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风暴式医学教程

Mosby's Crash Course

免疫、血液及淋巴系统

Immune, Blood, and Lymphatic Systems

Saimah Arif ⊙ Arjmand Mufti
***with* Daniel Horton-Szar as Series Editor**

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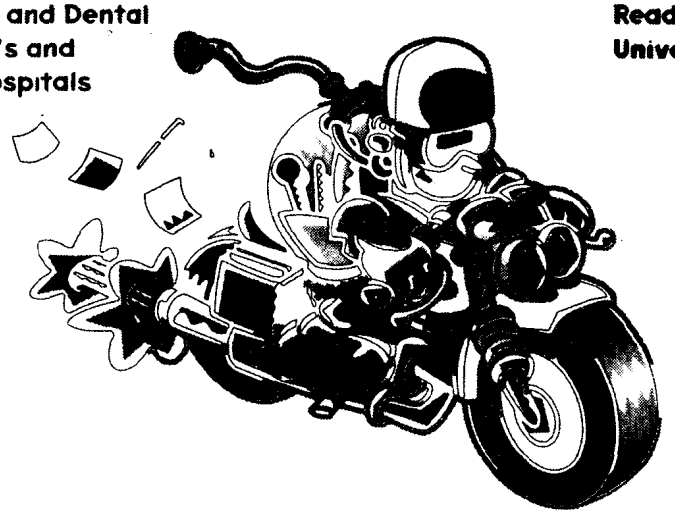
Series editor
Daniel Horton-Szar
BSc (Hons)
United Medical and Dental Schools of Guy's and St Thomas's Hospitals (UMDS), London

Faculty advisor
David B Jones
PhD
Reader in Pathology
University of Southampton



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Saimah Arif
BSc (Hons)
United Medical and Dental Schools of Guy's and St Thomas's Hospitals (UMDS), London

Arjmand Mufti
BSc (Hons)
United Medical and Dental Schools of Guy's and St Thomas's Hospitals (UMDS), London

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Preface

Immunology is a subject that many medical students find hard to master because of its conceptual nature. Haematology, for the medical student, is factual rather than conceptual, and the main problem is one of sifting through a large volume of information.

In this book, we have tried to present the information in a clear and concise manner, emphasizing points of particular importance to medical students (and to examiners!). The clinical aspects of these subjects are presented alongside the basic sciences so that the student can appreciate the link between the two, facilitating greater understanding and easier learning.

Enjoy!

Saimah Arif
Arjmand Mufti

Immunology, as with many areas of medicine, is a constantly evolving science. Nevertheless, the authors of this book have endeavoured to present all the relevant information relating to the current medical curriculum as recommended by the General Medical Council.

This volume fulfils the need to supply a revision text that covers the essential aspects of the normal physiology and pathology of the lymphoreticular system. The aim throughout has been to provide a concise and readable text with clearly drawn and easy-to-understand illustrations. In addition, hints and tips boxes and comprehension check boxes aid learning and understanding. At the end of the book there is a practice exam for self-assessment.

We hope that Crash Course Immune, Blood, and Lymphatic Systems will provide useful revision material which is relevant to the current revised medical curricula.

David Jones
Faculty Advisor

Preface

OK, no-one ever said medicine was going to be easy, but the thing is, there are very few parts of this enormous subject that are actually difficult to understand. The problem for most of us is the sheer volume of information that must be absorbed before each round of exams. It's not fun when time is getting short and you realize that: a) you really should have done a bit more work by now; and b) there are large gaps in your lecture notes that you meant to copy up but never quite got round to.

This series has been designed and written by senior medical students and doctors with recent experience of basic medical science exams. We've brought together all the information you need into compact, manageable volumes that integrate basic science with clinical skills. There is a consistent structure and layout across the series, and every title is checked for accuracy by senior faculty members from medical schools across the UK.

I hope this book makes things a little easier!

Danny Horton-Szar
Series Editor (Basic Medical Sciences)

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Figure Credits

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Figures 11.26 and 11.27 taken from *Blood in Systemic Disease*, Mosby, 1997.Courtesy of M. Makris and M. Greaves. .

