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IMMUNOLOGY

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Immunology

The most important function of the immune system is resisting against any foreign body, so people who have 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.

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.**

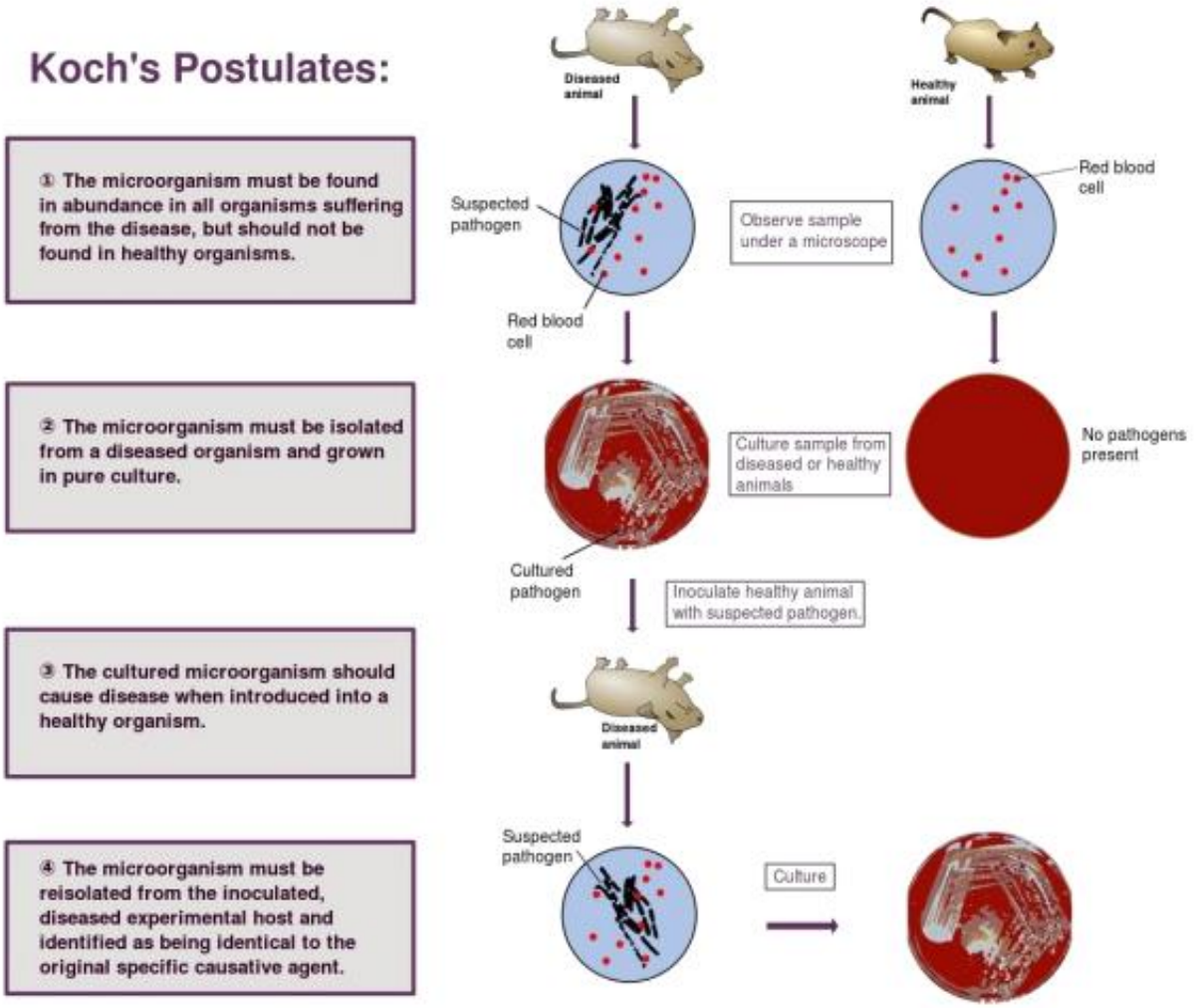
It is important to understand that the immune system will resist any foreign body, even if this body does not belong to microbes or viruses, for example: if any cell of your body turned into a cancer cell, the immune system will kill it. Therefore, the immune system can harm your body.

