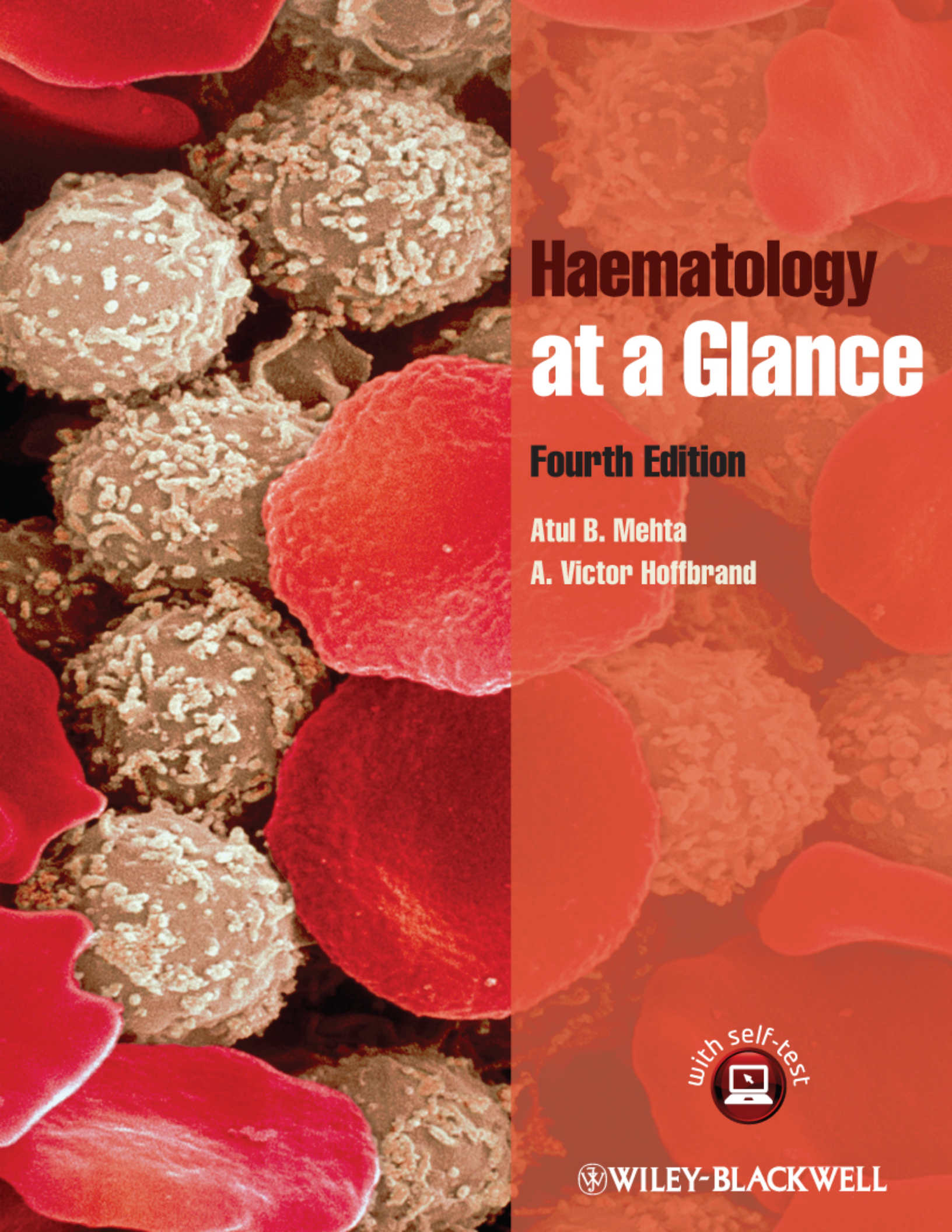


A microscopic image of blood cells, showing several red blood cells (erythrocytes) and white blood cells (leukocytes). The red blood cells are biconcave discs, and the white blood cells are larger with prominent nuclei. The image is overlaid with a semi-transparent orange-red gradient on the right side.

Haematology at a Glance

Fourth Edition

Atul B. Mehta

A. Victor Hoffbrand



 **WILEY-BLACKWELL**

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Haematology at a Glance

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Preface to the fourth edition

Major advances in classification, diagnostic techniques and treatment have occurred over the 4 years since the third edition of this book was published. Much of this new knowledge has depended on the application of molecular techniques for diagnosis and determining treatment and prognosis, particularly for the malignant haematological diseases. New drugs are now available, not only for these diseases but also for treatment of red cell, platelet, thrombotic and bleeding disorders. In order to keep the book to the *at a Glance* size and format, we have included only the new information which represents major change in haematological practice and omitted more detailed knowledge, appropriate for a postgraduate text. The number of diagrams and tables has been increased to make the new information readily accessible to the undergraduate student but overall size of the book has not increased thanks to omission of all obsolete material.

