Immune System in the Body

The human immune system consists of lymphoid organs, tissues, cells and soluble molecules like antibodies. As you have read, immune system is unique in the sense that it recognises foreign antigens, responds to these and remembers them. The immune system also plays an important role in allergic reactions, auto-immune diseases and organ transplantation.

Lymphoid organs:

These are the organs where origin and/or maturation and proliferation of lymphocytes occur. The primary lymphoid organs are **bone marrow** and **thymus** where immature lymphocytes differentiate into antigen-sensitive lymphocytes. After maturation the lymphocytes migrate to secondary lymphoid organs like spleen, lymph nodes, tonsils, Peyer's patches of small intestine and appendix. The secondary lymphoid organs provide the sites for interaction of lymphocytes with the antigen, which then proliferate to become effector cells. The location of various lymphoid organs in the human body is shown in Figure 1.

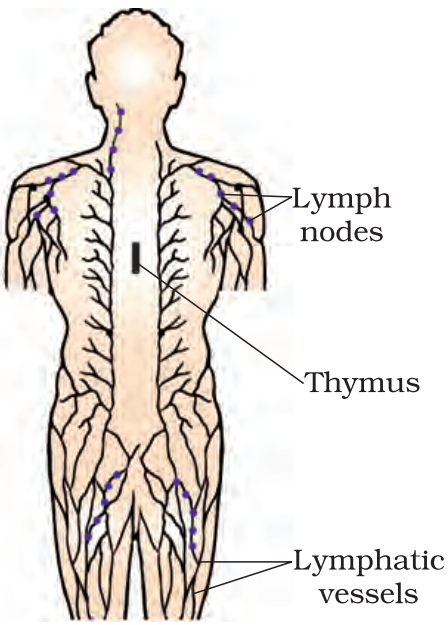


Figure 1 Diagrammatic representation of Lymph nodes

The bone marrow is the main lymphoid organ where all blood cells including lymphocytes are produced. The thymus is a lobed organ located near the heart and beneath the breastbone. The thymus is quite large at the time of birth but keeps reducing in size with age and by the time puberty is attained it reduces to a very small size. Both bone-marrow and thymus provide micro-environments for the development and maturation of T-lymphocytes. The spleen is a large bean-shaped organ. It mainly contains lymphocytes and phagocytes. It acts as a filter of the blood by trapping blood-borne micro-organisms. Spleen also has a large reservoir of erythrocytes. The lymph nodes are small solid structures located at different points along the lymphatic system. Lymph nodes serve to trap the micro-organisms or other antigens, which happen to get into the lymph and tissue fluid. Antigens trapped in the lymph nodes are responsible for the activation of lymphocytes present there and cause the immune response.

There is lymphoid tissue also located within the lining of the major tracts (respiratory, digestive and urogenital tracts) called **mucosa-associated lymphoid tissue** (MALT). It constitutes about 50 per cent of the lymphoid tissue in human body.

contact with the infected persons or their belongings should be avoided. For diseases such as malaria and filariasis that are transmitted through insect vectors, the most important measure is to control or eliminate the vectors and their breeding places. This can be achieved by avoiding stagnation of water in and around residential areas, regular cleaning of household coolers, use of mosquito nets, introducing fishes like *Gambusia* in ponds that feed on mosquito larvae, spraying of insecticides in ditches, drainage areas and swamps, etc. In addition, doors and windows should be provided with wire mesh to prevent the entry of mosquitoes. Such precautions have become all the more important especially in the light of recent widespread incidences of the vector-borne (*Aedes* mosquitoes) diseases like dengue and chikungunya in many parts of India.

The advancements made in biological science have armed us to effectively deal with many infectious diseases. The use of vaccines and immunisation programmes have enabled us to completely eradicate a deadly disease like smallpox. A large number of other infectious diseases like polio, diphtheria, pneumonia and tetanus have been controlled to a large extent by the use of vaccines. Biotechnology (about which you will read more in Chapter 12) is at the verge of making available newer and safer vaccines. Discovery of antibiotics and various other drugs has also enabled us to effectively treat infectious diseases.

IMMUNITY

Everyday we are exposed to large number of infectious agents. However, only a few of these exposures result in disease. Why? This is due to the fact that the body is able to defend itself from most of these foreign agents. This overall ability of the host to fight the disease-causing organisms, conferred by the immune system is called **immunity**.

Immunity is of two types: (i) Innate immunity and (ii) Acquired immunity.

1. Innate Immunity

Innate immunity is non-specific type of defence, that is present at the time of birth. This is accomplished by providing different types of barriers to the entry of the foreign agents into our body. Innate immunity consist of four types of barriers. These are —

(i) ***Physical barriers*** **:** Skin on our body is the main barrier which prevents entry of the micro-organisms. Mucus coating of the epithelium lining the respiratory, gastrointestinal and urogenital tracts also help in trapping microbes entering our body.

(ii) ***Physiological barriers*** **:** Acid in the stomach, saliva in the mouth, tears from eyes–all prevent microbial growth.

(iii) ***Cellular barriers*** **:** Certain types of leukocytes (WBC) of our body like polymorpho-nuclear leukocytes (PMNL-neutrophils) and

monocytes and natural killer (type of lymphocytes) in the blood as well as macrophages in tissues can phagocytose and destroy microbes.

(iv) ***Cytokine barriers*** **:** Virus-infected cells secrete proteins called **interferons** which protect non-infected cells from further viral infection.

