Table 27–1. Normal values for the cellular elements in human blood.

Cell	Cells/μL (average)	Approximate Normal Range	Percentage of Total White Cells
Total WBC	9000	4000–11,000	...
Granulocytes			
Neutrophils	5400	3000–6000	50–70 = 60%
Eosinophils	275	150–300	1–4 = 04%
Basophils	35	0–100	0.4 = 01%
Lymphocytes	2750	1500–4000	20–40 = 30%
Monocytes	540	300–600	2–8 = 05%

Table 19.3 Summary of Formed Elements in Blood

Name and Appearance	Number	Characteristics*	Functions
Red blood cells (RBCs) or erythrocytes 	4.8 million/μL in females; 5.4 million/μL in males.	7–8 μm diameter, biconcave discs, without a nucleus; live for about 120 days.	Hemoglobin within RBCs transports most of the oxygen and part of the carbon dioxide in the blood.
White blood cells (WBCs) or leukocytes	5000–10,000/μL.	Most live for a few hours to a few days.†	Combat pathogens and other foreign substances that enter the body.
Granular leukocytes			
Neutrophils 	60–70% of all WBCs.	10–12 μm diameter; nucleus has 2–5 lobes connected by thin strands of chromatin; cytoplasm has very fine, pale lilac granules.	Phagocytosis. Destruction of bacteria with lysozyme, defensins, and strong oxidants, such as superoxide anion, hydrogen peroxide, and hypochlorite anion.
Eosinophils 	2–4% of all WBCs.	10–12 μm diameter; nucleus has 2 or 3 lobes; large, red-orange granules fill the cytoplasm.	Combat the effects of histamine in allergic reactions, phagocytize antigen–antibody complexes, and destroy certain parasitic worms.
Basophils 	0.5–1% of all WBCs.	8–10 μm diameter; nucleus has 2 lobes; large cytoplasmic granules appear deep blue-purple.	Liberate heparin, histamine, and serotonin in allergic reactions that intensify the overall inflammatory response.
Agranular leukocytes			
Lymphocytes (T cells, B cells, and natural killer cells) 	20–25% of all WBCs.	Small lymphocytes are 6–9 μm in diameter; large lymphocytes are 10–14 μm in diameter; nucleus is round or slightly indented; cytoplasm forms a rim around the nucleus that looks sky blue; the larger the cell, the more cytoplasm is visible.	Mediate immune responses, including antigen–antibody reactions. B cells develop into plasma cells, which secrete antibodies. T cells attack invading viruses, cancer cells, and transplanted tissue cells. Natural killer cells attack a wide variety of infectious microbes and certain spontaneously arising tumor cells.
Monocytes 	3–8% of all WBCs.	12–20 μm diameter; nucleus is kidney shaped or horseshoe shaped; cytoplasm is blue-gray and has foamy appearance.	Phagocytosis (after transforming into fixed or wandering macrophages).
Platelets (thrombocytes) 	150,000–400,000/μL.	2–4 μm diameter cell fragments that live for 5–9 days; contain many vesicles but no nucleus.	Form platelet plug in hemostasis; release chemicals that promote vascular spasm and blood clotting.

Table 12.7 Types of white cell in Romanowsky-stained blood films.

WHITE-CELL TYPES

Cell	Diameter (μm)	Nucleus	Cytoplasm	% of total (adults)
Neutrophil	12–15	2–5 lobes	Pink, granular; fine purple granules	40–75
Lymphocyte	6–8 (small) 12–16 (large)	Round; heavy chromatin	Thin rim, pale blue; occasional granule	20–45
Monocyte	12–20	Large, irregular; fine chromatin	Bulky, pale blue-grey	2–10
Eosinophil	12–15	Two lobes	Many large, oval, orange-red granules	1–6
Basophil	12–15	Large; irregular lobes	Few dark-blue granules; often overlie nucleus	<1

Table 1.3 Ninety five per cent confidence limits for the concentrations of various types of circulating blood cell in adult Caucasians and their life-span in the blood.

