# CLS 241
# Basic Haematology

## Introduction to Haematology & Haemopoiesis

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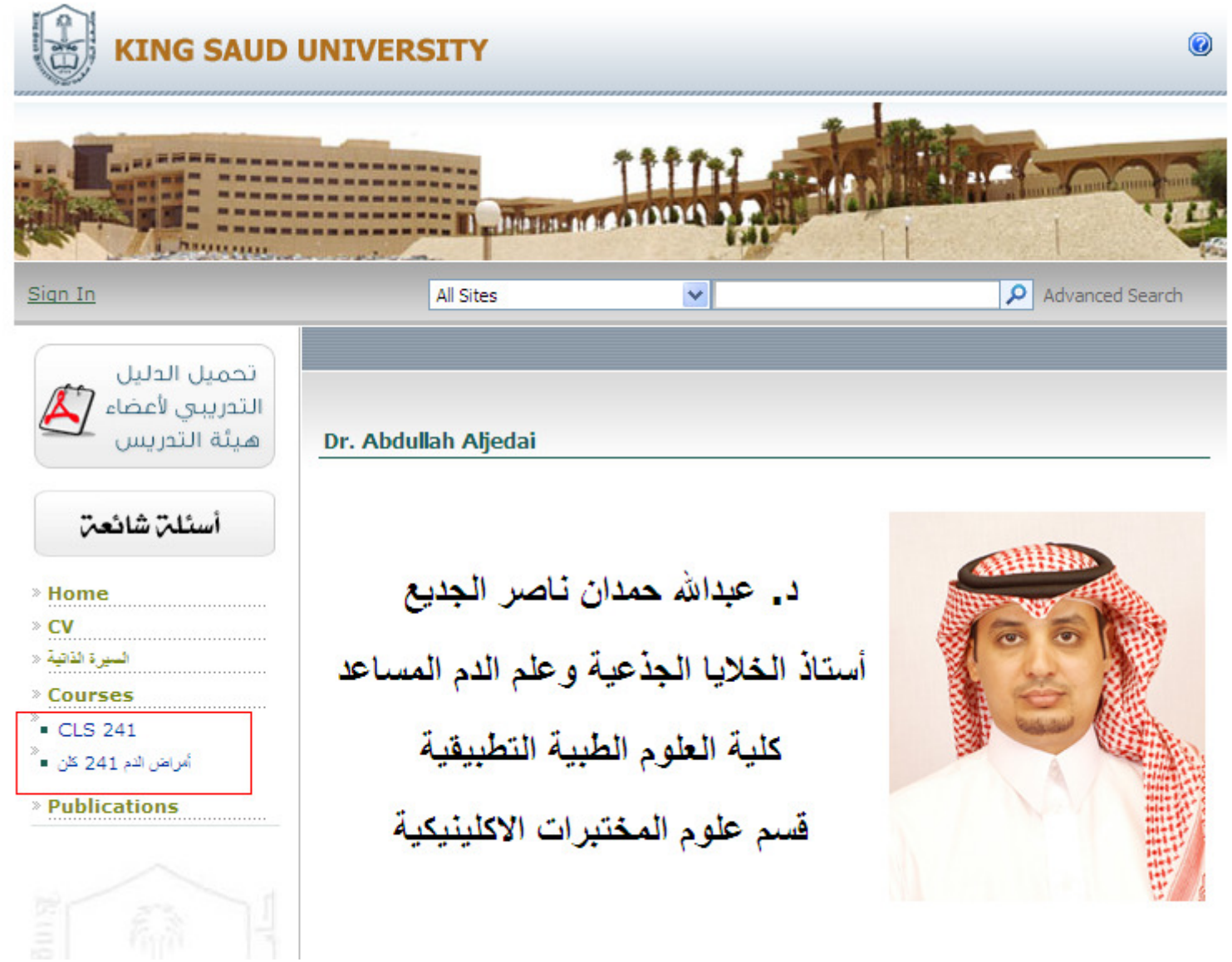


# Haematology

- (Hematology comes from the Greek words (*haima*) meaning "blood" and (*logos*), a root commonly employed to denote a field of study.).
- **Haematology** ( also spelled hematology) can be defind as The diagnosis, treatment, and prevention of diseases of the blood and bone marrow as well as of the immunologic, hemostatic and vascular systems. (Webster's New World Medical Dictionary).
- Because of the nature of blood, the science of haematology profoundly affects the understanding of many diseases.
- The laboratory work that goes into the study of blood and the investigation of blood disorders is frequently performed by a medical technologist (MT).
- Physicians specialized in haematology are known as **hematologists**. Their routine work mainly includes the care and treatment of patients with hematological diseases, although some may also work at the hematology laboratory viewing blood films and bone marrow slides under the microscope, interpreting various hematological test results.