Immunology is the study of the immune system, including its responses to microbial pathogens and damaged tissues and its role in disease.

History of Immunlogy :-

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.



- **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

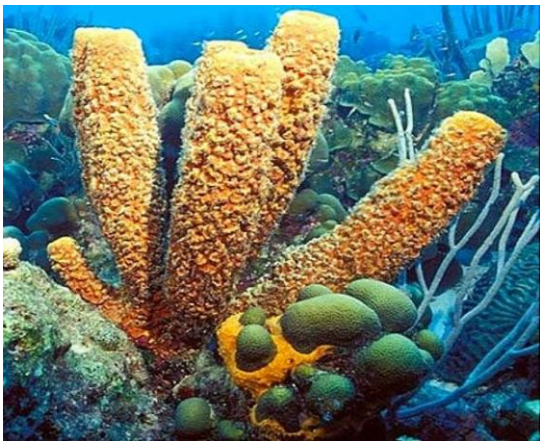
Immunology introduction:-

- 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 tell that something is foreign?
- Through their antigens
- The immune system works in three “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.
- Why the immune system needs to remember the pathogen?
- To respond faster and expend less energy.
- This "remember" part isn’t in all the organisms.
- Any living organism needs an immune system to help them fight against pathogens.

- 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.

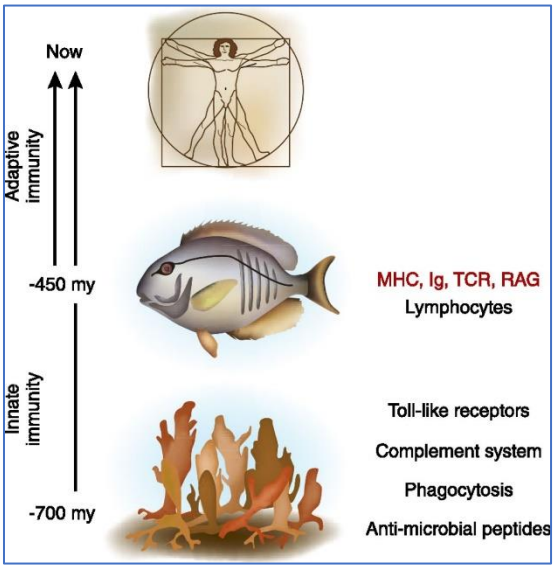
Some simple organisms like: See Sponges and See Cucumbers have non-specific immune response similar to humans.

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.

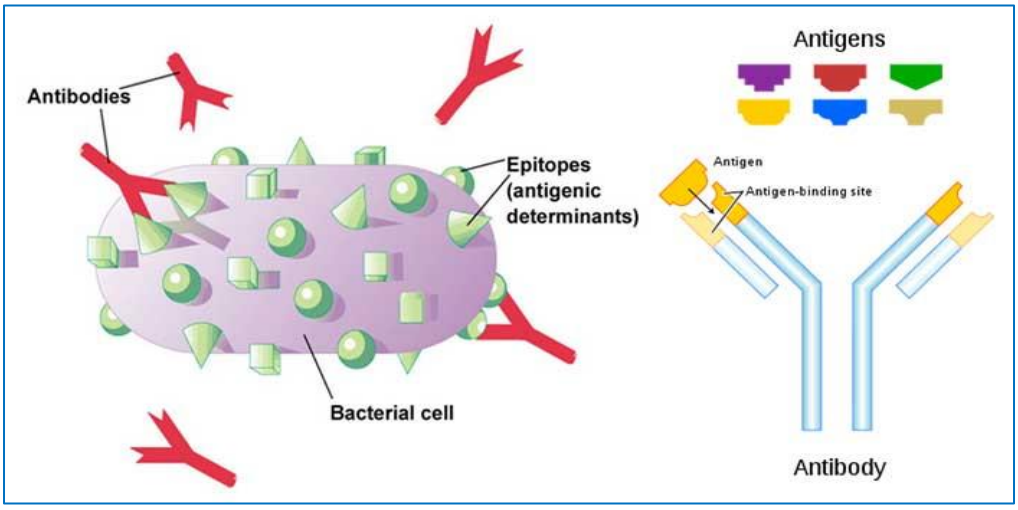


- Pathogens evolve new strategies to overcome immune mechanisms, and so the host defence becomes more complex to defend against invading pathogens.