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Atul B. Mehta
A. Victor Hoffbrand

December 2013

Preface to the first edition

With the ever-increasing complexity of the medical undergraduate curriculum, we feel that there is a need for a concise introduction to clinical and laboratory haematology for medical students. The *at a Glance* format has allowed us to divide the subject into easily digestible slices or bytes of information.

We have tried to emphasize the importance of basic scientific and clinical mechanisms, and common diseases as opposed to rare syndromes. The clinical features and laboratory findings are summarized and illustrated; treatment is briefly outlined.

This book is intended for medical students, but will be useful to anyone who needs a concise and up-to-date introduction to haematology, for example nurses, medical laboratory scientists and those in professions supplementary to medicine.

We particularly thank June Elliott, who has patiently word-processed the manuscript through many revisions, and Jonathan Rowley and his colleagues at Blackwell Science.

Atul B. Mehta
A. Victor Hoffbrand
January 2000

Glossary

Anaemia:	a haemoglobin concentration in peripheral blood below normal range for sex and age.
Anisocytosis:	variation in size of peripheral blood red cells.
Basophil:	a mature circulating white cell with dark purple-staining cytoplasmic granules which may obscure the nucleus.
Chromatin:	nuclear material containing DNA and protein.
Clone:	a group of cells all derived by mitotic division from a single somatic cell.
CT:	computerized scanning.
DIC:	disseminated intravascular coagulation.
Eosinophil:	mature circulating white cell with multiple orange-staining cytoplasmic granules and two or three nuclear lobes.
Fluorescent <i>in situ</i> hybridization (FISH):	the use of fluorescently labelled DNA probes which hybridize to chromosomes or sub-chromosomal sequences to detect chromosome deletions or translocations.
Haematocrit:	the proportion of a sample of blood taken up by red cells.
Haemoglobin:	the red protein in red cells which is composed of four globin chains each containing an iron-containing haem group.
Karyotype:	the chromosomal make-up of a cell.
Leucocytosis:	a rise in white cell levels in the peripheral blood to above the normal range.
Leucopenia:	a fall in white cell (leucocyte) levels in the peripheral blood to below the normal range.
Lymphocyte:	a white cell with a single, usually round, nucleus and scanty dark blue-staining cytoplasm. Lymphocytes divide into two main groups: B cells, which produce immunoglobulins; and T cells, which are involved in graft rejection and immunity against viruses.
Macrocytic:	red cells of average volume (MCV) above normal.
Mean cell volume (MCV):	the average volume of circulating red cells.
Mean corpuscular haemoglobin (MCH):	the average haemoglobin content of red blood cells.
Megaloblastic:	an abnormal appearance of nucleated red cells in which the nuclear chromatin remains open and fine despite maturation of the cytoplasm.

Microcytic:	red cells of average volume (MCV) below normal.
Monocyte:	mature circulating white cell with a few pink- or blue-staining cytoplasmic granules, pale blue cytoplasm and a single nucleus. There are usually cytoplasmic vacuoles. In the tissues, the monocyte becomes a macrophage.
MRI:	magnetic resonance imaging.
Myeloblast:	an early granulocyte precursor containing nucleoli and with a primitive nucleus; there may be some cytoplasmic granules.
Myelocyte:	a later granulocyte precursor containing granules, a single lobed nucleus and semi-condensed chromatin.
Neutrophil:	a mature white cell containing two to five nuclear lobes and many, fine, reddish or purple cytoplasmic granules.
Normoblast:	(erythroblast): nucleated red cell precursor normally found only in bone marrow.
Pancytopenia:	a fall in peripheral blood red cell, neutrophil and platelet levels to below normal.
Pappenheimer body:	an iron granule in red cells stained by standard (Romanovsky) stain.
Paraprotein:	a γ -globulin band on protein electrophoresis consisting of identical molecules derived from a clone of plasma cells.
PET scan:	positron emission tomography scan used to detect the sites of active disease, e.g. lymphoma.
Phagocyte:	a white blood cell that engulfs bacteria or dead tissue. It includes neutrophils and monocytes (macrophages).
Plasma cell:	usually an oval-shaped cell, derived from a B lymphocyte, which secretes immunoglobulin. Plasma cells are found in normal bone marrow but not in normal peripheral blood.
Platelet:	the smallest cell in peripheral blood, it is non-nucleated and involved in promoting haemostasis.
Poikilocytosis:	variation in shape of peripheral blood red cells.
Polycythaemia:	a haemoglobin concentration in peripheral blood above normal range for age and sex.
Red cell:	mature non-nucleated cell carrying haemoglobin. The most abundant cell in peripheral blood.
Reticulocyte:	a non-nucleated young red cell still containing RNA and found in peripheral blood.
Sideroblast:	a nucleated red cell precursor found in marrow and containing iron granules, which appear blue with Perls' stain.
Siderocyte:	a mature red cell containing iron granules and found in peripheral blood or marrow.
Stem cell:	resides in the bone marrow and by division and differentiation gives rise to all the blood cells. The stem

