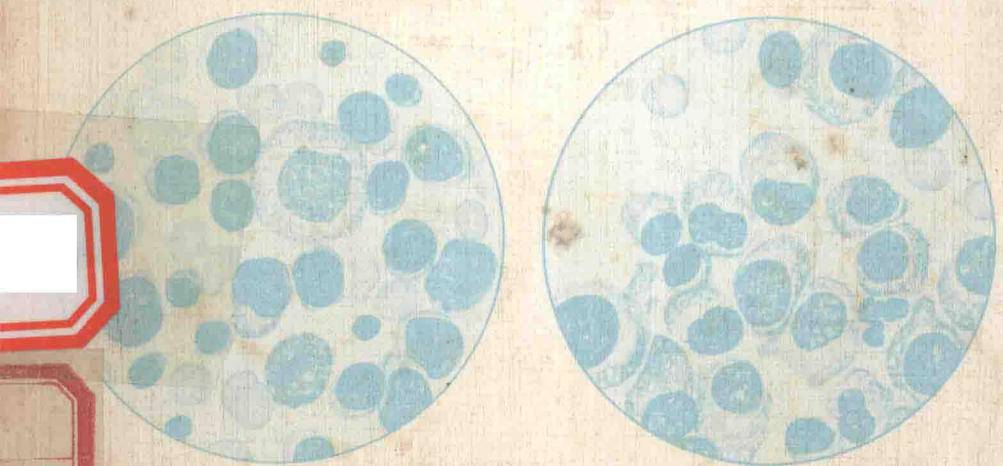
Blood and Bone Marrow Morphology Blood Coagulation

A Manual

Paul Frick

Translated by E. M. Gillis

3rd Revised and Enlarged Edition
44 Color Illustrations



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3rd Edition

Preface to the 3rd English Edition

The earlier editions of the "Manual of Blood and Bone Marrow Morphology" have been completely revised and enlarged. This new edition deals with blood coagulation as well because it is an integral part of the hematological training of medical laboratory technicians and medical students. In order to familiarize the reader with the close relationship between patient and laboratory findings, clinical aspects of hematological disorders are presented in greater detail. Various hematologic disorders that differ quantitatively or biochemically rather than morphologically from the normal have been included in the text for the first time (e.g., pancytopenia, agranulocytosis, polycythemia). Additional staining techniques used for the cytochemical characterization of the leukemias are described. Thus expanded, the new edition attempts to cover the whole field of practical hematological cytology and blood coagulation, taking into account the needs of both routine and specialized laboratories.

Zurich

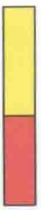
P. Frick

Contents

Normal Hematological Values

Blood Volume

The blood volume averages 75 ml/kg body weight in men, and 65 ml/kg body weight in women. The total blood volume consists of the cell volume and the plasma volume. The hematocrit gives the volume of packed red cells as a percentage of the total volume.



	Men ml/kg body weight	Women
Plasma volume	40	37
Cell volume	35	28
Total	75	65

Cellular Components of Blood

The normal values for the individual cellular components are given on page 3.

Erythrocytes and Hemoglobin

The erythrocyte is a biconcave round disk with a diameter of 7–7.8 μ and a maximum thickness of 2.5 μ. The most important component of the erythrocyte is hemoglobin. This pigment is the sole carrier of oxygen and partly also of carbon dioxide. Hemoglobin consists of four heme groups and globin (protein portion). Each heme group contains a divalent iron atom, and the globin consists of two α and two β chains. Each α chain consists of 141 amino acids and each β chain of 147 amino acids. Variations in the amino acid sequence of any one chain are the cause of hemoglobinopathies, e.g. hemoglobin S in sickle cell anemia.
The erythrocytes have a life-span of 120 days. The energy requirement of the erythrocytes is met by glucose; the erythrocyte mass of an adult requires 15–20 g glucose daily. About 90% of the intraerythrocytic glucose breakdown takes place via the anaerobic cycle and about 10% via the aerobic cycle.

