Doctor 021

IMMUNOLOGY

Sheet no. 1

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IMMUNOLOGY

Immunology is defined as the study of the immune system, including its responses to microbial pathogens and damaged tissues and its role in disease, and is a very important branch of the medical and biological sciences. The immune system protects us from infection through various lines of defense.

Immunity is defined as resistance to disease, specifically infectious diseases. The collection of cells, tissues, and molecules that mediate resistance to infections is called the **immune system**, and the coordinated reaction of these cells and molecules to infectious microbes comprises an **immune response**.

The main function of the immune system is to provide resistance against any foreign body such as viruses, bacteria, prions and fungi. Individuals with immune deficiency are always exposed to various infections. Conversely, stimulating immune responses against microbes through vaccination is the most effective method for protecting individuals against infections.

It is important to understand that the **immune system will resist** any foreign body, even if this body does not belong to microbes or viruses, for example: if any cell of your body turned into a cancer cell, the immune system will kill it. Therefore, the immune system can harm your body. For instance, the immune system in some cases resists bacteria in an excessive way, so it might cause your body more harm than bacterial poisons.

- Microbiology and immunology science established 150 years ago.
- Microbiology science began after the invention of the microscope by Antoni van Leeuwenhoek.
- In ancient times, people thought that the cause of any disease is **poisonous air**, because they noticed that diseases spread in areas containing trash.

Effectiveness of vaccination for some common infectious diseases.

Role of the immune system	Implications
Defense against infections	Deficient immunity results in increased susceptibility to infections; exemplified by AIDS Vaccination boosts immune defenses and protects against infections
Defense against tumors	Potential for immunotherapy of cancer
The immune system can injure cells and induce pathologic inflammation	Immune responses are the cause of allergic, autoimmune, and other inflammatory diseases
The immune system recognizes and responds to tissue grafts and newly introduced proteins	Immune responses are barriers to transplantation and gene therapy