Cell type	Normal range (95% confidence limits)	Life-span in blood
Red cells	Males 4.4–5.8 × 10^{12}/litre Females 4.1–5.2 × 10^{12}/litre	110–120 days
White cells (leucocytes)	4.0–11.0 × 10^{9}/litre	
Neutrophil granulocytes	1.5–7.5 × 10^{9}/litre	$t_{1/2}$ approx. 7 hours
Eosinophil granulocytes	0.02–0.60 × 10^{9}/litre	$t_{1/2}$ approx. 6 hours
Basophil granulocytes	0.01–0.15 × 10^{9}/litre	
Monocytes	0.2–0.8 × 10^{9}/litre	$t_{1/2}$ approx. 70 hours
Lymphocytes	1.2–3.5 × 10^{9}/litre	
Platelets	160–450 × 10^{9}/litre	9–12 days

The bone marrow is actually one of the largest organs in the body, approaching the size and weight of the liver. It is also one of the most active. Normally, 75% of the cells in the marrow belong to the white blood cell-producing myeloid series and only 25% are maturing red cells, even though there are over 600 times as many red cells in the circulation as there are white cells. This difference in the marrow reflects the fact that the average life span of white cells is short, whereas that of red cells is long.

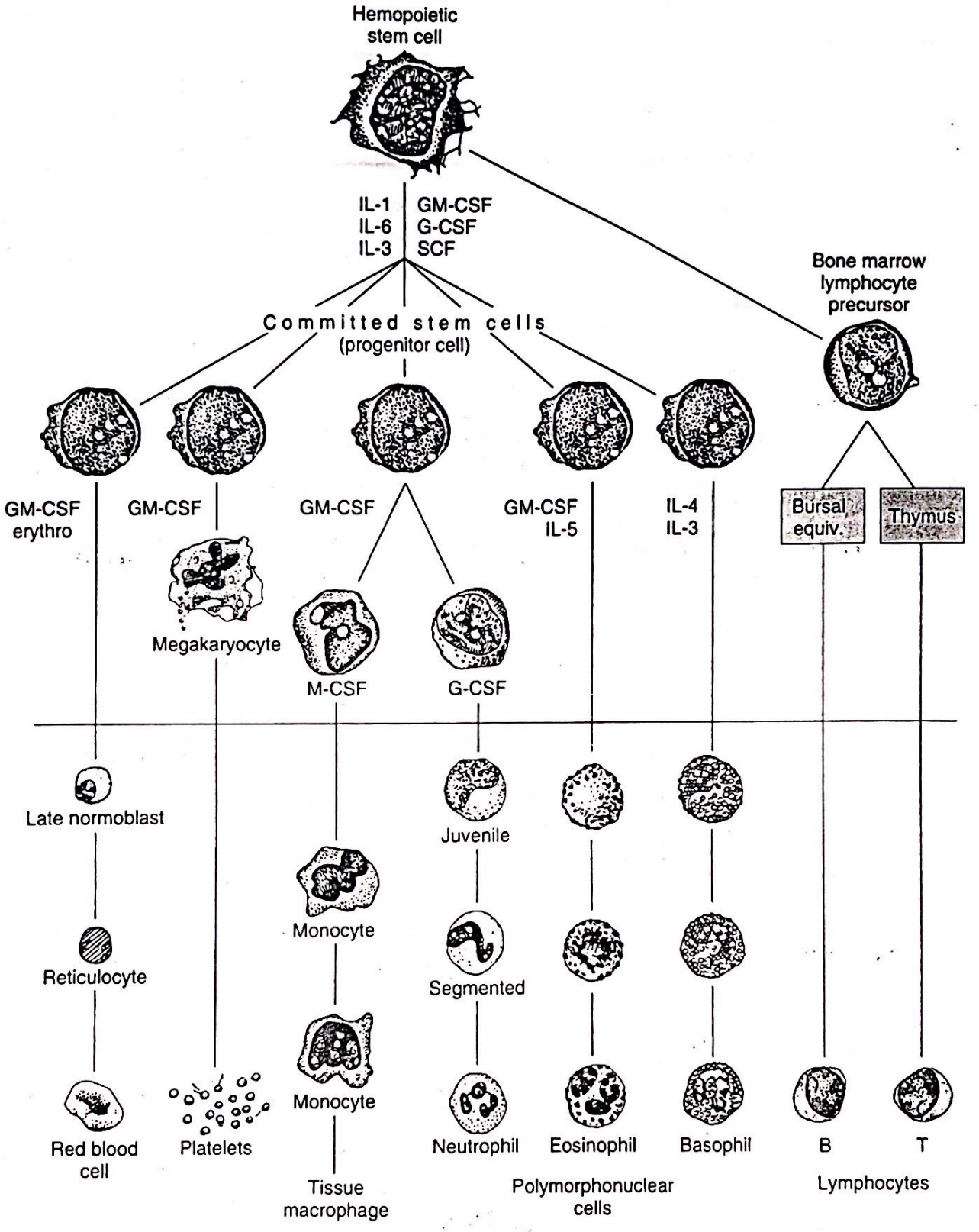

Figure 27–2 Development of various formed elements of the blood from bone marrow cells. Cells below the horizontal line are found in normal peripheral blood. The principal sites of action of erythropoietin (erythro) and the various colony-stimulating factors (CSF) that stimulate the differentiation of the components are indicated. G, granulocyte; M, macrophage; IL, interleukin; see Tables 27–2 and 27–3.

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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actin in the neutrophils does not polymerize normally, and the neutrophils move slowly. In another, there is a congenital deficiency of leukocyte integrins. In a more serious disease (chronic granulomatous disease), there is a failure to generate O_2^- in both the neutrophils and