# Blood

- **MODERN DEFINITION OF BLOOD**

Blood is a tissue and fluid of an organism that provides its constituent cells with:

a. Nutrients such as glucose, amino acids, and fatty acids

b. Supply of oxygen to tissues (bound to hemoglobin, which is carried in red cells)
c. Chemical regulatory information such as:

1. Regulation of body pH
2. Regulation of Ionic strength
3. Messenger functions, including the transport of hormones and the signaling of tissue damage

- d. Immunological functions, including circulation of white blood cells, and detection of foreign material by antibodies

- e. Elimination of wastes such as carbon dioxide, urea, and lactic acid.
- f. Coagulation, which is one part of the body's self-repair mechanism
- g. Regulation of body temperature

- In vertebrates, blood is composed of blood cells suspended in a liquid called blood plasma.

# Components of Blood

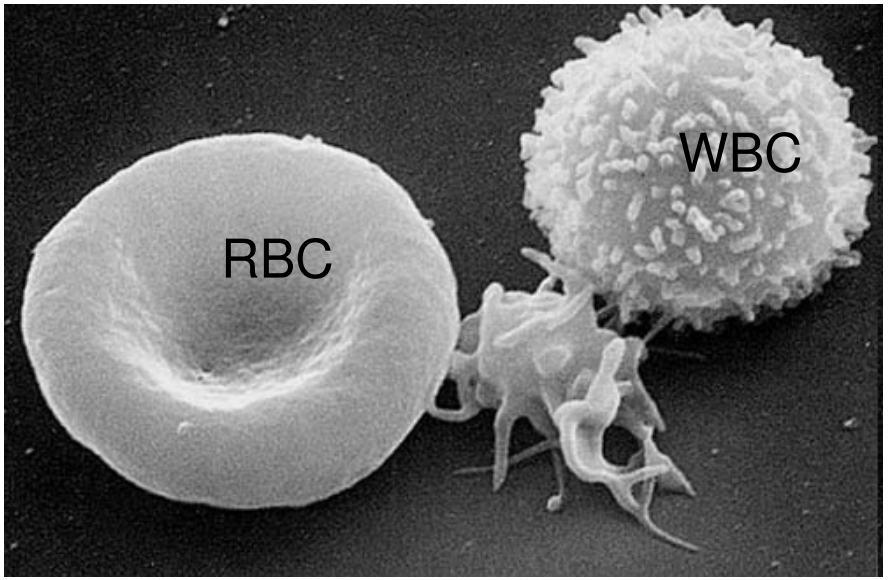
**A- plasma**: Plasma is the liquid portion of the blood that contains coagulation factors. It is separated from the blood cells by centrifugation. Constitutes about 54.3% of blood.

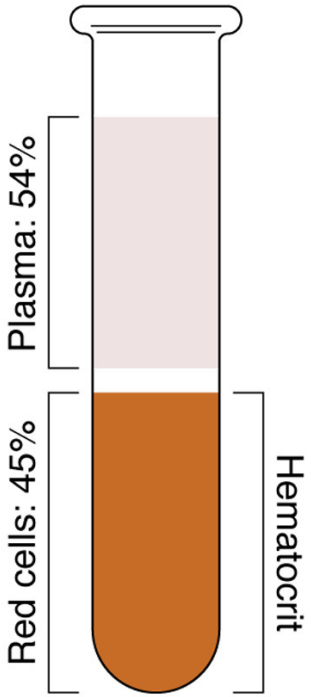
Colour……..

