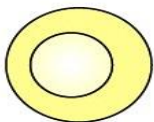


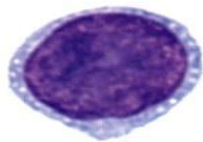
Circulating Blood Cells

Cell type	Proportion of leukocytes (%)
Neutrophil	40–75
Eosinophil	1–6
Basophil	<1
Monocyte	2–10
Lymphocyte	20–50

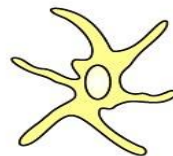
Figure 1.15 The Immune System, 3ed. (© Garland Science 2009)

Small lymphocyte

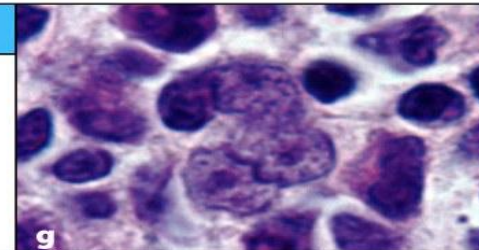
a



Production of antibodies (B cells) or cytotoxic and helper functions (T cells)

Dendritic cell

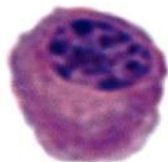
g



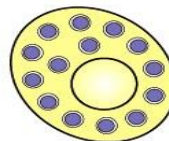
Activation of T cells and initiation of adaptive immune responses

Plasma cell

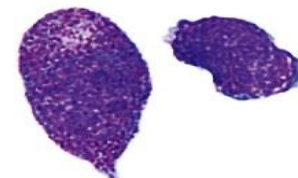
b



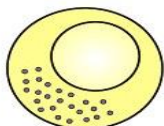
Fully differentiated form of B cell that secretes antibodies

Mast cell

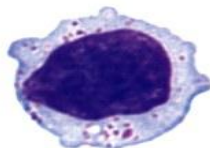
h



Expulsion of parasites from body through release of granules containing histamine and other active agents

Natural killer cell

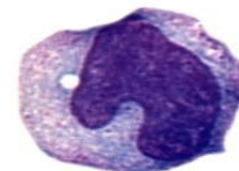
c



Kills cells infected with certain viruses

Monocyte

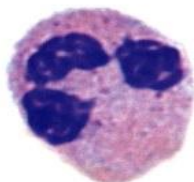
i



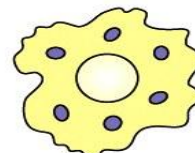
Circulating precursor cell to macrophage

Neutrophil

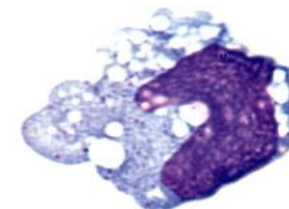
d



Phagocytosis and killing of microorganisms

Macrophage

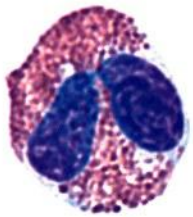
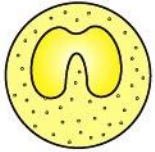
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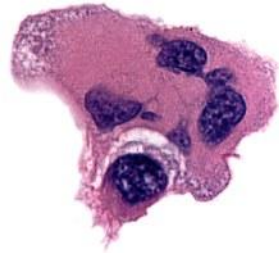
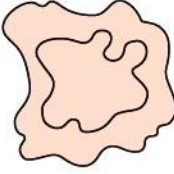


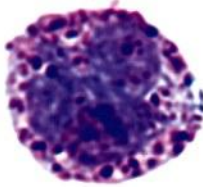

Phagocytosis and killing of microorganisms. Activation of T cells and initiation of immune responses

Figure 1.12 part 1 of 3 The Immune System, 3ed. (© Garland Science 2009)

Figure 1.12 part 2 of 3 The Immune System, 3ed. (© Garland Science 2009)

Eosinophil	 <p data-bbox="511 578 531 599">e</p>
	
<p data-bbox="125 614 869 678">Killing of antibody-coated parasites through release of granule contents</p>	

Megakaryocyte	 <p data-bbox="1420 578 1439 599">k</p>
	
<p data-bbox="1168 628 1642 664">Platelet formation, wound repair</p>	

Basophil	 <p data-bbox="511 985 531 1006">f</p>
	
<p data-bbox="193 1035 801 1071">Controlling immune responses to parasites</p>	



Erythrocyte	 <p data-bbox="1420 985 1439 1006">l</p>
	
<p data-bbox="1284 1035 1535 1071">Oxygen transport</p>	

Figure 1.12 part 3 of 3 The Immune System, 3ed. (© Garland Science 2009)

Granulocytes -- Also known as **polymorphonuclear leukocytes**. These are major inflammatory cells but they are not APCs.

A. Neutrophils (PMNs) - **Sixty to 70% of blood leukocytes and over 90% of circulating granulocytes**

Professional phagocytes or effector cells in the immune system

Morphology - polymorphonuclear vs mononuclear

End line cells with **oxygen dependent and independent killing systems**.

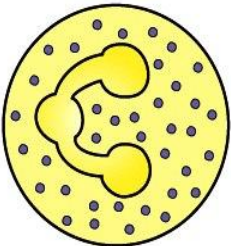
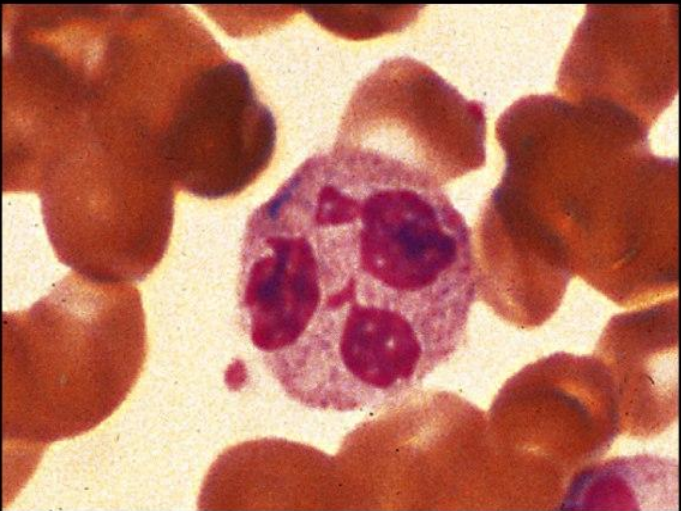
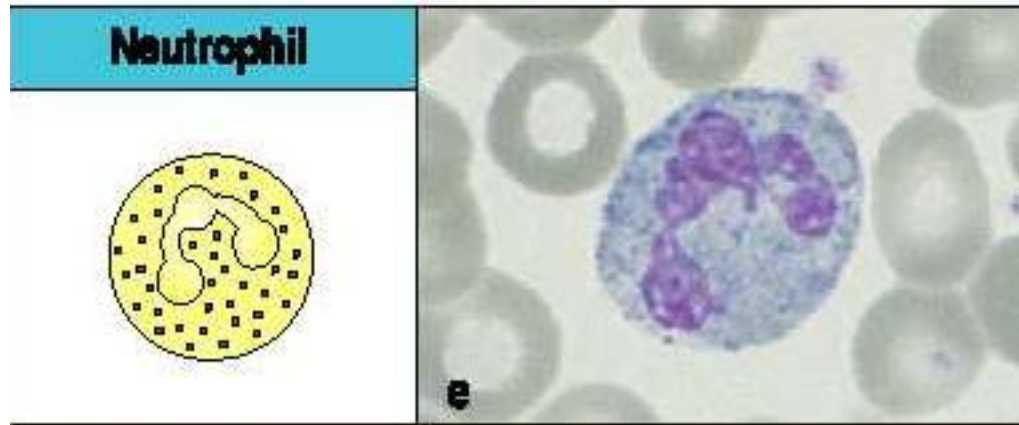
Cell	Activated function
<p data-bbox="247 791 537 848">Neutrophil</p> 	 <p data-bbox="1418 902 1754 1125">Phagocytosis and activation of bactericidal mechanisms</p>