monocytes and consequent inability to kill many phagocytosed bacteria. In severe congenital glucose 6-phosphate dehydrogenase deficiency, there are multiple infections because of failure to generate the NADPH necessary for O_2^- production. In congenital myeloperoxidase deficiency, microbial killing power is reduced because hypohalite ions are not formed.

Lymphocytes

Lymphocytes are key elements in the production of immunity (see below). After birth, some lymphocytes are formed in the bone marrow. However, most are formed in the lymph nodes (Figure 27–4), thymus, and spleen from precursor cells that originally came from the bone marrow and were processed in the thymus or bursal equivalent (see below). Lymphocytes enter the bloodstream for the most part via the lymphatics. At any given time, only about 2% of the body lymphocytes are in the peripheral blood. Most of the rest are in the lymphoid organs. It has been calculated that in humans, 3.5×10^{10} lymphocytes per day enter the circulation via the thoracic duct alone; however, this count includes cells that reenter the lymphatics and thus traverse the thoracic duct more than once. The effects of adrenocortical hormones on the lymphoid organs, the circulating lymphocytes, and the granulocytes are discussed in Chapter 20.

IMMUNITY

Overview

Insects and other invertebrates have **innate immunity.** The key to this system is receptors that bind sequences of sugars, fats, or amino acids in common bacteria and activate various defense mechanisms. The receptors are coded in the germ line, and their fundamental structure is not modified by exposure to antigen. The activated

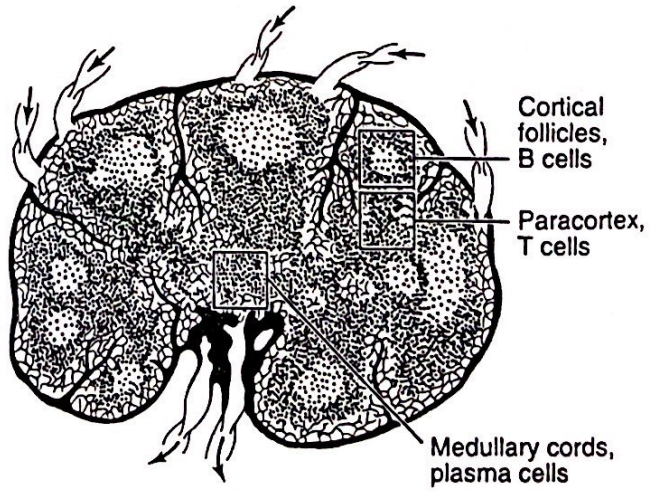

Figure 27–4 Anatomy of a normal lymph node. (After Chandrasoma. Reproduced, with permission, from McPhee SJ, Lingappa VR, Ganong WF [editors]: *Pathophysiology of Disease,* 4th ed. McGraw-Hill, 2003.)

