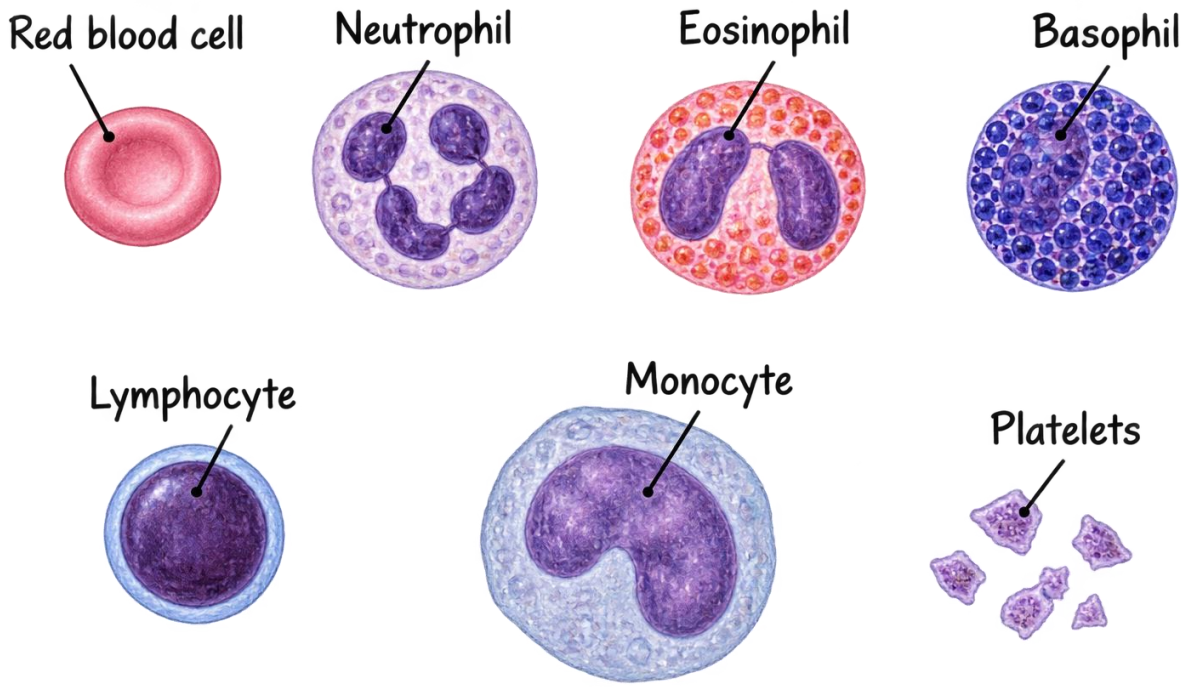
Physiology - Topic 2 - Haematology

Composition and Functions of Blood



The formed elements of blood show characteristic differences in size, nuclei and cytoplasmic granules

Blood as a Circulating Connective Tissue

- Blood is a fluid connective tissue that circulates through a closed system of vessels.
    - Its **plasma** carries dissolved substances, while red cells, white cells and platelets perform specialised functions.
    - **Blood** connects the respiratory, digestive, excretory and endocrine systems with the tissues.

Blood Volume and Packed Cell Fractions

- **Blood volume** is approximately 7–8% of body weight in a healthy adult, or about 70 mL/kg.
    - A 70 kg adult therefore has roughly 5 litres of **blood**.
    - The value varies with body size, sex, pregnancy and hydration, so it is an estimate rather than a fixed number.
- **Plasma** normally forms about 55% of blood volume, and packed red cells form about 45%.
    - A thin **buffy coat** of white cells and platelets lies between them after centrifugation.
    - The **haematocrit** is the fraction of whole blood occupied by red cells, not by all formed elements.

Acidity and Viscosity

- **Arterial blood pH** is normally 7.35–7.45.
- **Blood** is more viscous than water, mainly because of its cells and plasma proteins.

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- Increasing the **haematocrit** increases resistance to flow, particularly when it becomes markedly elevated.

