

INTRODUCTION- IMMUNOLOGY

- **Immunology** is a branch of science that deals with the body's resistance to infection or the of altered reactivity of the body following an exposure to a foreign substance or infection.
- **Immunity** means the body's ability to resist infection or in other words the state of the body which learns from the experience of past infection(s), how to deal more efficiently with subsequent infections.
- **The immune system** of an individual is consisting of its cells and molecules responsible for the immunity.
- **Immune Response** is the reaction of the body following an exposure to foreign antigen resulting in the formation of antibodies and lymphokines

HISTORY OF IMMUNOLOGY

- In Fifth century, B.C. (B.C. 430), Thucydides in Athens first mentioned immunity to an infection that he called 'plague' (but not probably bubonic plague). But the concept of immunity existed much before as the ancient Chinese custom to protect children against small pox was by subjecting them to inhale powder prepared from the skin lesions of patients recovered from small pox.
- By twelfth century, Chinese observed that the individuals who recovered from small pox were resistant to further attack and they deliberately infected infants by making small cut on the skin and rubbing the scabs collected from the infected person. The children survived from the infection and they were protected from small pox later in their life. Later with their experience they adopt a method of infecting children with the scabs collected from the mildest cases of small pox (**variolation**) and the incidence of death due to small pox dropped down from 20% to 1%. This news spread to Europe by the early eighteenth century and soon used widely.
- In 18th century, deaths among cattle due to Rinderpest (cattle plague) in Europe was common and soaking a piece of string with nasal discharge from the Rinderpest affected animal and inserting into dewlap by making an incision in susceptible animals reduced the incidence. In 1774, Benjamin Jesty, a farmer, inoculated his wife with vaccinia virus to protect her from small pox.
- In 1798, **Edward Jenner** (1749-1823) following the suggestion of a dairymaid inoculated a eight years old boy with blister fluid collected from cowpox and protected him from severe small pox. This technique is called **vaccination** (*vacca* means cow in Latin) and used extensively to eradicate small pox from the world. He is considered as the **Father of Immunology**.
- The concept of Jenner's observation was not realized till 1879 when **Louis Pasteur** (1822 – 1895) in France was working with bacterium now known as **Pasteurella multocida**. Once his assistant accidentally left the culture of this organism on a laboratory bench and went on summer vacation. When he returned and infected the chickens, they did not die. Pasteur prepared fresh culture and infected the same chickens but in his surprise he saw that birds were resistant to infection. Pasteur realized that this was similar to the principle of using cowpox for vaccination against small pox.
- In vaccination, exposure of an animal to less virulent or avirulent organism does not cause disease but produce immunity and prevent an attack against a virulent organism of same type or a closely related organism. Pasteur applied this technique for the control of anthrax. He made **Bacillus anthracis** bacteria avirulent by growing them at an unusual high temperature. In 1881, first he vaccinated one group of sheep with avirulent anthrax bacilli and invited people to watch as he challenged the sheep with virulent culture of **Bacillus anthracis**. The vaccinated sheep did not die. Pasteur's miracle for controlling diseases was spread widely. Since Rabies was a burning problem, he was asked to prepare a vaccine. He collected saliva from rabid dog and inoculated into rabbits. When rabbits died, he collected the brain and spinal cord, dried and made into powder. The powder was mixed with liquid and given to dogs; the vaccinated dogs did not suffer from rabies.
- In 1885, Pasteur administers first vaccine to Joseph Meister, a young boy who was bitten repeatedly by a rabid wolf. He could observe that the boy did not suffer from Rabies. Then he treated several patients. Pasteur established the Pasteur Institute at Paris. First human trial of Pasteur's rabies vaccine was made in 6 July 1885. This day is observed as zoonosis day.
- During the same time Salmon in USA demonstrated dead organisms could also be used as vaccines. He showed that heat killed culture of **Bacillus suipestifer** (present name **Salmonella choleraesuis**) believed to cause hog cholera could protect pigeons against the disease caused by that organism.
- In 1888 P.P. Emile Roux and Alexander Yersin at Pasteur institute, Paris demonstrated bacterial toxins in the culture filtrate of diphtheria bacilli and describe the immunity or antitoxin to such toxin. In

1890, Von Behring and Shibasaburo Kitasato (Berlin) demonstrated toxin and anti-toxin neutralization and transformation of antitoxin immunity to non-immune animal by transfer of immune serum. This finding had earned Noble Prize to Von Behring in Medicine in 1901. Although Pasteur was so successful in immunization against Fowl cholera, Rabies and Anthrax in animals but the mechanism of immunity remained obscure. Two different schools of thoughts developed simultaneously.