Interleukins IL-1 and IL-6 followed by IL-3 act in sequence to convert pluripotential uncommitted stem cells to committed progenitor cel

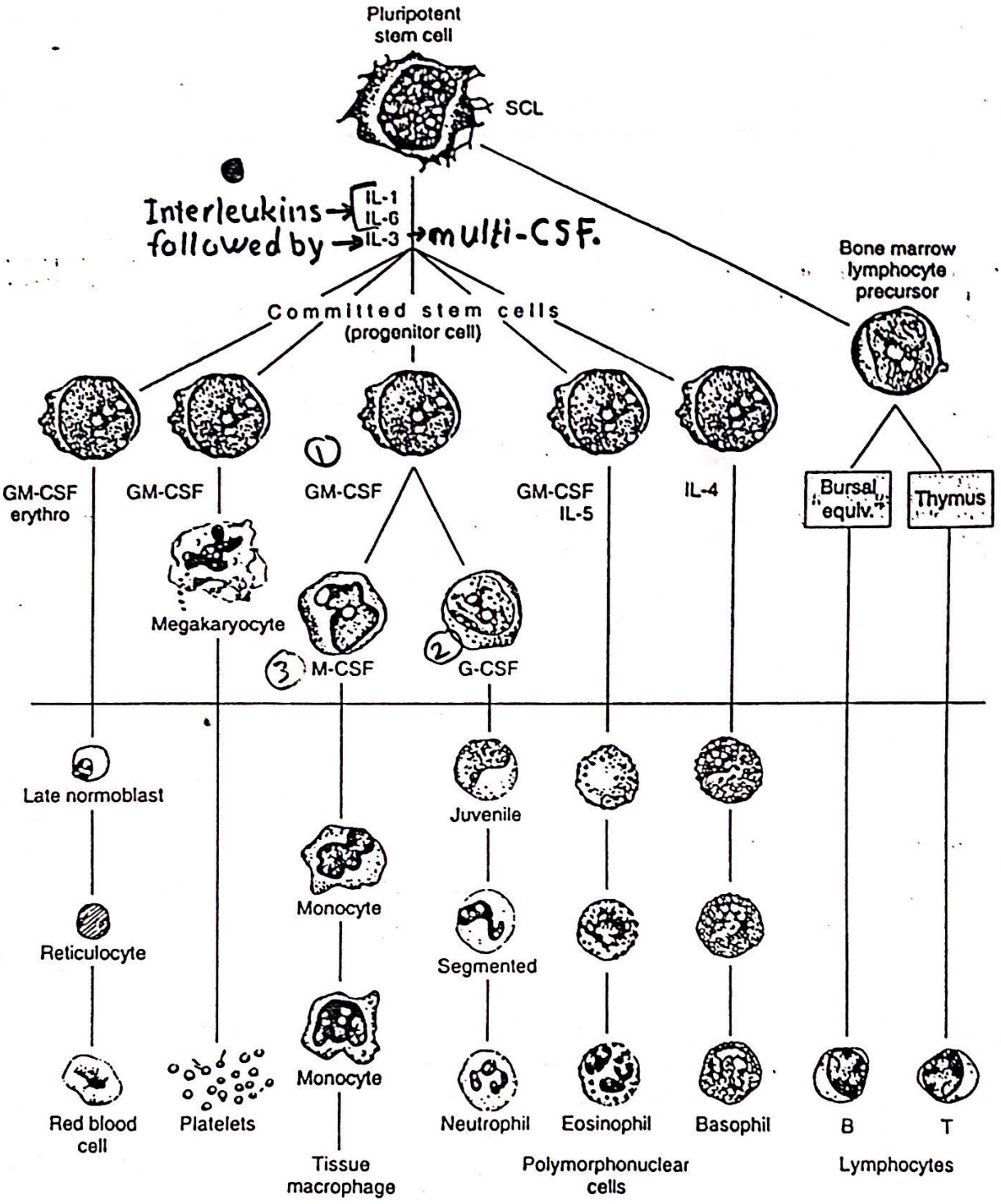

Figure 27–2. Development of various formed elements of the blood from bone marrow cells. Cells below the horizontal line are found in normal peripheral blood. The principal sites of action of erythropoietin (erythro) and the various colony-stimulating factors (CSF) that stimulate the differentiation of the components are indicated. G, granulocyte; M, macrophage; IL, interleukin; see Tables 27–2 and 27–4.