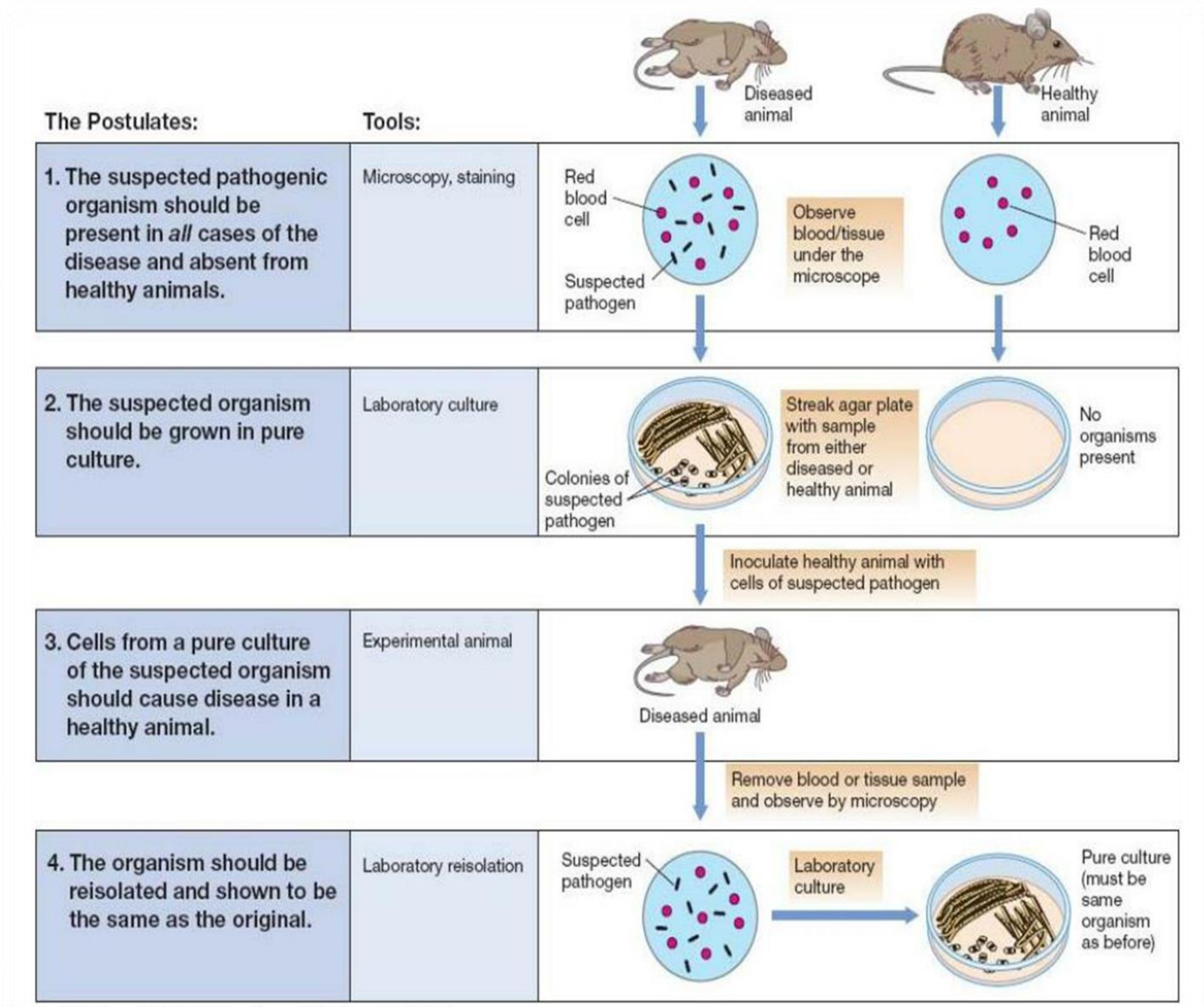
HISTORY OF IMMUNOLOGY

- **Pasteur** is renowned for his discoveries of the principles of vaccination, microbial fermentation and **pasteurization**, he was responsible for disproving the doctrine of spontaneous generation.

- **Robert Koch** was one of the main founders of modern bacteriology. He identified the specific causative agents of tuberculosis, cholera and anthrax and gave experimental support for the **concept of infectious disease (**germ theory), which included experiments on humans and other animals.

- In the final decades of the 19th century, Koch conclusively established that a particular germ could cause a specific disease. He did this by experimentation with anthrax. Using a microscope, Koch examined the blood of cows that had died of anthrax. He observed rod-shaped bacteria and suspected they caused anthrax. When Koch infected mice with blood from anthrax-stricken cows, the mice also developed anthrax. This led Koch to list four criteria to determine that a certain germ causes a particular disease. These criteria are known as Koch's Postulates and are still used today.

Koch's Postulates



Source: Madigan, Martinko, Dunlap and Clark, p. 15 (2009).

- **Paul Ehrlich** and others, , recognized that a specific antigen elicited the production of a specific antibody. Ehrlich hypothesized that these antibodies were specialized molecular structures with specific receptor sites that fit each pathogen like a lock and key. Thus, the first realization that the body had a specific defense system was introduced.

- The most important scientists in immunology are **Paul Ehrlich** and **Élie Metchnikoff.**

- The idea that specific cells could be directly involved with defending the body was first suggested in 1884 by Élie Metchnikoff.

IMMUNOLOGY INTRODUCTION

- The immune system includes the role of **physical barriers** (e.g.: -**skin cells tightly backed, full of keratin)**, **cellular**, and **chemical systems** (**molecular systems)** that are in place and that respond to all aspects of **foreignness.**

How can we determine that something is foreign? Basically, through their antigens.