Figure 1-4 part 3 of 6 Immunobiology, 7ed. (© Garland Science 2008)



Neutrophils: Phagocytes

- Origin and maturation: Bone marrow
- Antigen receptors: No
- Function: Phagocytosis and killing of microorganisms
- Where: in blood circulation
- Sites of function: infection sites
- Short life span

Induced by the cytokines IL-3, GM-CSF and G-CSF

II. Mononuclear Phagocytes -- Primary function is phagocytosis and these cells take up particulates efficiently.

A. Development -- These cells are derived from bone marrow monoblasts and enter the circulatory system as monocytes.

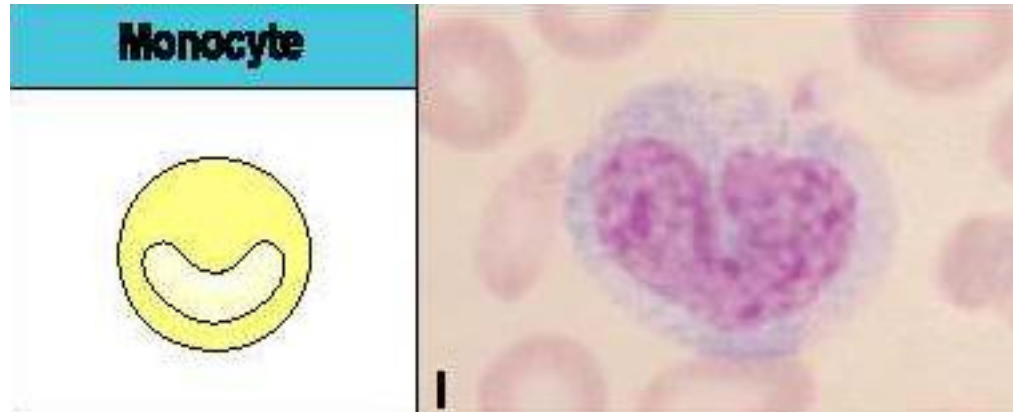
1. When monocytes are appropriately activated or enter into appropriate tissues they become macrophages. (e.g microglia in CNS, Kupffer cells in liver, alveolar macrophages in the lung).

2. Basic features of the monocyte/macrophage series:

a. Professional phagocytes found through out the body.

b. Morphology - large cells, kidney shaped nucleus.

c. Surface markers include receptors for Fc, CD35, MHC class II (Ia in mouse and DR in human), and CD14.



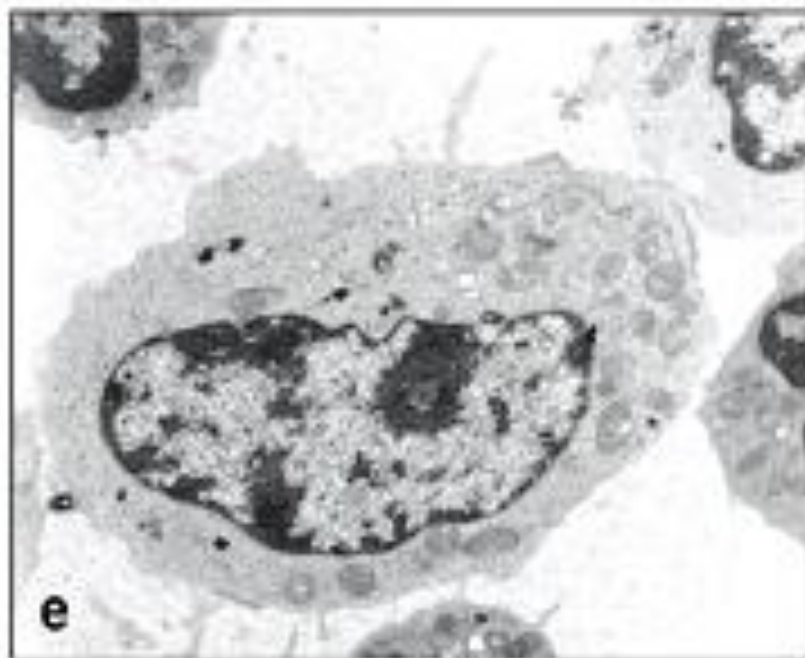
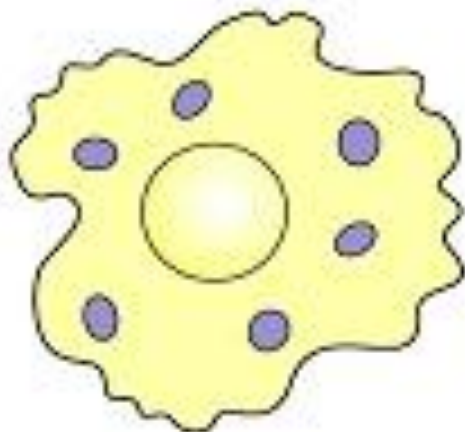
Monocytes: Macrophage precursors

- Origin : bone marrow
- Antigen receptors: No

- Function: to become macrophages
- Present in blood circulation

IL-3, GM-CSF and M-CSF induce monocytes

Macrophage



Macrophages express receptors for many microbial constituents

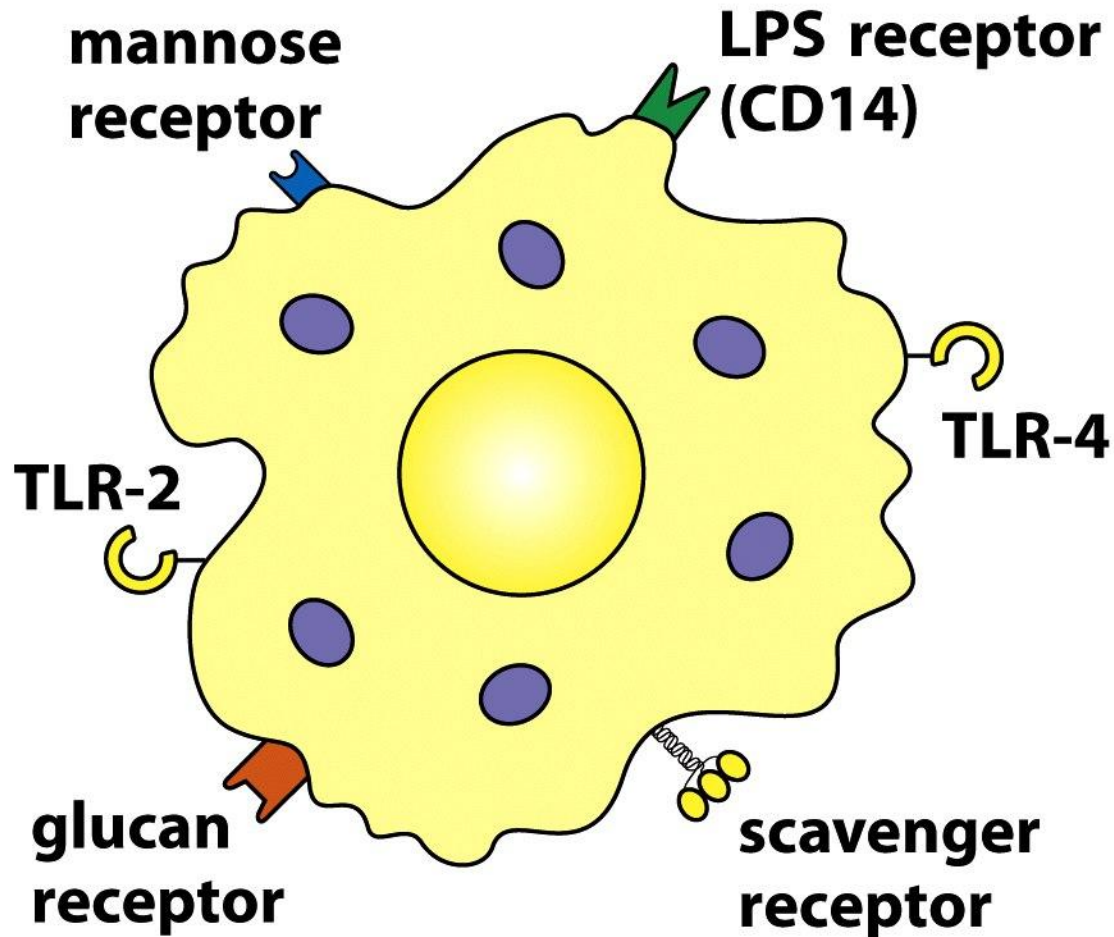


Figure 1-10 Immunobiology, 7ed. (© Garland Science 2008)