THEORIES OF IMMUNOLOGY

Cellular Immunity Theory

- In 1882 the Russian Zoologist Elie Metchnikoff (1845-1916) observed that when a rose thorn is introduced into the larvae of a starfish, within a few hours it was surrounded by motile cells and could be observed in the transparent starfish larvae.
- In 1883 he observed that fungal spores could be attacked by the blood cells in Daphnia, a metazoan under microscope (being transparent). He extended his investigation to mammalian leukocytes, showing their ability to engulf micro-organisms, a process which he termed **phagocytosis**. Thus he arrived to a polarized view that phagocytosis is the main defense against infection. He defined that the phagocytosis is due to two types of circulating phagocytes:
 - The polymorphonuclear leukocytes (microphage) and
 - The larger macrophages.
- Many people accepted the cellular theory of Metchnikoff but some pathologist criticized it as they observed immunity in absence of cells and about 50 years later again it became an area of extensive study.

Humoral Theory

- After Pasteur discovered that immunity can be produced by vaccination, it was soon recognized that substances produced immunity are present in blood or in body fluid (Humor).
- Fodor in 1886 observed a direct action of immune serum on anthrax bacilli. George Nuttall in 1888 observed the bactericidal action of blood in certain animals.
- In 1889 Hans Buchner showed that cell free serum is bactericidal and failed to have that effect after heating at 55 °C for one hour. The heat labile substance causing bactericidal effect was termed alexin (later named as cytolysin or complement).
- In 1890 Von Behring and Kitasato demonstrated the neutralizing antitoxic activity by serum from immunized animals with diphtheria or tetanus toxin. This was the first proof of humoral immunity.
- Thus both theories developed simultaneously.

A CHRONOLOGY OF IMPORTANT ACHIEVEMENTS IN IMMUNOLOGY

Year	Scientists Involved	Findings
1798	Edward Jenner	Vaccination against small pox
1862	Ernst Haeckel	Phagocytosis
1877	Paul Ehrlich	Mast cells
1879	Louis Pasteur	Attenuated vaccine for Fowl cholera,
1881	Louis Pasteur	Attenuated vaccine for Anthrax and swine erysipelas
1883	Eolie Metchnikoff	Phagocytosis and cellular theory of immunity

1885	Louis Pasteur	Anti rabies vaccine
1888	Pierre Roux and Alexander Yersin	Bacterial toxins
1890	Emil A von Behring and Shibasaburo kitasato	Antitoxins in serum for diphtheria and tetanus
1891	Robert Koch	Delayed type of hypersensitivity
1894	Richard Pfeiffer and Vasily Isaeff	Bacteriolysis
1894	Jules Bordet	Complement and bacteriolysis
1900	Paul Ehrlich	Antibody formation theory(side chain theory)
1901	Karl Landsteiner	ABO blood group
1901	Bordet and Gengou	Complement Fixation Test
1902	Charles Richet and Paul J. Portier	Anaphylaxis
1903	Nicholas Arthus	Specific tissue destruction -Arthus Phenomenon
1903	Sir Almoth Wright	Opsonization (antibodies could help in Phagocytosis)
1905	Von Pirquet	Studied Serum Sickness
1906	Clemens Pirquet	Allergy (introduced the term allergy)
1912	Bacille, Albert Clamette and Camille Guerin	B.C.G. vaccination against Tuberculosis
1917	Karl Landsteiner	Hapten
1921	Carl Prausnitz and Heinz Kustner	Cutaneous allergic reaction
1930	Friedrich Breinl and Felix Haurowitz	Template theory of antibody formation
1934	John Marrack	Antigen-Antibody binding hypothesis (Lattice theory)
1936	Grover	Major Histocompatibility Complex (MHC)
1939	Tiselius and Kabat	Antibodies are gamma globulins
1940	Karl Land Steiner and Alexander Weiner	Identification of Rh antigen

1941	Albert H. Coons and others	Fluorescence labeling immunofluorescence
1942	Jules Freund and Katherine McDermott	Adjuvants
1944	Peter Medwar and Frank MacFarlane Burnet	Theory of acquired immunological tolerance
1948	Orjan Ouchterlony and Stephen D Elek	Double diffusion of antigen and antibody in gels.
1948	Fagraeus	Antibody production in Plasma B cells.
1952	James Riley and Geoffy Westt	Histamine in Mast cell
1955-59	Frank MacFarlane Burnet and Neils K. Jerne	Clonal selection theory of antibody formation
1955	Glick	Bursa of Fabricius
1957	Isaacs and Lindenmann	Discovery of interferon
1958	J. Dausset and F. Rapaport	Histocompatibility antigens on human leukocytes
1959	R.R. Porter, Gerald M.Edelman and Alfred Nisonoff	Discovery of antibody structure
1961-62	Miller and Good	Discovery of thymus involvement in cellular Immunity
1964-68	Claman	T and B cell co-operation in immune response
1975	George Koehler and Caesar Milstein	Monoclonal antibodies
1976	Susuma Tonegawa	Gene arrangements in antibody production
1995	Shimon Sakaguchi	Regulatory T cells