Erythrocyte cell indices are calculated as follows:

Mean hemoglobin content of individual erythrocytes (Mean Corpuscular Hemoglobin, MCH)

$$\text{MCH} = \frac{\text{Hb (g/100 ml)} \times 10}{\text{erythrocytes } (10^6)/\text{mm}^3} = 29 \pm 2 \text{ pg (picogram)}$$

Mean hemoglobin concentration in erythrocytes (Mean Corpuscular Hemoglobin Concentration, MCHC)

$$\text{MCHC} = \frac{\text{Hb (g/100 ml)} \times 100}{\text{hematocrit}} = 33 \pm 2\%$$

Mean erythrocyte volume (Mean Corpuscular Volume, MCV)

$$\text{MCV} = \frac{\text{hematocrit} \times 10}{\text{erythrocytes } (10^6)/\text{mm}^3} = 89 \pm 5 \text{ fl (femtoliter)}$$

The cell indices allow the classification of anemias according to cell size, hemoglobin content and hemoglobin concentration.

Leucocytes

The number of leucocytes varies from 4000 to 9500 cells per mm^3. If the value lies below 4000 one speaks of leucopenia, and if the value exceeds 9500 leucocytosis is present. An increase in the band neutrophils of more than 16% is designated as shift to the left. The half-life of the neutrophilic granulocytes in the circulating blood is only 6–7 hours. The most important functions of neutrophilic granulocytes are phagocytosis and the destruction of bacteria. The eosinophilic granulocytes are increased in allergic conditions. Monocytes have similar functions to the neutrophilic leucocytes. The lymphocytes and plasma cells take part in immunological defense. Plasma cells and B-lymphocytes produce antibodies against bacterial and viral agents, and T-lymphocytes play an important role in cellular immunity, i.e. against fungal infections.

Bone Marrow

The bone marrow obtained by puncture from the sternum and iliac crest consists of half fat and of half cells. The quantitative cell distribution is listed on page 10. Erythrocytes, granulocytes, monocytes and platelets are formed exclusively in the bone marrow; lymphocytes and plasma cells originate mainly in lymph nodes and spleen and, to only a very small extent, in the bone marrow and liver.

Hemogram with Normal Values

Name _____ Date _____

Hemoglobin	____g%	(♂ 14–18) (♀ 12–16)	MCHC:	____%	(31–35)
Erythrocytes	____/mm³	(♂ 5±0.5 × 10⁶) (♀ 4.5±0.5 × 10⁶)	MCH:	____pg	(27–31)
Hematocrit	____%	(♂ 45±4) (♀ 40±4)	MCV:	____fl	(84–94)
Reticulocytes	____‰	(5–15)	**Leucocytes:**	____/mm³	(4–9500)
			Platelets:	____/mm³	(150–350000)

Differential blood picture

Erythroblasts			
Myeloblasts		%	
Promyelocytes		%	
Myelocytes	immature	%	
	semi-mature	%	
	mature	%	
Metamyelocytes		%	
Neutrophils	band	%	(5–16)
	segmented	%	(40–60)
Eosinophils		%	(2–4)
Basophils		%	(½–1)
Monocytes		%	(6–10)
Lymphocytes		%	(20–35)
Plasma cells		%	

Erythrocytes

Hb staining
Normocytosis
Anisocytosis
Microcytosis
Macrocytosis
Megalocytes
Ovalocytes
Poikilocytosis
Polychromasia
Basophilic stippling
Target cells
Howell-Jolly bodies
Stomatocytes
Fragmentocytes
Acanthocytes
Inclusion-bodies

Neutrophils	Nuclei:	normal segmentation, hypersegmented, pyknotic
	Plasma:	orthochromic, vacuoles, basophilic zones
	Granules:	fine, semi-coarse, coarse
Monocytes	Nucleus:	juvenile, old, granules
Lymphocytes	Nuclei:	small, large, indented
	Plasma:	basophilic, pale, wide, narrow, azurophilic granules
Platelets	Number:	assessed as normal, decreased, increased
	Quality:	giant platelets

Erythropoiesis
(Fig 1)

Megaloblasts and normoblasts must be strictly distinguished from each other morphologically. Megaloblasts are present only at the embryonic stage of development and in anemias due to vitamin B_{12} or folic acid deficiency. Megaloblasts develop into megalocytes, and normoblasts into normocytes.

The **megaloblast** is a very large cell with a slightly oval nucleus usually situated eccentrically. The chromatin forms a delicate network.

The **normal erythroblast** is smaller than the megaloblast and as a rule differs from it by a narrow cytoplasmic rim and a much denser, lumpier nuclear chromatin. The maturation process of the two cell types is the same.