2. Acquired Immunity

Acquired immunity, on the other hand, is pathogen specific. It is characterised by memory. This means that our body when it encounters a pathogen for the first time produces a response called **primary response** which is of low intensity. Subsequent encounter with the same pathogen elicits a highly intensified secondary or anamnestic response. This is ascribed to the fact that our body appears to have memory of the first encounter.

The primary and secondary immune responses are carried out with the help of two special types of lymphocytes present in our blood, i.e., **B**-lymphocytes and **T**-lymphocytes.The B-lymphocytes produce an army of proteins in response to pathogens into our blood to fight with them. These proteins are called antibodies. The T-cells themselves do not secrete antibodies but help B cells produce them. Each antibody molecule has four peptide chains, two small called **light chains** and two longer called **heavy chains**. Hence, an antibody is represented as H_2L_2. Different types of antibodies are produced in our body. IgA, IgM, IgE, IgG are some of them. A cartoon of an antibody is given in Figure 2. Because these antibodies are found in the blood, the response is also called as **humoral immune response**. This is one of the two types of our acquired immune response – antibody mediated. The second type is called cell-mediated immune response or **cell-mediated immunity** (CMI). The T-lymphocytes mediate CMI. Very often, when some human organs like heart, eye, liver, kidney fail to function satisfactorily, transplantation is the only remedy to enable the patient to live a normal life. Then a search begins – to find a suitable donor. *Why is it that the organs cannot be taken from just anybody? What is it that*

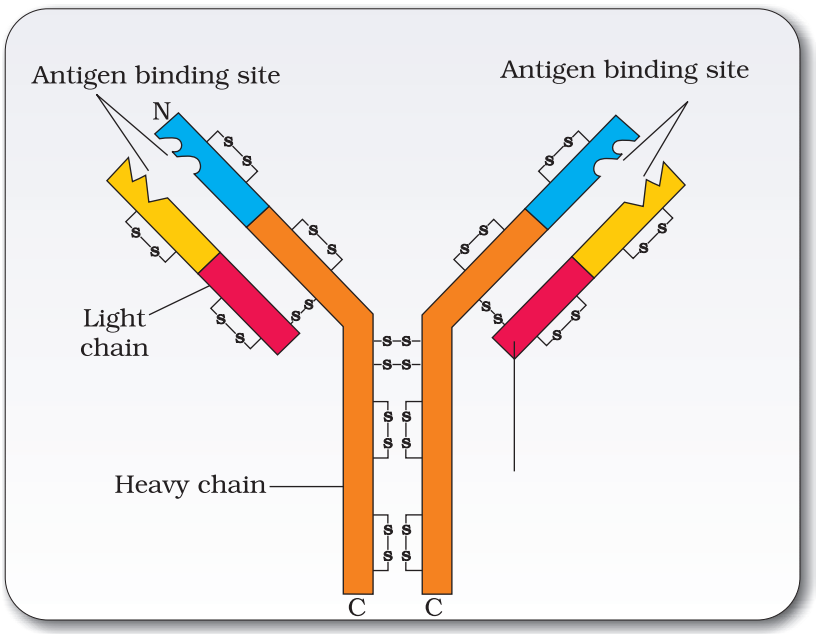


Figure 2 Structure of an antibody molecule

the doctors check? Grafts from just any source – an animal, another primate, or any human beings cannot be made since the grafts would be rejected sooner or later. Tissue matching, blood group matching are essential before undertaking any graft/transplant and even after this the patient has to take immuno–suppresants all his/her life. The body is able to differentiate 'self' and 'nonself' and the cell-mediated immune response is responsible for the graft rejection.

3. Active and Passive Immunity

When a host is exposed to antigens, which may be in the form of living or dead microbes or other proteins, antibodies are produced in the host body. This type of immunity is called **active immunity.** Active immunity is slow and takes time to give its full effective response. Injecting the microbes deliberately during immunisation or infectious organisms gaining access into body during natural infection induce active immunity. When ready-made antibodies are directly given to protect the body against foreign agents, it is called **passive immunity**. *Do you know why mother's milk is considered very essential for the new-born infant*? The yellowish fluid **colostrum** secreted by mother during the initial days of lactation has abundant antibodies (IgA) to protect the infant. The foetus also receives some antibodies from their mother, through the placenta during pregnancy. These are some examples of passive immunity.

4. Vaccination and Immunisation

The principle of immunisation or vaccination is based on the property of 'memory' of the immune system. In vaccination, a preparation of antigenic proteins of pathogen or inactivated/weakened pathogen (vaccine) are introduced into the body. The antibodies produced in the body against these antigens would neutralise the pathogenic agents during actual infection. The vaccines also generate memory – B and T-cells that recognise the pathogen quickly on subsequent exposure and overwhelm the invaders with a massive production of antibodies. If a person is infected with some deadly microbes to which quick immune response is required as in tetanus, we need to directly inject the preformed antibodies, or antitoxin (a preparation containing antibodies to the toxin). Even in cases of snakebites, the injection which is given to the patients, contain preformed antibodies against the snake venom. This type of immunisation is called **passive immunisation**.

Recombinant DNA technology has allowed the production of antigenic polypeptides of pathogen in bacteria or yeast. Vaccines produced using this approach allow large scale production and hence greater availability for immunisation, e.g., hepatitis B vaccine produced from yeast.

