

Introduction

Medical microbiology is the study of organisms that cause human infections, diseases they produce, their diagnosis, their prevention by vaccines, chemoprophylaxis and treatment.

History

Antony van Leeuwenhoek who had the habit of grinding lenses, first observed bacteria under microscope.

Major development in the field was brought by Louis Pasteur.

LOUIS PASTEUR (Fig. 1.1)

He was a French chemist. His discovery of fermentation built up his interest in further research into microbiology.

He is known as the **father of modern microbiology**. His important contributions are as follows:

- He coined the term 'microbiology'.
- He identified silkworm disease. He established that fermentation was the result of microbial activity. He also showed that different types of fermentation are associated with different organisms.



Fig. 1.1: Louis Pasteur

- He developed the techniques of bacteriology.
- He introduced the techniques of sterilization, e.g. steam sterilizer, autoclave, hot air oven, flaming, and pasteurization.
- He also proved that microbes arose from their like and not *de novo*. He along with Robert Koch showed that living organisms were the cause of disease.
- He established the importance of cotton plugs for protection of culture media from aerial contamination.
- He suggested method of pasteurization of milk.
- He introduced concept of liquid media and used nutrient broth for culture of bacteria.
- He introduced the use of complex media.
- He accidentally observed that culture of *Chicken cholera* bacillus left on the bench for several weeks lost its pathogenic property but retained its ability to protect the birds against subsequent infection. This led to the process of attenuation and development of live vaccines (1880).
- He prepared anthrax vaccine by attenuating anthrax bacilli at high temperature (42–43°C) in 1881. In 1881, he took part in a public trial of his vaccine against anthrax in domestic animals. He coined the term 'vaccine' for such prophylactic preparations. He also proved that inoculation of vaccine in animals induces specific protection against anthrax.
- He developed a vaccine for rabies in 1881. He obtained fixed virus of rabies by serial intracerebral passage in rabbits. The vaccine was prepared by dried pieces of spinal cord from rabies infected with fixed virus. This was proven effective in humans when he inoculated Joseph Mister, 9-year-old boy who had been bitten badly with dog having rabies.

JOSEPH LISTER

- Joseph Lister is known as the **father of antiseptic surgery**.

- He realized that microorganisms prevalent in the atmosphere might be responsible for postoperative wound infections.
- He was interested in the prevention of postoperative sepsis.
- He introduced **antiseptic techniques** in surgery using carbolic acid as a spray during operation or on the wound in postoperative stage. It was a revolution and an important milestone in surgical practice.

ROBERT KOCH (Fig. 1.2)

- Robert Koch is known as the **father of bacteriology**.
- He invented hot air oven and steam sterilizer.
- He introduced solid media for bacterial culture. Method of isolation of bacteria in pure culture is also introduced by him.
- While in general practice in Berlin, he isolated anthrax bacillus and showed a specific organism as a cause of disease.
- He was the founder of germ theory of disease. He brought clarity in medicine—until then diseases were attributed to miasmas or mists, to punishments from Gods or devils or to unfortunate conjunctions of stars and planets.
- He became first to grow bacteria in colonies, initially on potato slices and later on, with his pupil Petri, on gelatin media.
- He perfected bacteriological techniques.
- He introduced methods for isolation of bacteria in pure cultures using solid media.



Fig. 1.2: Robert Koch

- Method of study of motility by hanging drop method is invented by him.
- He was the first to isolate anthrax bacilli in pure culture and to show spores in anthrax bacilli.
- He introduced staining techniques.
- He discovered tubercle bacilli and *Vibrio cholerae*.
- He was the first person to see motility of bacteria by hanging drop method.
- He discovered old tuberculin.

Koch's Postulates and Molecular Koch's Postulates

Robert Koch postulated the criteria for proving that a microorganism isolated from a disease was indeed caused due to it.

According to these postulates, a microorganism can be accepted as the causative agent of the disease only if the following conditions are satisfied.

- The microorganism should be constantly associated with the lesions of the disease.
- It should be possible to isolate the organism in pure culture from the lesions of the disease.
- Inoculation of such pure culture in suitable laboratory animals should produce a similar disease in animals.
- It should be possible to reisolate the organism in pure culture from lesions produced in the experimental animals.
- An additional criterion introduced subsequently states that specific antibodies to that organism should be demonstrated in the serum of patients.

These postulates have proved to be useful in confirming doubtful claims made regarding the causative agents of infectious diseases.

Exceptions to Koch's Postulates

- *Treponema pallidum* and *Mycobacterium leprae* are unable to grow on artificial media.
- Viruses and *Rickettsia* are unable to grow on artificial media.

Molecular Koch's Postulates

With the evolution of genetics and identification of genes responsible for the virulence of organism, **molecular Koch's postulates** are added as follows:

- The phenotype or the property under investigation should be significantly associated with the pathogenic strains of the species and not with nonpathogenic strains of the disease.
- Specific inactivation of gene or genes associated with virulence trait should lead to measurable decrease in pathogenicity or virulence.