The immune system works in three processes symbolled "R"s:-

1- Recognize, 2- Restore, 3- Remember

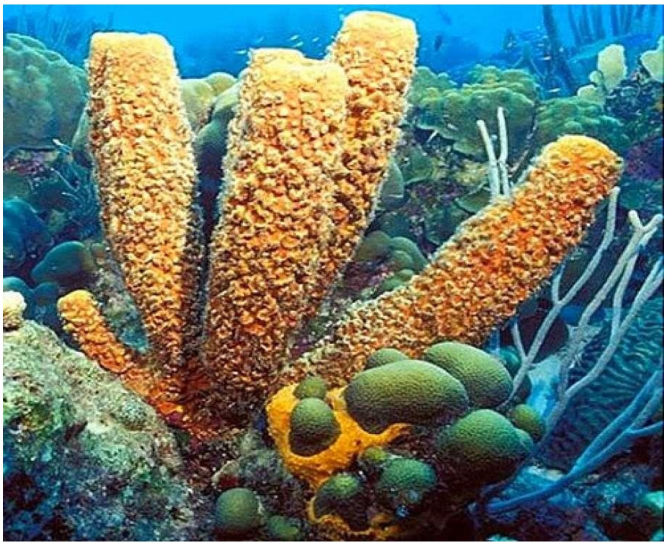
- The immune system targets any "foreign" object, so the first step is to **recognize** what is self and non- self.
- The second step is to **restore** homeostasis by eliminating the foreign object.
- The third step is to **remember** the invading pathogen to respond better the next time it is encountered.

The immune system is required to memorize the pathogen, in order to response faster and expend less energy. "Remembering" part isn't available in all organisms.

- The immune system is not **only** active when danger arises, but is constantly sensing danger and **is important for normal physiology and homeostasis** similar to the cardiovascular and renal systems**.**

Some simple organisms like: See Sponges and See Cucumbers have non-specific immune response similar to humans.

- Transplantation of parts of sponge to other sponges is met by an immune response.

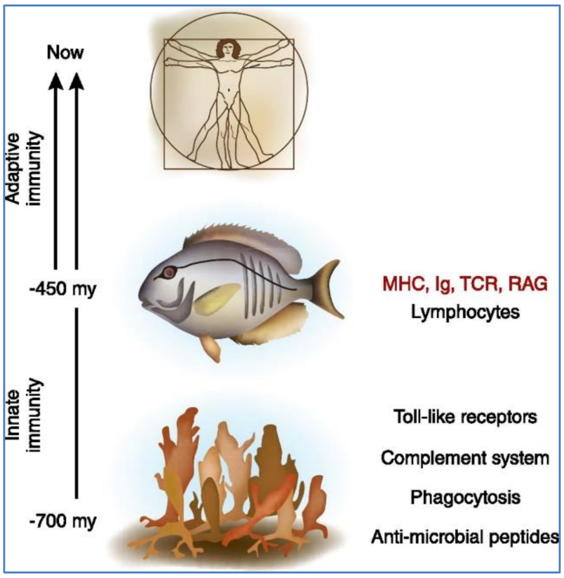


- Mechanisms for discriminating "**self" from "non-self"** evolved to accomplish the task of fighting pathogens, launching a long history of **host-pathogen co-evolution.**

- Virtually all organisms have at least one form of defence that helps repel disease-causing organisms.

- Pathogens evolve new strategies to overcome immune mechanisms, and so the host defence becomes more complex to defend against invading pathogens.

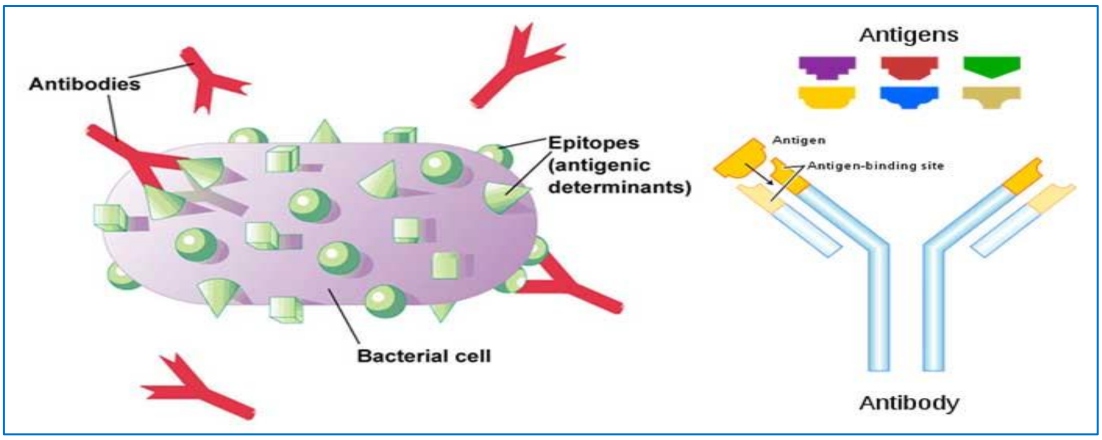
- **Jawed vertebrates** have developed higher complexity of defence reflected in the **adaptive immune response**.