5. Allergies

When you have gone to a new place and suddenly you started sneezing, wheezing for no explained reason, and when you went away, your symptoms dissappeared. Did this happen to you? Some of us are sensitive to some particles in the environment. The above-mentioned reaction could be because of allergy to pollen, mites, etc., which are different in different places.

The exaggerated response of the immune system to certain antigens present in the environment is called **allergy**. The substances to which such an immune response is produced are called allergens. The antibodies produced to these are of IgE type. Common examples of allergens are mites in dust, pollens, animal dander, etc. Symptoms of allergic reactions include sneezing, watery eyes, running nose and difficulty in breathing. Allergy is due to the release of chemicals like histamine and serotonin from the mast cells. For determining the cause of allergy, the patient is exposed to or injected with very small doses of possible allergens, and the reactions studied. The use of drugs like anti-histamine, adrenalin and steroids quickly reduce the symptoms of allergy. Somehow, modern-day life style has resulted in lowering of immunity and more sensitivity to allergens – more and more children in metro cities of India suffer from allergies and asthma due to sensitivity to the environment. This could be because of the protected environment provided early in life.

6. Auto Immunity

Memory-based acquired immunity evolved in higher vertebrates based on the ability to differentiate foreign organisms (e.g., pathogens) from self-cells. While we still do not understand the basis of this, two corollaries of this ability have to be understood. One, higher vertebrates can distinguish foreign molecules as well as foreign organisms. Most of the experimental immunology deals with this aspect. Two, sometimes, due to genetic and other unknown reasons, the body attacks self-cells. This results in damage to the body and is called **auto-immune** disease. Rheumatoid arthritis which affects many people in our society is an auto-immune disease.

Immune System

Much progress has been made over the last several decades in unraveling the complex nature of our immune system. The ability of our immune system to protect us is dependent upon the ability of immune cells to communicate with one another in order to coordinate activities. Cells are able to communicate with one another through cell-to-cell contact or by secreting small signaling proteins called cytokines. Cell-to-cell contact and/or reaction to cytokines is mediated through a diverse variety of membrane bound receptors and ligands that are expressed on the surface of the cell at the right moment. Ligands are molecules that bind to receptors initiating a signal. Literally hundreds of these receptors and ligands have been identified by immunologists all over the world. Today each receptor is referenced using an international language called the "Cluster of Differentiation" or CD. A number identifying the order in which the receptor was discovered follows the letters CD. For example, all T lymphocytes express the receptor CD3. However, a special type of T lymphocyte called a "Helper" T Cell, also expresses the receptor referred to as CD4.

Key Elements of Immunity

Before examining the specifics of oral infections and the host response, several key elements involved in immunity will be summarized. In higher animals, resistance to a pathogen includes a non-adaptive, non-specific or innate response (natural immunity) and an adaptive or acquired response, which act in concert to protect the host. A simple way to remember this is to consider innate immunity as what you are born with. The innate response occurs in the same way and to the same extent regardless of how many times a pathogen is encountered. In contrast, an adaptive or acquired response occurs after a pathogen comes into contact with the host and a "specific response" to that pathogen is developed and stored in a memory bank for any future contact. On second contact with the pathogen, a more rapid and heightened immune response ensues to eliminate it.

Innate immunity includes the following component parts:

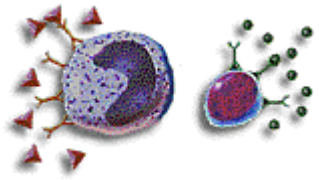
- External barriers such as skin, oral mucosa, body secretions and even endogenous (normal) microbial inhabitants
- Physiological factors as body pH and temperature
- Blood and tissue leukocytes (neutrophils, monocytes, macrophages, mast cells, basophils, eosinophils and natural killer cells)
- Dendritic cells for immune surveillance and antigen presentation
- Primary and secondary lymphoid tissue
- Soluble mediators of inflammation including acute phase proteins, complement and cytokines

The adaptive or acquired immune response system is mediated by T and B lymphocytes which are commonly referred to as T Cells and B Cells. There are three important characteristics to adaptive immunity:

- Self-recognition (or recognition of non-self)
- Specificity
- Memory

Three Important Characteristics to Adaptive Immunity

Self-Recognition



In healthy, immune competent individuals, immune responses are not produced against "*self*"-components. In vertebrates, Major Histocompatibility Complexes (MHC) exist that allow for differentiation between self and non-self antigens. In humans it is called the Human Leukocyte Antigen System (HLA) and it is responsible for genetically encoding our cells for recognition by the Immune System as either self or non-self.

Nucleated cells express MHC Class I genes, whereas a subgroup of immune cells called antigen presenting cells (APCs) express MHC Class II genes. In a healthy cell, a MHC Class I molecule coupled with one of the cell's peptides is expressed at the cell surface. This complex acts as a signal to circulating Natural Killer lymphocytes or cytotoxic T cells not to attack. However, if that cell is invaded by a pathogen, the MHC Class I molecule couples to a non-self peptide of the pathogen which then signals the cytotoxic lymphocytes to attack and destroy the cell. Tissue cells that undergo malignant transformation may also express peptides with the MHC Class I molecules that are no longer recognized as self; thus promoting the destruction of these cancerous cells.