B. Activation and Function

1. Phagocytosis of foreign particles and serves as scavengers to clean up damaged tissues.

2. Monocytes produce important molecular messages or cytokines also called monokines (e.g. IL-1). Many of these monokines work on lymphocytes and lymphocytes produce lymphokines that stimulate monocytes (e.g. IFN- γ).

3. Monocytes serve as "Accessory Cells". Accessory cells are "supplementary cells" that improve lymphocyte activity. These cells are predominantly of the monocyte macrophage lineage. They cooperate with T and B lymphocytes in the formation of antibody and cell mediated immune reactions.

These accessory cells are antigen presenting cells (APC).

4. Macrophages are very important effector cells involved in many forms of cell mediated immunity.

III. Dendritic cells

A. Dendritic cells (DC) are bone marrow derived and are in most tissues of the body. They are the most effective and efficient at presenting Ag to T cells and serve as sentinels for the immune system. They are responsible for the initial presentation of antigen to T cells (Virgin T cells). Dendritic cells in the lymph nodes are called interdigitating cells, in the skin as Langerhans cells, and in the lymph as veiled cells.

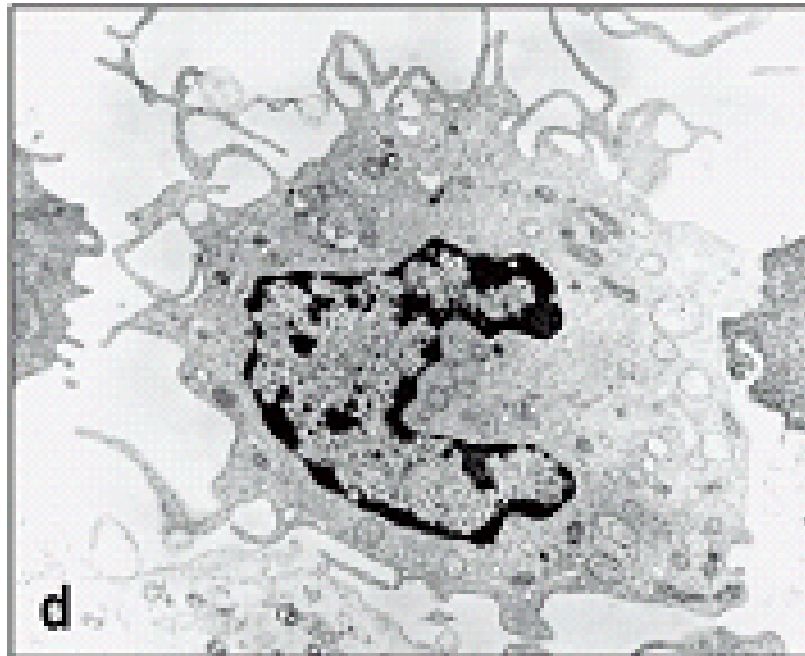
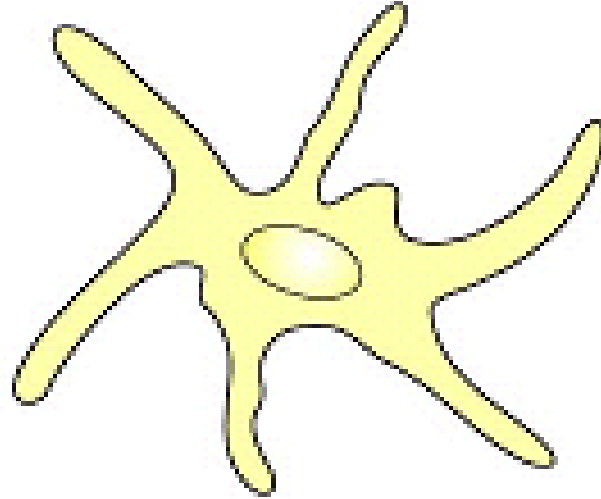
1. Interdigitating cells (IDC)

- a. Many DCs are in the thymus and T cell regions of lymphoid tissues.
- b. Morphology - they often appear star shaped cells with large dendritic processes.
- c. Surface markers: They are rich in MHC class II (Ia or DR)
- d. Processes and presents antigen to T cells in the context of MHC antigens. They represent “professional” antigen presenting cells.

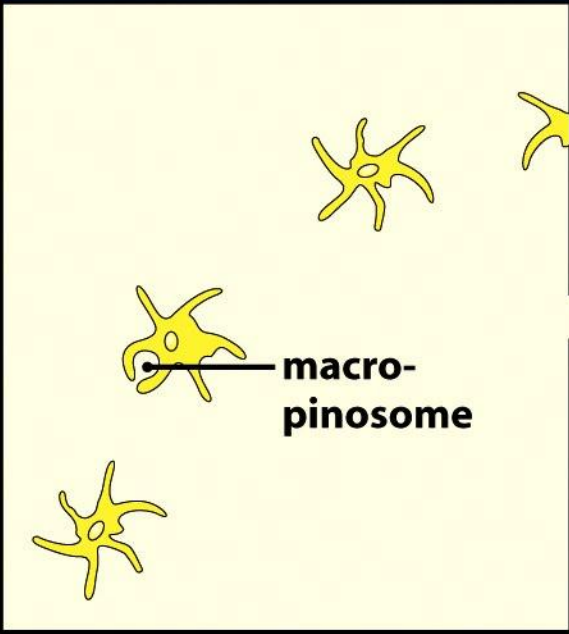
B. Follicular Dendritic Cells (FDCs)

1. Non-phagocytic, found in germinal centers, which are in the B cell regions
2. Large cells with numerous fine processes
3. Surface markers: Receptor for Fc and complement fragments used in trapping antigen in the form of antigen-antibody complexes.
4. Presents native antigen to B cells.