The factors stimulating the production of committed stem cells include 1 + 2 + 3 ↑. These factors are called colony-stin factors (CSFs), because they cause appropriate single stem cells to proliferate forming colonies in culture medium. Each of the CSFs a predominant action, but all the CSFs and interleukins also have other overlapping actions. Also activate and

See the last page,

Table 27–2. Factors regulating hematopoiesis.

Name	Cellular Sources	Cell Type Produced in Increased Numbers
SCL	?	Pluripotential cells
Erythropoietin	Kidney cells, Kupffer cells	Red blood cells
G-CSF	Monocytes, fibroblasts, endothelial cells	Neutrophils
M-CSF	Monocytes, fibroblasts, endothelial cells	Monocytes
GM-CSF	T cells, monocytes, fibroblasts, endothelial cells	Neutrophils, monocytes, eosinophils, megakaryocytes, red blood cells
IL-1	Macrophages, fibroblasts, endothelial cells	Neutrophils, monocytes, eosinophils, basophils, megakaryocytes, red blood cells
IL-3	T cells	
IL-4	T cells	Basophils
IL-5	T cells	Eosinophils
IL-6	Macrophages, fibroblasts, endothelial cells	Neutrophils, monocytes, eosinophils, basophils, megakaryocytes, red blood cells

Functions of the Leucocytes:-

All leucocytes possess, to some degree, four basic properties that relate to their functions in the body.

They are able to pass through the walls of capillaries, to enter the tissue spaces in accordance with the local needs. This process (I) is known as *diapedesis*. Once within the tissue spaces, the leukocytes (particularly the polymorphonucleocytes) have the ability to move through the tissues by an (II) ameboid motion at speeds of up to 40 μm min^{-1}. Furthermore, they seem to be attracted by certain chemical substances released by bacteria or by inflamed tissues (III) (*chemotaxis*).

(IV) Phagocytosis: The ability to engulf and digest or kill bacteria and products of cell death.

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.

Table 1.4 Main functions of blood cells.

Type of cell	Main functions
Red blood cells (erythrocytes)	Transport O_2 from lungs to tissues; transport CO_2 from tissues to lungs
Granulocytes	
Neutrophil	Chemotaxis, phagocytosis, killing of phagocytosed bacteria
Eosinophil	All neutrophil functions listed above, effector cells for antibody-dependent damage to metazoal parasites, regulate immediate type hypersensitivity reactions (inactivate histamine and slow-reacting substance of anaphylaxis released by basophils and mast cells)
Basophil	Mediate immediate-type hypersensitivity (IgE-coated basophils react with specific antigen and release histamine and slow reacting substance of anaphylaxis), modulate inflammatory responses by releasing heparin and proteases
Monocytes	Chemotaxis, phagocytosis, killing of some microorganisms, become macrophages
Platelets	Adhere to subendothelial connective tissue, participate in blood clotting (see p. 162)
Lymphocytes	Involved in immune responses

Table 1.2 Morphology of normal white cells in Romanowsky-stained smears of peripheral blood.

Cell type	Cell size (μm)	Cytoplasm			Nucleus
		Colour	Ratio of cytoplasmic volume to nuclear volume	Granules	
Neutrophil granulocytes	9–15	Slightly pink	High	Numerous, very fine, faint purple	Usually 2–5 segments
Eosinophil granulocytes	12–17	Pale blue	High	Many, large and rounded, reddish-orange	Usually two segments
Basophil granulocytes	10–14		High	Several, large and rounded, dark purplish-black	Usually two segments, granules overlie nucleus
Monocytes	15–30	Pale greyish-blue, cytoplasmic vacuoles may be seen	Moderately high or high	Variable number, fine, purplish-red	Various shapes (rounded, C- or U-shaped, lobulated), skein-like or lacy chromatin
Lymphocytes	7–12 (small lymphocytes); 12–16 (large lymphocytes)	Pale blue	Low or very low	Few, fine, purplish-red	Rounded with large clumps of condensed chromatin

- Interleukins IL-1 and IL-6 followed by IL-3 act in sequence to convert pluripotential uncommitted stem cells to committed progenitor cells.

- The factors stimulating the production of committed stem cells include (1+2+3↑). These factors are called colony-stin factors (CSFs), because they cause appropriate single stem cells to proliferate forming colonies in culture medium. Each of the CSFs a predominant action, but all the CSFs and ILs also have other overlapping actions. Also activate and sustain mature blood cells.