Immunology

Dr. Ekhlas M. Idan & Dr. Zahra'a A. Ahmed

University of Baghdad / College of Science for Women/
Department of Biology

This influx causes swelling and other physiological changes that collectively are called inflammation. Such local innate and inflammatory responses usually are beneficial for eliminating pathogens and damaged or dead cells and promoting healing.

- Increased levels of antimicrobial substances and phagocytic cells help to eliminate pathogens, and dendritic cells take up pathogens for presentation to lymphocytes, activating adaptive immune responses.
- Despite the multiple layers of the innate immune system, some pathogens may evade the innate defenses leading to the activation of adaptive immune responses (B and T lymphocytes), which generate antibodies, and effector T cells that specifically recognize and neutralize or eliminate the invaders.

➢ Innate immunity

Innate immunity is an immediate response to a pathogen that does not confer long-lasting protective immunity. It is a nonspecific defense system and includes barriers to infectious agents, such as the skin (epithelium) and mucous membranes. It also includes many immune components important in the adaptive immune response, including phagocytic cells, natural killer (NK) cells, toll-like receptors (TLRs), cytokines, and complement.

The epithelial cell layer has tight junctions and produces a number of powerful antimicrobial peptides that help provide protection against invading pathogens. Lysozyme is an example of an antimicrobial peptide that dissolves some bacterial cell walls. Another major peptide of innate host defense with antimicrobial properties is defensin. Defensins are positively charged peptides located primarily in the gastrointestinal tract and lower respiratory tracts that create holes in bacterial cell walls and hence disrupt the bacterial membrane.

The mucosal epithelium of the respiratory tract offers another mode of protection from infection. Mucus, a complex mixture of mucins, proteins, proteases, and protease inhibitors, is a major component of the mucosal epithelium. The presence of mucus limits bacterial adhesion to these cell surfaces. Also, once entrapped in the mucus, the bacteria are removed by ciliary clearance.

Thus, the mucosal surface and the ciliated epithelial cells tend to inhibit microbial adhesion and limit exposure time. Likewise, the gastrointestinal tract has mechanisms to inhibit bacteria. The acidity of the stomach and the proteolytic enzymes of the small intestine make this environment hostile to many bacteria.

In addition, to the physiologic barriers of protection, the innate system has both **cells and proteins** (such as cytokines and complement). Phagocytic leukocytes, such as polymorphonuclear neutrophilic (PMN) leukocytes (neutrophils), and macrophages along with NK cells are the primary cellular components to combat microbes. The interaction of the invading microbe with these cells and other cells throughout the body triggers the release of complement and numerous cytokines.

- **Cellular Components and Phagocytosis**

Granulocytes are at the front lines of attack during an immune response and are considered part of the innate immune system.

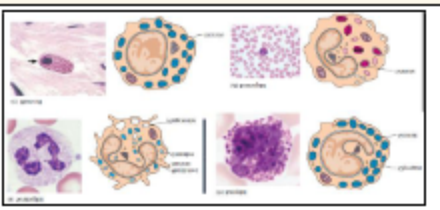
Granulocytes are white blood cells (leukocytes) that are classified as **neutrophils, basophils, mast cells, or eosinophils** based on differences in cellular morphology and the staining of their characteristic cytoplasmic granules.

All granulocytes have multilobed nuclei that make them visually distinctive and easily distinguishable from lymphocytes, whose nuclei are round. The cytoplasm of all granulocytes is replete with granules that are released in response to contact with pathogens.

These granules contain a variety of proteins with distinct functions: Some damage pathogens directly; some regulate the trafficking and activity of other white blood cells, including lymphocytes; and some contribute to the remodeling of tissues at the site of infection.

Examples of proteins in neutrophil, eosinophil, and basophil granules

Cell type	Molecule in granule	Function
Neutrophil	Proteases	Tissue remodeling
	Antimicrobial proteins	Direct harm to pathogens
	Protease inhibitors	Regulation of proteases
Eosinophil	Ribonucleases	Vasodilation, basophil degranulation
	Cytokines	Antiviral activity
	Chemokines	Modulation of adaptive immune responses
		Attract leukocytes
Basophil/Mast Cell	Cytokines	Modulation of adaptive immune response
	Lipid mediators	Regulation of inflammation
	Histamine	Vasodilation, smooth muscle activation



During infection, circulating **phagocytic cells** increase. Any antigen (microorganism) that enters the body through the lymphatics, lung, or bloodstream is engulfed by phagocytic cells. Therefore, phagocytes, present in the blood, lymphoid tissue, liver, spleen, lung, and other tissues, are the cells responsible for the uptake and removal of foreign antigen.

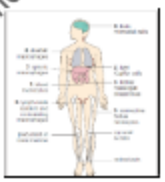
Phagocytes include (1) monocytes and macrophages (2) neutrophils and (3) dendritic cells.

Neutrophils have a short half-life and are important phagocytic cells that destroy pathogens within intracellular vesicles. **Eosinophils and basophils** are less abundant and store granules containing enzymes and toxic proteins that can be released upon activation of the cells.

Monocytes are circulate in the blood and mature into macrophages that can be found in almost all tissues. For example, they are known as Kupffer cells in the liver and microglial cells in the nervous tissue.

Macrophages are essential cells that engulf and kill pathogens, process and present antigens, and regulate immune reactivity by producing a variety of molecules (eg, cytokines).

Dendritic cells are also phagocytic and can degrade pathogens; however, their main role is to activate T cells in the adaptive immune response by acting as an antigen-presenting cell and by producing regulatory cytokines.



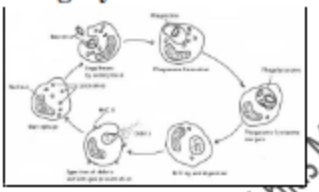
Phagocytosis is a multistep process whereby a phagocytic cell recognizes the pathogen, ingests it, and then destroys the engulfed organism.

Once a pathogen enters the blood or tissue, the phagocytic cell (ex: neutrophils) migrates to that site. This migration is dependent on the release of chemoattractant signals produced by cells of the host. One chemoattractant is IL-8 (CXCL8), a potent chemotactic cytokine, which attracts neutrophils to peripheral tissues.

In the initial stage of the migration process, neutrophils attach to the endothelial cell surface through adhesion molecules, such as P-selectin. Neutrophils follow the chemokine attraction and migrate from the circulation through the endothelium into the tissues and to the site of infection.

Here the neutrophil recognizes, engulfs, and internalizes the pathogen into an endocytic vesicle called a phagosome. Once inside the neutrophil, the pathogen is killed.

Phagocyte Mobilization



The phases of phagocytosis

1. Chemotaxis; **2.** Contact and ingestion (formation of a phagosome); **3.** Formation of phagolysosome (lysosome fuse with phagosome); **4.** Microbe is killed and then digested by lysosomal enzymes; **5.** Release of debris from cell.

- Phagocytosis can occur without antibody. However, phagocytosis is more efficient when antibodies are available to coat the surface of bacteria and

facilitate their ingestion. This process is called **opsonization**, and it can occur by the following mechanisms:

1. Antibody alone can act as opsonin.
2. Antibody and antigen can trigger the complement system (via the classic pathway) to generate opsonin.
3. opsonin may be produced when the alternative pathway is activated and C3 is generated.

Macrophages have receptors on their membranes for the **Fc portion** of an antibody and for the **complement component C3**. Both of these receptors facilitate the phagocytosis of the antibody coated pathogen.