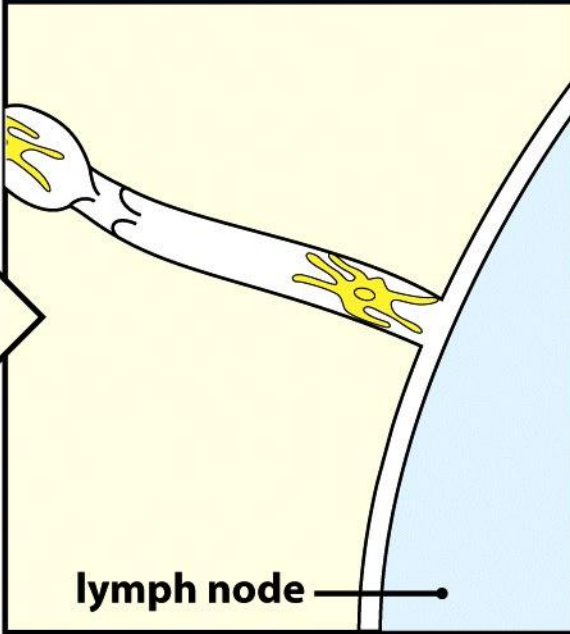
Dendritic cell



**Immature dendritic cells
reside in peripheral
tissues**



**Dendritic cells migrate
via lymphatic vessels to
regional lymph nodes**



**Mature dendritic cells
activate naive T cells
in lymphoid organs
such as lymph nodes**

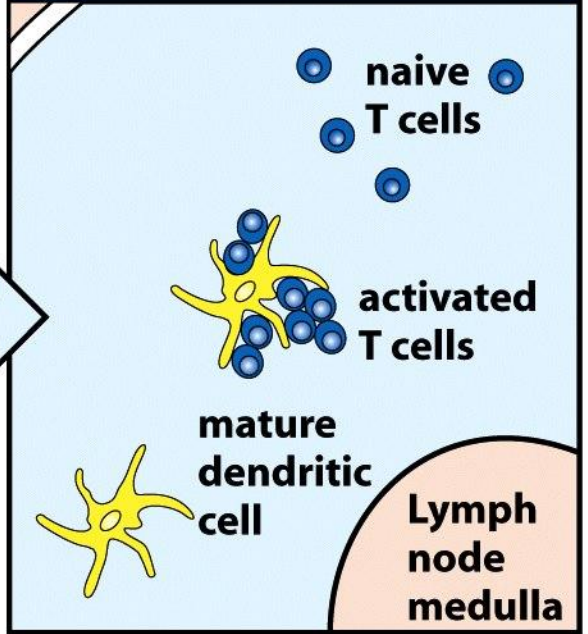
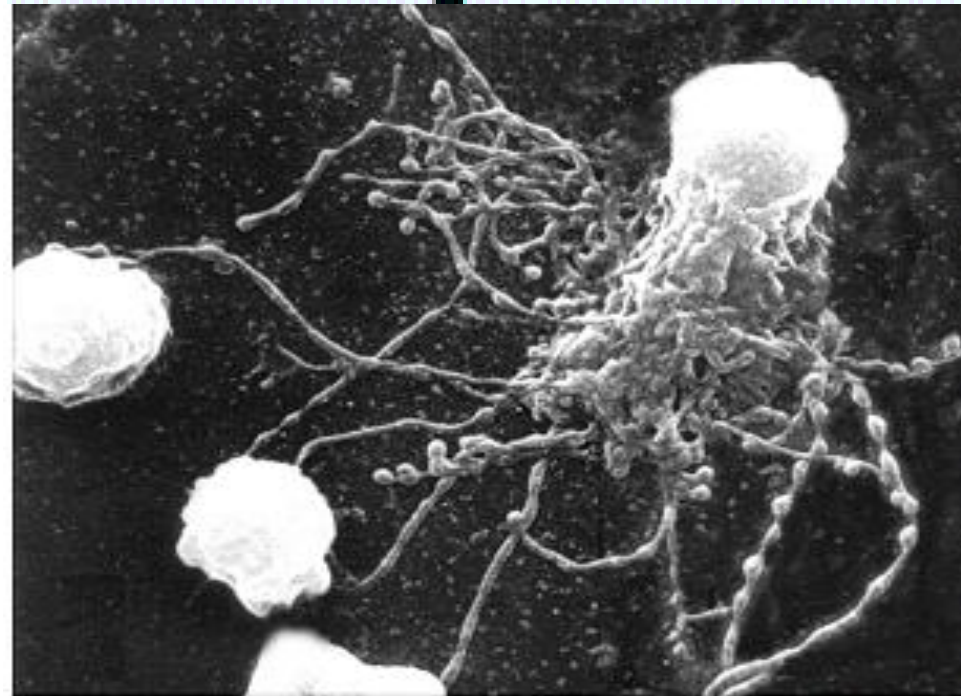
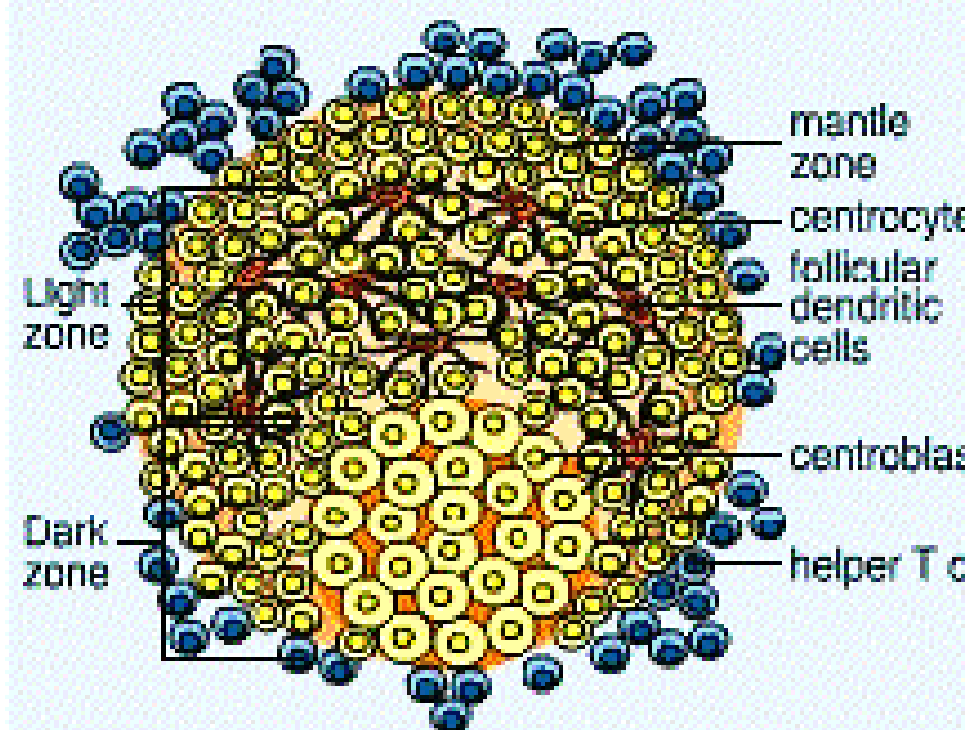


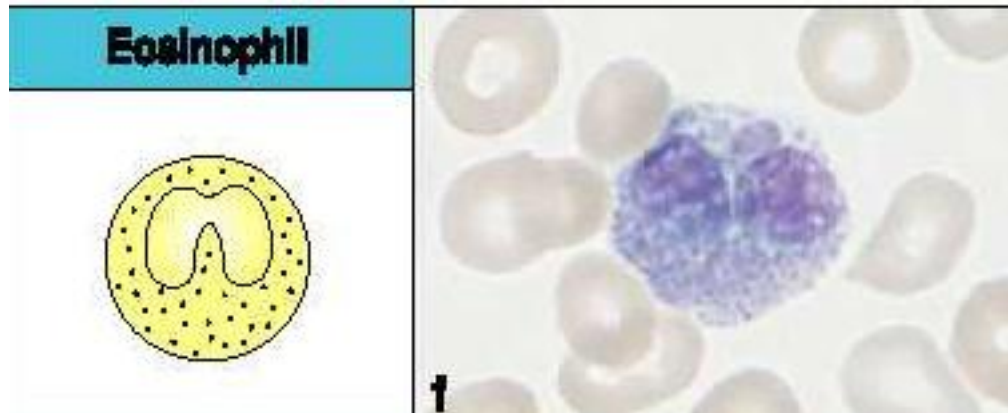
Figure 1-9 Immunobiology, 7ed. (© Garland Science 2008)

Follicular Dendritic Cells (FDCs)

Cardinal features of FDCs

1. Located in the follicles of secondary lymphoid tissue.
2. Dendritic morphology -- Note the numerous processes wrapped "spaghetti-like" and the beads (Iccosomes) on scanning electron micrograph of the FDC.
3. Binds and retains immune complexes (ICs).

