(1)

Leucocytes

Classification

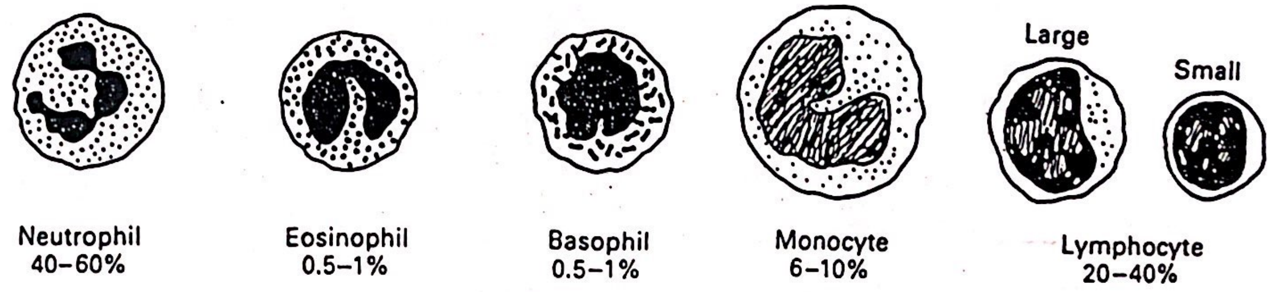
The blood leucocytes (white blood cells) are a heterogeneous population of nucleated cells lacking haemoglobin. There are five distinct morphological types classified into two groups on the basis of the presence or absence of granules in their cytoplasm:

1 **Granulocytes** (with cytoplasmic granules): these are the neutrophils, eosinophils and basophils.

2 **Agranulocytes** (without cytoplasmic granules): these are the monocytes and lymphoctyes.

Figure 2.5 gives the dimensions and morphological characteristics of the leucocytes.

2)



Morphological features: Diameter 10–16μm	Diameter 12–18μm	Diameter 10–14μm	Diameter 15–20μm	Diameter 5–8μm (small lymphocyte) 9–15μg (medium and large lymphocyte)
Nucleus: Lobulated (2–5 lobes) connected by chromatin strands. Nucleus is made of dense masses which take the purple stain	Made usually of 2 lobes—stains less deeply than neutrophil	Rarely segmented and its margins are usually obscured by the overlying cytoplasmic granules	Usually kidney shaped. Nuclear chromatin made of interwoven threads which are without compact blocks. Stains faintly	Rounded or slightly indented. Nuclear chromatin is clumped in the form of dark masses
Cytoplasm: Contains fine granules which stain purplish	Contains the characteristic large spherical bright red granules	Contains large coarse rounded or oval dark deeply staining granules which overlie the nucleus	Grey-blue giving a ground glass appearance with fine reddish azurphilic granules	Large lymphocyte has abundant cytoplasm which usually takes pale blue stain and may contain fine reddish granules Small lymphocyte has a very scanty cytoplasm forming a small rim around the nucleus

Fig. 2.5 The shapes, dimensions and special morphological features of the various types of leucocytes.

3

Formation of leucocytes (leucopoiesis)

Sites of formation

1 **Granulocytes:** bone marrow.

2 **Lymphocytes:** bone marrow, thymus, lymph nodes and other collections of lymphoid tissues, e.g. wall of the intestine.

3 **Monocytes:** bone marrow.

Formation of granulocytes (granulopoiesis)

The life history of the granulocytes begins in the bone marrow, where there is progressive division and maturation from the earliest cell, the stem cell, successively through the cell types myeloblast, promyelocyte, myelocyte, metamyelocyte, band neutrophil and segmented neutrophil. The myeloblasts, promyelocytes and myelocytes are capable of mitotic division and cell replication; hence, these are collectively called the **proliferating granulocyte pool**. From the metamyelocyte stage onwards, no cell division occurs and therefore the metamyelocytes, band neutrophils and segmented neutrophils are together referred to as the **maturation pool**. Maturation takes the form of biochemical and morphological changes in both the nucleus and the cytoplasm. The nucleus becomes condensed and broken up into lobes. In addition, fine neutrophilic granules appear in the cytoplasm. The maturation pool is sometimes called the **marrow granulocyte reserve**, as it is believed to be the main source of extra neutrophils which enter the bloodstream in acute infections and other pathological states. The mature neutrophils, once released into the bloodstream, stay there for about 7–10 hours before they migrate to the tissues, where they function as mobile phagocytes.