- Why the simple organisms have a **less complex immune system than the more complex organisms**?
  - ➢ With time, the immune system **becomes more complex because of the huge number of pathogens**, and as a result, both the pathogens and the immune system are always becoming more complex.

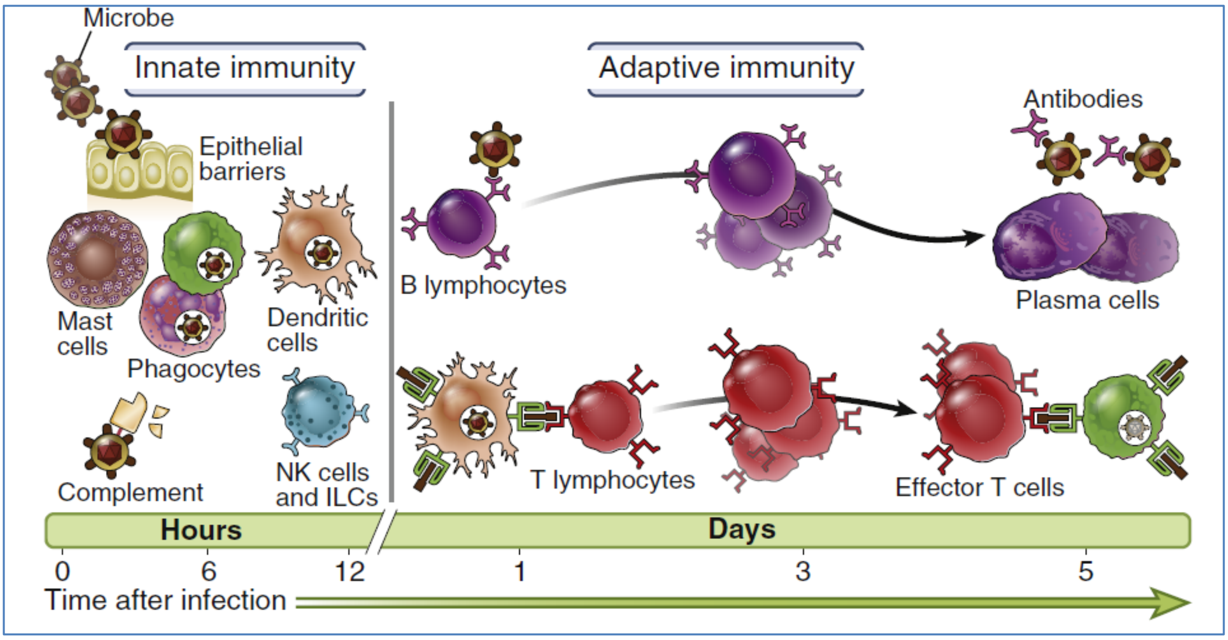
- **Antigens** are any substance that stimulates the immune system to produce **antibodies**. **Antigens** can be bacteria, viruses, or fungi that cause infection and disease.

- **Antigens** may also originate from within the body ("self-antigen"), but should not be attacked by the immune system in normal situations.



Note: Antigen: antibody generating molecule.

