IMMUNOLOGY

3rd Year – Microbiology

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Introduction

The main function of our immune system is to protect us from infection in its various forms, and one of the greatest discoveries in medicine, immunization, was put into use and saved millions of lives one and half century before there were any real scientific understanding of the mechanism involved. But the immune system is a coin with two sides. For a few people, when the coin spins, it falls into the unfavorable side, and then instead of functioning purely as a protective mechanism, immune reactions harmful to the host are produced.

Because immune reaction can involve any system of the body, immunology has spread its roots into most branches of medicine. In addition of dealing with harmful conditions resulting from activity of the immune system, clinicians are now more involved than ever in dealing with patients who have diminished immune function.

Clearly therefore, an understanding of immunology leads to a wider appreciation of the role of the immune system in health and disease conditions such as tumors and hopefully in the future to improved management through immune therapy.

The Components of the Immune System

The function of the immune system is **to protect the body from damage caused by invading microorganisms**.

This function is carried out by the **lymphocytes**, **phagocytes**, and a number of **accessory cells** which are distributed through out the body but tend to cluster in lymphoid organs. The various cells interact with each other, producing a coordinated immune response.

Lymphocytes

Lymphocytes are derived from the **bone marrow stem cells,** which give rise to all blood cells, Figure 1.

Lymphocytes are the key cells controlling the immune response. They specifically recognize foreign material and distinguish them from the body's self components.

Lymphocytes recognize foreign material by means of specific surface receptor molecules called **antigen receptors.**

There are two major types of lymphocytes:

B-Lymphocytes: synthesize and secrete antibodies, which mediate humoral immune responses.

T-Lymphocytes: do not make antibodies but they participate in **cell-mediated immune responses.**

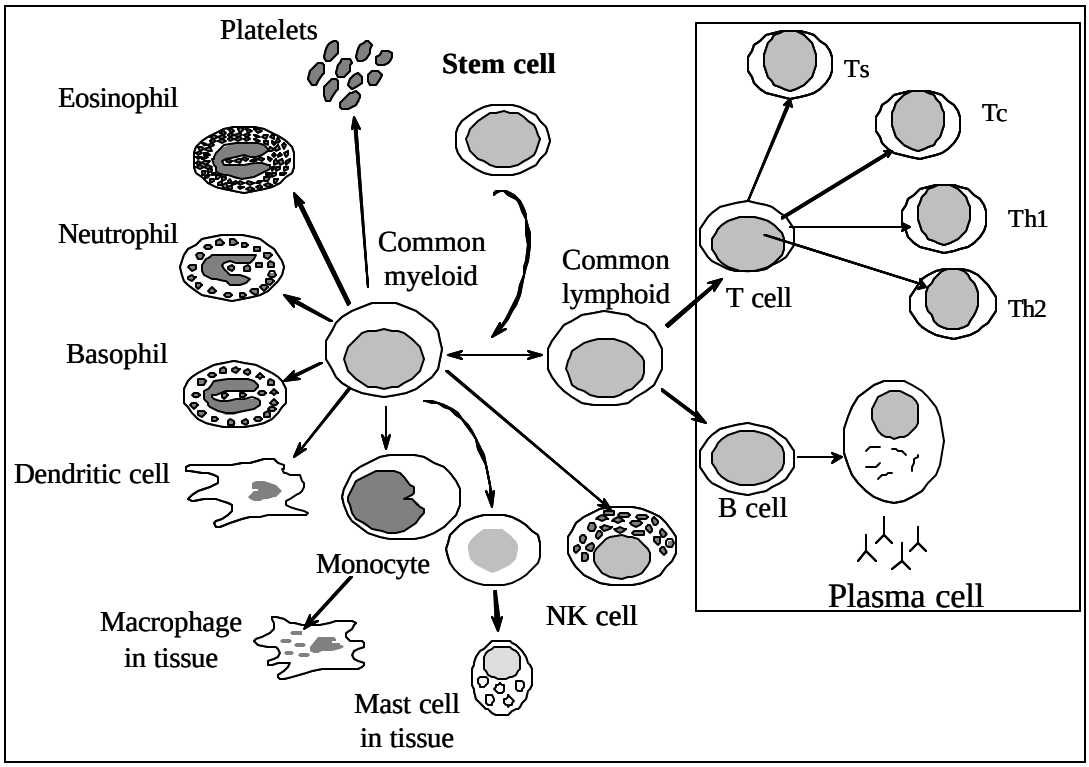


Figure 1: The cells of the immune system.