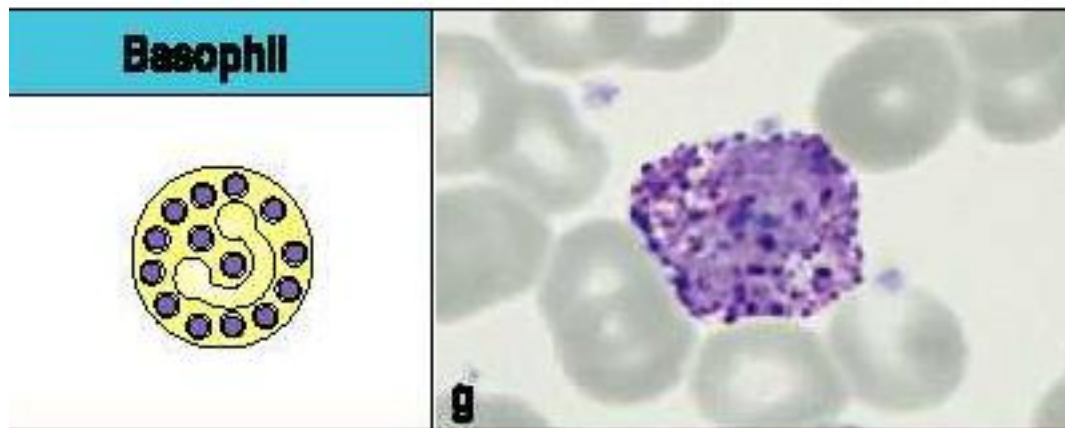




Eosinophils: worm (parasites) killers

- Origin : bone marrow
- Antigen receptors: No
- Function: killing of antibody-coated parasites through release of killing mix (cytotoxic granules)
- IgE&IgG receptors
- Effector machinery: cytotoxic granules, lipid mediators, cytokines and chemokines

T-cell-derived IL-5 induces eosinophil proliferation



Basophils: relatives of mast cells and eosinophils

- Origin : bone marrow
- Antigen receptors: No
- Function: important effector cells in allergic disorders and immune responses to parasites
- Sensor: IgE receptor
- Effector machinery: cytotoxic granules, lipid mediators, cytokines and chemokines

- V. Mast Cells. **Note the granules** in the mast cell shown below.
- 1. These cells bind IgE and contain the mediators of immediate hypersensitivity including histamine.
 - 2. These cells are found in the tissues including connective tissue and mucosal tissue.
 - 3. Although best known for their role in allergy, mast cells are involved in wound healing and defense against pathogens.

Cell		Activated function
Mast cell		Release of granules containing histamine and active agents

Figure 1-4 part 6 of 6 Immunobiology, 7ed. (© Garland Science 2008)

I. Lymphocytes -- These are the only cells **capable of specific recognition** and that derives from the fact that they **express BCR or TCR for Ag.**

A. Lymphocyte Development and Heterogeneity -- note that lymphocytes have a **common morphology.** See (See Fig. 1.5) illustrating resting lymphocytes.

1. **T cells** -- Development in the bone marrow and **thymus.**

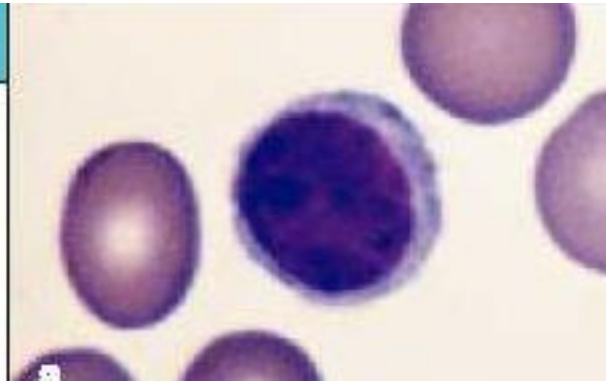
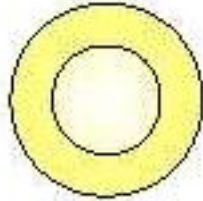
Prothymocytes, and thymocytes are in the thymic cortex, and mature cells are in the thymic medulla and peripheral lymphoid organs.

a. T cell receptor for antigen is a **heterodimer.** The **alpha & beta chains** (TCR-2; >90% of human blood T cells) and **gamma & delta chains** (TCR-1; <10% of human blood T cells).

b. T lymphocyte surface antigens. The CD markers (CD = **cluster of differentiation**) have diagnostic value and relate to cell function. In addition to the T cell specific markers we have MHC and other common antigen systems. Important CD molecules for T cells include: **Pan T cell markers: TCR, CD3, CD2, CD28, & Thy-1 (mouse only).** **Helper T cells** are indicated by **CD4** and **cytotoxic T cells** by **CD8.**

c. **Fluorescent Abs reactive with CD antigens help identify the cell types and gives clinically useful information.**

Small lymphocyte



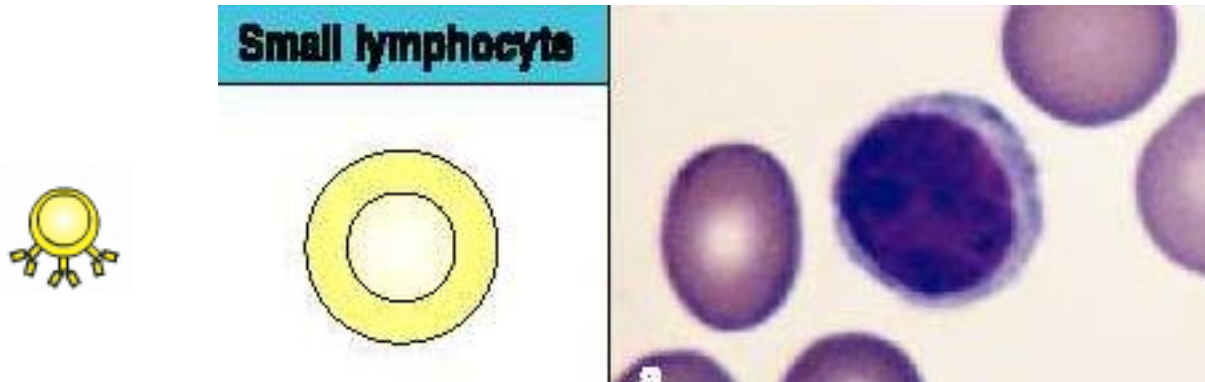
T lymphocytes: master regulators of the immune system

- Origin: Bone marrow
- Maturation: Thymus
- Differentiation to effector cells in secondary lymphoid tissues (lymph nodes, spleen, Peyer's patch, and tonsils)

- Antigen receptors: Yes
- CD4+, CD8+
- Function: regulate humoral and cell-mediated immune responses
- Mechanisms: cytokines, cell surface molecules, cytotoxic granules.