Specificity

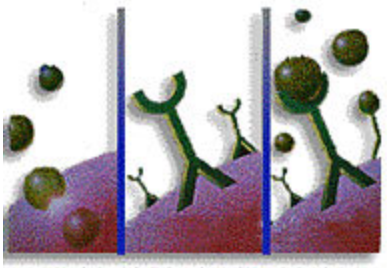
This property refers to the ability of the immune system to recognize non-self antigens and respond in a specific manner to them, rather than responding in a random manner. Specificity is initiated by Antigen Presenting Cells such as activated T Cells, B Cells, macrophages, dendritic cells and thymic epithelial cells. The APCs express MHC Class II molecules at their surface, which are coupled to antigenic peptides. When this antigenic peptide is presented to a T cell, the T cell becomes activated and in turn helps stimulate B cells to proliferate and differentiate into Plasma Cells which make antibodies "specific" to that antigen only. When the body encounters the measles virus, for example, and responds to it, it does not respond against all other viruses.

Response to one organism does not give protection against another unrelated organism.

Memory

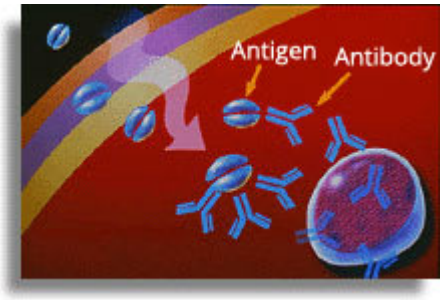
The initial contact with a molecule eliciting an immune response (antigen) leaves an imprint of information. With the help of the activated T cell, B cells also produce memory cells with antigen-specific antibodies expressed on their surface as B cell Receptors. These memory cells live for a longer period of time and, on second contact with an antigen, can respond more robustly and more quickly to eliminate it. We rarely suffer twice from measles, mumps, etc. The first contact imprints "*memory*" so that the body repels the next invasion.

Vaccines are synthetic forms or processed natural antigens used to stimulate the production of antibodies. Every time that antigen invades the body, the body remembers (memory), and an appropriate and specific response is produced by the host immune cells and antibodies.



Cells are imprinted with memory from previous contact with antigen (e.g. infectious agent)

Immunogens and Antigens



Foreign material, including microorganisms, can contain chemical groups recognizable by the body as foreign. In general terms, molecules of any chemical group that elicit an immune response are termed immunogens. More specifically, a molecule that is capable of ***gen***erating an ***anti***body is termed an ***antigen***. Antigenicity is determined by areas on the molecule termed antigenic determinants or epitopes. If a microorganism bypasses the body's other defenses, the immune system will produce a specific response that is directed against a particular antigenic epitope of this microorganism.

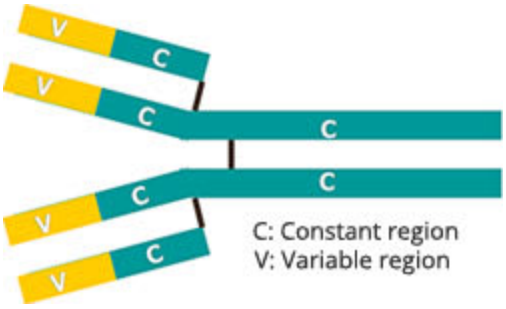
Most antigens are pure proteins, glycoproteins or lipoproteins. T Cells recognize the small peptides of proteins but not polysaccharides or nucleic acids. An Antigen Presenting Cell (APC) can present one of these antigenic peptides to the T Cell, thereby activating it. The activated T cell will in turn join to a B Cell stimulating it to differentiate into a Plasma Cell, which will produce specific antibodies to that particular antigen. This type of antigen that requires a T Cell to B Cell interaction for antibody production to occur is referred to as a T-dependent antigen. On the other hand, B Cells can express antibodies on their surface membrane, which are called B Cell Receptors (BCR). These receptors recognize not only proteins, but also polysaccharides and nucleic acids. These latter molecules are large and contain several different antigenic epitopes each of which can cross-link the membrane bound cell receptors (antibodies) on different clones of B Cells stimulating each cell to produce an antibody to one of the epitopes. This pathway is referred to Polyclonal B Cell stimulation. Since these antigens do not require a T Cell to B Cell interaction in order to produce antibodies, they are referred to as T-independent antigens. Examples include bacterial polysaccharides such as Lipopolysaccharide (LPS), a virulent product of many gram-negative bacteria.

Immunoglobulins

Immunoglobulins (Ig) are gamma globulin proteins present in bodily fluids (e.g. blood serum) and mucosal secretions (e.g., saliva, tears, vaginal secretions), and may also be found at the site of inflammation within the tissue. They are produced by plasma cells, which are differentiated B lymphocytes or B cells. Based on structure and protein composition, immunoglobulins are divided into five classes, two of which are further sub classified. Each has its own distinct chemical structure and specific biological function.

Typical Immunoglobulin Structure

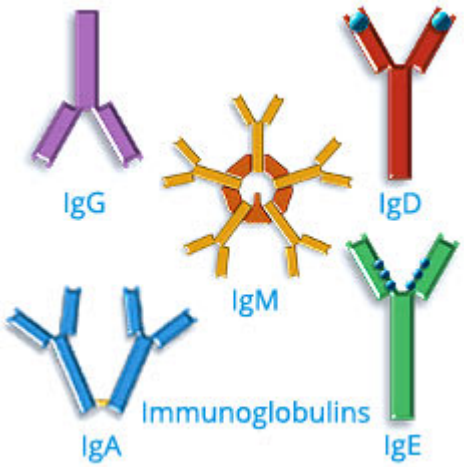
The immunoglobulin molecule is composed of a Constant region and Variable regions.