Functions and subpopulation of T lymphocytes

1- Cooperation with B cells to enhance the production of antibodies. Such T cells are called T-helper-2 (TH2).

2- **Inflammatory effects.** On activation, a certain T cell subpopulation induces the activation of monocytes and macrophages leading to **delayed-type hypersensitivity.** This subpopulation is called **T-helper-1 (TH1).**

3- **Cytotoxic effect.** The T cells in this subset become cytotoxic killer cells. These T cells are termed **T cytotoxic cells (Tc).**

4- **Regulatory effect.** Some T cells are able to suppress the immune response leading to **downward modulation** or a shutoff in reactivity of other cells. These cells are called **T-suppresser cells (Ts).**

5- **Signal via cytokines**. Cytokines are soluble mediators released by cells. Those released by lymphocytes are also termed **lymphokines**. Both helpers **(TH1, TH2)** subpopulation exert numerous effects on many cells through many cytokines that they release.

Phagocytes

Phagocytes include blood monocytes, macrophages and neutrophils. Their function is to take up pathogens, foreign material, and cell debris and break it down. This function is known as **phagocytosis.**

Phagocytic cells contain granules (lysosomes) filled with hydrolytic enzymes. They also produce peroxide and superoxide radicals that are toxic to many microorganisms. Some granules also contain bactericidal proteins such as Lactoferrin, Figure 2.

Macrophages constitute an essential part of the immune system. They include a variety of histologic forms that are included in the so called reticuloendothelial system (RES**).** In general macrophages have three major functions:

They **engulf and destroy** particulate materials and antigens by a process known as **phagocytosis.** Thus these cells play a key role in the removal of bacteria and parasites from the blood.

2. Antigen presentation.

3. cytokine production.

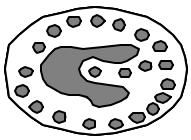
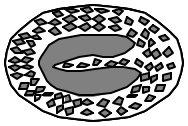
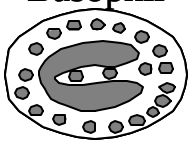
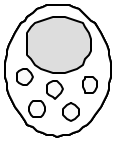
Cells	Function of activated cells
Macrophage 	Phagocytosis, Antigen presentation Cytokine production
Neutrophil 	Phagocytosis and activation of bactericidal mechanisms
Eosinophil 	Killing of antibody coated parasites
Basophil 	As mast cells
Mast cell 	Release of granules containing histamine and other active agents

Figure 2: The phagocytes and some accessory cells.

Accessory cells

Accessory cells include Eosinophils, Basophils, Mast Cells, Platelets, and Antigen Presenting Cells.

Eosinophils have a role in damaging parasites and controlling inflammation.

Basophil, Mast Cells, and Platelets contain a variety of molecules which mediate inflammation. They are thus important in linking immune responses and inflammatory reactions.

The function of the **Antigen Presenting Cells (APC)** is to take up antigen, process it, and present it to T cell. Antigen presenting cells include several cell types such as **Dendritic Cells** in lymph nodes and **Langerhans Cells** in the skin which present antigen to lymphocytes.

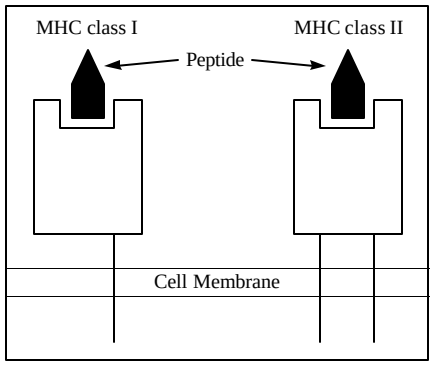


Figure 3: MHC molecules display peptide fragments of antigens on the surface of antigen presenting cell.