Volume…….Litre

Plasma Vs Serum

**B- Cellular components:** RBC (45%), WBC, & Platelets = About (0.7%)% of blood.




**WBC & Platelets??**

# STRUCTURE & COMPOSITION OF BLOOD

- **1- PLASMA**

**A. Composition** - liquid portion - 55% of blood volume –

- 91.5% Water - solvent for solids heat transfer
- 8.5% - Solutes - Salts, contain LMW substance such as Vit., hormones,
- 7.0% - Proteins
- - More than 100 known 1975, currently 1500
- - Conc. range
- 40 mg/ml . 1mM (Alb)
- 4-10 mg/ml . 25 µM (IgG)
- 4-10 µg/ml . 25 pM (IgE) to trace amounts
- MW range 106 < p. proteins < 15 kDa
- - 6.5% - Serum = (Plasma - Fibrinogen & other clotting factors)
- **B. Definition:** Plasma protein
- 1. present in plasma
- 2. synthesized in liver or RES (total pool of marrow, blood, & tissue
- monocyte & macrophages)
- 3. I° function carried out in vascular system
- 4. Actively secreted into blood
- 5. Relatively the highest concentration in blood
- **C. Identification & Separation of Plasma Proteins**
- 1. Solubility (albumins soluble in water; globulins soluble in salt solution)
- 2. Sedimentation & Hydrodynamics
- 3. Electrophoresis
- 4. Immunological
- 5. Bioassay

- **D. Nomenclature - confusing**
- α, β, γ - electrophoresis patterns not indicative of structure or function.
- **E. Protein Systems - To revisit**
- **1. Carrier Proteins**
- a. Regulate diffusion/interaction/transport of small molecules
- b. Regulate specific inteactions
- c. Regulate toxicity
- d. Contol osmotic pressure i.e. a water carrier
- e. Albumin
- f. Lipoproteins, Transport proteins, Carrier proteins
- Phospholipid, Triglyceride, Cholesterol transport
- Fatty acid transport
- Hydrophobic vitamin & cofactor transport
- Hormone transport
- Peptide transport protection from proteases
- Health Importance: In lipid metabolism, atherosclerosis

## 2. Immunoproteins

a. Immunoglobins - γ globulins
5 classes IgG (75%); A (15%); M (5-10%); D (1%); E (<0.1%)
*Importance*: (Auto)Immunity, Allergy, Host Defense,Inflammation
b. Complement System - 11 proteins and inhibitors –
*Health Importance* - host defense, inflammation.

**3. Coagulation Proteins -**

proenzymes, enzymes, adhesive protein, inhibitors, activators,
*Health Importance: Hemophilia*
Proteases and Inhibitors - mostly α globulins
Health Importance: Inflammation
Signalling proteins -- Hormones, Cytokines

# Cellular components of blood

- All blood cells are divided into three lineages.
- Erythroid cells are the oxygen carrying red blood cells (RBC). Both reticulocytes and erythrocytes are functional and are released into the blood. In fact, a reticulocyte count estimates the rate of erythropoiesis.
- Lymphoid cells are the cornerstone of the adaptive immune system. They are derived from common lymphoid progenitors. The lymphoid lineage is primarily composed of T-cells and B-cells.
- Myeloid cells, which include granulocytes, megakaryocytes and macrophages and are derived from common myeloid progenitors, are involved in such diverse roles as innate immunity, adaptive immunity, and blood clotting.

One microliter of blood contains:

(a) 4.7 to 6.1 million (male), 4.2 to 5.4 million (female) RBC

b) 4,000–11,000 WBC

C) 200,000–500,000 thrombocytes (PLATELETS)

# FUNCTIONS OF WBC

| Cell type | Function | Count (% of leukocytes) |
|---|---|---|
| Neutrophilic band granulocytes (band neutrophil) | Precursors of segmented cells that provide antibacterial immune response | 0–4% |
| Neutrophilic segmented granulocyte (segmented neutrophil) | Phagocytosis of bacteria; migrate into tissue for this purpose | 50–70% |
| Lymphocytes (B- and T-lymphocytes, morphologically indistinguishable) | B-lymphocytes (20% of lymphocytes) mature and form plasma cells → antibody production. T-lymphocytes (70%): cytotoxic defense against viruses, foreign antigens, and tumors. | 20–50% |
| Monocytes | Phagocytosis of bacteria, protozoa, fungi, foreign bodies. Transformation in target tissue | 2–8% |
| Eosinophilic granulocytes | Immune defense against parasites, immune regulation | 1–4% |
| Basophilic granulocytes | Regulation of the response to local inflammatory processes | 0–1% |

# RBC & PLATELETS

- **Erythrocytes** are the oxygen carriers for all oxygen-dependent metabolic reactions in the organism. They are the only blood cells without nuclei, since this allows them to bind and exchange the greatest number of O2 molecules. Their physiological biconcave disk shape with a thick rim provides optimal plasticity.

- **Thrombocytes (Platelets)** form the aggregates that, along with humoral coagulation factors, close up vascular lesions. During the aggregation process, in addition to the mechanical function, thrombocytic granules also release factors that promote coagulation.