1	**Promegaloblast.** Fine nuclear structure with nucleoli; cytoplasm basophilic, cloudy
2, 3	**Basophilic megaloblasts**
4, 5, 6	**Polychromatic megaloblasts**
7, 8	**Oxyphilic megaloblasts**
9	**Megalocyte**
10	**Pronormoblast**
11, 12	**Basophilic normoblasts**
13, 14, 15	**Polychromatic normoblasts**
16, 17	**Oxyphilic normoblasts**
18	**Normocyte**
19	**Karyorrhexis**
20	**Howell-Jolly body**

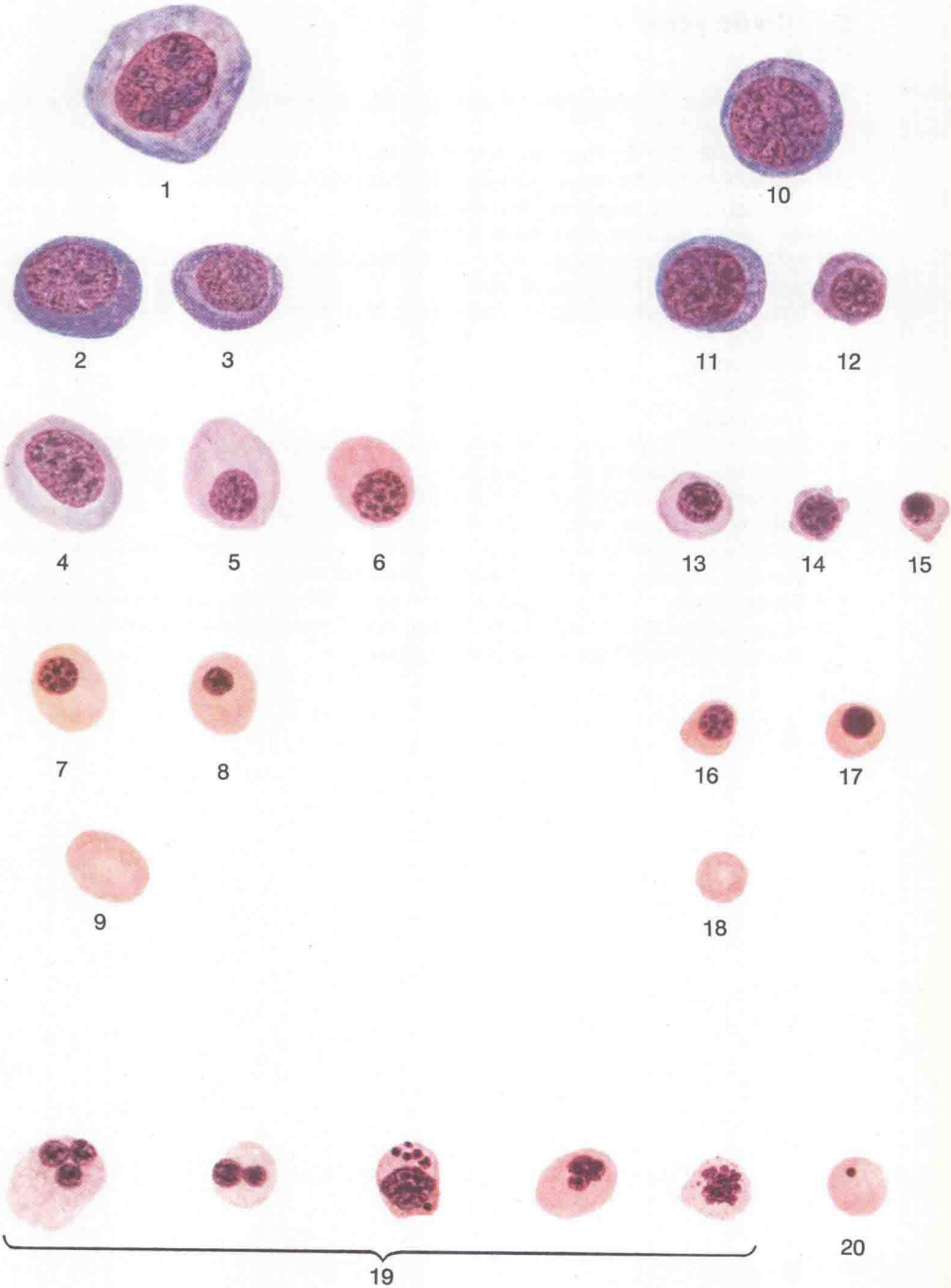


Fig 1 Erythropoiesis

Erythrocytes

(Fig 2)

