Immunology

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Immunology

- The term "**immunology**" is derived from the Latin word "**immunise**" which means exempt (protection from infectious diseases). It is a state of protection against foreign pathogens or substances (antigens).
- The immune system is equipped with a rapid response mechanism, exquisite specificity, adaptability, an intricate regulatory network, and memory to accomplish this goal.
- Over the past several decades, dramatic progress has occurred in the immunology field. Consequently, significant advances have been realized not only in the research field but also in the diagnostic and clinical arena. These advances have allowed us to better understand how the immune system works and have provided insight into a variety of immune disorders, such as infectious diseases, allergies, autoimmunity, immunodeficiency, cancer, and transplantation. This information has led to better diagnoses, new treatment strategies, and improved management for patients with these disorders.
- The fully functional immune system involves so many organs, molecules, cells, and pathways in such an interconnected and circular process.
- Recent advances in cell imaging, genetics, bioinformatics, as well as cell and molecular biology have helped us to understand many of the individual players in great molecular detail. Indeed, the field of immunology can be credited with the vaccine that eradicated smallpox, the ability to transplant organs between humans, and the drugs used today for treatment.

A Historical Perspective of Immunology

The discipline of immunology grew out of the observation that individuals who had recovered from certain infectious diseases were therefore protected from the disease.

Perhaps the earliest written reference to the phenomenon of immunity can be traced back to Thucydides. In describing a plague in Athens, he wrote in 430 BC that only those who had recovered from the plague could nurse the sick because they would not contract the disease a second time. Although early societies recognized the phenomenon of immunity, almost 2000 years passed before the concept was successfully converted into medically effective practice.

Pasteur showed that vaccination worked, but he did not understand how. Some scientists believe that immune protection in vaccinated individuals were mediated by cells, while others postulated that a soluble agent delivered protection. The

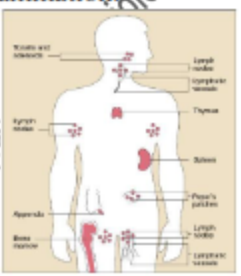
experimental work of Emil von Behring and Shibasaburo Kitasato in 1890 gave the first insights into the mechanism of immunity, earning von Behring the Nobel Prize in Physiology or Medicine in 1901.

Nobel Prizes for immunologic research

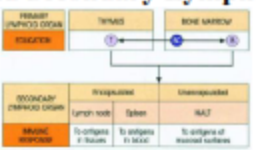
Year	Recipient	Country	Research
1901	Emil von Behring	Germany	Serum antitoxins
1905	Robert Koch	Germany	Cellular immunity to tuberculosis
1908	Elie Metchnikoff Paul Ehrlich	Russia Germany	Role of phagocytosis (Metchnikoff) and antitoxins (Ehrlich) in immunity
1913	Charles Richet	France	Anaphylaxis
1919	Jules Bordet	Belgium	Complement-mediated bacteriolysis
1930	Karl Landsteiner	United States	Discovery of human blood groups
1951	Max Theiler	South Africa	Development of yellow fever vaccine
1957	Daniel Bovet	Switzerland	Antihistamines
1960	F. Macfarlane Burnet Peter Medawar	Australia Great Britain	Discovery of acquired immunological tolerance
1972	Rodney R. Porter	Great Britain	Chemical structure of antibodies
1977	Rosalyn R. Yalow	United States	Development of radioimmunoassay
1980	George Snell Jean Dausset Baruj Benacerraf	United States France United States	Major histocompatibility complex
1984	Niels K. Jerne Cesar Milstein Georges E. Köhler	Denmark Great Britain Germany	Immune regulatory theories (Jerne) and technological advances in the development of monoclonal antibodies (Milstein and Köhler)
1987	Susumu Tonegawa	Japan	Gene rearrangement in antibody production
1991	E. Donnall Thomas Joseph Murray	United States United States	Transplantation immunology
1996	Peter C. Doherty Rolf M. Zinkernagel	Australia Switzerland	Role of major histocompatibility complex in antigen recognition by T cells
2002	Sydney Brenner H. Robert Horvitz J. E. Sulston	South Africa United States Great Britain	Genetic regulation of organ development and cell death (apoptosis)
2008	Harald zur Hausen Françoise Barré-Sinoussi Luc Montagnier	Germany France France	Role of HPV in causing cervical cancer (Hausen) and the discovery of HIV (Barré-Sinoussi and Montagnier)
2011	Jules Hoffman Bruce Beutler Ralph Steinman	France United States United States	Discovery of activating principles of innate immunity (Hoffman and Beutler) and role of dendritic cells in adaptive immunity (Steinman)

Organs of the Immune System

- Normally, the immune system comprises primary (or central) and secondary (or peripheral) organs.
- The primary organs, which include the thymus and bone marrow, enable cell commitment and immunoregulation functions. The bone marrow is the "maternity home" for all types of cells and is the "academy" for B lymphocytes (B cells). The thymus represents the "immunological government" to master the whole immune system and plays a role as the "academy" for T lymphocytes (T cells).
- The protective reactions and responses proceed in the secondary organs such as the lymph nodes, spleen, and mucosae-associated lymphoid tissue (MALT) divided into nasal-associated lymphoid tissue (NALT), bronchus-associated lymphoid tissue (BALT), gut-associated lymphoid tissue (GALT), and skin-associated lymphoid tissue (SALT). A variety of competent immunological islets are present in other organs (e.g., the liver, kidneys, synovia, etc.).
- Tertiary lymphoid tissues or organs are pathologically ectopic accumulations of lymphoid cells and various cell types at the sites of unresolved immune responses and chronic inflammation.



