Joseph Lister (Father of modern Surgery):** Indirect evidence that microorganisms were agents of human disease came from the work of the English surgeon **Joseph Lister** (1827–1912) on the prevention of wound infections.
- Lister impressed with Pasteur's studies on the involvement of microorganisms in fermentation and putrefaction, developed a system of antiseptic surgery designed to prevent microorganisms from entering wounds.
- Instruments were heat sterilized, and phenol was used on surgical dressings and at times sprayed over the surgical area.
- It also provided strong indirect evidence for the role of microorganisms in disease because phenol, which killed bacteria, also prevented wound infections.
- **Robert Koch :** The first direct demonstration of the role of bacteria in causing disease came from the study of anthrax by the German physician **Robert Koch** (1843–1910).
- Winner of noble price in 1905.

German physician Robert Koch

- Koch used the criteria proposed by his former teacher, Jacob Henle (1809–1885), to establish the relationship between *Bacillus anthracis* and anthrax, and published his findings in 1876.
- Koch injected healthy mice with material from diseased animals, and the mice became ill.
- After transferring anthrax by inoculation through a series of 20 mice, he incubated a piece of spleen containing the anthrax bacillus in beef serum.
- The bacilli grew, reproduced, and produced spores.
- When the isolated bacilli or spores were injected into mice, anthrax developed.
- His criteria for proving the causal relationship between a microorganism and a specific disease are known as **Koch's postulates.**

Koch's postulates

- The microorganism must be present in every case of the disease but absent from healthy organisms.
- The suspected microorganism must be isolated and grown in a pure culture.
- The same disease must result when the isolated microorganism is inoculated into a healthy host.
- The same microorganism must be isolated again from the diseased host.

- Koch's proof that *Bacillus anthracis* caused anthrax was independently confirmed by Pasteur and his coworkers.
- They discovered that after burial of dead animals, anthrax spores survived and were brought to the surface by earthworms.
- Healthy animals then ingested the spores and became ill.

...Robert Koch

Staining techniques: He described methods for the easy microscopic examination of bacteria in dried, fixed films stained with aniline dyes (1877).

Hanging drop method: He was the first to use hanging drop method by studying bacterial motility.

Methods for isolating pure cultures of bacteria: He devised a simple method for isolating pure cultures of bacteria by plating out mixed material on a solid culture medium and to isolate pure cultures of pathogens.

GOLDEN ERA OF MEDICAL BACTERIOLOGY

- Koch's postulates permitted Koch and his students to identify many of the causes of the most infectious diseases of humans and animals. Koch had now assembled the techniques needed to investigate the bacterial causes of many communicable diseases.
- The powerful methodology developed by Koch introduced the "Golden era of medical bacteriology".
- By 1882 Koch had used these techniques to isolate bacillus of tuberculosis.

PAUL EHRLICH (1854-1915)

- "Father of chemotherapy"

1. Stains to cells and tissues: He applied stains to cells and tissues for the purpose of revealing their function.
2. Acid-fastness of tubercle bacillus: He reported the acid-fastness of tubercle bacillus.
3. Methods of standardizing toxin and antitoxin: He introduced methods of standardizing toxin and antitoxin and coined the term minimum lethal dose.
4. Side chain theory of antibody production: He proposed side chain theory of antibody production.
5. Salvarsan introduction: He introduced salvarsan, an arsenical compound, sometimes called the 'magic bullet'. It was capable of destroying the spirochete of syphilis with only moderate toxic effects. He continued his experimentation until 1912 when he announced the discovery of neosalvarsan. Thus he created a new branch of medicine known as chemotherapy.

Fleming discovered penicillin and Waksman streptomycin. Subsequently, several fungi have

The discovery of viruses and their role in disease was made possible when Charles Chamberland (1851–1908), one of Pasteur's associates, constructed a porcelain bacterial filter in 1884.

DISCOVERY OF VIRUSES

- By the end of 19th century many infectious diseases had been proven to have a bacterial aetiology. The trend continued in 20th century. But yet there remained many diseases of common occurrence for which no bacterium could be demonstrated. These included smallpox, chickenpox, measles and common cold. Advent of electron microscopy in 1934 by Ruska made morphological examination of viruses possible. The first human disease proven to have a virus aetiology was yellow fever.
- Iwanowski (1892), and Martinus Beijrinck (1898) in Holland, attributed the cause of tobacco- mosaic disease to the infectious agents in bacteria-free filtrates to be living, but fluid—contagium vivum fluidum and introduced the term virus (Latin for 'poison') for such filterable infectious agents.
- In 1930s viruses could be grown in bacteria free, living chick embryo—a technique perfected by Goodpasteur.
- By 1940, growth in tissue culture of susceptible mammalian cells was established. The availability of well defined cell lines have now replaced tedious methods of growing viruses in the living animals.
- The discovery of viral and cellular oncogenes have put forth the possible mechanisms of viral oncogenesis. Positive proof a virus causing of human malignancy was established when the virus of human T-cell leukemia was isolated in 1980.

Immunological Studies

- In this period progress also was made in determining how animals resisted disease and in developing techniques for protecting humans and livestock against pathogens.
- During studies on chicken cholera, Pasteur and Roux discovered that incubating their cultures for long intervals between transfers would attenuate the bacteria, which meant they had lost their ability to cause the disease.
- If the chickens were injected with these attenuated cultures, they remained healthy but developed the ability to resist the disease.
- He called the attenuated culture a vaccine [Latin *vacca, cow] in honor of Edward Jenner because, many years earlier,* Jenner had used vaccination with material from cowpox lesions to protect people against smallpox .
- Shortly after this, Pasteur and Chamberland developed an attenuated anthrax vaccine in two ways: by treating cultures with potassium bichromate and by incubating the bacteria at 42 to 43°C.

- References:

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Prescott's Microbiology