cell also reproduces itself. Some stem cells circulate in the peripheral blood.

Thrombocytopenia: a platelet level in peripheral blood below the normal range.

Thrombocytosis: a platelet level in peripheral blood above the normal range.

Tissue factor: a protein on the surface of cells which initiates blood coagulation.

White cell (leucocyte): nucleated cell that circulates in peripheral blood and whose main function is combating infections. White cells include granulocytes (neutrophils, eosinophils, and basophils), monocytes and lymphocytes.

von Willebrand factor: a plasma protein that carries factor VIII and mediates the adhesion of platelets to the vessel wall.

Normal values

Normal peripheral blood count

Cell	Normal concentration
Haemoglobin	115–155 g/L (female)
	135–175 g/L (male)
Red cell	$3.9\text{--}5.6 \times 10^{12}/\text{L}$ (female)
	$4.5\text{--}6.5 \times 10^{12}/\text{L}$ (male)
Reticulocyte	0.5–3.5%
	$\sim 25\text{--}95 \times 10^9/\text{L}$
White cells	$4.0\text{--}11.0 \times 10^9/\text{L}$
Neutrophils	$1.8\text{--}7.5 \times 10^3/\text{L}$
	$(1.5\text{--}7.5 \times 10^9/\text{L}$ in black people)
Eosinophils	$0.04\text{--}0.4 \times 10^9/\text{L}$
Basophils	$0.01\text{--}0.1 \times 10^9/\text{L}$
Monocytes	$0.2\text{--}0.8 \times 10^9/\text{L}$
Lymphocytes	$1.5\text{--}3.0 \times 10^9/\text{L}$
Haematocrit	0.38–0.54
Mean cell volume	80–100 (Fig. 8.2)
Mean cell haemoglobin	27–33 (Fig. 8.2)
Haematinics	
Serum iron	10–30 $\mu\text{mol}/\text{L}$
Total iron binding capacity	40–75 $\mu\text{mol}/\text{L}$ (2–4 g/L as transferrin)
Serum ferritin	40–340 $\mu\text{g}/\text{L}$ (males)
	15–150 $\mu\text{g}/\text{L}$ (females)
Serum folate	3.0–15.0 $\mu\text{g}/\text{L}$ (4–30 nmol/L)
Red cell folate	160–640 $\mu\text{g}/\text{L}$ (360–1460 nmol/L)
Serum vitamin B ₁₂	160–925 $\mu\text{g}/\text{L}$ (120–682 pmol/L)

About the companion website



Visit the companion website at:

www.ataglanceseries.com/haematology

The website includes:

- Multiple-Choice Questions
- Case studies from the book

All of these are interactive so that you can easily test yourself on the topics in each chapter.