These cells express on their surface proteins referred to as **MHC class 1 and class II molecules**, coded for by **genes of the major histocompatibility complex (MHC).** The outer extracellular par of every MHC class I and MHC class II molecules contains a groove that functions as the peptide - binding site.

Lymphatic organs

The lymphatic organs are those organs where **lymphocyte maturation, differentiation, and proliferation take place**.

The lymphoid organs are generally divided into two categories:

1- The **primary or central lymphoid organs** are those in which the maturation of T and B lymphocytes into antigen-recognizing lymphocytes occurs.

2- The **secondary lymphoid organs** are those organs in which antigen-driven proliferation and differentiation take place.

Primary lymphoid organs

T and B lymphocytes develop in primary lymphoid organs. Their initial development-maturation process is independent of antigen. There are two major primary lymphoid organs, one in which the T cells develop and the other in which the B cell develop, Figure 4.

1- **The Thymus gland**. Progenitor cells from the bone marrow migrate to the thymus gland where they differentiate into T-lymphocytes.

2- **Bone marrow**. B cells differentiate from stem cells in the fetal liver. After birth and for the life of the individual this function moves to the bone marrow.

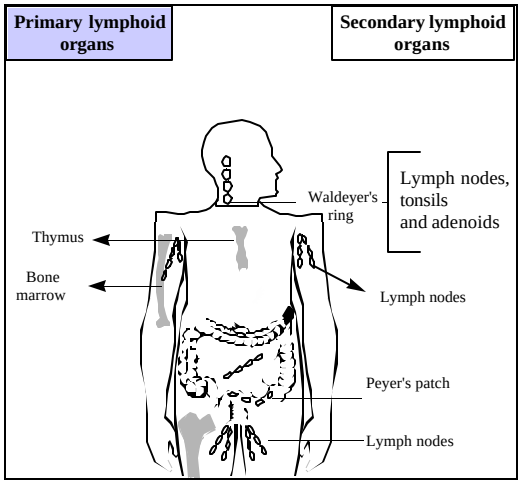


Figure 4: The distribution of lymphoid tissues in the body.

Secondary lymphoid organs

The major secondary lymphoid organs are the **spleen** and **lymph nodes**. In addition tonsils, appendix, cluster lymphocytes distributed in the lining of small intestines (payer's patches), as well as lymphoid aggregates spread through out mucosal tissues are considered secondary lymphoid organs, Figure 4.

The secondary lymphoid organs have two major functions:

1- They are highly efficient in trapping and concentrating foreign substances.

2- They are the main sites of production of antibodies and the generation of antigen specific T lymphocytes.

The spleen

The spleen is the major organ in the body in which antibodies are synthesized and from which they are released into circulation.

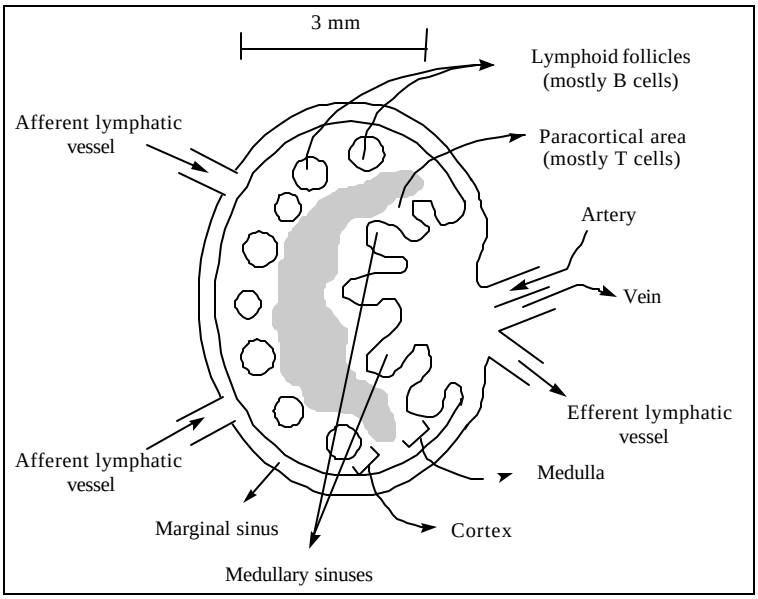


Figure 5: A schematic overview of a lymph node.