- Reversion or replacement of mutated gene with wild type gene should lead to restoration of pathogenicity or virulence.

Koch's Phenomenon

Robert Koch observed that guinea pig sensitized by infection with tubercle bacilli responded with an exaggerated manner following injection of TB bacilli or its protein.

PAUL EHRLICH (Fig. 1.3)

- He is known as **father of chemotherapy**. He initialized the search for chemotherapeutic agent for killing of bacteria.
- He discovered arsenic compound for treatment of syphilis.
- He reported acid-fast nature of tubercle bacilli.
- He proposed side chain theory for antibody production.
- He introduced methods of standardizing toxin and antitoxins.



Fig. 1.3: Paul Ehrlich

Important discoveries by other scientists

Lepa bacillus	Hansen 1874
Gonococcus	Neisser 1881
Diphtheria bacillus	Klebs 1883-Löffler 1884
Pneumococcus	Frankel 1886
Tetanus bacillus	Kitasato 1889
Meningococcus	Weichselbaum 1887

IMPORTANT LANDMARKS IN VIROLOGY

- Pasteur while working with rabies postulated that the causative agent is ultramicroscopic.
- Yellow fever was first human disease proved to be of viral origin and it was discovered by Walter Reid 1902.
- Landsteiner demonstrated that poliomyelitis is due to filterable virus.
- Goodpasture developed techniques of viral cultivation in chick embryo.
- Bacteriophage was discovered by Twort in 1915.

SOME IMPORTANT DISCOVERIES IN IMMUNOLOGY

- Pfeiffer and Bordet contributed in understanding of complement.
- Metchnikoff discovered phenomenon of phagocytosis while Wright discovered opsonization.
- Richet for the first time observed the phenomenon of anaphylaxis.
- Jerne proposed natural selection theory of antibody formation.
- Burnet postulated clonal selection theory.
- Burnet also developed concept of immunological surveillance.
- Medawar and Burnet made first transplant successful by using immunosuppression.

OTHER DEVELOPMENTS

- Ruska developed electron microscope.
- Alexander Fleming discovered first antibiotic penicillin.

NOBEL LAUREATES IN PHYSIOLOGY AND MEDICINE

Year	Name	Work
1901	Emil A von Behring	Serum therapy
1902	Ronald Ross	Malaria life cycle
1905	Robert Koch	Tuberculosis
1907	C LA Laveran	Role of protozoa in causing disease
1908	P Ehrlich and E Metchnikof	Immunity
1913	Charles Robert Ricket	Anaphylaxis
1919	Jules Bordet	Immunity
1926	Johannes Fibiger	<i>Spiroptera carcinoma</i>
1928	Charles Nicolle	Typhus
1930	Karl Landsteiner	Discovery of human blood groups
1939	Gerhard Domagk	Prontosil
1945	A Fleming Boris Chain and Howard Walter Florey	Penicillin
1951	Max Theiler	Yellow fever
1952	Selman A Waksman	Streptomycin
1954	Franklin Enders H Weller and F C Robbins	Poliomyelitis culture in tissue
1958	George Beadle and E LTatun and Lederberg	Gene action and genetic recombination
1960	F M Burnet and P B Medawar	Acquired immunological tolerance
1965	Francois Jacob, Andre Lwoff and Jacques Monod	Genetic control of enzymes
1966	Peyton Rous	Tumor inducing viruses
1969	M Delbruck, A D Hershey and S E Luria	Replication mechanism and genetic structure of viruses
1972	Gerald M Edelman and Rodney R Porter	Chemical structure of antibodies
1975	D Baltimore, R Dulbecco and H Martin Temin	Interaction between tumor viruses and genetic material of cell
1976	Baruch S Blumberg and D Carleton Gajdusek	New mechanisms of infectious diseases dissemination
1978	Werner Arber, Daniel Nathans and Hamilton O Smith	Restriction enzymes
1980	Baruj Benacerraf, Jean Dausset and George D Snell	Immunological regulation by cell surface
1984	Niels K Jerne, Georges J F Kohler and Cesar Milstein	Control of immune system and monoclonal antibodies
1987	Susumu Tonegawa	Generation of antibody diversity
1989	J Michael Bishop and Harold Varmus	Origin of retroviral oncogenes
1996	Peter C Doherty and Rolf M Zinkernagel	Specificity in cell-mediated defense
1997	Stanley B Prusiner	Prions
2005	Barry J Marshall and J Robin Warren	<i>Helicobacter pylori</i>
2008	Herald Hausen and Francoise Barre-S and L Montagnier	Human papillomaviruses, human immunodeficiency virus
2011	Bruce A Beutler, Jules A Hoffman, Ralph M Steinman	Activation of innate immunity, and dendritic cells and their role in adaptive immunity
2012	Sir John B Gurdon, Shinya Yamanaka	Mature cells can be programmed to become pluripotent