- **All Jawed vertebrates** have developed higher complexity of defence reflected in the **adaptive immune response**. (their immmune system can remember the pathogenes).

  - **Why the simple organisms have a less complex immune system than the more complex organisms?**

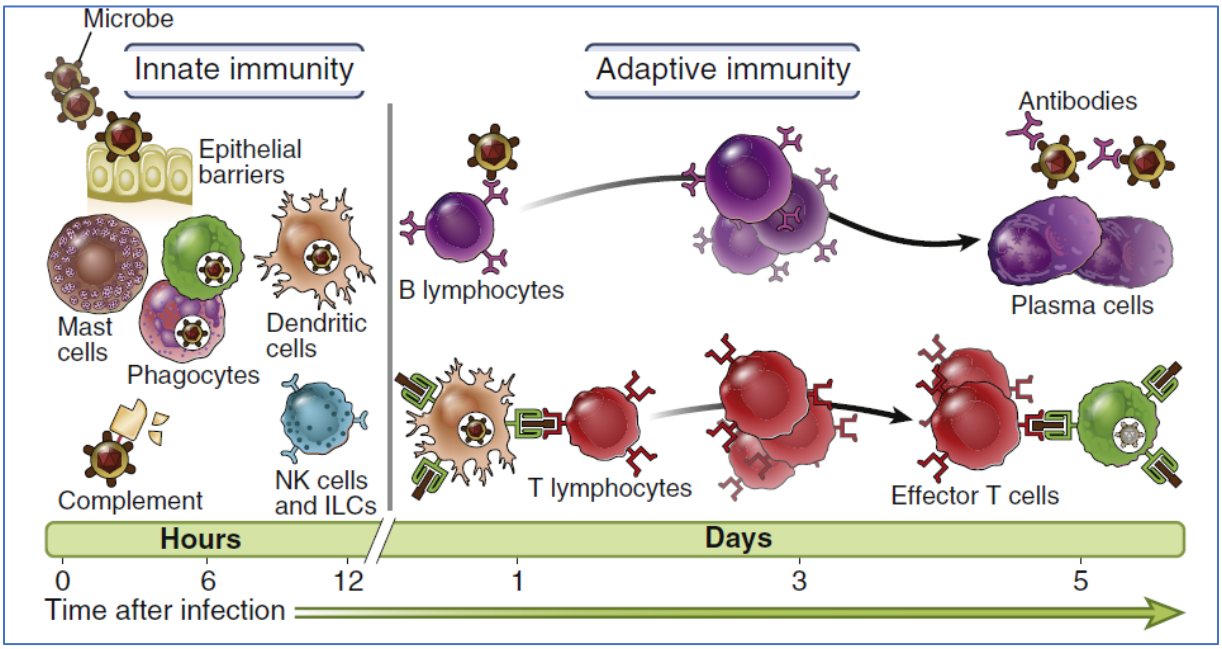
  - With time, the immune system becomes more complex because of the huge number of pathogens, and as a result, both the pathogens and the immune system are always becoming more complex.



Antigen: antibody generating molecule.

- **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.

Innate and Adaptive Immunity:-



- Host defences are grouped under **innate** immunity, which provides **immediate** protection against microbial invasion, and **adaptive** immunity, which develops **more slowly** and provides more specialized defence against infections.
- The immune system is divided into **innate immuntity** and **adaptive 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 respone 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.

- The adaptive immuntiy 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 .

