Components of the Immune System
The process of cell development that produces cells of the immune system, as well as red blood cells and platelets, is called **hematopoiesis**.

Begins in the yolk sac of embryos, then fetal liver and spleen. Transition to bone marrow just before birth. Occurs in the **bone marrow** of newborns and older. (Fig. 1.13)

1. Cells
   It all starts with one cell type - **pluripotent hematopoietic stem cell**

Overview (Fig.1.14)
Pluripotent hematopoietic stem cells proliferate and either self-renew or differentiate into:
- Common lymphoid **progenitor** (a.k.a.precursor)
- Common myeloid progenitor
- Common erythroid megakaryocyte progenitor

Common lymphoid progenitors give rise to:
- **B cells**
- **T cells**
- **NK (natural killer) cells**
  - there is an intermediate NK/T progenitor

Common myeloid progenitors give rise to two distinct progenitors:
 Common granulocyte progenitors that give rise to:
  -Granulocytes:
    - neutrophils, eosinophils, and basophils
    “Unknown” progenitor that gives rise to:
      - **Monocytes**: these are the bloodborne precursors of tissue macrophages and dendritic cells
      - **Mast cells**

Erythroid progenitors differentiate into:
- **Megakaryocytes**, from which platelets are derived
- Erythroblasts, from which **red blood cells** (RBC, erythrocytes) are derived

Pictures and schematic representations of all cell types in Fig. 1.12

Macrophages
- One of the two major **phagocyte** types (the other is neutrophil)
- eat not only pathogens but also dead host cells and cell debris
- Widely distributed in the body. First to respond to invaders in tissues (before neutrophils leak out of the blood).
- Immature form is called **monocytes**: when they migrate from the blood into tissues they differentiate into macrophages.
- Major **antigen presenting cell** (APC)
Dendritic Cells
- Immature dendritic cells reside in tissues and continuously ingest surrounding fluid by phagocytosis and macropinocytosis; after taking up pathogen, they mature and migrate to lymph nodes where they serve as APCs. Cellular messengers that inform lymphocytes in lymph nodes of a nearby infection. Crucial bridge between innate and adaptive immunity.

Granulocytes
- Three types (neutrophil, basophil, eosinophil).
- They release contents of their granules (toxic granule proteins and free radicals) that can combat pathogens.
- They also produce factors (prostaglandin, leukotrienes and cytokines) that amplify the inflammatory response by recruiting and activating further leukocytes and epithelial cells.
- Also called polymorphonuclear leukocytes (PMN) because of their oddly shaped nuclei.
- Relatively short-lived and produced in large numbers during infection/inflammation.

*neutrophils
- Also acts as a major phagocytic cell: macrophages and neutrophils are major phagocytes that engulf bacteria.
- Most numerous among granulocytes. (Fig. 1.15)
- Move rapidly into sites of infection, eat microorganisms and then die (Fig. 1.16)
- Deficiency in neutrophils leads to overwhelming bacterial infection.

*eosinophils
- Named because of they way they stain: their granules contain basic proteins that stain bright orange by the acidic stain eosin.
- Only a small number found in circulation -most are found in tissues, especially in the connective tissues underneath respiratory, gut, and genitourinary epithelium.
- Plays a role during parasite infection but also causes tissue damage in some allergic reaction.

*basophils
- Stains with basic dyes like hematoxylin
- Least abundant and not much known; may have similar function to that of mast cells; basophils circulate whereas most mast cells are resident in tissues. Recent advances suggest that basophils can “convert” to a dendritic cell phenotype and initiate adaptive immune responses that lead to allergy.

Lymphoid progenitor cells differentiate into three kinds of lymphocyte:

B cells
- Produce immunoglobulin (Ig), also known as antibody
- Cell surface form of Ig is called the B cell receptor (BCR) for antigen
- Third major type of APC
T cells
- express T cell receptor (TCR) for antigen
- Two main types: helper T lymphocytes and cytotoxic T lymphocytes (CTL)
- The two types can be distinguished by their surface protein expression: T helper cells express CD4, whereas CTLs express CD8.
Most T helper cells secrete cytokines that activate other immune cells. However, there are several subtypes of CD4 T cells with different functions, and some actually suppress responses of other immune cells.
- CTLs can attack tumor cells or cells that are infected with virus, and also secrete cytokines.

T cells and B cells are activated by antigen initially in lymphoid organs (defined below), not tissues. Antigens are brought here by lymph fluid and by dendritic cells, and possibly basophils.

NK cells
- Recognize and kill certain tumor cells and virally infected cells.
- They do not express TCR- or BCR-type receptors. Considered part of innate immunity.
- larger and more granular than B cells and T cells, sometimes called large granular lymphocytes

Mast Cells
- Major cell type involved in allergy
- activation by recognition of allergen leads to release of granules whose contents (histamine, etc.) cause the allergic reaction.

2. Organs of the immune system (Fig. 1.18)

Primary (central) lymphoid organs: generation of immune cells (hematopoiesis)

1. Bone marrow
- In sternum, vertebrae, iliac bones, and ribs
- Site of proliferation and differentiation of stem cells and progenitor cells

2. Thymus
- Bi-lobed organ above the heart
- T cells mature and undergo selection in the thymus
- Immature T cells undergoing differentiation and selection are called thymocytes.

Secondary (peripheral) lymphoid organs: major sites of lymphocyte activation

Although not an “organ” per se, the lymphatic vessels are an essential component of the immune system. The lymphatic vessels collect fluids, proteins and cells that have leaked out of the vascular system into the tissues, and return then back to the blood. Fragments of destroyed pathogens in tissues also enter the lymphatic system, as well as dendritic cells carrying antigens.
The fluid in these vessels is called **lymph** and is first filtered through lymph nodes. **Afferent** lymphatic vessels carry lymph to lymph nodes, which are the site of immune "sampling". **Efferent** lymphatic vessels eventually drain into thoracic duct, which returns lymph back to the peripheral blood system via a vein near heart. Lymphocytes (T and B cells) enter lymph nodes from blood capillaries, exit via the efferent lymph. (Fig. 1.19, 1.20)

1. **Lymph nodes** (Fig. 1.20, 1.21, 1.22)
   - Site of convergence/hub of the lymphatic system. Clusters of lymph nodes are found in neck, abdominal cavity, groin, etc.
   - Lymphocytes enter lymph nodes from blood by squeezing through vessel walls.
   - Antigens that enter the body are carried by APC (mainly dendritic cells, possibly basophils); they present antigens to T lymphocytes for sampling in “T cell area” of lymph nodes. The lymph node that receives fluid and cells from an infected site is called the **draining lymph node**
   - B cells found mainly in **follicles** and **germinal centers**
   - Filtered lymph leaves via efferent vessels, which also carries lymphocytes back to the blood

2. **Spleen** (Fig.1.23)
   - Organ found in the abdomen behind the stomach
   - Collects antigens from blood
   - Its main function is to initiate immune response to blood-borne antigen, whereas lymph nodes respond to antigens in tissues
   - Also the site of RBC disposal (in red pulp area)
   - White pulp area is where lymphocytes are organized much like in lymph nodes

3. **Mucosal** secondary organs (Fig. 1.25)
   - Diffuse lymph node-like structures underlying mucosal epithelia
   - **GALT** (gut-associated lymphoid tissue): tonsils, adenoids, appendix, Peyer's patches in the small intestine
   - **BALT** (bronchial-associated lymphoid tissue)
   - **MALT** (mucosal-associated lymphoid tissue) = GALT + BALT