Figure 1-6 Immunobiology, 7ed. (© Garland Science 2008)

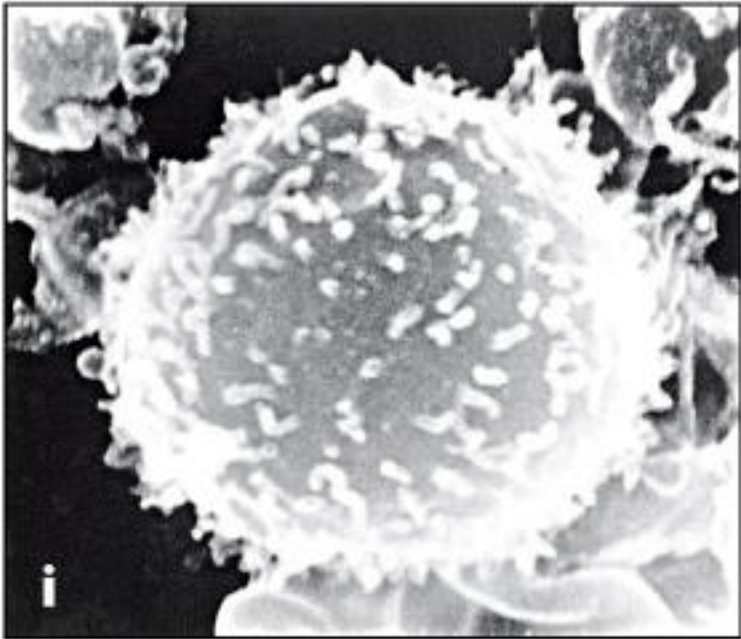
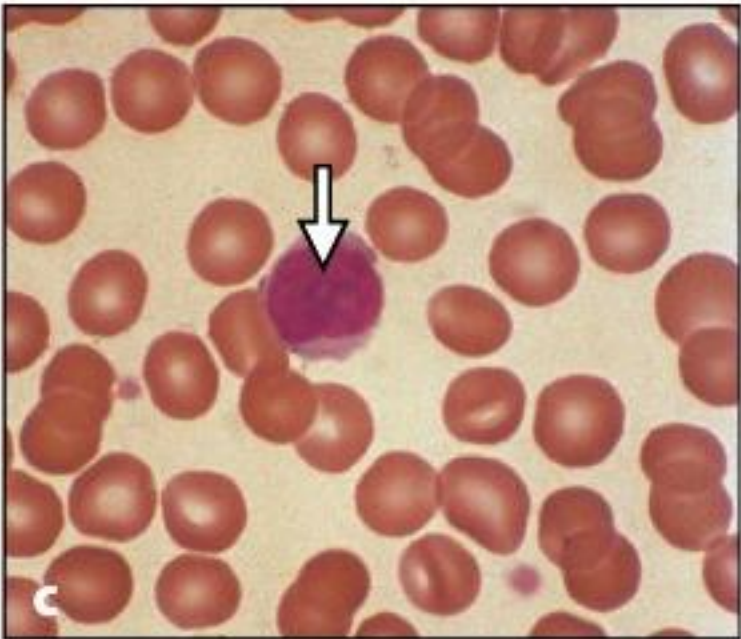
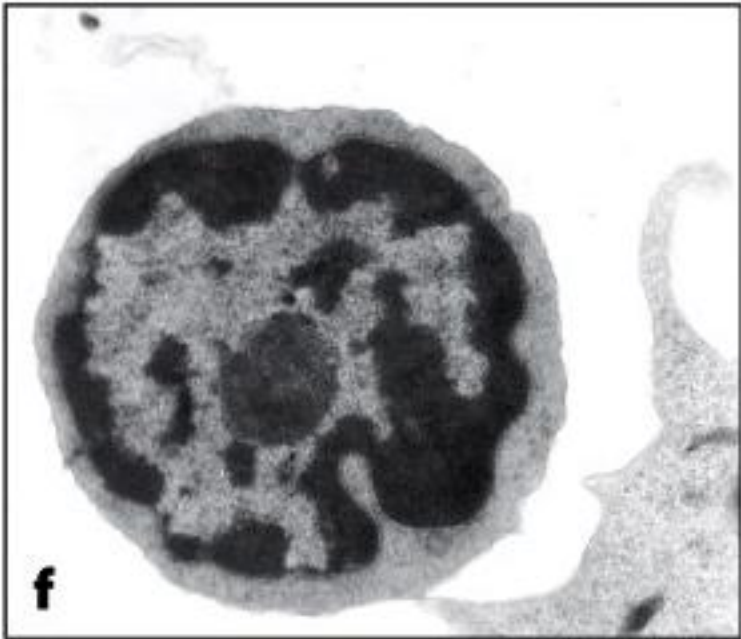
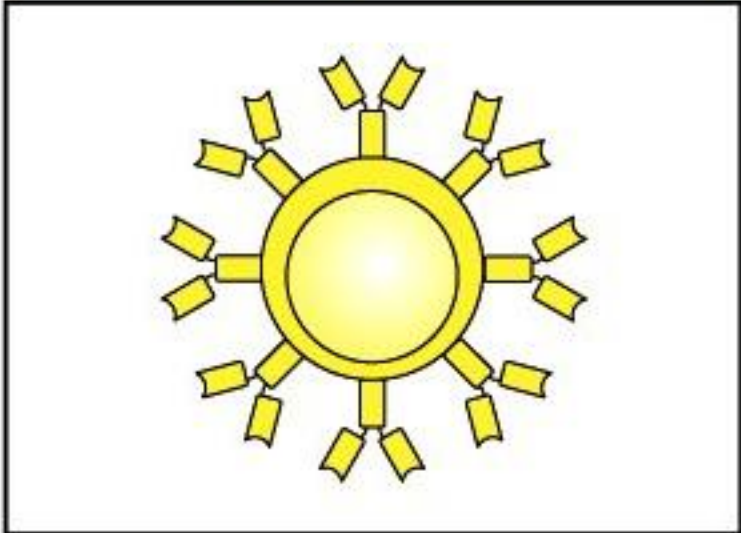


B lymphocytes: antibody producers

- Origin and maturation: Bone marrow
- Differentiation to plasma B cells in secondary lymphoid tissues (lymph nodes, spleen, Peyer's patch, and tonsils)
- CD19+CD20+
- Antigen receptors: B cell receptor (cell surface immunoglobulins)
- Function: Production of antibodies (IgM, IgE, IgA, and IgG)
- Regulated by T cells

2. B cells -- Bursa of Fabricius (birds) or mammalian bone marrow.
 - a. BCR or surface Ig receptors for antigen -- IgM and IgD of a single specificity (idiotype) on mature B cells.
 - b. Important surface markers include: BCR or surface Ig, CD19, CD21, CD35, FcγRII or CD32, CD40, CD5, and HLA-class II (See Fig. A-25).
 - c. Surface Ig traps antigen - may process antigen for presentation to T cells using HLA-class II or Ia in the case of the mouse.

B lymphocyte

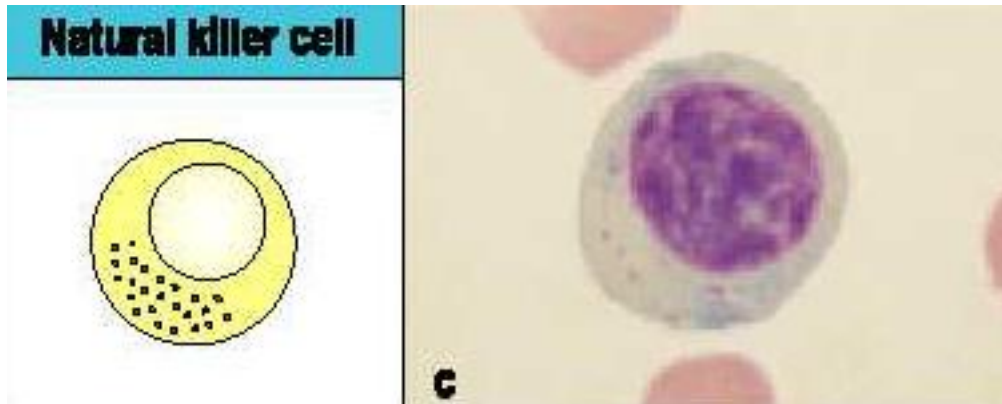


3. Natural Killer Type Cells or Null Cells --- Morphologically the activated cells may be large granular lymphocytes (LGLs). Defined as null cells -- **null meaning they lack BCR and TCR**. However, some LGLs do have some T cell markers and probably represent a heterogeneous population. Cluster of differentiation **CD56, CD57 and CD16** are important cell surface markers.