Primary and Secondary Lymphoid Organs



Functions of lymphoid organs

- **The Thymus** is a primary immune organ in which thymocytes are differentiated into T cells, and a variety of immunoregulatory substances are produced. The thymus is located in the anterior mediastinum (above the heart and is largest

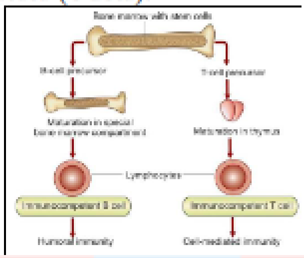
before puberty, when it begins to shrink). There are three parenchymal zones of the thymus, subcapsular, cortical, and medullary, that accord with major stages of T-cell lymphopoiesis. In the first and second zones, many thymic follicles are available, whereas in the third zone, thymic corpuscles (Hassall's) occur. In the thymus, suspension thymocytes account for approximately 97%. Giant epithelial "nurse" cells, macrophages, thymic dendritic cells, and Natural killer (NK) cells make up less than 1% in total. These cells are constant representatives of the thymic microenvironment, "professors," which teach "students," the thymocytes.

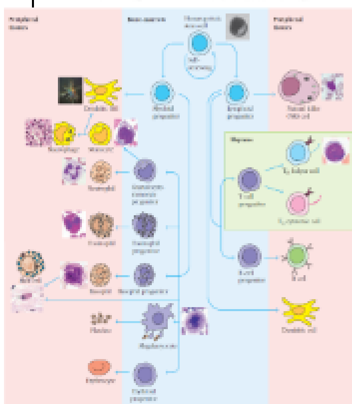
- **The Bone marrow** is a primary immune organ that is the source of all cell lines used by the immune system and the place of B cell maturation. There are two types of bone marrow, "red bone marrow," which is made up of hematopoietic tissue including cells of the immune system, and "yellow bone marrow," which consists of fat cells.

The bone marrow's stroma provides the hematopoietic microenvironment that facilitates hematopoiesis, in particular, B-cell lymphopoiesis, through the parenchymal cells that produce colony-stimulating factors (CSFs) and other cytokines. The blood vessels of the bone marrow create a blood-marrow barrier, which inhibits immature cells from leaving the bone marrow.

- **Hematopoiesis:** All red and white blood cells develop from a pluripotent hematopoietic stem cell during a highly regulated process called hematopoiesis. In the adult, hematopoiesis occurs in the bone marrow.
- Hematopoietic stem cells give rise to two main blood cell progenitors: common **myeloid progenitors** and common **lymphoid progenitors**.
- Four main types of cells develop from common myeloid progenitors: red blood cells (erythrocytes), monocytes (which give rise to macrophages and myeloid dendritic cells), granulocytes (which include the abundant neutrophils and less abundant basophils, eosinophils, and mast cells), and megakaryocytes.

- There are three types of lymphoid cells: B cells, T cells, and natural killer (NK) cells. B cells synthesize and display membrane antibody, and T cells synthesize and display T-cell receptors (TCRs).





Hematopoiesis. Self-renewing hematopoietic stem cells give rise to lymphoid and myeloid progenitors. Most immune cells mature in the bone marrow and then travel to peripheral organs via the blood. Some, including mast cells and macrophages, undergo further maturation outside the bone marrow. T cells develop to maturity in the thymus.

- **The spleen** is a secondary lymphoid organ where defensive immune processes proceed if pathogens invade the body through the blood. Thus, the spleen is of important in fighting infections that have invaded the blood. It is similar in structure to a large lymph node located in the left upper quadrant of the abdomen. However, the spleen has the splenic artery, splenic vein, and only efferent lymphatic vessels. It consists of red pulp and white pulp. The red pulp plays a role in blood clearance, removing old erythrocytes, maintaining an additional reservoir of blood, and metabolizing hemoglobin.

The white pulp is composed of lymphoid follicles, rich in B cells; marginal zones (MZ), rich in MZ B cells; and periarteriolar lymphoid sheaths (PALS), rich in T cells. The white pulp is vital for the immune processes including B-cell-mediated

responses, synthesis of antibodies, removal of antibody-coated microbes, and storage of monocytes.

- **Lymph nodes** are secondary lymphoid organs in which adaptive immune responses and other processes take place if pathogens invade the body through barrier tissues. Some blood fluid from the bloodstream leaks out into tissues and because of the pressure gradient is absorbed into the lymphatic system becoming the lymph (**Lymph, also called lymphatic fluid, is a collection of the extra fluid that drains from cells and tissues in your body and isn't reabsorbed into your capillaries. Lymph contains many different substances, including proteins, minerals, fats, damaged cells, cancer cells and germs**). In the course of lymph flow, the lymph picks up antigens, antigen-presenting cells (APC), and lymphocytes throughout the body and carries them via lymphatics into the lymph nodes.

  The lymph nodes are among the secondary organs of the immune system, widely present in many parts of the body, and have an artery, vein, and afferent and efferent lymphatic vessels. The afferent lymphatics are multiple and wider than efferent vessels, so cells and molecules can easily enter the lymph nodes.

  Each lymph node is divided into lymph nodules, which contain a cortical zone of primary follicles with B cells, a paracortical zone of T cells, and a basal part of the nodule in the medulla. The primary follicles develop into secondary follicles in the course of B-cell-mediated immune responses.