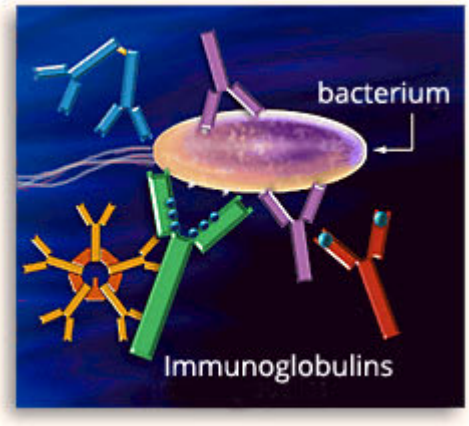


The Constant region generally is unique to the Ig Class or Ig Subclass and confers its biologic activity. The Variable regions form a complex, conformational molecular arrangement for the attachment of each specific antigen.

Five Classes [subclasses] of Immunoglobulins

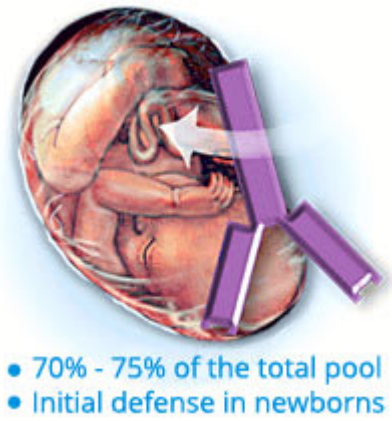
- Immunoglobulin G (IgG) [subclass IgG1, IgG2, IgG3, IgG4]
- Immunoglobulin A (IgA) [subclass IgA1, IgA2]
- Immunoglobulin M (IgM)
- Immunoglobulin D (IgD)
- Immunoglobulin E (IgE)





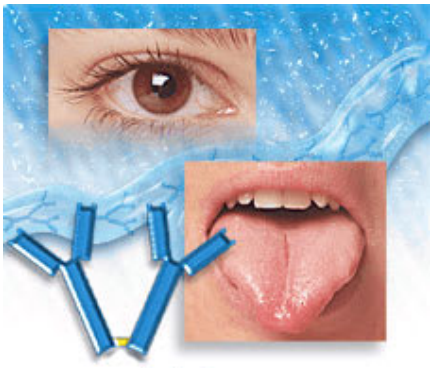
The five classes [subclasses] of immunoglobulins include:

IgA



Immunoglobulin G is the main immunoglobulin present in the blood and represents 70% to 75% of the total immunoglobulin pool. Several forms (subclasses) of IgG cross the placental barrier and are responsible for defense against infection in the first few months of a baby's life.

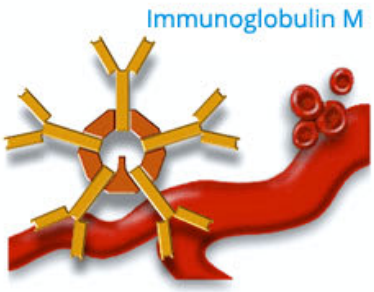
IgA



Immunoglobulin A (secretory)

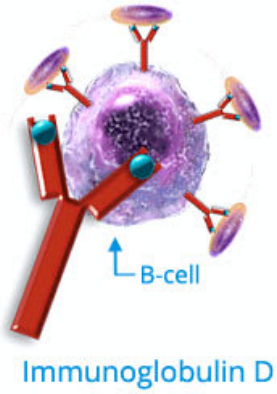
Immunoglobulin A provides localized antibody protection on mucosal surfaces. It is found in mucosal secretions such as saliva, tears, sweat, nasal fluids, fluids of the lung and colostrum, genito-urinary tract, and gastro-intestinal tract. It is a primary defense against microorganisms attacking exposed mucosal surfaces. IgA functions by preventing the microorganism from adhering to, and penetrating, the mucosal epithelial lining.

IgM



Immunoglobulin M is the major immunoglobulin present on the surface of immature B cells and is effective against microbes by binding with complement and causing agglutination and bacteriolysis. It is the first immunoglobulin to take part in the immune response and plays an important role in controlling bacteria that find their way into the blood stream (bacteremia).

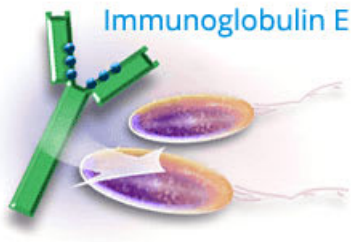
IgD



Immunoglobulin D

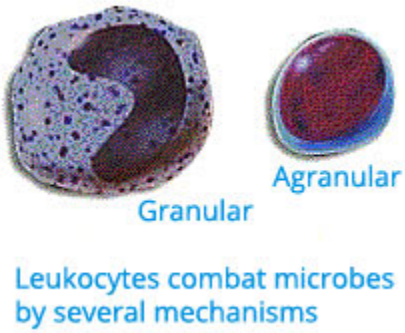
Immunoglobulin D is a trace antibody in the serum and is present on the surface of B cells. It may be involved in stimulating and suppressing these antibody producing cells in the manufacture of antibodies.

IgE



Immunoglobulin E is found in very low concentration in human serum, but it increases during allergic reactions and some parasitic infections. IgE is bound to high affinity membrane receptors (FceRI) on mast cells in the tissue and basophils in the blood. Cross-linking of cell bound IgE by an allergen elicits the release of inflammatory mediators like histamine and several cytokines. IgE is also the main immunoglobulin responding to infection caused by certain parasites.