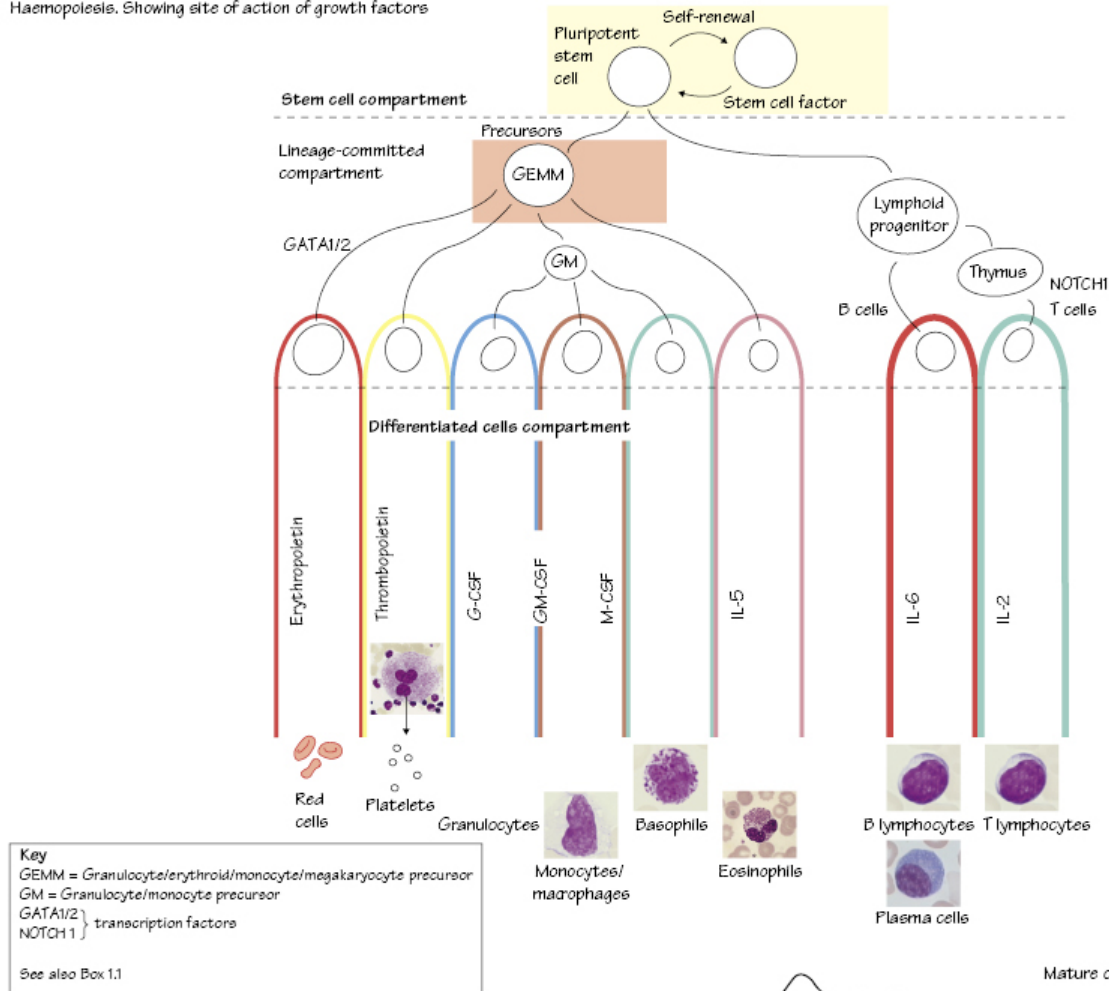


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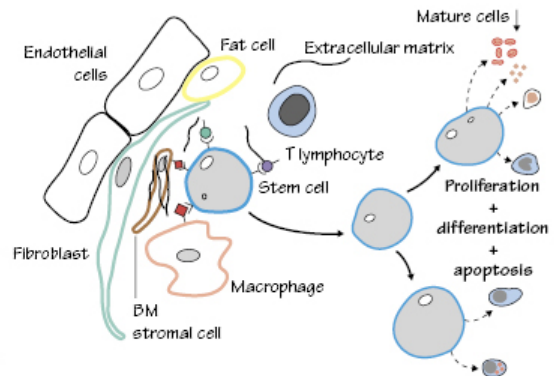
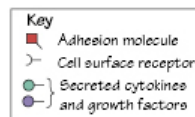
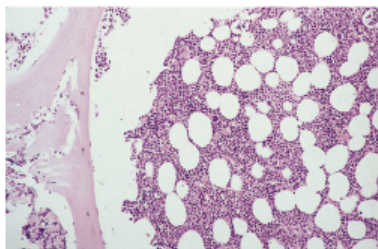
1