INNATE AND ADAPTIVE IMMUNITY



- Host defenses are grouped under innate immunity, which provides immediate protection against microbial invasion, and adaptive immunity, which develops more slowly and provides more specialized defense against infections

- The immune system is subdivided into Innate immunity and adaptive immunity.

❖ INNATE IMMUNITY

- The innate immunity responses non-specificly to any danger signals within hours and restore homeostasis. It's fast and non-specific.
- The innate immunity isn't as important as the adaptive immunity because sometimes the innate response needs the adaptive response.
- The Innate immune system is active all the time and is non-specific, if it can't overcome the microbes, the adaptive immune system will be activated.

❖ ADAPTIVE IMMUNITY

- The adaptive immunity is very specific and slowly takes about 10-14 days to develop antibodies.
- The adaptive immunity is quiet silent, it needs a signal from the innate immunity to be active.

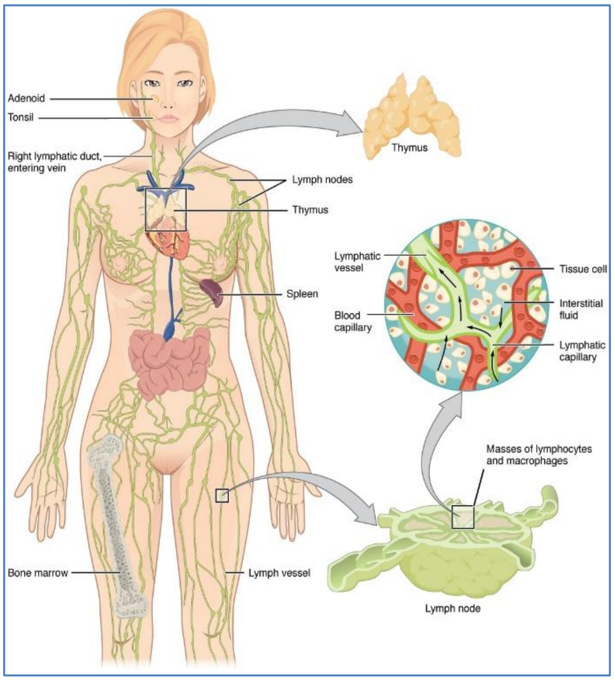
	Innate immunity	Adaptive Immunity
Components	 1. Physical and chemical barriers 2. Phagocytic leukocytes 3. Dendritic cells 4. Natural Killer cells 5. Plasma proteins (complement)	 1. Humoral immunity (B cells, which mature into antibody secreting plasma cells) 2. Cell-mediated immunity (T cells, which mature into effector helper and cytotoxic T cells)
Activity	Always present	Normally silent
Response and potency	Immediate response, but has a limited and lower potency	Slower response (over 1-2 weeks, but is much more potent
Specificity	General: can recognize general classes of pathogens (i.e. bacteria, viruses, fungi, parasites) but cannot make fine distinctions	Recognizes highly specific antigens
Course	Attempts to immediately destroy the pathogen, and if it can't, it contains the infection until the more powerful adaptive immune system acts.	Slower to respond; effector cells are generally produced in 1 week and the entire response occurs over 1-2 weeks. However, this course can vary somewhat during different responses in an individual.

LOCATION OF THE IMMUNE SYSTEM

- The immune system duty is to survey the whole body so it should be present everywhere.
  - (Because we can have pathogens anywhere in the body so the immune system must exist everywhere).
- But there are **sites where immune cells collect to fulfil their function** (e.g. lymph nodes).
  - Every tissue has immune cells, but they mainly exist in the circulation.

- For example, in the small intestine there is lymphatic tissue that surveys intestinal pathogens called Peyer's patches.

- The bone marrow is an important place for generation of immune and non-immune blood cells.