Blood Leukocytes



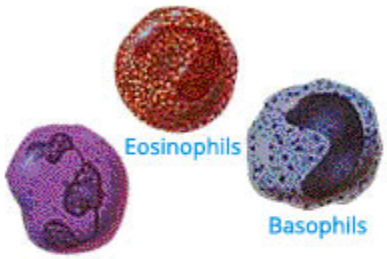
Leukocytes combat microbes by several mechanisms

White blood cells, or leukocytes, can be classified into five major categories based on morphological and functional characteristics. They may also be classified as granular or agranular based on the presence or lack of granules (small particles) within the cell cytoplasm. Leukocytes defend against invading microorganisms either by stimulating specific cellular or humoral (antibody production) immune responses, or by phagocytosis.

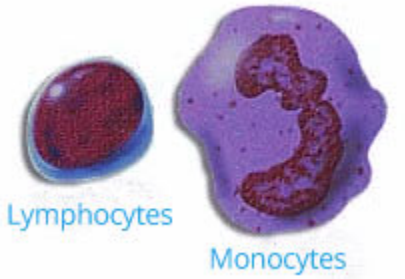
There are three types of granular leukocytes (granulocytes):

1. Neutrophils or polymorphonuclear leukocytes (PMNs)
2. Eosinophils
3. Basophils

Their names reflect the staining characteristics of the granules present in their cytoplasm. The name polymorphonuclear leukocyte also refers to the number of lobes comprising the nucleus of that cell type.



Neutrophils or polymorphonuclear (PMNs) leukocytes



Monocytes, the fourth group of leukocytes, have few granules and a typically kidney-shaped nucleus. In tissue, monocytes become macrophages. Macrophages are capable of surviving months to years thereby providing important immune surveillance within the tissue of the various organ systems.

The last major group of leukocytes includes the lymphocytes. They are agranular round cells, with a proportionally large nucleus. Lymphocytes are primarily responsible for adaptive or acquired immunity.

Granulocytes

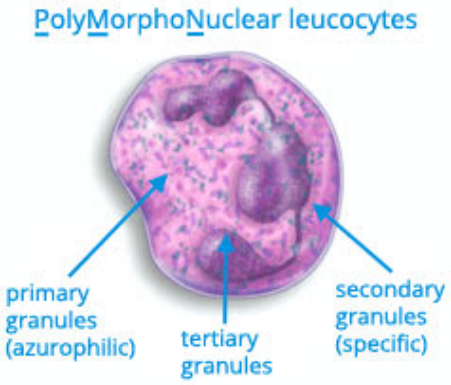
Neutrophils or PMNs are generally the first cells to migrate to the site of an invading microorganism or the site of trauma. This directed migration (chemotaxis) is caused by the release of signaling molecules called chemokines which can be released by several different cell types at the site of inflammation. The PMNs eliminate invaders by phagocytosis and other mechanisms. PMNs comprise 50-70% of the circulating leukocytes and more than 90% of the circulating granulocytes.

PMN's have three types of granules:

1. The primary or azurophilic granules are lysosomes that contain powerful digestive enzymes including acid hydrolases, elastase, myeloperoxidase and other proteins such as lysozyme and defensins.

2. Secondary or specific granules contain lactoferrin, lysozyme, collagenase and other proteins.

3. Tertiary granules contain gelatinase and other enzymes.



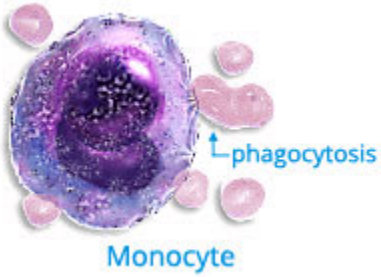
Eosinophils are involved in defense against parasitic infections and in control of allergic (hypersensitivity) reactions. Eosinophils comprise 1% to 3% of blood leukocytes.

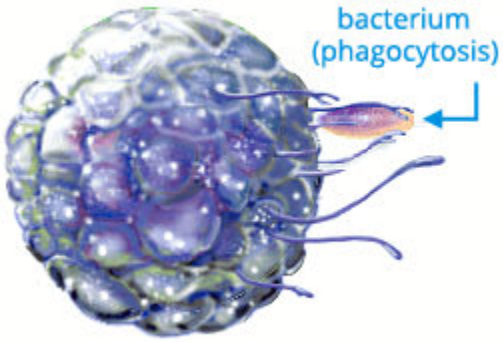
Circulating basophils comprise less than 1% of leukocytes. Granules in basophils contain heparin, histamine, and serotonin. When these (and other) chemicals are released from the cell, they cause an acute inflammatory response, which is why they are collectively called mediators of inflammation. Basophils are related to mast cells, which are found in the tissues only. Mast cells and basophils are the cells involved in immediate hypersensitivity (Type I) reactions (anaphylaxis).

Monocytes - Macrophages

Monocytes, which constitute 3-7% of leukocytes, are usually the second cell type to move to the site of injury or inflammation. Monocytes, like PMNs, can eliminate pathogens and debris by phagocytosis. After leaving the circulation, monocytes develop into tissue macrophages.

Macrophages are active against infectious agents by phagocytosis. They are also important antigen presenting cells that take up antigen and, after processing, present the antigen to lymphocytes. Thus, macrophages can help orchestrate the immune response.