Haemopoietic growth factors

The formation of all blood cells is sustained throughout life by a group of glycoprotein growth factors, the *haemopoietic growth factors* (collectively called *colony-stimulating factors*, CSF). The first to be discovered was erythropoietin. Others which control the production of white blood cells include: multipotential CSF, granulocyte–macrophage CSF and granulocyte CSF. Recently, these growth factors have found important clinical uses by stimulating the bone marrow activity in disease conditions such as bone marrow failure, haematological malignancies and infectious diseases.

Neutrophils in the bloodstream

Mature neutrophils leave the bone marrow to enter the blood. Some of them join the blood circulation—the so-called circulating granulocyte pool. These are the cells available for blood sampling and counting. Others are deposited along the walls of the small vessels (**marginal granulocyte pool**), where they are in a state of rapid and continuous exchange with the circulating cells, and from this site they can be mobilized by exercise or by an adrenaline (epinephrine) injection. The entry of these cells into the circulating pool accounts for the increased white cell count (leucocytosis) that accompanies exercise and other stressful situations.

Functions of leucocytes

The general function of leucocytes is defence against infection. However, the different types of leucocytes contribute to a different extent towards this general function.

Functions of neutrophils

The neutrophils are also called **polymorphonuclear leucocytes** because the nucleus is formed of two to five lobes. This cell is the most important cell in the cellular defences of the body against infection. To achieve this goal, neutrophils execute several integrated functions: (i) the neutrophils must reach the site of infection (**chemotaxis**); (ii) they must ingest the foreign organism (**phagocytosis**); and (iii) they must kill or inhibit the multiplication of the microorganism (**microbial killing**).

Chemotaxis

The neutrophils are actively motile cells; they can move more rapidly than any other cell in the body. Their movement is directed towards bacteria in a purposeful manner, being attracted to bacteria or the site of infection or inflammation by a variety of chemotactic substances, e.g. products of certain bacteria, damaged leucocytes or other tissue components. The property of directed movement of the neutrophils is named **chemotaxis**. It accounts for the accumulation of neutrophils at sites where they are needed, e.g. infected wounds. Impaired chemotaxis can lead to increased susceptibility to infectious diseases, especially in children.

When neutrophils approach the infected site, they lie along the walls of the closest capillaries—a process called **margination**. Then individual neutrophils squeeze themselves between endothelial cells and gradually move out from the capillary—a process called **diapedesis**. Since neutrophils are motile cells, they move towards the bacteria.

Phagocytosis

Phagocytosis is the process whereby a cell eats particulate matter (Fig. 2.6).

7)

Blood

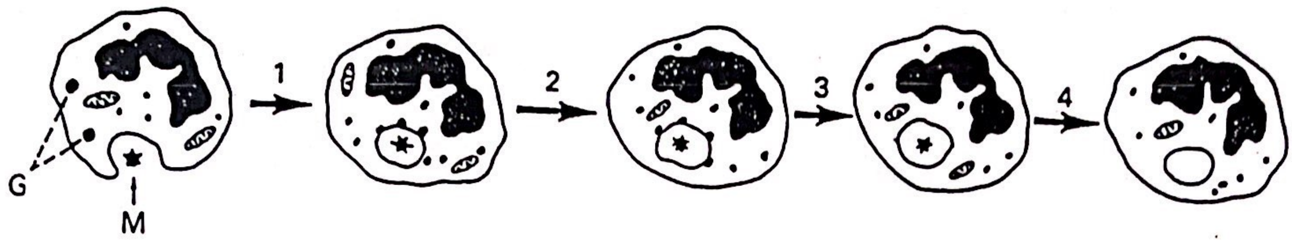


Fig. 2.6 Schematic diagram of the process of phagocytosis by a neutrophil. An ops onized microbe (M) after being recognized by th neutrophil is contained in an invagination of the neutrophil membrane. T hereafter, the particle is enclosed in a phagocytic vaauole. So of the neutrophil granules (G) stick to the wall of the vacuole and th en release their bactericidal substances, which induce klling and ultimate digestion of the microbe.

