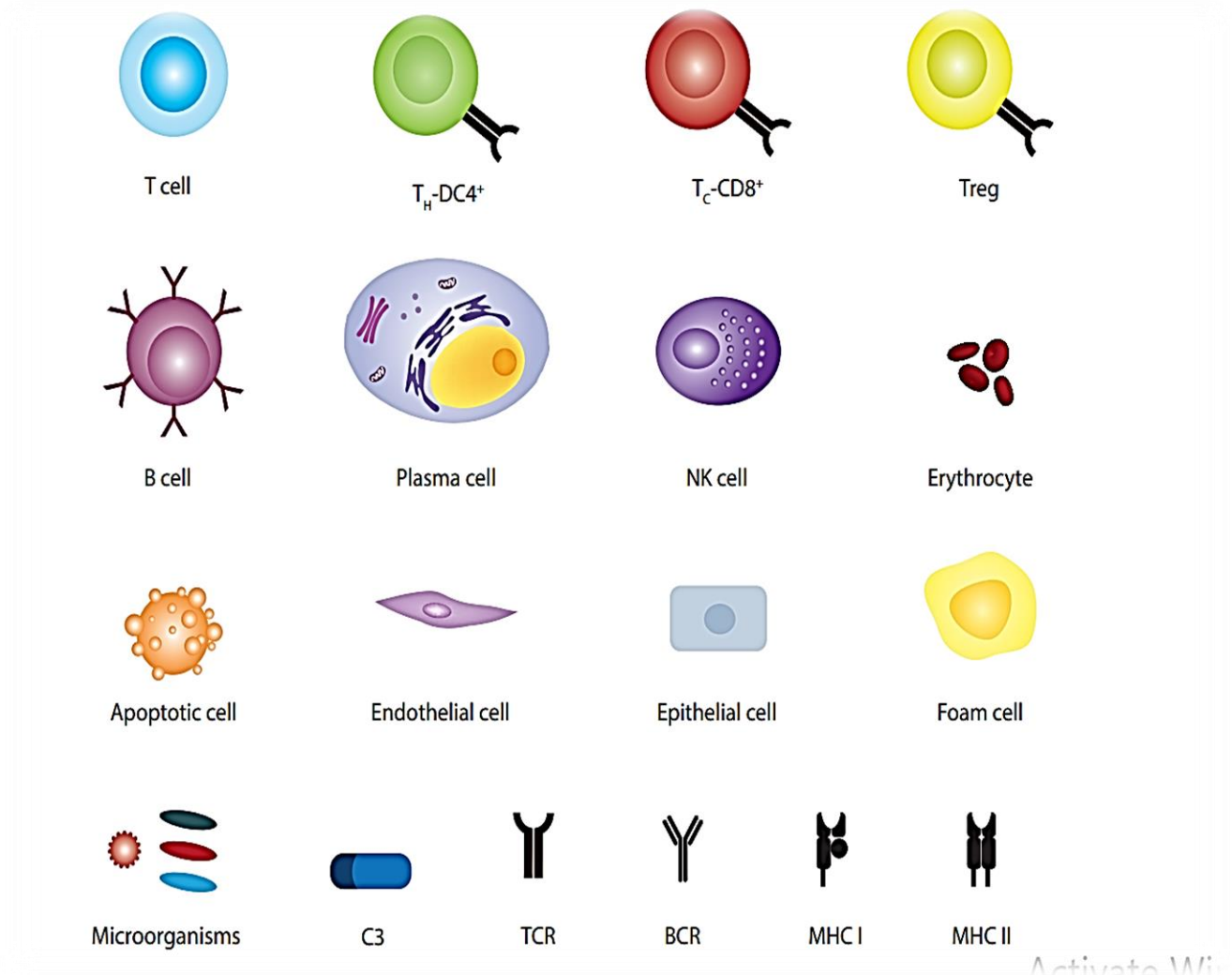


Lect.3 Cells of the Immune System