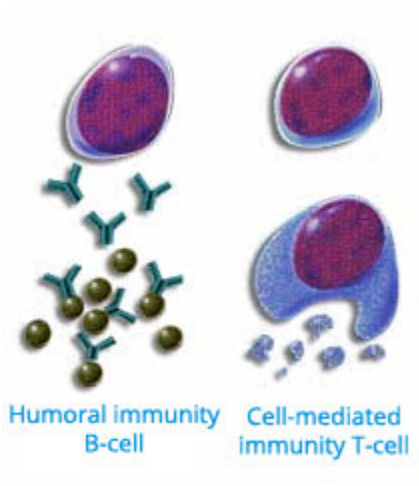
Lymphocytes

Lymphocytes comprise about 30% of the circulating leukocytes. Lymphocytes are involved in the development of adaptive or acquired immune responses. There are two major types of lymphocytes: T-cells and B-cells, both having surface receptors for antigen.

The Antigen-Antibody Reaction

When an antigen enters the body, two types of adaptive immune responses can occur:

- The synthesis and release of free antibody into the blood and other body fluids, called Humoral Immunity, is provided by B-cells.
- The production of sensitized lymphocytes called T-cells that are effectors of Cell-mediated Immunity.



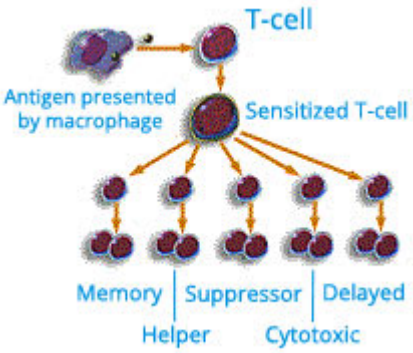
Cellular Immunity involving T-cells is effective against fungi, many parasites, intracellular bacteria, most viruses, cancer cells, and surgically transplanted or transfused foreign tissues. This is the type of response associated with graft rejection in transplant cases, and also with transfusion incompatibility.

Humoral Immunity, through circulating antibodies, is effective against extracellular organisms, including bacteria, some parasites, and some viruses.

Lymphocytes are produced in bone marrow from stem cells. A portion of the lymphocytic precursor cell population migrates to the thymus to mature into T-cells, while others are processed in the bone marrow to become B-cells. It should be mentioned that at 8-9 weeks of fetal development, B cells form in the liver but, soon after, the bone marrow becomes the primary site of production. The thymus gland and bone marrow are considered primary lymphoid organs while peripheral lymph nodes, mucous associated lymphoid tissue and the spleen are considered secondary lymphoid organs.

Maturity of T and B Cells

The T Cell:
T-cells mature in the thymus gland or in the lymph nodes. Since the thymus is only 10-15% functional in the adult, the lymph nodes take on greater importance in the maturation process.



Thymus Gland: T Cells migrating to the Thymus gland from the bone marrow will undergo a process of selection to eliminate not only the weakest cells, but also those so strong that they may attack healthy tissue cells (autoimmunity). Cells educated in the Thymus generally are either Helper (CD4+) or Suppressor/Cytotoxic (CD8+) cells. Other types of T-helper cells include T-helper 17, T regulatory cells, and T follicular helper cells.

Lymph Node: Naïve T cells in the paracortex of the lymph node may be activated by dendritic cells that have internalized and processed pathogenic antigens that made their way to the lymph node via lymphatic drainage from the site of infection or inflammation; or, by dendritic cells that have migrated to the lymph node from the site of infection. Once activated, T cells undergo clonal expansion and differentiate into functional effector cells (short-lived) or memory effector cells (long-lived). Functional effector cells migrate to the site of infection or inflammation where they orchestrate T helper (CD4+) or T cytotoxic/suppressor (CD8+) functions to combat pathogens. Memory cells may enter the circulation or healthy tissue sites, or remain in the lymph node.

The B Cell: B cells mature in the bone marrow or in the lymph node.

Bone Marrow: Mature B cells express antibodies on their surface, which are specific for a particular antigen. The antibodies are expressed on the cell surface and are primarily IgM with some IgD. These cells circulate in the blood or home to sites of infection or inflammation. However, until they are activated by T-cells, they do not proliferate or differentiate to form antibody producing Plasma Cells.

Lymph Node: Antigen-dependent B cells in the cortex of the lymph node may be stimulated by Helper T cells to proliferate and differentiate into Plasma Cells and memory cells. Immunoglobulin (antibody) class switching of the B cell from IgM to IgG, IgA or IgE may also take place as a result of the T cell interaction.

Learning Objectives

Upon completion of this topic, you should be able to:

- Define innate and adaptive or acquired immunity.
- Describe principal components of innate and acquired immunity.
- Compare and contrast the five classes of immunoglobulins.
- Name the major types of leukocytes.
- Discuss the origin, maturation, and function of T-cells and B-cells.

The Immune System - Key terms

IMMUNE SYSTEM:

A network of organs, glands, and tissues that protects the body from foreign substances.

IMMUNITY:

The condition of being able to resist a particular disease, particularly through means that prevent the growth and development or counteract the effects of pathogens.

IMMUNOLOGY:

The study of the immune system, immunity, and immune responses.

TISSUE:

A group of cells, along with the substances that join them, which form part of the structural materials in plants or animals.

GLAND:

A cell or group of cells that filters material from the blood, processes that material, and secretes it either for use again in the body or to be eliminated as waste.

