

History of Immunology

Derived from the Latin word IMMUNIS (EXEMPT)

The word “immunity” (Latin: immunis – free of/ exempt) was used in the context of being free of the burden of taxes or military conscription. The history of immunology is really slightly more than 100 years.

- Immunity refers to resistance exhibited by the body towards foreign entity i.e., microorganism and their products.
- Immunity refers to mechanisms used by the body as protection against environmental agents that are foreign to the body i.e., Microorganisms, Foods, Chemicals, Drugs, Pollen etc.

Immunology is a branch of biology involved with the study of the immune system, components of the immune system, its biological processes, the physiological functioning of the immune system, types, its disorders.

- **Two Arms of the Adaptive Immune System**
Humoral immunity (Antibodies)
Cell-mediated immunity (T-cells)

Historical aspect

- ~ 430 B.C: Peloponnesian War, Thucydides describes plague – the ones who had recovered from the disease could nurse the sick without getting the disease a second time.
- 12th century: Chinese and Turks use dried crusts of smallpox as “vaccine”
- The term “*immunity*” was first used in 1775 by **Van Sweiten**, a Dutch physician, as “*immunitas*” to describe the effects induced by an early attempt at variolization.

Discovery of Humoral Immunity -1890 von Behring and Kitasato

A Student of Koch, With Kitasato and Wernike, discovered anti-toxin for Diphtheria and Tetanus and applied as therapy.

Filtrates from cultures of *Clostr. tetani* can confer protection.

Serotherapy, Serum of vaccinated people had substances that specifically bound to the relevant pathogen (ANTIBODIES)

Louis Pasteur (1822-1895)

Stereochemist: molecular asymmetry. Fermentation and silk worker disease, Pasteurisation , Germ Theory of disease. Thus started microbiology

Attenuated vaccines for cholera, anthrax, and rabies

On July 4, 1886, 9-year-old Joseph Meister was bitten repeatedly by a rabid dog. Pasteur treated him with his attenuated rabies vaccine two days later. Meister survived.

Robert Koch (1843-1910)

German physician; also started to work on Anthrax in 1870's. Identified the spore stage.

First time the causative agent of an infectious disease was identified.

Koch's postulates: conditions that must be satisfied before accepting that particular bacteria cause particular diseases.

Discovered the tubercle bacillus and tuberculin. Detailed tuberculin skin test (DTH).

Paul Ehrlich (1845-1915)

Developed a series of tissue-staining dyes including that for tubercle bacillus.

Worked with Koch. **Developed anti-toxin (Diphtheria)**

Side-chain theory of antibody formation: "surface receptors bound by lock & key; Ag stimulated receptors"

Elie Metchnikoff (1845-1916)

Embryologist studying starfish development.

Found phagocytosis. Formed the basis of leukocyte **phagocytosis.**

Birth of **cellular immunology**

Sir Frank Macfarlane Burnet

Trained as MD

Important work on influenza. Discovery of an influenza viral enzyme with the specificity for particular forms of neuramic acid.

Clonal selection theory to explain **tolerance**

Discovery of **acquired immunological tolerance.** **Rejection of donor grafts** was due to an immunological reaction and that tolerance can be built up by injections into embryos.

Gerald M. Edelman 1929 and Rodney R. Porter 1917-1985

1972 Nobel Prize for their discoveries concerning the **chemical structure of antibodies.**

Baruj Benacerraf, Jean Dausset & George D. Snell

Discovered genes that regulate immune responses (Ir gene),

Now known as the **major histocompatibility antigens**

Niels K. Jerne (1912-1994)

Antibody avidity maturation, Plaque forming assay

Pre-existing repertoire (in host DNA) theory helped the formation of **clonal selection theory.**

Host MHC is the driving force for the maturation and selection of T cells in the thymus.

Idiotypic network

Nobel Prize, 1984, for theories concerning "the specificity in development and control of the immune system" and the discovery of "the principle for production of monoclonal antibodies."