1 **Normocytes** Erythrocytes of normal size (7.4 μ), shape and hemoglobin content
2 **Macrocytes** Larger than normocytes, round
3 **Megalocytes** Very large, elliptical erythrocytes, well-filled with hemoglobin (present only in megaloblastic anemias)
4 **Microcytes** Smaller than normocytes
5 **Spherocytes** Small, round, dark red erythrocytes with abundant hemoglobin, usually without pale central area
6 **Hypochromic erythrocytes** Large, pale central area due to low hemoglobin content
7 **Ovalocytes**
8 **Sickle cells**
9 **Target cells**
10 **Poikilocytes** Erythrocytes of irregular shape, frequently pear-shaped
11 **Crenated forms** Shrinkage products
12 **Anisocytosis** Erythrocytes of varying size
13 **Polychromasia** Juvenile erythrocytes with a bluish tint
14 **Basophilic stippling** Erythrocytes with blue stippling. Sign of regeneration in anemias. Present in large numbers in lead poisoning.
15 **Reticulocytes** Young erythrocytes with substantia granulofilamentosa. Normally 5–15 per 1000 erythrocytes. An increase indicates vigorous regeneration of erythrocytes in the bone marrow.

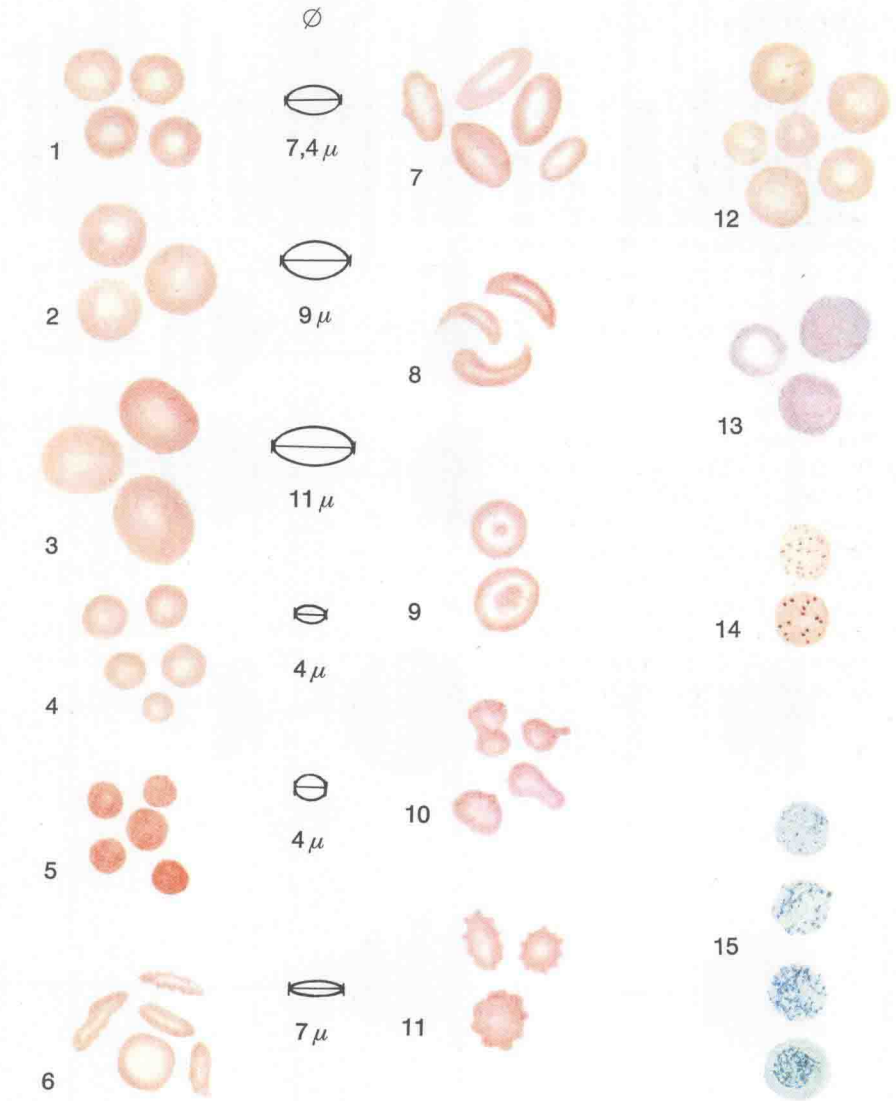


Fig 2 Erythrocytes

Leuco- and Thrombopoiesis

(Fig 3)