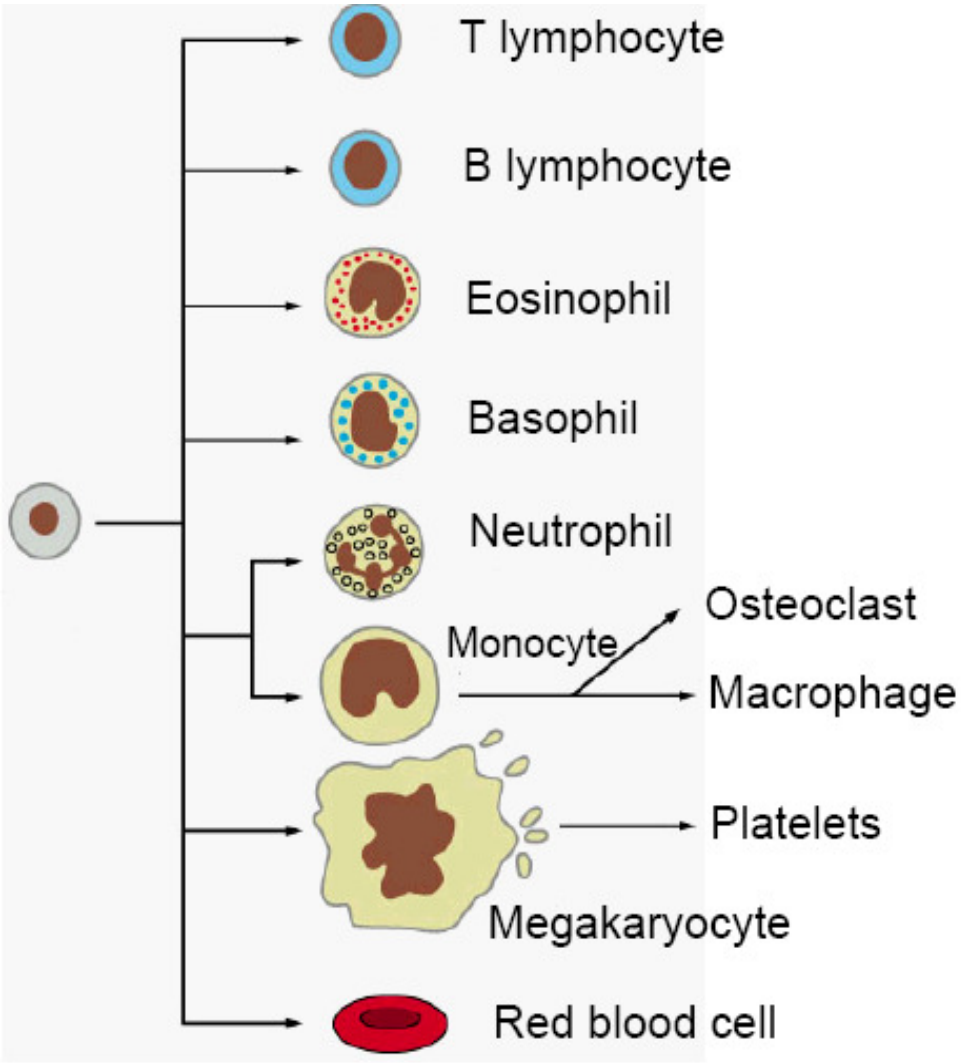
- Thrombocytes develop from polyploid megakaryocytes in the bone marrow. They are the enucleated, fragmented cytoplasmic portions of these progenitor cells.