By Dr. Agharid Ali Hussein



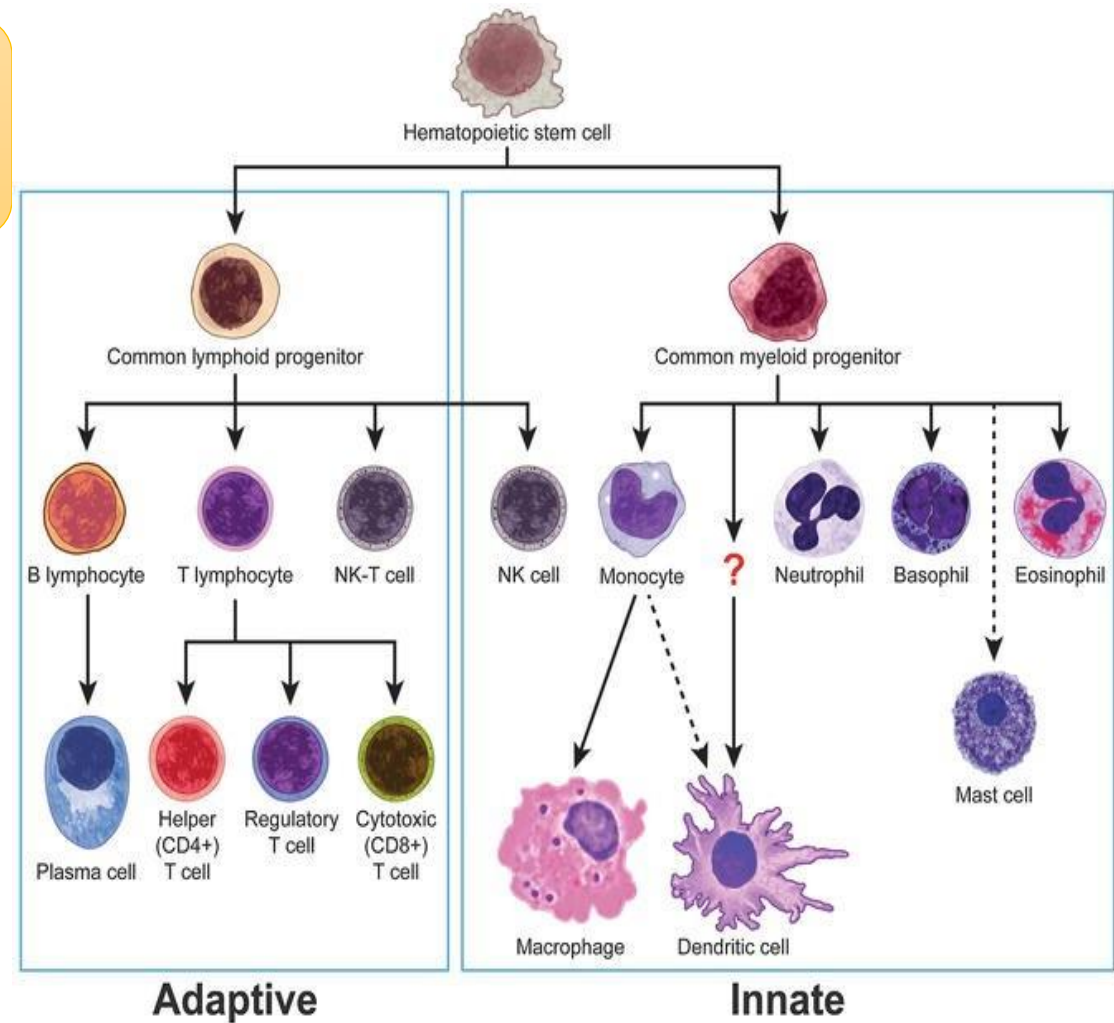