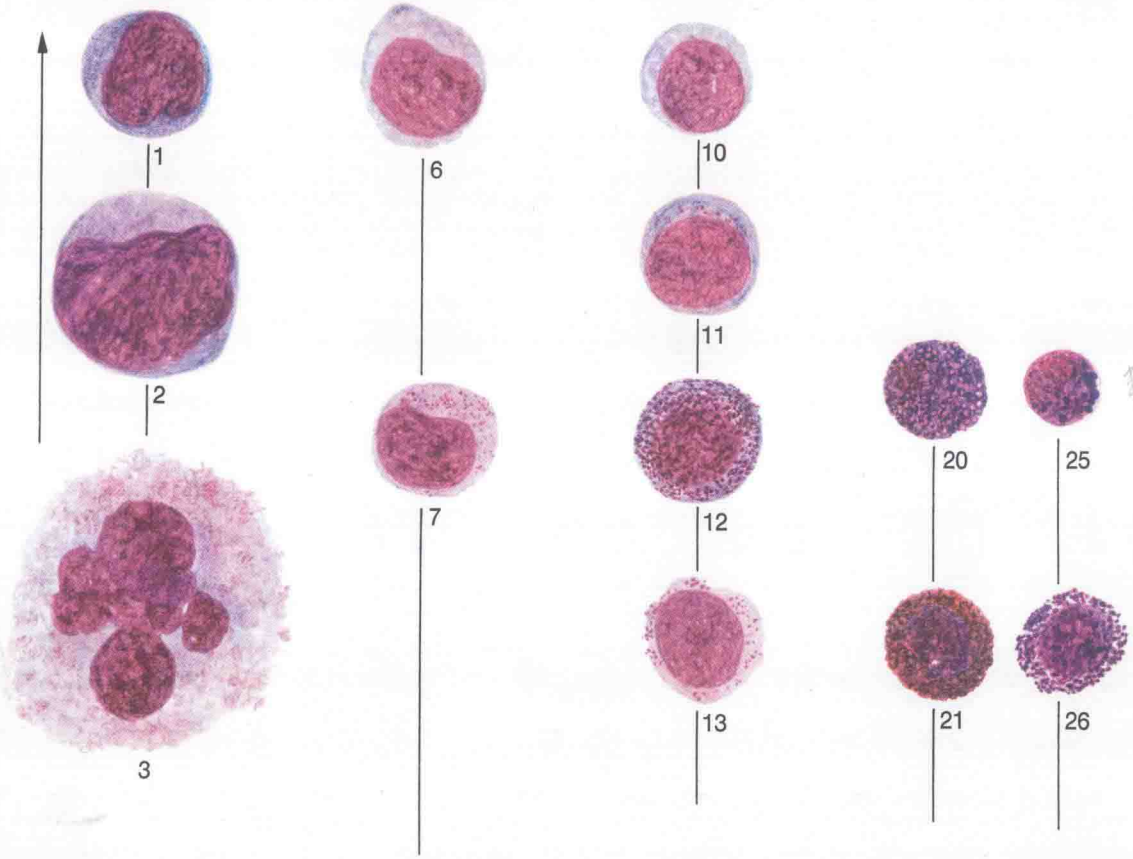
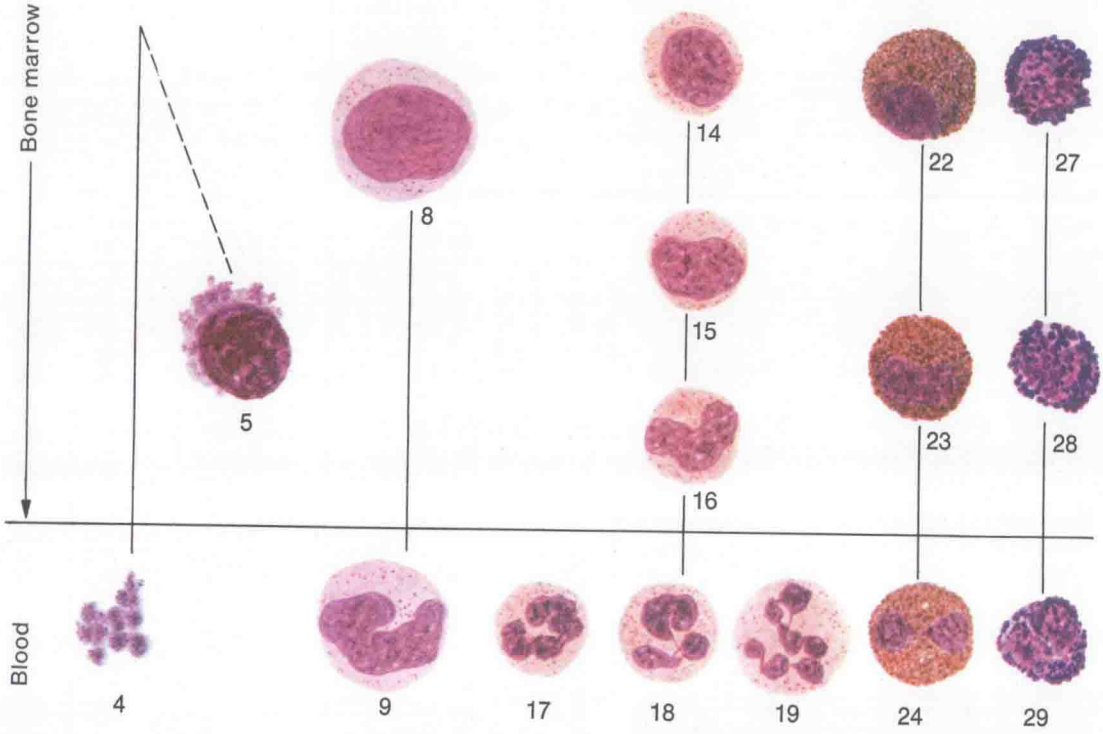