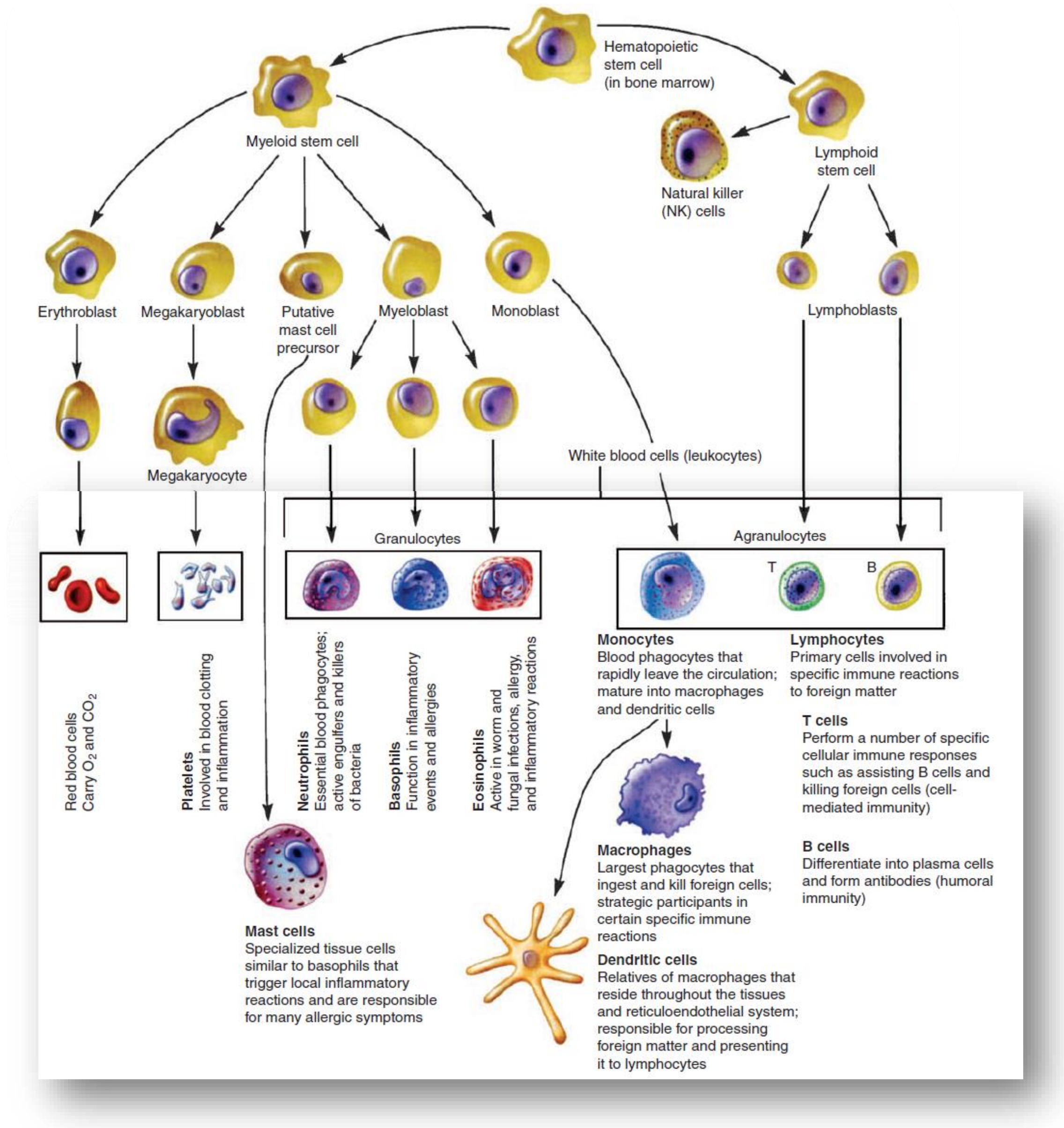
CONCLUSION

- Immunology is a relatively **recent science** with **applications** that extend to other medical sciences, thus it is important for medical students.
- The immune system in an **ancient** defence mechanism composed of tissues, cells and molecules that interact with each other with **great complexity**.
- Parts of the immune system are continuously active, and help in maintaining **homeostasis**.
- Specialized immune cells are mainly in the **bone marrow** and then circulate the blood or aggregate in lymph nodes.
- The immune system arms can be divided in general into **innate** and **adaptive**.

