Introduction to Immunology as a Science

The immune system is the body's biological defense mechanisms that protect against foreign invaders. Only in the last century, the components of that system and the ways they work were discovered and found.

The true roots of the study of the immune system were from 1796 when an English physician, **Edward Jenner**, discovered a method of **smallpox vaccination**. He noted that dairy workers who contracted **cowpox** from milking infected cows were resistant to smallpox (they didn't get infected during work with infected cows).

In 1796, the scientist Jenner injected a young boy with material from a milkmaid who had an active case of cowpox. After the boy recovered from his own resulting cowpox, Jenner inoculated him with smallpox; the boy was immune (didn't show disease clinical signs). After Jenner published these results Jenner's vaccination spread rapidly.

It was **Louis Pasteur** who established the cause of infectious diseases and the medical basis for **immunization**. First, Pasteur wrote his **germ theory of disease**, the concept that disease is caused by a **microorganisms**. In 1880, Pasteur discovered that aged cultures of cholera **bacteria** lost their power to induce disease in chickens but can cause **immunity** against the disease when injected. He also used attenuated (weakened) cultures of **anthrax** and **rabies** to vaccinate against those diseases.

Another historical development by **Louis Pasteur,** in 1884, Pasteur used weakened cultures of *Bacillus anthracis*, the causative agent of anthrax, and inactivated sample from the spinal cords of rabbits infected with the rabies virus to produce immunity to anthrax and rabies. Pasteur's

method started the development of other active immune protective vaccines like oral poliomyelitis vaccine that developed by Albert Sabin in the 1950s.

The American scientists **Theobald Smith** (1859–1934) and **Daniel Salmon** (1850–1914) showed in 1886 that bacteria killed by heat could also induce immunity.

In 1888, **Pierre-Paul-Emile Roux** (1853–1933) and **Alexandre Yersin** (1863–1943) showed that **diphtheria** bacillus produced a toxin that the body responded to it by producing an antitoxin.

Emil von Behring and **Shibasaburo Kitasato** found a similar toxin-antitoxin reaction in **tetanus** in 1890. Von Behring discovered that small doses of tetanus or diphtheria toxin produced immunity, and that this immunity could be transferred from animal to animal by serum. Von Behring concluded that the immunity happened by substances produced in the blood, which he called antitoxins, or antibodies.

Hans Buchner (1850–1902) in 1893 discovered another important blood substance called **complement** (Buchner's named it **alexin**), and **Jules Bordet** in 1898 found that this complement enabled the antibodies to combine with antigens (foreign substances) and destroy or eliminate them.

Karl Landsteiner was able to use this specific antigen-antibody reaction (that each **antibody** reacted only against a specific **antigen)** to distinguish the different blood groups (ABO System Grouping).

A new element was introduced during the 1880s by the Russian microbiologist **Elie Metchnikoff**. He discovered cell-based immunity: white blood cells (leucocytes), which Metchnikoff called phagocytes (cells that ingested and destroyed foreign particles).

A theory of immunity was written by **Paul Ehrlich** in the 1890s; he said: "side-chain" theory explained that antigens and antibodies combine chemically in fixed ways, like a key fits into a lock.

Until this time, the immune responses were seen as beneficial and necessary to protect human body from infectious agents. But, in 1902, **Charles Richet** and **Paul Portier** showed that extreme immune reactions in test animals (laboratory animals used in experiments), had become sensitive

to antigens by previous exposure. This phenomenon of hypersensitivity, called **anaphylaxis**, showed that immune responses could cause damage to the body itself. Hypersensitivity to antigens also explained **allergies**, this term was named by **Pirquet** in 1906.

Much more was learned about antibodies in the middle of twentieth century, including the fact that they are proteins of the type gamma globulin portion in plasma and they are produced by plasma cells; their molecular structure was also found.

An important advance in **Immunochemistry** came in 1935 when **Michael Heidelberger** and **Edward Kendall** (1886–1972) developed a method to detect and measure amounts of different Immunity: active, passive, and delayed.

A cellular research showed that there are two types of lymphocytes; B-lymphocytes, which secrete antibody, and **T-lymphocytes**, which regulate the B-lymphocytes and also kill foreign substances directly (killer **T cells**) or stimulate macrophages to do so (helper T cells). Lymphocytes recognize antigens by characteristics on the surface of the antigen-carrying molecules.

Knowledge about the immune system's role in rejection of transplanted tissue became extremely important as organ transplantation became surgically important. **Peter Medawar's** work in the 1940s showed that such rejection was an immune reaction to antigens on the foreign tissue.

Donald Calne showed in 1960 that immunosuppressive drugs (drugs that suppress immune responses), able to reduce transplant rejection, and these drugs were first used on human patients in 1962.

In the 1940s, **George Snell** discovered in mice a group of tissue-compatibility genes, the **MHC**, which played an important role in controlling acceptance or resistance to tissue grafts.

Autoimmune reaction, in which the body has an immune response to its own substances, also may be a cause of a number of diseases, like multiple sclerosis. During 1960s, **Ion Gresser** discovered that the protein **interferon** acts against cancerous tumors during cancer treatment

experiments. After the development of genetically engineered interferon in 1980s; that made it available for treatment of cancer.

The invention of monoclonal antibodies in the mid-1970s was a grate and effective method to fight one of the most serious immune system disorders, **AIDS**.

The **cytokines**, proteins produced by the body that help the immune system cells to communicate with each other and activate them to fight infection. The researches on cytokines opened new windows to improve treatment of difficult diseases like cancers and AIDS.