Fig 3

1 **Megakaryoblast**
2 **Immature megakaryocyte**
3 **Mature megakaryocyte**
4 **Platelets (thrombocytes)**
5 **Megakaryocyte nucleus with platelets**
6 **Monoblast** Fine-meshed nucleus, frequently still containing nucleoli, basophilic cytoplasm
7, 8 **Young monocytes**
9 **Mature monocyte** Lobed, coarse-meshed nucleus, grayish-blue cytoplasm with fine, dust-like red granules
10 **Myeloblast** Fine-meshed nucleus with 2–3 nucleoli, basophilic cytoplasm without granulation
11 **Promyelocyte**
12 **Immature myelocyte**
13 **Semimature myelocyte**
14 **Mature myelocyte**
12, 13, 14 With maturation, the nuclei become more coarse-meshed, the basophilic cytoplasm changes to oxyphilic



and the basophilic granules become fine and oxyphilic

15 **Metamyelocyte** Kidney-shaped, indented nucleus

16 **Juvenile nonsegmented, band neutrophilic leucocyte**

17 **Mature band neutrophilic leucocyte**

18 **Segmented neutrophilic leucocyte**

19 **Hypersegmented neutrophilic leucocyte**

20, 21, 22, 23 **Eosinophilic myelocytes**
20 Nucleus covered with coarse eosinophilic and partly basophilic granules. 21–23 Maturing forms

24 **Eosinophilic leucocyte** Nucleus segmented, granules eosinophilic

25, 26, 27, 28 **Basophilic myelocytes**
Nuclei round to indented. Granules coarse, blue-black

29 **Basophilic leucocyte**

Normal Cell Distribution in Bone Marrow

	Normal values		
Pronormoblasts	1	22	100
Basophilic normoblasts	3		
Polychromatic normoblasts	6		
Oxyphilic normoblasts	12		
Myeloblasts	1	78	
Promyelocytes	4		
Myelocytes, immature			
Myelocytes, semi-mature	12		
Myelocytes, mature			
Metamyelocytes	7		
Band neutrophils	30		
Segmented neutrophils	6		
Eosinophils	4		
Basophils	0–1		
Monocytes	2		
Lymphocytes and lymphoid cells	8		
Plasma cells	2		
Reticulum cells	1		
Macrophages	0–1		
Tissue mast cells			
Megakaryocytes			