Haemopoiesis: physiology and pathology

1.1 Haemopoiesis. Showing site of action of growth factors

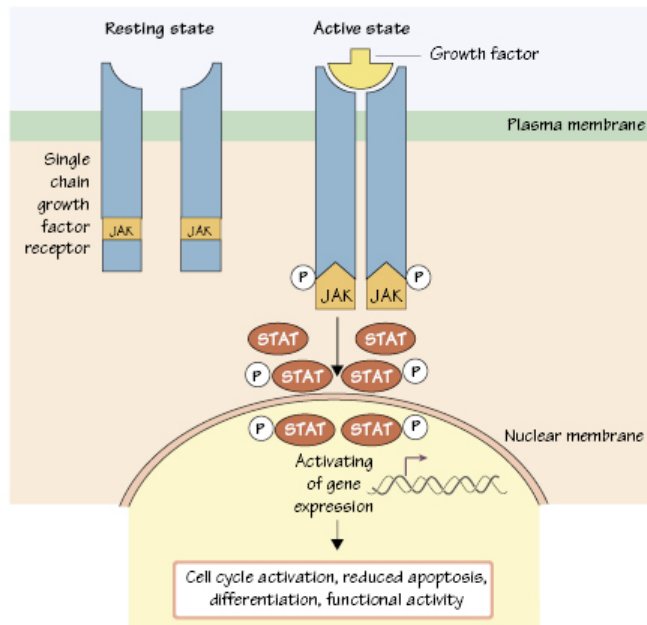


1.2 Low power microscopic view of bone marrow trephine biopsy

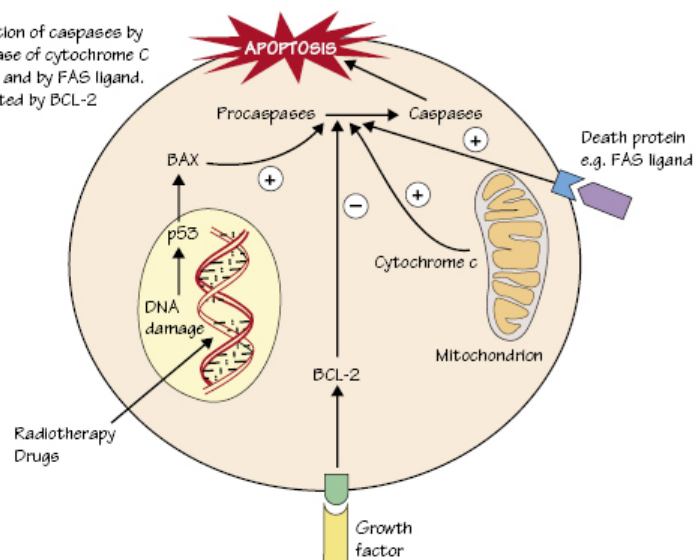


1.3 Haemopoiesis occurs within bone marrow microenvironment ('niche') where haemopoietic stem cells are brought into contact with a range of other cell types. Cell-cell communication is by binding, via cell surface receptors, to adhesion molecules and to fixed or secreted cytokines and growth factors. This binding triggers signal transduction which regulates gene transcription leading to proliferation, differentiation and inhibition or activation of apoptosis

1.4 The signal transduction pathway. This is a series of biochemical pathways whereby a message from the cell surface can be transmitted to the nucleus (see pg 12)



1.5 Apoptosis. Activation of caspases by DNA damage, release of cytochrome C from mitochondria and by FAS ligand. Apoptosis is inhibited by BCL-2



Definition and sites

Haemopoiesis is the process whereby blood cells are made (Fig. 1.1). The yolk sac, and later the liver and spleen, are important in fetal life, but after birth normal haemopoiesis is restricted to the bone marrow.

Infants have haemopoietic marrow in all bones, but in adults it is in the central skeleton and proximal ends of long bones (normal fat to haemopoietic tissue ratio of about 50 : 50) (Fig. 1.2). Expansion of haemopoiesis down the long bones may occur in bone marrow malignancy, e.g. in leukaemias, or when there is increased demand, e.g. chronic haemolytic anaemias. The liver and spleen can resume extramedullary haemopoiesis when there is marrow replacement, e.g. in myelofibrosis, or excessive demand, e.g. in severe haemolytic anaemias such as thalassaemia major.

Stem and progenitor cells

Haemopoiesis involves the complex physiological processes of proliferation, differentiation and apoptosis (programmed cell death). The bone marrow produces more than a million red cells per second in addition to similar numbers of white cells and platelets. This capacity can be increased in response to increased demand. A common primitive stem cell in the marrow has the capacity to self-replicate and to give rise to increasingly specialized or committed progenitor cells which, after many (13–16) cell divisions within the marrow, form the mature cells (red cells, granulocytes, monocytes, platelets and lymphocytes) of the peripheral blood (Fig. 1.1). The earliest recognizable red cell precursor is a pronormoblast and for granulocytes or monocytes, a myeloblast. An early lineage division is between lymphoid and myeloid cells. Stem and progenitor cells cannot be recognized morphologically; they resemble lymphocytes. Progenitor cells can be detected by *in vitro* assays in which they form colonies (e.g. colony-forming units for granulocytes and monocytes, CFU-GM, or for red cells, BFU-E and CFU-E). Stem and progenitor cells also circulate in the