- a. Do not require a **thymus or bursa**.
- b. Kill tumor or virus infected cells in **a nonspecific fashion** (NK-activity).
- c. They are involved in **antibody dependent cellular cytotoxicity (ADCC)** and this is called K-cell activity (K for killer cell). Need CD16 or Fc receptor for this activity.

Natural Killer (NK) Cells

- Also called large granular lymphocytes
- Make up 5–10% of circulating lymphocytes
- Responsible for immunological surveillance
- Attack:
 - foreign cells
 - virus-infected cells
 - cancer cells



NK cells: natural killers

- Origin : Bone marrow and thymus
- Antigen receptors: No
- Function: Kill tumor and virus-infected cells
- Effector machinery (=weapons): perforins and granzymes
- Activating or inhibitory receptors; Fc receptors

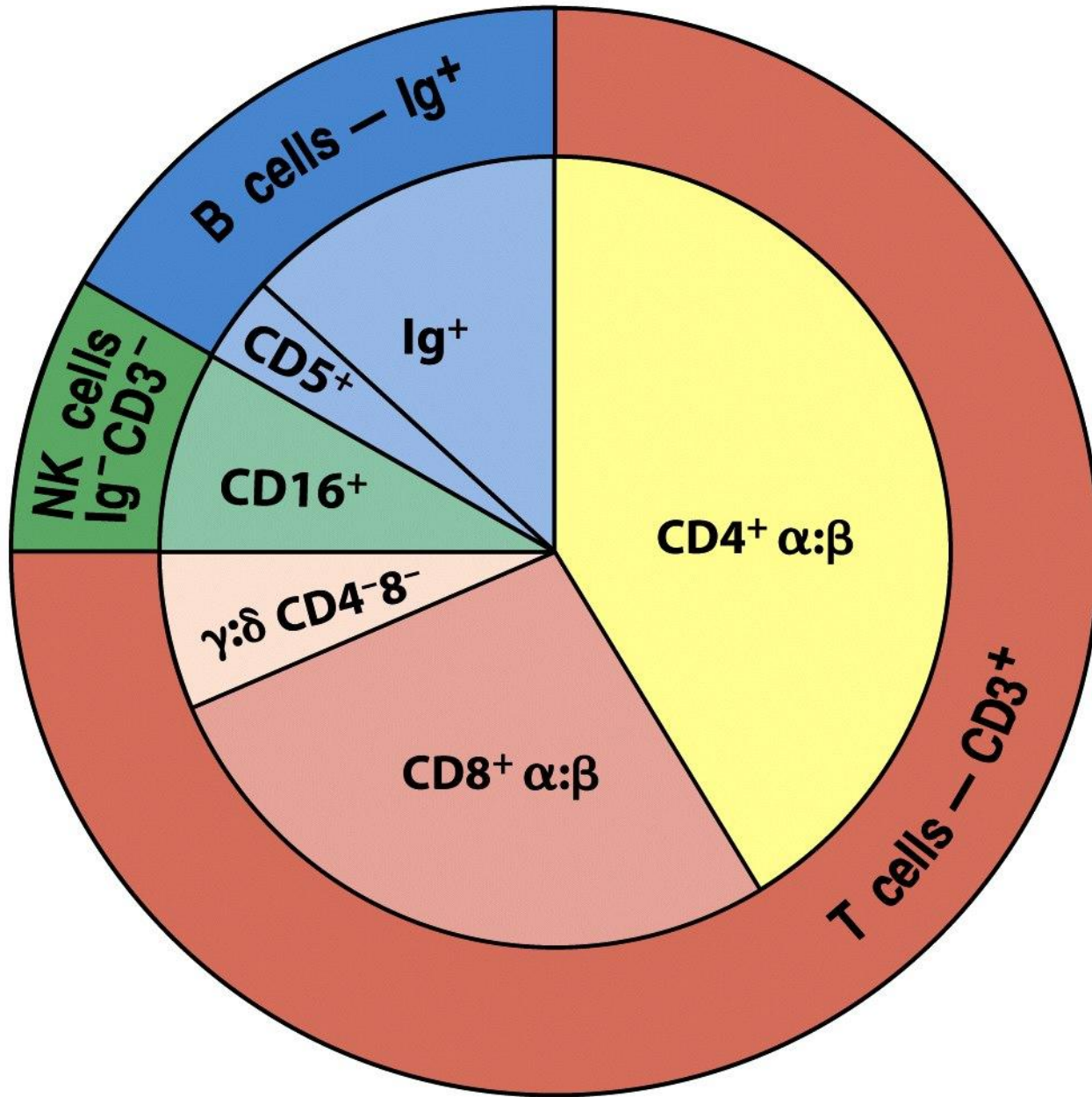
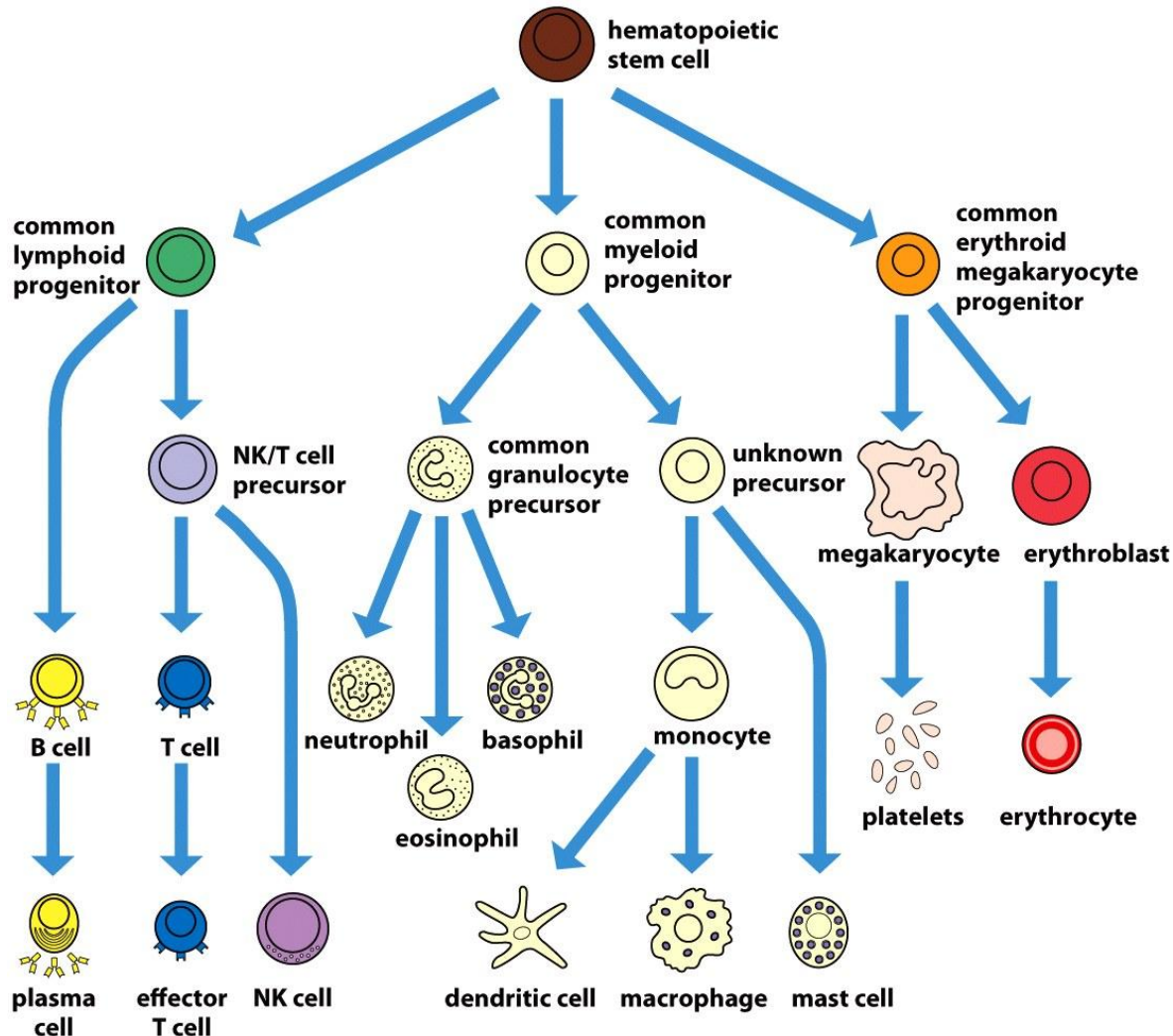