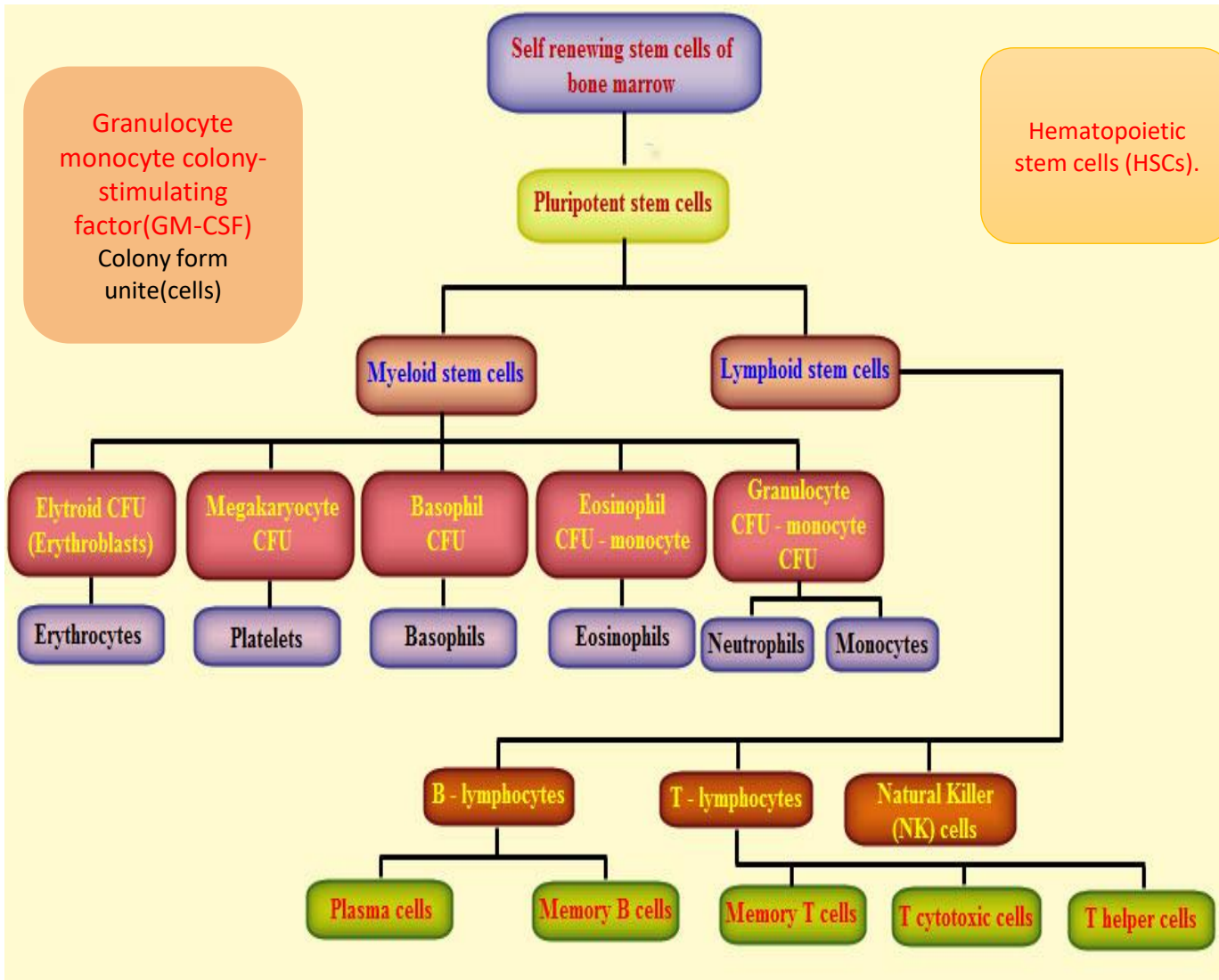
CELLS OF IMMUNE SYSTEM