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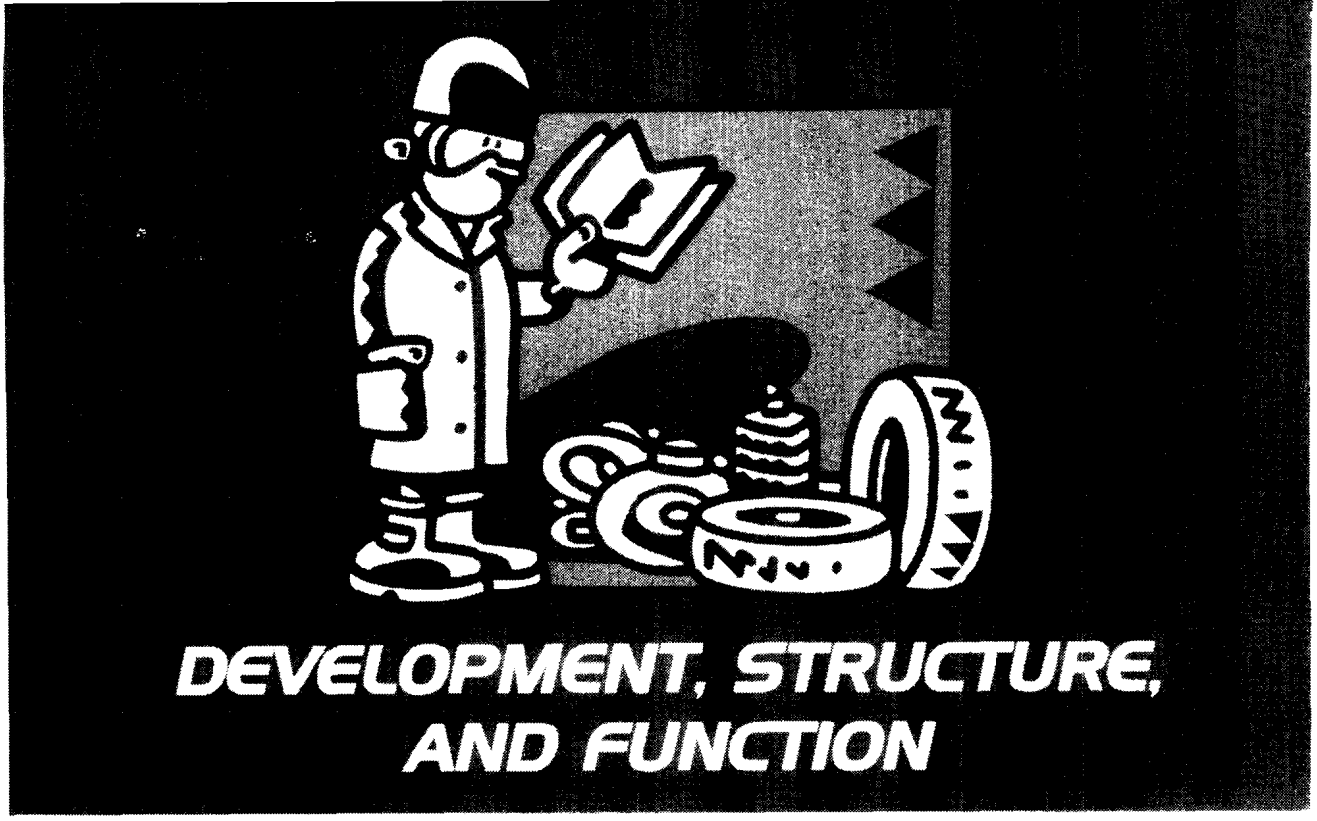

DEVELOPMENT, STRUCTURE, AND FUNCTION

1. Overview of the Immune, Blood, and Lymphatic Systems

THE PLAYERS—AN OVERVIEW OF THE CELL LINES

All mature blood cells are derived from a common stem cell. Haemopoiesis is the formation and development of red and white blood cells from these undifferentiated stem cells. Haemopoietic stem cells are pluripotent, i.e. they are capable of differentiating along a number of pathways and have an unlimited capacity for self-renewal, thus maintaining a reserve population.

Stem cells yield one of three main cell lineages:

- Erythroid → erythrocytes.
- Lymphoid → lymphocytes.
- Myeloid → neutrophils, basophils, eosinophils, monocytes, and megakaryocytes.

Subsequent differentiation of the erythroid, lymphoid, and myeloid cells gives rise to specialized progenitor cells for each type of mature blood cell. These cells are not capable of self-renewal (Fig. 1.1).