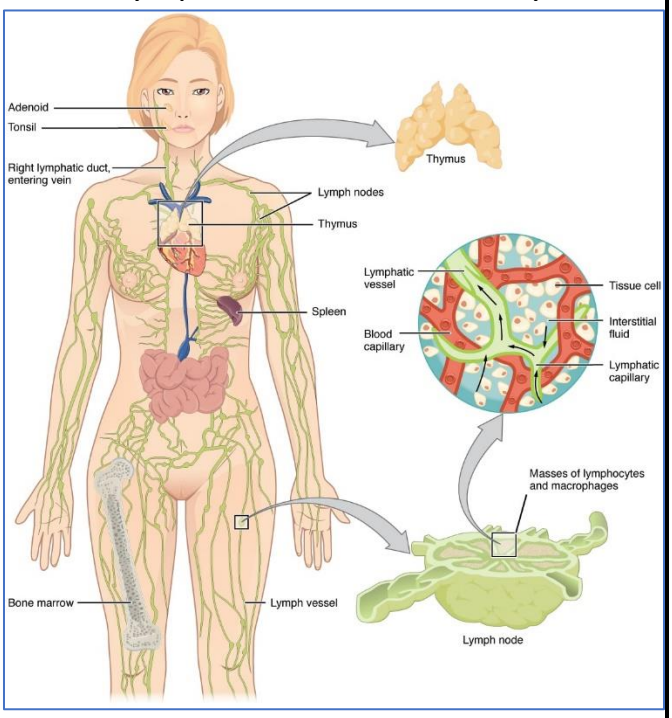
	Innate immunity	Adaptive Immunity
Components	 1. Physical and chemical barriers 2. Phagocytic leukocytes 3. Dendritic cells 4. Natural Killer cells 5. Plasma proteins (complement)	 1. Humoral immunity (B cells, which mature into antibody secreting plasma cells) 2. Cell-mediated immunity (T cells, which 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 are aggregated to fulfil their function (e.g. lymph nodes).**
- Every tissue has immune cells but the majority of the immune cells are in the circulation.