- **The cells that serve specialized roles in innate and adaptive immune responses are phagocytes, dendritic cells, antigen specific lymphocytes, and various other leukocytes that function to eliminate antigens.**
- **The numbers of some of these cell types in the blood are listed in Table 1.**
- **Although most of these cells are found in the blood, their responses to microbes are usually localized to tissues and are generally not reflected in changes in the total numbers of circulating leukocytes.**

	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

ORIGINS OF IMMUNE SYSTEM CELLS

- **Stem cells are undifferentiated cells that divide continuously and give rise to additional stem cells and to cells of multiple different lineages of hematopoietic system.**
- **The stem cells that form blood and immune cells are known as hematopoietic stem cells (HSCs).**
- **They are ultimately responsible for the constant renewal of blood and the production of billions of new blood cells each day. Origins of cells of hematopoietic and immune systems are as below**



CELLS OF NON-SPECIFIC IMMUNE SYSTEM(Myeloid lineage)

- **Non-specific immune response is the first line of defense to remove the infection, when a microorganism enters the body, it is trapped and destroyed by phagocytes.**
- **Phagocytes belong to two complementary systems: neutrophils and macrophages.**

Neutrophils and macrophages, are cells whose primary function is to identify, ingest, and destroy microbes.

1. The functional responses of phagocytes in host defense consist of sequential steps:

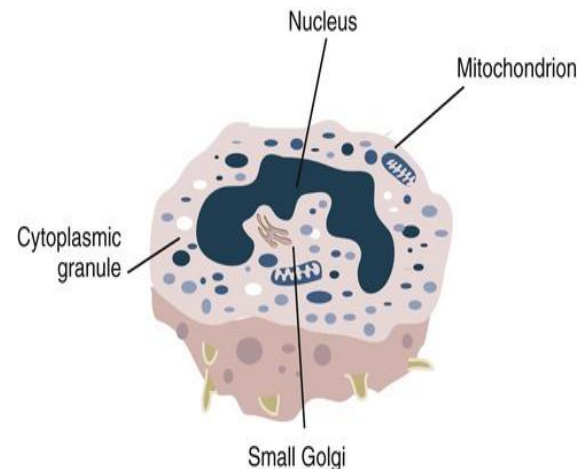
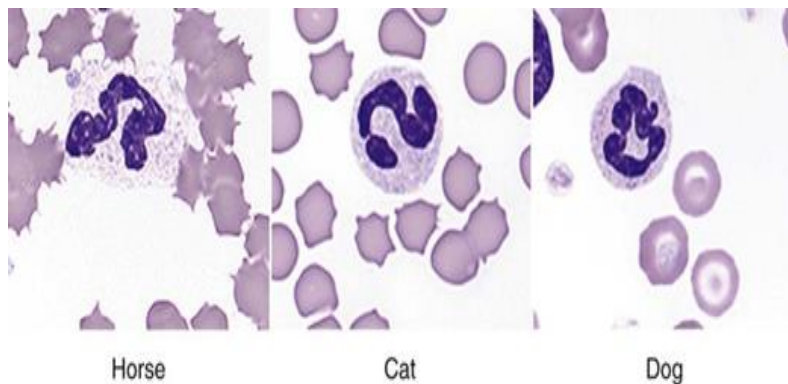
- **Recruitment of the cells to the sites of infection,**
- recognition of and activation by microbes,
- ingestion of the microbes by the process of phagocytosis,
- and destruction of ingested microbes.

2. In addition, through direct contact and by secreting proteins, phagocytes communicate with other cells in ways that promote or regulate immune responses

Neutrophils

Neutrophils, also called polymorphonuclear leukocytes, are the most abundant population of circulating white blood cells and mediate the earliest phases of inflammatory reactions.

Neutrophils circulate as spherical cells about 12 to 15 μm in diameter with numerous membranous projections. The nucleus of a neutrophil is segmented into three to five connected lobules, hence the synonym polymorphonuclear leukocyte (Fig.1). The cytoplasm contains granules of two types. The majority, called specific granules, are filled with enzymes such as lysozyme, collagenase, and elastase. These granules do not stain strongly with either basic or acidic dyes (hematoxylin and eosin, respectively), which distinguishes neutrophil granules from those of two other types of circulating granulocytes, called basophils and eosinophils. The remainder of the granules of neutrophils, called azurophilic granules, are lysosomes containing enzymes and other microbicidal substances, including defensins and cathelicidins



(Fig.1 : 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 pale cytoplasmic granules

Mononuclear Phagocytes

1. **The mononuclear phagocyte system consists of cells whose primary function is phagocytosis and that play central roles in innate and adaptive immunity.**
2. **The cells of the mononuclear phagocyte system originate from a common precursor in the bone marrow, circulate in the blood, and mature and become activated in various tissues.**
3. **The cell type in this lineage that enters the peripheral blood from the marrow is incompletely differentiated and is called the monocyte.**
4. **Monocytes are 10 to 15 μm in diameter, and they have bean-shaped nuclei and finely granular cytoplasm containing lysosomes, phagocytic vacuoles, and cytoskeletal filaments.**
5. **Monocytes are heterogeneous and consist of at least two subsets, which are distinguishable by cell surface proteins and kinetics of migration into tissues.**
6. **One population is called inflammatory because it is rapidly recruited from the blood into sites of tissue inflammation.**
7. **The other type may be the source of tissue resident macrophages and some dendritic cells.**
8. **monocytes mature when once they enter tissue and become macrophages.**

Macrophages

Macrophages in different tissues have been given special names to designate specific locations. For instance, in the central nervous system, they are called microglial cells; when lining the vascular sinusoids of the liver, they are called Kupffer cells; in pulmonary airways, they are called alveolar macrophages; and multinucleate phagocytes in bone are called osteoclasts. Macrophages perform several important functions in innate and adaptive immunity.



