HEMATOLOGY
&LYMPH SYSTEM

Histology Handout

Number 3

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Leukocytes (White Blood Cells)

White blood cells (WBCs) are also called **leukocytes**. There are five kinds of WBCs; all are larger than RBCs and have nuclei when mature. The nucleus may be in one piece or appear as several lobes. Special staining for microscopic examination gives each kind of WBC a distinctive appearance.

A normal WBC count (part of a CBC) is 5,000 to 10,000 per mm^3. Notice that this number is quite small compared to a normal RBC count. Many of our WBCs are not within blood vessels but are carrying out their functions in tissue fluid.

Classification and sites of production

The five kinds of white blood cells may be classified in two groups: granular and agranular. The granular leukocytes are produced in the red bone marrow; these are the **neutrophils**, **eosinophils**, and **basophils**, which have distinctly colored granules when stained. The agranular leukocytes are **lymphocytes** and **monocytes**, which are produced in the lymphatic tissue of the spleen, lymph nodes , and thymus, as well as in the red bone marrow. A **differential WBC count** (part of a CBC) is the percentage of each kind of leukocyte.

Functions

White blood cells all contribute to the same general function, which is to protect the body from infectious disease and to provide immunity to certain diseases. Each kind of leukocyte has a role in this very important aspect of homeostasis.

Neutrophils and **monocytes** are capable of the **phagocytosis** of pathogens. Neutrophils are the more abundant phagocytes, but monocytes are the more efficient phagocytes, because they differentiate into **macrophages**, which also phagocytize dead or damaged tissue at the site of any injury, helping to make tissue repair possible.

Eosinophils are believed to detoxify foreign proteins. This is especially important in allergic reactions and parasitic infections. **Basophils** contain granules of heparin and histamine. **Heparin** is an anticoagulant that helps prevent abnormal clotting within blood vessels. **Histamine** is released as part of the inflammation process, and it makes capillaries more permeable, allowing tissue fluid, proteins and white blood cells to accumulate in the damaged area.

There are two major kinds of lymphocytes: T cells and B cells. **T cells** (or T lymphocytes) recognize foreign antigens, may directly destroy some foreign antigens, and stop the immune response when the antigen has been destroyed. **B cells** (or B lymphocytes) become **plasma cells** that produce antibodies to foreign antigens.

Leukocytes function in **tissue fluid** as well as in the **blood**. Many WBCs are capable of self-locomotion (ameboid movement) and are able to squeeze between the cells of capillary walls and out into tissue spaces. Macrophages provide a good example of dual location of leukocytes. Some macrophages are "fixed", that is stationary in organs such as the liver, spleen, and red bone marrow (part of the tissue macrophage or RE system) and in the lymph nodes. They phagocytize pathogens that circulate in blood or lymph through these organs (these are the same macrophages that also phagocytize old RBCs). Other "wandering" macrophages move about in tissue fluid, especially in the connective tissue of mucous membranes and below the skin. Pathogens that gain entry into the body through natural openings or through breaks in the skin are usually destroyed by the leukocytes in connective tissue before they can cause serious disease. **Neutrophils**

Stages of Granulopoiesis

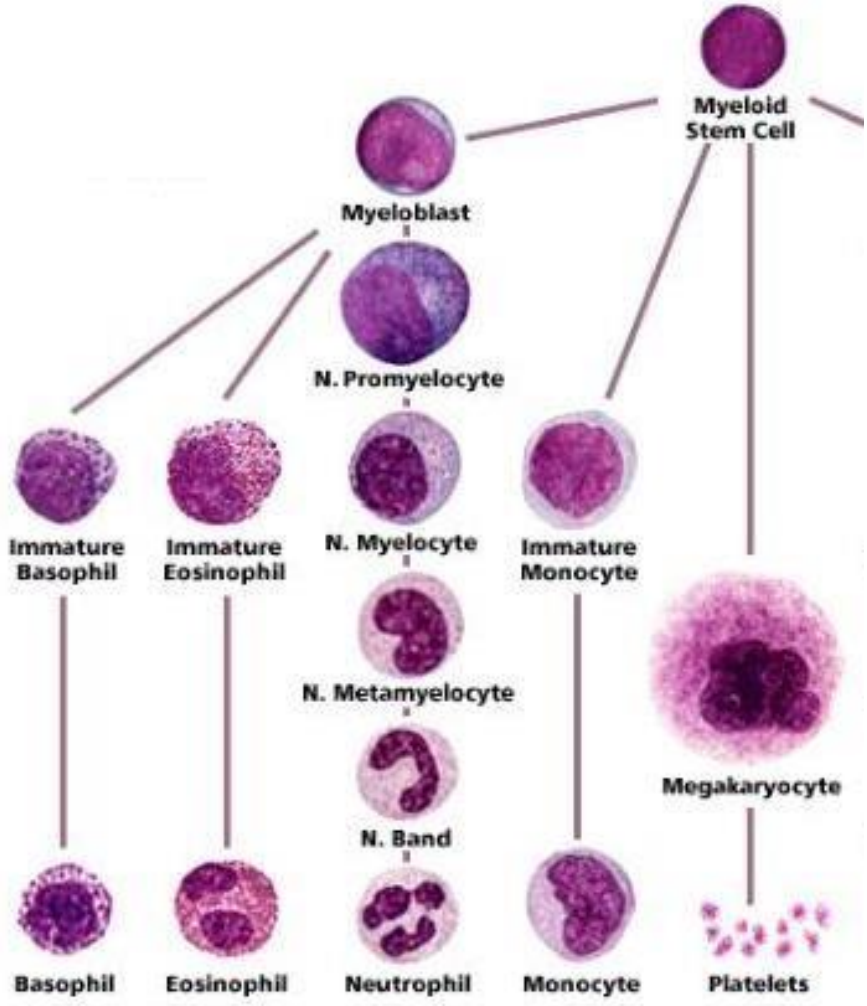
The maturation sequence in granulopoiesis is myeloblast, promyelocyte, myelocyte, metamyelocyte, band cell, and segmented granulocyte. This process occurs within the bone marrow. G-CSF is a key regulator of neutrophil production.