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

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



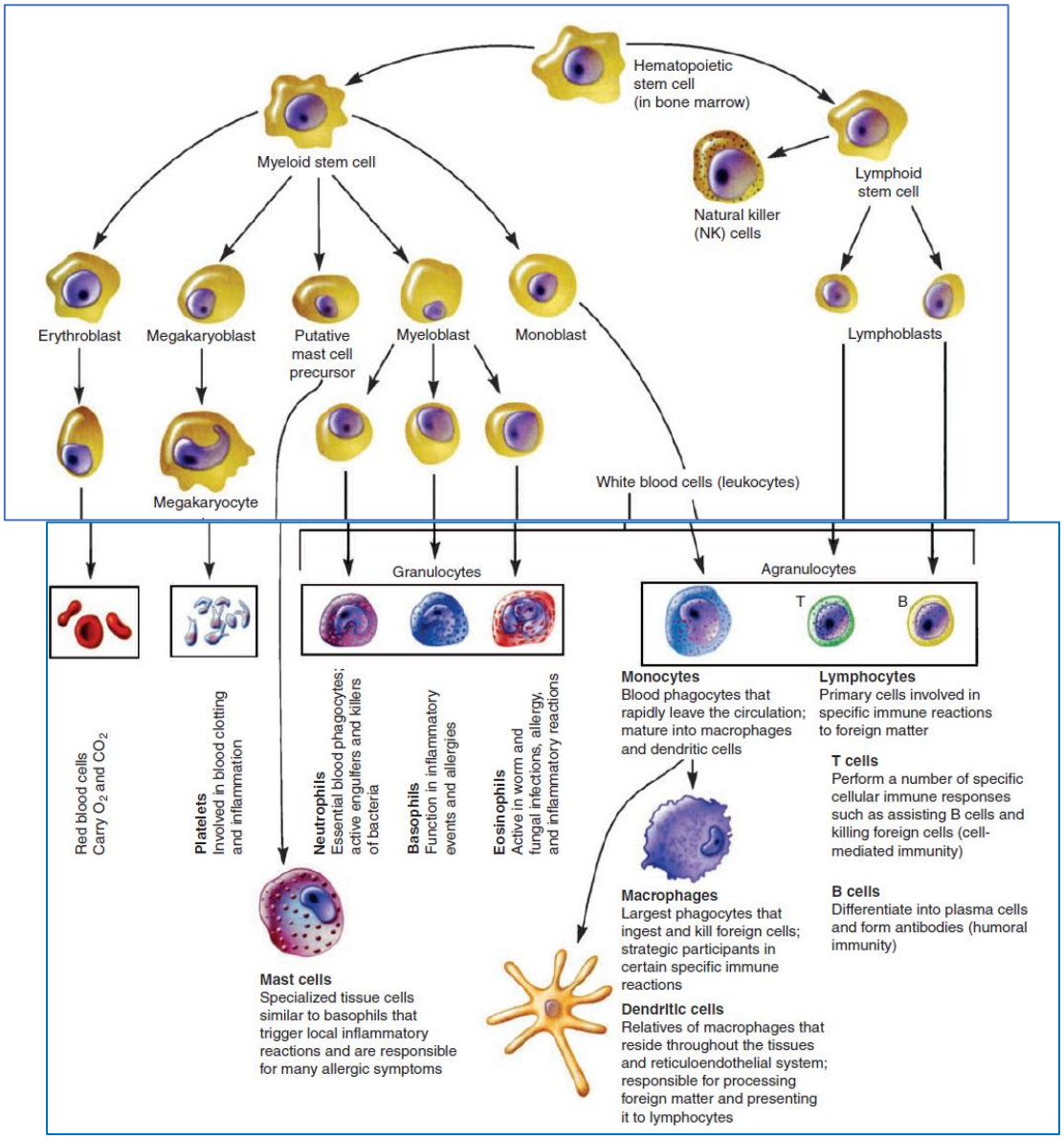
Conclusions:-

- 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 they circulate in the blood or aggregate in lymph nodes.
- The **immune system arms** can be divided in general into **Innate** and **Adaptive**

Cell 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 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.