Lymph nodes

The **lymph nodes** are highly organized lymphoid structures that are the sites of convergence of an extensive system of vessels that collect the extracellular fluid

from tissues and return it to the blood. The fluid is called **lymph**, and the vessels that carry it **lymphatic vessels**.

The **afferent lymphatic vessels** which drain fluid from the tissues also carry antigens from sites of infection in most parts of the body to the lymph nodes, where they are trapped.

In the lymph nodes, B lymphocytes are localized in **follicles**, with T cells more diffusely distributed in the surrounding **paracortical areas**. Some of the B cells follicles contain central areas called **germinal centers**, where B cells are undergoing intense proliferation after encountering antigen, Figure 6.

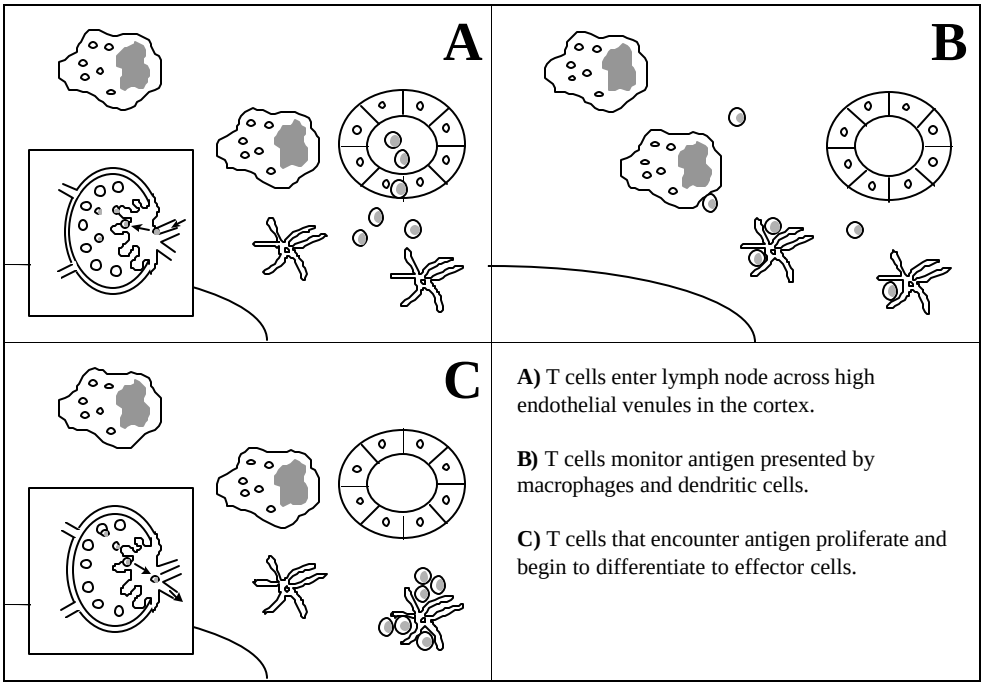


Figure 6: Naïve T cells encounter antigen during their recirculation through lymphoid organs.

The fate of antigen after penetration

Three major routes may be followed by an antigen after is has penetrated the interior of the body:

The antigen may enter the body through the blood stream. In this case, it is carried to the spleen.

The antigen may lodge in the epidermal or subcutaneous tissue. From these tissues the antigen is transported into the regional draining lymph node.

The antigen may enter the gastrointestinal or respiratory tract where it lodges in the mucosa associated lymphoid tissue (MALT).