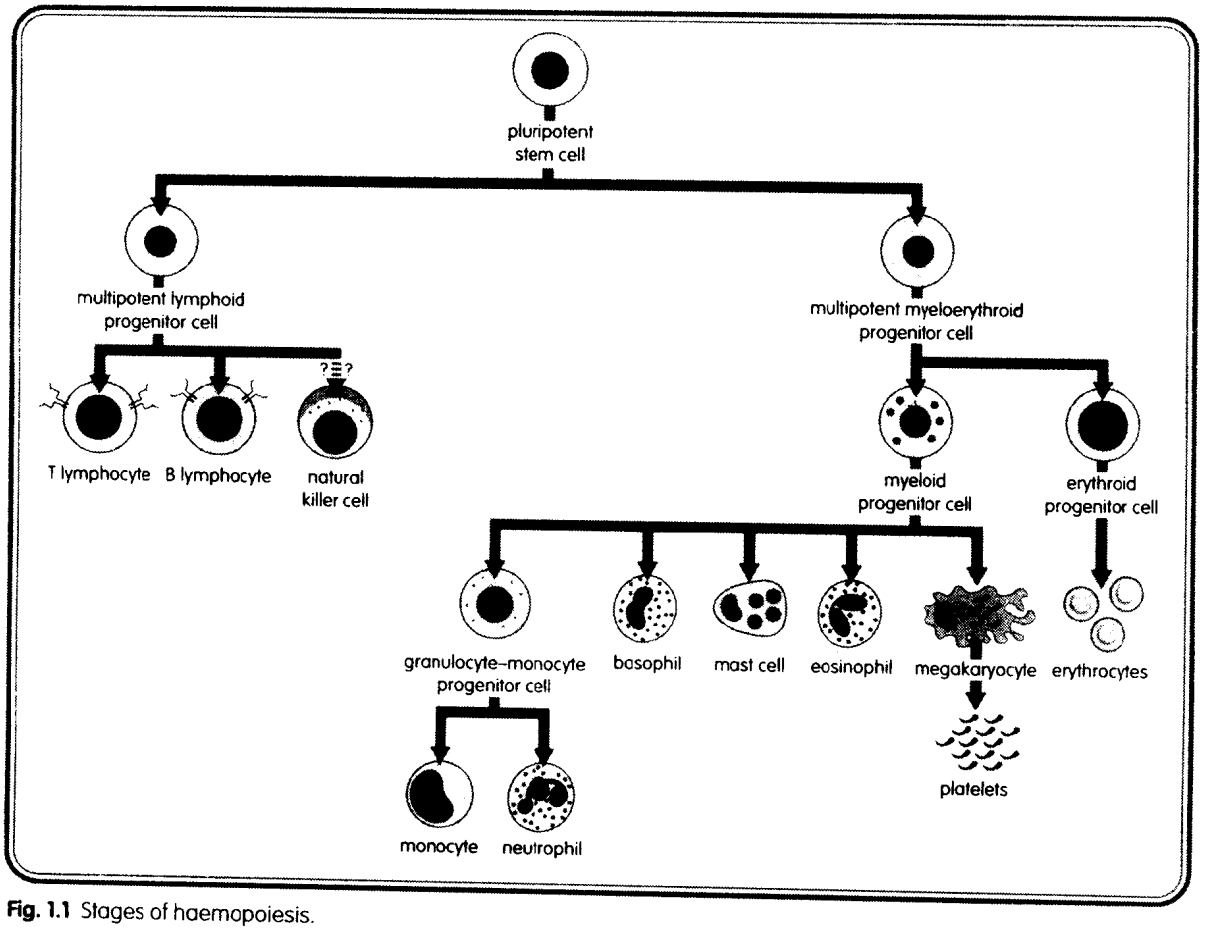

Fig. 1.1 Stages of haemopoiesis.

Sites of haemopoiesis

The site of haemopoiesis changes according to developmental age:

- Birth to 6 weeks—fetal yolk sac.
- From 6 weeks to 6 months—fetal liver.
- From 6 months onwards—bone marrow.

Myeloid cells

The first progenitor cell produced when haemopoietic stem cells are grown *in vitro* is the colony-forming unit (CFU). This is capable of giving rise to granulocytes, erythrocytes, monocytes, and megakaryocytes (CFU-GEMM). Various growth factors, or cytokines, are required for the proliferation and differentiation of haemopoietic cells, including colony-stimulating factors (CSFs). Major CSFs that have been identified include:

- Multilineage CSF (also known as interleukin-3).
- Granulocyte–macrophage CSF (GM-CSF).
- Macrophage CSF (M-CSF).
- Granulocyte CSF (G-CSF).