Milstein (b. 1927) and Köhler (1946-1995)

Monoclonal antibody production

Susumu Tonegawa (b. 1939)

Cloning of the Immunoglobulin gene.

Discovery of "the genetic principle for generation of antibody diversity".

Peter C. Doherty and Rolf M. Zinkernagel

Two signals· 1996 Nobel Prize for "**the specificity of the cell- mediated immune defence**".

History of Immunology Time Line

1798	Edward Jenner	Smallpox vaccination
1862	Ernst Haeckel	Recognition of phagocytosis
1877	Paul Erlich	recognition of mast cells
1879	Louis Pasteur	Attenuated chicken cholera vaccine development
1883	Elie Metchnikoff	Cellular theory of vaccination
1885	Louis Pasteur	Rabies vaccination development
1888	Pierre Roux & Alexandre Yersin	Bacterial toxins
1888	George Nuttall	Bactericidal action of blood
1891	Robert Koch	Delayed type hypersensitivity
1894	Richard Pfeiffer	Bacteriolysis
1895	Jules Bordet	Complement and antibody activity in bacteriolysis
1900	Paul Erlich	Antibody formation theory
1901	Karl Landsteiner	A, B and O blood groupings
1902	Paul Portier & Charles Richet	Anaphylaxis
1903	Almroth Wright & Stewart Douglas	Opsonization reactions
1906	Clemens von Pirquet	coined the word allergy
1907	Svante Arrhenius	coined the term immunochemistry
1910	Emil von Dungern, & Ludwik Hirsfeld	Inheritance of ABO blood groups
1910	Peyton Rous	Viral immunology theory
1917	Karl Landsteiner	Haptens
1924	L Aschoff	Reticuloendothelial system
1926	Lloyd Felton & GH Bailey	Isolation of pure antibody preparation
1934	John Marrack	Antigen-antibody binding hypothesis
1940	Karl Lansteiner & Alexander Weiner	Identification of the Rh antigens

1941	Albert Coons	Immunofluorescence technique
1942	Jules Freund & Katherine McDermott	Adjuvants
1944	Peter Medwar	Immunological hypothesis of allograft rejection
1948	Astrid Fagraeus	Demonstration of antibody production in plasma B cells
1949	Macfarlane Burnet & Frank Fenner	Immunological tolerance hypothesis
1950	Richard Gershon and K Kondo	Discovery of suppressor T cells
1952	Ogden and Bruton	discovery of agammagobulinemia (antibody immunodeficiency)
1953	Morton Simonsen and WJ Dempster	Graft-versus-host reaction
1953	James Riley & Geoffrey West	Discovery of histamine in mast cells
1953	Rupert Billingham, Leslie Brent Peter Medwar, & Milan Hasek	, Immunological tolerance hypothesis
1955-59	Niels Jerne, David Talmage, Macfarlane Burnet	Clonal selection theory
1957	Ernest Witebsky et al.,	Induction of autoimmunity in animals
1957	Alick Isaacs & Jean Lindemann,	Discovery of interferon (cytokine)
1958-62	Jean Dausset et al.,	Human leukocyte antigens
1959-62	Rodney Porter et al.,	Discovery of antibody structure
1959	James Gowans,	Lymphocyte circulation
1961-62	Jaques Miller et al.,	Discovery of thymus involvement in cellular immunity
1961-62	Noel Warner et al.,	Distinction of cellular and humoral immune responses
1964-8	Anthony Davis et al.,	T and B cell cooperation in immune response
1965	Thomas Tomasi et al.,	Secretory immunoglobulin antibodies
1974	Rolf Zinkernagel & Peter Doherty,	MHC restriction
1975	Kohler and Milstein,	Monoclonal antibodies used in genetic

		analysis
1984	Robert Good,	Failed treatment of severe combined immunodeficiency (SCID, David the bubble boy) by bone marrow grafting.
1985	Tonegawa, Hood et al.,	Identification of immunoglobulin genes
1985-7	Leroy Hood et al.,	Identification of genes for the T cell receptor
1990	Yamamoto et al.,	Molecular differences between the genes for blood groups O and A and between those for A and B