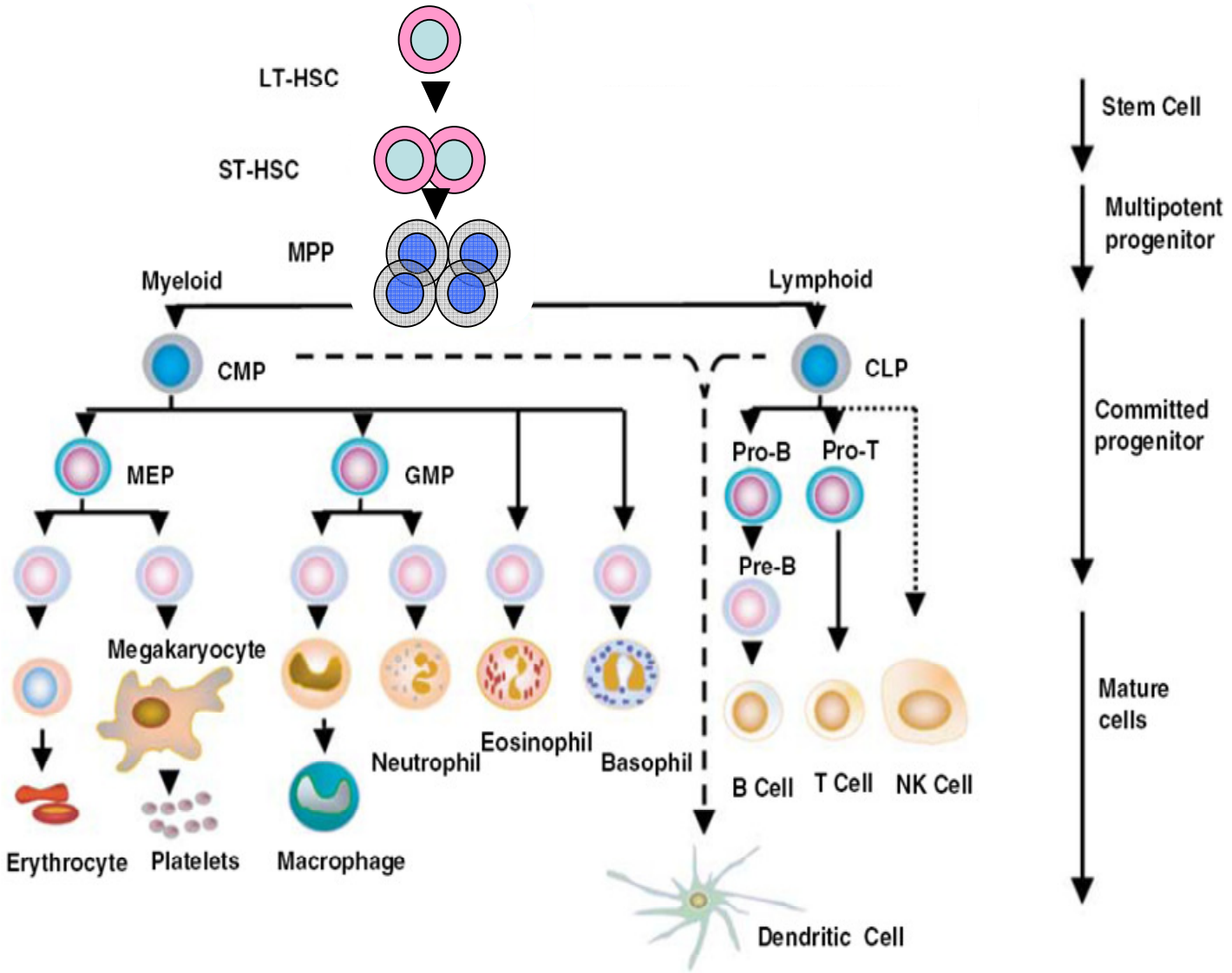
# Stem cells and haemopoiesis

- Haemopoiesis is the lifelong process of blood cells production in haemopoietic tissues.
- Why? Mature circulating blood cells have a limited lifespan and need to be replaced.
- $10^{13}$ new cells must be replaced each day to maintain steady-state blood counts.
- The stem cells are the most important cells in haemopoietic cell production.
- Hematopoietic stem cells (HSCs) reside in the medulla (bone marrow) and have the unique ability to give rise to all of the different mature blood cell types.
- Hematopoietic stem cell is a cell isolated from the blood or bone marrow that can renew itself, can differentiate to a variety of specialized cells, can mobilize out of the bone marrow into circulating blood, and can undergo programmed cell death, called apoptosis.

- Haemopoiesis can be described as hierarchical with the rare HSCs at the top of the hierarchy giving rise first to progenitors and then to precursors with single lineage commitment and ending in differentiated mature cells of different lineages (red cells, granulocytes, monocytes, platelets and lymphocytes).


HSC from bone marrow produces all cells found in blood stream.