CELLS OF THE IMMUNE SYSTEM

- The cells of the immune system originate from the **bone marrow**, in the bone marrow there are **stem cells** which can differentiate into **lymphoid stem** cells and **myeloid stem cells**.
- The most common cells of the immune system can be categorized as lymphocytes (T cells, B cells, and NK cells), neutrophils, and monocytes/ macrophages. These are all types of white blood cells.

- The cells of the innate and adaptive immune system are normally present as circulating cells in the blood and lymph, as anatomically defined collections in lymphoid organs, and as scattered cells in virtually all tissues.



- The stem cells in the bone marrow can differentiate into **lymphoid stem cells** and **myeloid stem cells**, depending on the signal type that is received.

- The **lymphoid stem cells** differentiate into **Natural Killer (NK) cells, B cells and T cells** which are adaptive immune cells.

- The Natural Killer cell is non-specific immune cell so it's from the Innate cells.

- The **myeloid stem cells** differentiate into:
  - **Erythroblasts** which give the RBCs.
  - **Megakaryocytes** give the platelets.

TYPES OF THE IMMUNE CELLS

We will be discussing about four types of immune cells.

- **Phagocytes.**
- **Mast Cells, Basophils, Eosinophils**
- **Antigen-Presenting Cells.**
- **Lymphocytes.**

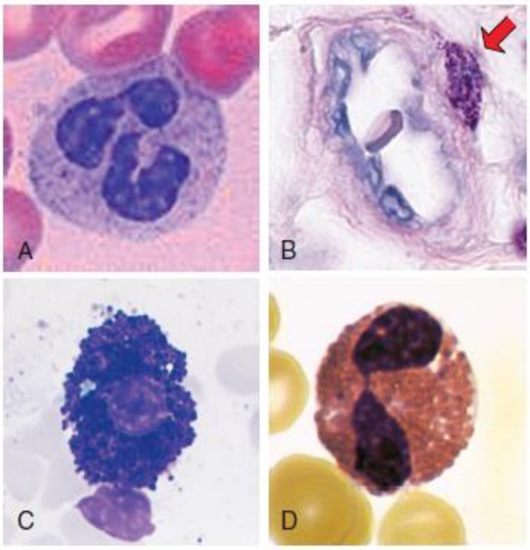


FIGURE 2–1 Morphology of neutrophils, mast cells, basophils, and eosinophils. A, The light micrograph of a Wright-Giemsa–stained blood neutrophil shows the multilobed nucleus, because of which these cells are also called polymorphonuclear leukocytes, and the faint cytoplasmic granules. **B,** The light micrograph of a Wright-Giemsa–stained section of skin shows a mast cell *(arrow)* adjacent to a small blood vessel, identifiable by the red blood cell in the lumen. The cytoplasmic granules in the mast cell, which are stained purple, are filled with histamine and other mediators that act on adjacent blood vessels to promote increased blood flow and delivery of plasma proteins and leukocytes into the tissue. *(Courtesy of Dr. George Murphy, Department of Pathology, Brigham and Women's Hospital, Boston, Massachusetts.)* **C,** The light micrograph of a Wright-Giemsa–stained blood basophil shows the characteristic blue-staining cytoplasmic granules. *(Courtesy of Dr. Jonathan Hecht, Department of Pathology, Brigham and Women's Hospital, Boston, Massachusetts.)* **D,** The light micrograph of a Wright-Giemsa–stained blood eosinophil shows the characteristic segmented nucleus and red staining of the cytoplasmic granules.

TABLE 2–1 Normal Blood Cell Counts

	Mean Number per Microliter	Normal Range
White blood cells (leukocytes)	7400	4500-11,000
Neutrophils	4400	1800-7700
Eosinophils	200	0-450
Basophils	40	0-200
Lymphocytes	2500	1000-4800
Monocytes	300	0-800

- Although most of these cells are found in the blood, their responses to microbes are usually **localized to tissues.**