A group of cytokines called interleukins (ILs) are also involved in the regulation of haemopoiesis. They are produced primarily by the bone marrow stromal cells. Stem cell factor (SCF), also secreted by the bone marrow stromal cells, acts on primitive stem cells.

CSFs act in a sequential manner:

1. Multi-CSF acts early in differentiation, to induce formation of all non-lymphoid blood cells including erythrocytes, granulocytes, monocytes, and megakaryocytes.
2. GM-CSF acts on the same cell lines at a later stage.
3. M-CSF and G-CSF act later still, to stimulate the formation of monocytes and neutrophils, respectively.

Specific cytokine receptors are expressed on the membrane of each progenitor cell and are pivotal in subsequent differentiation and maturation, e.g. the macrophage progenitor cell expresses specific receptors for M-CSF, the binding of which stimulates cellular proliferation and differentiation.

Erythropoietin, a haemopoietic cytokine, is produced by the kidney. It is involved in terminal erythrocyte development and regulates red blood cell production.

Lymphoid cells

Lymphoid progenitor cells differentiate to form three distinct cell types:

- B cell.
- T cell.
- Natural killer (NK) cell.

Lymphocytes comprise 20–40% of the body's white blood cells. They circulate in the blood and lymph, and also have the capacity to migrate into tissue spaces and lymphoid organs. The B cell receptor is a membrane-bound antibody molecule; the T cell expresses the T cell receptor.

B and T cells share the following features:

- Diversity.
- Specificity.
- Memory.
- Discrimination between self and non-self.

NK cells do not express antigenic receptors and hence do not express specificity. However, they have been implicated in tumour lysis and protection against viral infections, although the exact mechanisms remain unclear.

A general overview of the functions of different blood cells is shown in Fig. 1.2.

- **Describe the concepts underlying haemopoiesis.**
- **What are the processes via which myeloid and lymphoid cells are produced?**
- **Summarize the functions of blood cells.**

Blood cell functions	
Cell type	**Functions**
erythrocytes	carry O_2 from lungs to tissues, and CO_2 from tissues to lungs
neutrophils	usually first to arrive at point of inflammation by chemotaxis—phagocytosis and the killing of phagocytosed bacteria
basophils	non-phagocytic—major role in allergic responses via release of mediators, e.g. histamine; may also play role in immunity against parasites
eosinophils	as for neutrophils, although decreased phagocytic function, play major role in defence against parasites; dampen inflammatory response in immediate-type hypersensitivity via release of histaminase and aryl sulphatase, which inactivate mast cell products such as histamine
monocytes	phagocytosis and removal of antigen; act as antigen-presenting cells (APCs)
platelets	adhere to exposed subendothelial connective tissue and participate in blood clotting
lymphocytes	key players in adaptive immune response; release haemopoietic substances

Fig. 1.2 Blood cell functions.

2. Organization of the Lymphoid System

Lymphoid organs and tissues are classified as primary (central) or secondary (peripheral).

PRIMARY LYMPHOID ORGANS

The bone marrow and thymus comprise the primary lymphoid organs and are the main sites of lymphocyte development and maturation.

Bone marrow

Haemopoietic tissue fills all of the bone cavities in the newborn, but in the adult, haemopoiesis is restricted principally to the sternum, vertebrae, pelvis, and ribs. The total volume of haemopoietic tissue is 1–2 litres. Because of its macroscopic appearance, this tissue is known as red marrow. Approximately 50% of red marrow consists of fat. The marrow in the peripheral skeleton—yellow marrow—contains mainly fat. However, yellow marrow still contains a small population of precursor cells that may be reactivated when the demand for blood cells is sufficiently high. Similarly, the liver and spleen can resume their fetal haemopoietic role if required.

The red marrow provides a suitable micro-environment for stem cell growth and development. It has two main components:

- Specialized fibroblasts, known as adventitial reticular cells, which secrete a framework of reticulin fibres (fine collagen fibres), forming a meshwork that plays an essential role in supporting the developing blood cells.
- A network of blood sinusoids, lined by a single layer of endothelial cells, which interconnect via tight junctions and thus effectively separate the vascular and extravascular spaces.