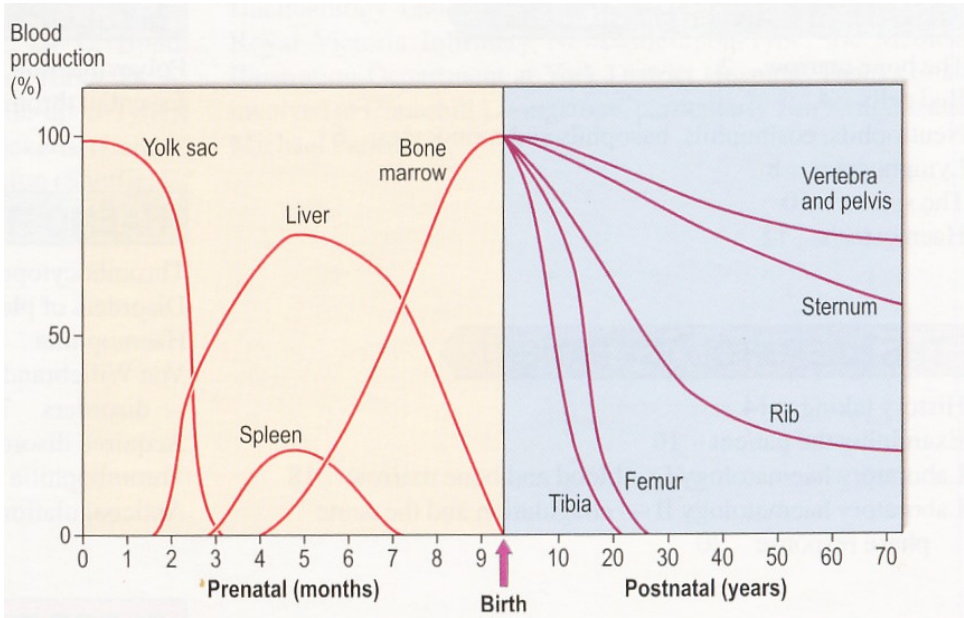





Haemopoietic tree (Modified from Larsson and Karlsson, 2005)

# Sites of haemopoiesis

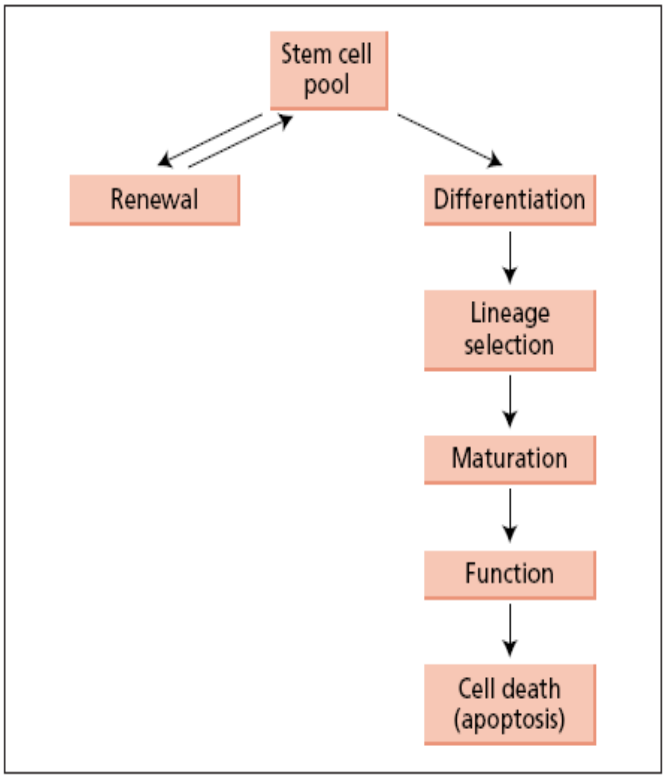
-In developing embryos, blood formation occurs in aggregates of blood cells in the yolk sac, called blood islands.
- As development progresses, blood formation occurs in the spleen, liver and lymph nodes.
-After birth normal haemopoiesis is restricted to the bone  marrow.
-In children, haemopoiesis occurs in the marrow of the long bones such as the femur and tibia.
-In adults, it occurs mainly in the pelvis, cranium, vertebrae, and sternum.
-Expansion of haemopoiesis down the long bones may occur. e.g. in leukaemias and 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.



1 Sites of blood production in the fetus and after birth.

# Regulation of haemopoiesis

-Estimates of stem cell frequency in human bone marrow are about one stem cell per 20 million nucleated cells.
-Haemopoiesis is regulated by soluble factors (growth factors).
-In addition to the haemopoietic system, the bone marrow contains stromal stem cells (mesenchymal stem cells) which are important for constructing the haemopoietic microenvironment.
- **Mobilization** of blood cells involves detachment from the microenvironment and migration to the blood stream.



# Homing & mobilization of stem cells