Figure A-25 Immunobiology, 7ed. (© Garland Science 2008)

Hematopoiesis

- (1) The process to produce immune cells
- (2) Stem cells and cytokines
- (3) Hematopoiesis in bone marrow is regulated by some cytokines such as stem cell factor, IL-1, IL-3, IL-6, IL-7, GM-CSF, EPO, G-CSF and M-CSF

Hematopoiesis generates immune cells



Hematopoietic stem cells:

1. Self renewal
2. Totipotency

They are in bone marrow after birth

They make immune cells, platelets, and RBCs

T cell progenitors migrate to thymus and generate T cells

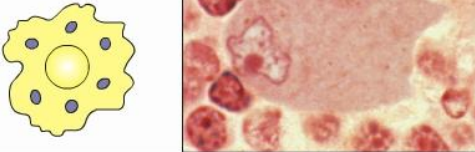
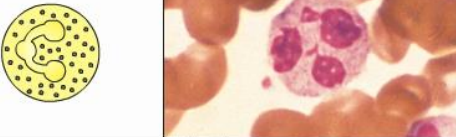
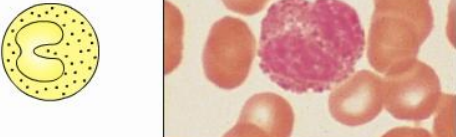
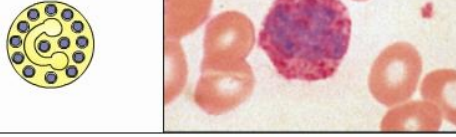

B cell progenitors reside in bone marrow to make naïve B cells

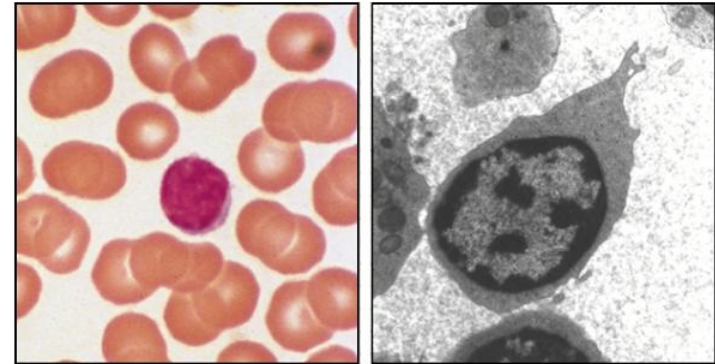
Myeloid vs. Lymphoid cells

Myeloid cells

Stem cells

Lymphoid cells

Cell		Activated function
Macrophage		Phagocytosis
Neutrophil		Phagocytosis and activation of bactericidal mechanisms
Eosinophil		Killing of antibody-coated parasites
Basophil		Unknown
Mast cell		Release of granules containing histamine and other active agents



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T cells: T cell antigen receptor
 B cells: B cell antigen receptor
 NK cells: no antigen-specific receptor

Hematopoiesis occurs in the adult bone marrow

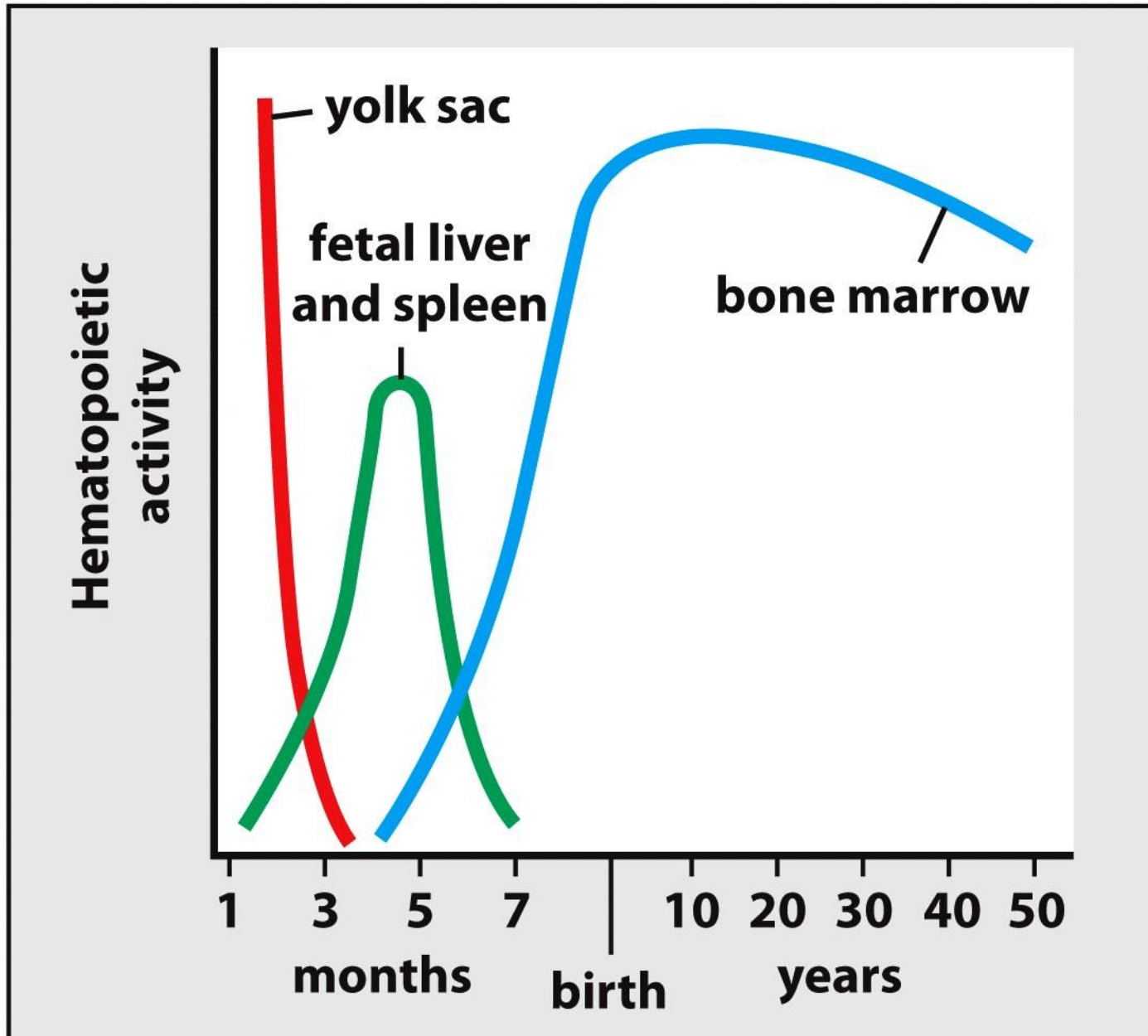


Figure 1.13 The Immune System, 3ed. (© Garland Science 2009)