One of the remarkable features of neutrophils is their fine capacity to distinguish foreign cells like bacteria from homologous body cells and aged or damaged cells from fresh ones. This is due to the presence in plasma of certain substances (**opsonins**), such as **γ-globulins** (especially immunoglobulin G (IgG)) and **complement C4**, which coat bacteria and ageing cells, thereby making them 'palatable' to neutrophils. To opsonize means to prepare for eating. An opsonin is an agent in plasma which acts on foreign particles to increase their palatability to phagocytes.

Recognition is followed by close adhesion between the outer membrane of the neutrophil and the bacterium. This is followed by invasion of the neutrophil membrane and complete encirclement of the bacterium by pseudopodia. The pseudopodia fuse to enclose the bacterium in a phagocytic vacuole.

9) *Microbial killing*

Following the ingestion (phagocytosis) of the bacterium, the following sequence of events take place:

1 The fusion of the neutrophilic granules with the phagocytic vacuole.

2 Discharge of antimicrobial agents from the granules into the vacuole. These agents include lysozymes, myeloperoxidase and lactoferrin, which are capable of destroying a wide range of bacteria.

3 Killing and digestion of the ingested organism.

Functions of eosinophils (acidophils)

The eosinophils are characterized by the presence of coarse, bright red granules in their cytoplasm. These granules contain an arginine-rich basic protein which attracts red acidic dyes like eosin. The eosinophil nucleus is often seen as two large lobes. Eosinophil functions are not very different from those of the neutrophil.

Chemotaxis

Unlike neutrophils, eosinophils are attracted more towards areas of chronic inflammation rather than acute inflammation. **Chemotactic substances** for eosinophils include histamine, antigen–antibody complexes, 5-hydroxytryptamine (5-HT), bradykinin and a specific 'eosinophil chemotactic factor'.

Eosinophils tend to accumulate at the sites of histamine release, as is seen in allergic diseases of the skin or lungs.

Phagocytosis

Eosinophils are capable of ingesting a variety of particles, ranging from bacteria and destroyed cells to antigen–antibody complexes. Phagocytosis involves the same sequence of events as already described for neutrophils. However, antimicrobial activity is considerably less than that of the neutrophil. Eosinophils also release **major basic protein** (MBP) which is highly toxic to larvae of parasites.

Table 27-2. Principal cytokines.

Cytokine	Cell Lines Stimulated	Cytokine Source
IL-1	Erythrocyte Granulocyte Megakaryocyte Monocyte	Multiple cell types
IL-3	Erythrocyte Granulocyte Megakaryocyte Monocyte	T lymphocytes
IL-4	Basophil	T lymphocytes
IL-5	Eosinophil	T lymphocytes
IL-6	Erythrocyte Granulocyte Megakaryocyte Monocyte	Endothelial cells Fibroblasts Macrophages
IL-11	Erythrocyte Granulocyte Megakaryocyte	Fibroblasts Osteoblasts
Erythropoietin	Erythrocyte	Kidney Kupffer cells of liver
SCF	Erythrocyte Granulocyte Megakaryocyte Monocyte	Multiple cell types
G-CSF	Granulocyte	Endothelial cells Fibroblasts Monocytes
GM-CSF	Erythrocyte Granulocyte Megakaryocyte	Endothelial cells Fibroblasts Monocytes T lymphocytes
M-CSF	Monocyte	Endothelial cells Fibroblasts Monocytes
Thrombopoietin	Megakaryocyte	Liver, kidney

Key: IL = interleukin; CSF = colony stimulating factor; G = granulocyte; M = macrophage; SCF = stem cell factor.

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