The nutrient artery of the bone marrow branches into a network of vascular sinuses that support the haemopoietic cells. These drain into a large central sinus that channels the blood into the systemic venous circulation. Haemopoiesis takes place in haemopoietic cords or islands located between the vascular sinuses.

Macrophages are found within the haemopoietic cords at the centre of each focal group and contain stored iron in the form of ferritin and haemosiderin. They have three main functions:

- Transfer of iron to developing erythroblasts for haemoglobin synthesis.
- Phagocytosis of the cellular debris of haemopoiesis.
- Regulation of haemopoietic cell differentiation and maturation.

Newly formed cells from the haemopoietic system enter the bloodstream in areas where the endothelial cell cytoplasm lining the sinusoids thins to approaching a double plasma membrane in thickness.

The thymus

T cell progenitors enter the thymus gland as immature thymocytes and emerge as mature, antigen-specific, immunocompetent T cells. The thymus is a bilobed

In humans, B cells mature in the bone marrow, and T cells in the thymus. (B cells acquire their title from their site of development in birds—the bursa of Fabricius.)

gland located in the anterior part of the superior mediastinum, posterior to the sternum and anterior to the great vessels and upper part of the heart. It may extend superiorly into the roof of the neck and inferiorly into the anterior mediastinum. Each lobe is surrounded by a capsule and divided into multiple lobules by fibrous septa known as trabeculae. Each lobule is divided into two regions (Fig. 2.1):

- An outer cortex.
- An inner medulla.

It is thought that T cells enter the thymus via the cortex, where they rapidly proliferate. The thymus exhibits a high rate of cell death, and a much smaller and more mature group of thymocytes survives to enter the medulla. The thymocytes continue to mature here and eventually leave the thymus via the postcapillary venules.

A network of epithelial cells is present in the thymic lobules:

- The 'nurse' cells of the outer cortex.
- The cortical epithelial cells.
- The medullary epithelial cells.

These are all vital in the development of thymocytes into mature T cells. A 'nurse' cell is capable of engulfing up to 50 thymocytes with its long membranous processes. Cortical epithelial cells have long, interconnecting, cytoplasmic processes that interact with thymocytes. In addition, bone-marrow-derived interdigitating (ID) cells and macrophages are present, especially at the corticomedullary junction, and they also have long processes that interact with thymocytes. Collectively, these cells are known as stromal cells.

Thymic epithelial cells produce hormones that are essential for the differentiation and maturation of thymocytes. Four hormones have been isolated so far:

- α thymosin.
- β_4 thymosin.
- Thymulin.
- Thymopoietin.

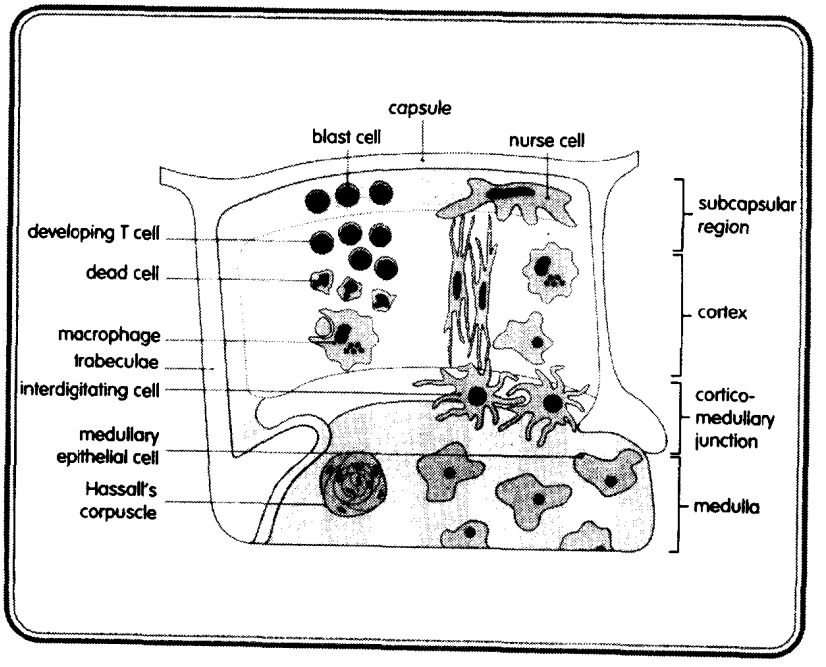

Fig. 2.1 Ultrastructure of the thymus, showing the cells present in the cortex and medulla.