And so on… * look at the figure in the previous page (IMPORTANT) ↑↑

We will talk about 4 types of the immune cells: -

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

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

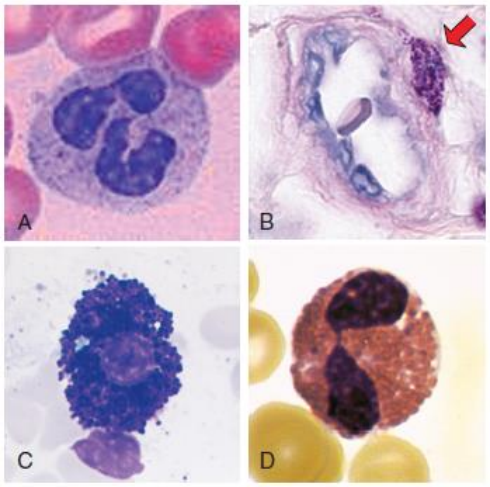


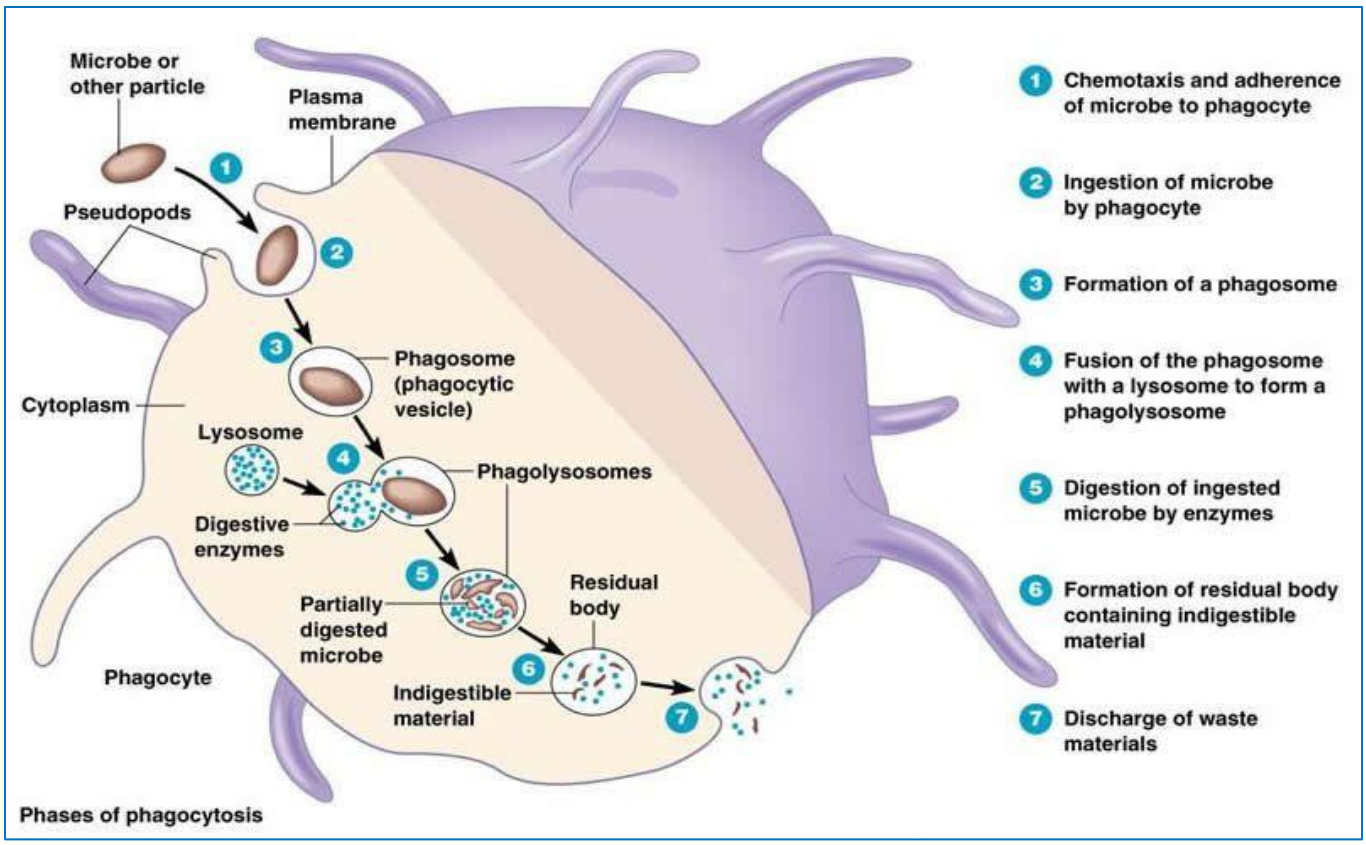
FIGURE 2–1 Morphology of neutrophils, mast cells, basophils, and eosinophils. A, The light micrograph of a Wright-Giemsa–stained blood neutrophil shows the multilobed nucleus, because of which these cells are also called polymorphonuclear leukocytes, and the faint cytoplasmic granules. **B,** The light 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.

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

Phagocytes: -

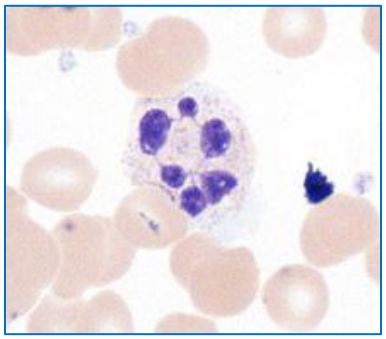
- **Phagocytes**, including **neutrophils** and **macrophages**, are cells whose primary function is to identify, ingest, and destroy microbes.
- Phagocytes also communicate with other cells in ways that promote or regulate immune responses.

The mechanism of phagocytosis is explained in the picture:

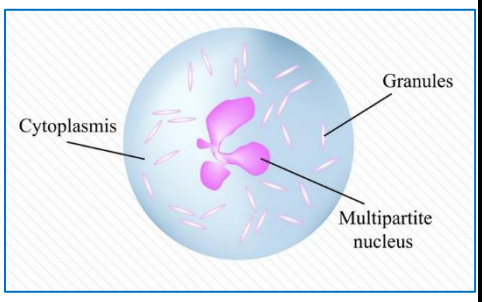


*Extra info about Chemotaxis:
Chemotaxis is the movement of the cell that is directed in response to an extracellular chemical stimulus, it is clearly an advantage for bacteria to be able to carry out chemotaxis, since by it they can avoid unfavourable conditions and seek optimum surroundings. Chemotaxis involves dynamic remodelling of cytoskeleton.