LYMPH:

That portion of the blood that includes white blood cells and plasma but not red blood cells.

LYMPH NODES:

Masses of tissue at certain places in the body that act as filters for blood.

HEMOGLOBIN:

An iron-containing protein in red blood cells that is responsible for transporting oxygen to the tissues and removing carbon dioxide from them. Haemoglobin is known for its deep red colour.

ALLERGY:

A change in bodily reactivity to an antigen as a result of a first exposure. Allergies bring about an exaggerated reaction to substances or physical states that normally would have little significant effect on a healthy person.

WHITE BLOOD CELLS:

Blood cells that are colourless, lack haemoglobin, White blood cell, also called leukocyte or white corpuscle, a cellular component of the blood, is capable of motility, and defends the body against infection and disease by ingesting foreign materials and cellular debris.

In turn, **there** are three **types** of WBC—lymphocytes, monocytes, and granulocytes—and three main **types** of granulocytes (neutrophils, eosinophils, and basophils).

LEUCOCYTE:

a colourless cell which circulates in the blood and body fluids and is involved in counteracting foreign substances and disease; a white (blood) cell. There are several types, all amoeboid cells with a nucleus, including lymphocytes, granulocytes, and monocytes.

LYMPHOCYTE:

A type of white blood cell, varieties of which include B cells and T cells, or B lymphocytes and T lymphocytes.

B CELL:

A type of white blood cell that gives rise to antibodies. Also known as a *B lymphocyte.*

T CELL:

A type of white blood cell, also known as a *T lymphocyte,* that plays a key role in the immune response. T cells include cytotoxic T cells, which destroy virus-infected cells in the cell-mediated immune response; helper T cells, which are key participants in specific immune responses that bind to APCs, activating both the antibody and cell-mediated immune responses; and suppressor T cells, which deactivate T cells and B cells.

MONOCYTE:

A type of white blood cell that phagocytizes (engulfs and digests) foreign microorganisms.

PHAGOCYTE:

A cell that engulfs and digests another cell.

MACROPHAGE:

A type of phagocytic cell derived from monocytes. A type of white blood cell that surrounds and kills microorganisms, removes dead cells, and stimulates the action of other immune system cells.

PATHOGEN:

A disease-carrying parasite, usually a microorganism.

ANTIGEN:

A substance capable of stimulating an immune response or reaction. An antigen is any substance that causes your immune system to produce **antibodies** against it. This means your immune system does not recognize the substance and is trying to fight it off.
An **antigen** may be a substance from the environment, such as chemicals, bacteria, viruses, or pollen.

ANTIBODIES:

Proteins in the human immune system that help fight foreign invaders, especially pathogens and toxins.

MALT

The main sites of entry for microbes into the body are through mucosal surfaces. It is therefore not surprising that more than 50% of the total body lymphoid mass is associated with these surfaces. These are collectively called mucosa-associated lymphoid tissues (MALT) and include NALT, BALT, GALT and lymphoid tissue associated with the genitourinary system (see Section O).

NALT

The nasal-associated lymphoid system is composed of the lymphoid tissue at the back of the nose (pharyngeal, tonsil and other tissue) and that associated with the Waldeyer's ring (palatine and lingual tonsils). The strategic location of these lymphoid tissues suggests that they are directly involved in handling airborne microbes. Their composition is similar to that of lymph nodes but they are not encapsulated and are without lymphatics. Antigens and foreign particles are trapped within the deep crypts of their lympho-epithelium from where they are transported to the lymphoid follicles (*Fig. 1*). The follicles are composed mainly of B cells surrounded by T cells and the germinal center within the follicle is the site of antigen-dependent B cell proliferation.

GALT

The primary role of GALT is to protect the body against microbes entering the body via the intestinal tract. It is primarily made up of lymphoid aggregates and lymphoid cells (IELs) between epithelial cells and within the lamina propria. In order to distinguish between harmful invaders or harmless food, the gut has a 'sampling' mechanism that analyzes everything that has been ingested

BALT

Bronchus-associated lymphoid tissue is similar to Peyers patches. It is composed mainly of aggregates of lymphocytes organized into follicles that are found in all lobes of the lung and are situated under the epithelium mainly along the bronchi. The majority of lymphocytes in the follicles are B cells. Antigen sampling is carried out by epithelial cells lining the surface of the mucosa and by way of M cells which transport antigens to underlying APCs and lymphocytes.

MUCOSA-ASSOCIATED LYMPHOID TISSUES

MALT

The majority (>50%) of lymphoid tissue in the human body is located within the lining of the respiratory, digestive and genitourinary tracts, as they are the main entry sites for microbes into the body; subdivided into NALT, GALT and BALT.

NALT

Nasal-associated lymphoid tissue (NALT) includes immune cells underlying the throat and nasal passages and especially the tonsils. The architecture of these lymphoid tissues, although not encapsulated, is similar to that of the lymph nodes and consists of follicles composed mainly of B cells.

GALT

Gut-associated lymphoid tissue (GALT) is composed of lymphoid complexes (also called Peyer's patches in the ileum) that consist of specialized epithelium, antigen-presenting cells and intraepithelial lymphocytes. These structures occur strategically at specific areas in the digestive tract.

BALT

The lymphoid tissue associated with the bronchus (BALT) is structurally similar to Peyer's patches and other lymphoid tissues of the gut. It consists of lymphoid aggregates and follicles and is found along the main bronchi in the lobes of the lungs.