1. **A major function of macrophages in host defense is to ingest and kill microbes. The mechanisms of killing, include the enzymatic generation of reactive oxygen and nitrogen species that are toxic to microbes, and proteolytic digestion.** In addition to ingesting microbes, macrophages also ingest dead **host cells as part of the cleaning up process after infection or sterile tissue injury.** **For example, they phagocytose dead neutrophils, which rapidly accumulate in sites of infection or tissue death caused by trauma or interrupted blood supply. Macrophages also recognize and engulf apoptotic cells before the dead cells can release their contents and induce inflammatory responses, as part of many physiologic processes, such as development, growth, and renewal of healthy tissues, and the dead cells must be cleaned up by macrophages.**
2. **Activated macrophages secrete proteins, called cytokines, that bind to signaling receptors other cells and thereby instruct those cells to respond in ways that contribute to host defense.** **For example, some cytokines act on endothelial cells lining blood vessels to enhance the recruitment of more monocytes from the blood into sites of infections, thereby amplifying the protective response against the microbes.** There are many different cytokines that are involved in every aspect of immune responses.
3. **Macrophages serve as APCs(Antigen presenting cells) that display antigens to and activate T lymphocytes. This function is important in the effector phase of T cell–mediated immune responses.**

4. Another important function of macrophages is to promote repair of damaged tissues by stimulating new blood vessel growth (angiogenesis) and synthesis of collagen-rich extracellular matrix (fibrosis). This function is mediated by certain cytokines secreted by the macrophages that act on various tissue cells.

5. Macrophages are activated to perform their functions by recognizing many different kinds of microbial molecules as well as host molecules produced in response to infections. These various activating molecules bind to specific signaling receptors located on the surface of or inside the macrophage. An example of these receptors is the Toll-like receptors, which are of central importance in innate immunity.

6. Macrophages are also activated when receptors on their plasma membrane bind opsonins on the surface of microbes. Opsonins are substances that coat particles for phagocytosis. Examples of these opsonin receptors are complement receptors and antibody

7. Macrophages typically respond to microbes nearly as rapidly as neutrophils do, but macrophages survive much longer at sites of inflammation. Unlike neutrophils, macrophages are not terminally differentiated and can undergo cell division at an inflammatory site. Therefore, **macrophages are the dominant effector cells of the later stages of the innate immune response, several days after infection.**

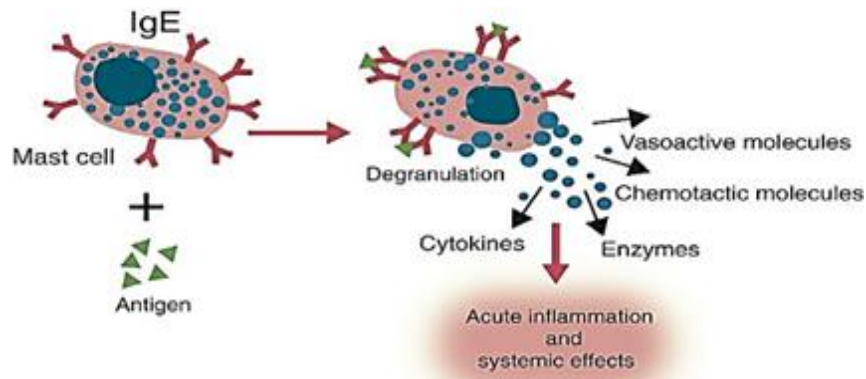
Mast Cells

Mast cells are bone marrow–derived cells that are present in the skin and mucosal epithelium and contain abundant cytoplasmic **granules filled with cytokines histamine, and other mediators.**

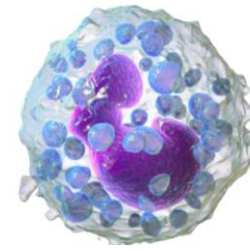
Normally, mature mast cells are not found in the circulation but are constitutively present in healthy tissues, usually adjacent to small blood vessels and nerves. Human mast cells vary in shape and have round nuclei, and the cytoplasm contains membrane-bound granules. The granules contain acidic proteoglycans that bind basic dyes

Mast cells express plasma membrane receptors for IgE and IgG antibodies and are usually coated with these antibodies. When these antibodies on the mast cell surface also bind antigen, signaling events are induced that lead to release of the cytoplasmic granule contents into the extracellular space.