Neutrophils: -



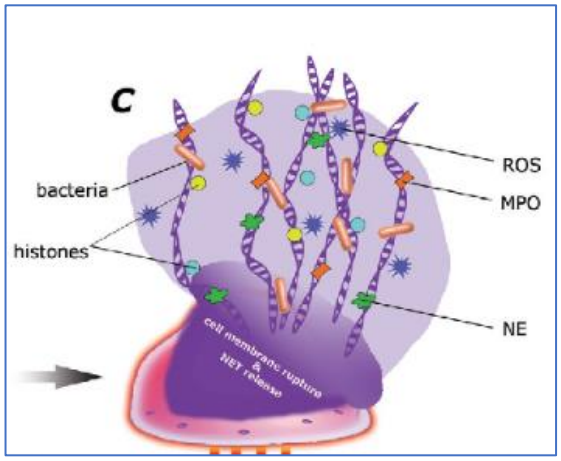
- Neutrophils, also called **polymorphonuclear leukocytes,** are the most abundant population of circulating white blood cells and mediate the earliest phases of inflammatory reactions.
- **Polymorphonuclear leukocytes → white blood cell with many shapes of the nucleus.**
- The nucleus of a neutrophil is **segmented** into 3-5 connected **lobules.**

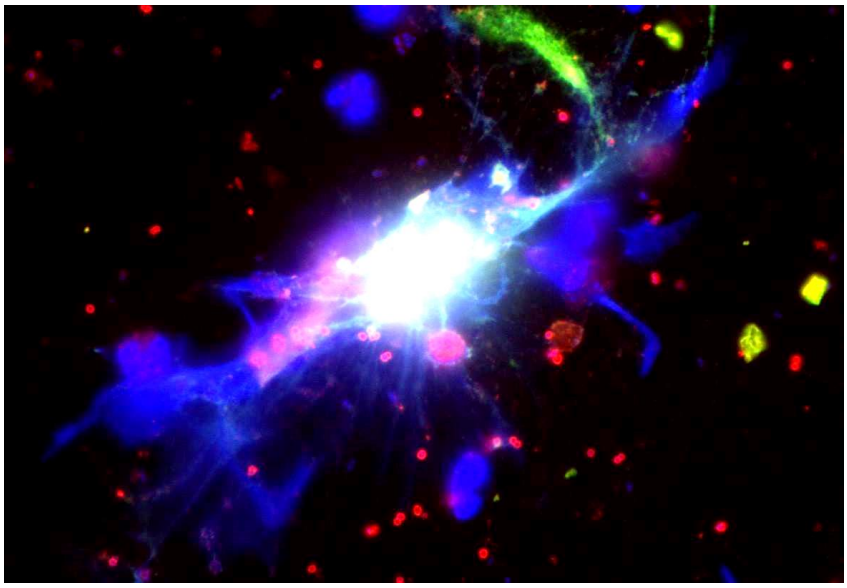


- **Have a Short lifespan,** they circulate for about 6 hours.
  The Production of neutrophils is **stimulated by granulocyte colony-stimulating factor (G-CSF)**. An adult human produces more than 1×10^{11} neutrophils per day.
- **They are the most abundant cells in the circulation.**
- **They mediate the earliest phases of inflammatory reactions** (They arrive firstly at the site of injury).

- **The cytoplasm contains granules of two types**. The majority, called **specific granules**, are filled with enzymes such as **lysozyme** (breaks down the bacterial cell wall), **collagenase**, and **elastase** and these enzymes are important because when the neutrophils enter the tissue, they need to penetrate the ECM and reach the site of infection, so these enzymes help the cell to move easily in the tissue.
- The remainder are **azurophilic granules**, which are lysosomes-containing enzymes and other microbicidal substances.
- Neutrophils may migrate to sites of infection **within a few hours** after the entry of microbes.
- After entering tissues, neutrophils function for a few hours and then die.

Also, the neutrophil has a mechanism that is discovered recently, it is called **Neutrophil Extracellular Traps (NETs)**. Scientists have found that some neutrophils ,when they arrive to the site of infection, **get** their DNA (which is inside the nucleus around the histone proteins) out the cell, and when the DNA gets outside the nucleus, it will cover a large area and bind to the microbe and kill it.





Their DNA contains certain proteins, enzymes and Radical Oxygen Species (ROS) that can kill the microbe.

- ✓ **Neutrophil Extracellular Traps (NETs) are networks of extracellular fibers, primarily composed of DNA from neutrophils, which bind to pathogens.**

تم بحمد الله

The End