The **myeloblast** is derived from the granulocyte monocyte progenitor cell, which is in turn derived from the common myeloid progenitor cell. The myeloblast is the earliest recognizable cell in the granulocytic maturation process. It is about 15 to 20 um in diameter, with a large round to oval nucleus, and small amount of basophilic cytoplasm, with no granules. The nucleus contains 2 to 5 nucleoli and nuclear chromatin is fine and reticular. The next stage in the maturation is **promyelocyte** which is slightly larger in size than myeloblast. Primary or azurophilic granules appear at the premyelocyte stage. The nucleus contains nucleoli as in myeloblast stage, but nuclear chromatin shows slight condensation.

Myelocyte stage is characterized by the appearance of secondary or specific granules (neutrophilic, eosinphilic, or basophilic). **Neutrophilic myelocyte** is a

small cell with round to oval eccentrically placed nucleus, more condensation of chromatin than in premyelocyte stage, and absence of nucleoli. Cytoplasm is relatively greater in amount than in the premyelocyte stage and contain both primary and secondary granules. Myelocyte is the last cell capable of mitotic division. In the **neurtophilic metamyelocyte** stage, the nucleus becomes indented and kidney shaped, and the nuclear chromatin becomes moderately coarse. Cytoplasm contains both primary and secondary granules. The **band (stab) cell** stage is characterized by horseshoe shape of the nucleus with constant diameter throughout and condensed nuclear chromatins. Band cells are rarely seen in blood film. An increase in band neutrophils typically means that the bone marrow has been signaled to increase production of leukocytes, also known as a "left shift". Most often this is due to infection or inflammation in the body.

With Leishman's stain, the nucleus of the **segmented (polymorphonuclear) neutrophil** appears deep purple with 2 to 5 lobes which are joined by thin filamentous strands. Nuclear chromatin pattern is coarse. The cytoplasm stains light pink and has small specific granules.



Neutrophilic granules

The neutrophil granules are of two types: primary or azurophilic granules and secondary or specific granules. Azurophilic granules contain myeloperoxidase, lysozyme, acid phosphatase, elastases, collagenases, and acid hydrolases. Specific granules contain lysozyme, lactoferrin, alkaline phosphatases, and other substances.

Function of neutrophils

After their formation, neutrophils remain in bone marrow for 5 more days as a reserve pool. Neutrophils have a life span of only 1 to 2 days in circulation. In

response to infection and inflammation, neutrophils come to lie closer to endothelium (margination) and adhere to endothelial surface (sticking). This is followed by escape of neutrophils from blood vessels to extravascular tissue (emigration). The escape of neutrophils is guided by chemotactic factors present in the inflammatory zone. Phagocytosis follows, which involves three steps: antigen recognition, engulfment, and killing the organism.

Neutrophils are the most abundant type of leukocytes in the blood. Their main function is in the acute inflammatory response. An increase in the number of neutrophils is termed **neutrophilia**, mostly seen in the course of bacterial infections. Some drugs, such as prednisone, have the same effect as cortisol and adrenaline (epinephrine), causing marginated neutrophils to enter the blood stream, causing neutrophilia.

Eosinophils

The eosinophil forms via the same stages as the neutrophil,with the exception that IL-5 ismost implicated in eosinophil production. Eosinphilic specific granules first become evident at the **myelocyte** stage. The size of the eosinophil is slightly greater than that of a neutrophil. The nucleus is often bilobed and the cytoplasm contains numerous, large, bright orange-red granules. The granules contain major basic protein, cationic protein, and peroxidase (which is distinct from myeloperoxidase). Eosinophilic peroxidase along with iodide and hydrogen peroxide may be responsible for some defense against helminthic parasites. Maturation time for eosinophils in bone marrow is 2 to 6 days and half-life in blood is less than 8 hours. In tissues, they reside in skin, lungs, and gastrointestinal tract.

Basophils

Basophils are small, round to oval cells which contain very large, coarse, deep purple granules. The nucleus has condensed chromatin and is covered by granules. Basophil granules contain histamine, chondroitin sulfate, heparin, proteases and peroxidase. Basophils bear surface membrane receptors for IgE. Upon reaction of antigen with membrane-bound IgE, histamine and other granular contents are released which play a role in immediate hypersensitivity reaction. Basophils are also involved in some cutaneous basophil hypersensitivity reactions.

Monocytes

The initial cell in development is **monoblast**, which is indistinguishable from myeloblast. The next cell is promonocyte which has an oval or clefted nucleus with fine chromatin pattern and 2 to 5 nucleoli. The monocyte is a large cell (15-20 um) with irregular shape, oval or clefted (often kidney-shaped) nucleus, and fine delicate chromatin. Cytoplasm is abundant, blue-grey with ground glass appearance and often contains fine azurophilic granules and vacuoles.

Monocytes circulate in blood for about 1 day and then enter and settle in tissues where they differentiate into macrophages. Macrophage phagocytosis is slower as compared to neutrophils. In some organs, macrophages have distinctive morphologic and functional characteristics. Examples include Kupffer cells in the liver, Alveolar macrophages in the lungs, osteoclasts in the bone, and others.