The released contents of the granules, including cytokines and histamine, promote changes in the blood vessels that cause inflammation. **Mast cells provide defense against helminths but are also responsible for symptoms of allergic diseases .**

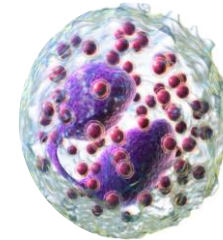


□ Basophils



Basophils are blood granulocytes with many structural and functional similarities to mast cells. Like other granulocytes, basophils are derived from bone marrow progenitors (a lineage different from that of mast cells), mature in the bone marrow, and circulate in the blood. Basophils constitute less than 1% of blood leukocytes. **Basophils contain granules that bind basic dyes, and they are capable of synthesizing many of the same mediators as mast cells.** Like mast cells, basophils express IgG and IgE receptors, bind IgE, and can be triggered by antigen binding to the IgE. **Because basophil numbers are low in tissues, their importance in host defense and allergic reactions is uncertain.**

□ Eosinophils



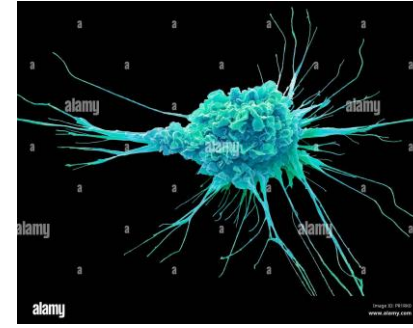
Eosinophils are blood granulocytes that express cytoplasmic granules containing enzymes that are harmful to the cell walls of parasites but can also damage host tissues. The granules of eosinophils contain basic proteins that bind acidic dyes such as eosin . Like neutrophils and basophils, eosinophils are bone marrow derived. **GM-CSF, IL-3, and IL-5 promote eosinophil maturation from myeloid precursors.**

Some eosinophils are normally present in peripheral tissues, especially in mucosal linings of the respiratory, gastrointestinal, and genitourinary tracts, and their numbers can increase by recruitment from the blood in the setting of inflammation

□ Antigen-Presenting Cells

Antigen-presenting cells (APCs) are cell populations that are specialized to capture microbial and other antigens, display them to lymphocytes, and provide signals that stimulate the proliferation and differentiation of the lymphocytes. By convention, APC usually refers to a cell that displays antigens to T lymphocytes. The major type of APC that is involved in initiating T cell responses is the dendritic cell. Macrophages and B cells present antigens to T lymphocytes in different types of immune responses, and a specialized cell type called the follicular dendritic cell displays antigens to B lymphocytes during particular phases of humoral immune responses. APCs link responses of the innate immune system to responses of the adaptive immune system, and therefore they may be considered components of both systems.

Dendritic Cells



Dendritic cells are the most important APCs for activating naive T cells, and they play major roles in innate responses to infections and in linking innate and adaptive immune responses. They have long membranous projections and phagocytic capabilities and are widely distributed in lymphoid tissues, mucosal epithelium, and organ parenchyma.

Dendritic cells are part of the myeloid lineage of hematopoietic cells and arise from a precursor that can also differentiate into monocytes but not granulocytes. **Similar to macrophages, dendritic cells express receptors that recognize molecules typically made by microbes and not mammalian cells, and** they respond to the microbes by secreting cytokines. **The majority of dendritic cells are called conventional dendritic cells. In response to activation by microbes, conventional dendritic cells in skin, mucosa, and organ parenchyma become mobile, migrate to lymph nodes, and display microbial antigens to T lymphocytes.** Thus, these cells function in both innate and adaptive immune responses and are a link between these two components of host defense.

One subpopulation of dendritic cells, **called plasmacytoid dendritic cells,** are early cellular responders to viral infection. They recognize nucleic acids of intracellular viruses and produce soluble proteins called type I interferons, which have potent antiviral activities.

Follicular Dendritic

Cells Follicular dendritic cells (FDCs) are cells with membranous projections that are found to **become mixed together and in specialized collections of activated B cells, called germinal centers, in the lymphoid follicles of the lymph nodes, spleen, and mucosal lymphoid tissues.** FDCs are not derived from precursors in the bone marrow and are unrelated to the dendritic cells that present antigens to T lymphocytes. FDCs trap antigens complexed to antibodies or complement products and display these antigens on their surfaces for recognition by B lymphocytes.



Follicular dendritic cells