Functions of Blood

1. Transport

- Red cells transport oxygen through **haemoglobin** and contribute to carbon dioxide transport.
- **Plasma** carries nutrients, hormones, waste products, electrolytes and much of the carbon dioxide as bicarbonate.
  - Transport allows distant organs to work together.

2. Regulation

- **Blood** distributes heat and helps maintain extracellular fluid volume, osmotic balance and acid–base balance.
- **Haemoglobin**, plasma proteins and bicarbonate provide buffering.
- The circulation carries excess acid and **carbon dioxide** to organs that eliminate them.

3. Protection

- White cells, **antibodies** and complement defend against infection.
- **Platelets** and coagulation proteins limit blood loss after vascular injury.
  - These protective processes must remain local and controlled, because an unnecessary clot can obstruct a healthy vessel.

Plasma and Serum

Plasma

- Plasma is the liquid obtained when anticoagulated blood is centrifuged.
  - It contains **fibrinogen** and other coagulation proteins.

Serum

- **Serum** is the liquid remaining after blood has clotted; fibrinogen has been consumed in forming fibrin, and several other constituents have changed during clotting.

Composition of Plasma

- **Plasma** is about 90–92% water.
  - Its proteins, electrolytes, nutrients, gases and waste products make up the remaining portion.
- Sodium and its accompanying anions are the major contributors to extracellular osmolality, whereas plasma proteins are important for **colloid osmotic pressure**.

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Plasma Proteins

Origin, Forms and Normal Concentrations

- Total **plasma** protein is commonly about 6–8 g/dL in adults.
    - **Albumin** is approximately 3.5–5.0 g/dL, **globulins** about 2–3.5 g/dL and fibrinogen about 200–400 mg/dL.
    - Laboratories use their own reference intervals, and **plasma** protein is slightly higher than serum protein because plasma retains fibrinogen.

Sites of Protein Synthesis

- The **liver** synthesises albumin, fibrinogen and most other plasma proteins.
- **Plasma cells** synthesise immunoglobulins.
- The globulin fraction includes **antibodies**, transport proteins, complement proteins and several enzymes, so it is a mixed group rather than a single substance.

Electrophoretic Fractions and Interpretation

- **Protein electrophoresis** separates serum proteins into albumin and alpha-1, alpha-2, beta and gamma fractions.
    - The gamma region contains most **immunoglobulins**.
    - A broad increase suggests a polyclonal response, whereas a narrow band can indicate a monoclonal protein and requires further investigation.

Functions and Clinical Implications of Plasma Proteins

1. Albumin

- **Albumin** is the main contributor to plasma colloid osmotic pressure because of its high concentration and large number of molecules.
    - **Albumin** helps retain fluid within the circulation and transports bilirubin, fatty acids, calcium, hormones and many drugs.

2. Globulins

- **Globulins** transport specific substances and take part in immunity.
    - **Transferrin** transports iron, and ceruloplasmin carries copper.

3. Fibrinogen

- **Fibrinogen** forms the fibrin mesh of a clot.

Shared Functions of Plasma Proteins

- **Plasma proteins** also buffer hydrogen ions and contribute to blood viscosity.

Protein Loss and Concentration Changes

- Severe **liver** disease reduces synthesis of albumin and several clotting factors.

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- **Nephrotic syndrome** causes urinary protein loss, and extensive burns can cause protein loss through damaged tissue.
- Reduced **plasma oncotic pressure** favours oedema, although hydrostatic pressure, capillary permeability and lymph drainage also determine fluid movement.
- Dehydration can raise the measured protein concentration without increasing total body protein.
- Pregnancy and fluid overload may lower it by dilution.
- **Albumin** is a negative acute-phase protein, whereas fibrinogen and many other inflammatory proteins increase during an acute-phase response.
- The albumin-to-globulin ratio is normally greater than one, commonly about **1.2–1.8**, although the method and population affect the reference interval.
- A reversed ratio may result from reduced albumin, increased globulins or both and must be interpreted with the clinical setting.

Protein Binding and Interpretation

- A low **albumin** concentration can lower total measured calcium even when ionised calcium is normal.
- Changes in protein binding can also alter the free fraction of a drug.
- Clinical interpretation therefore considers both the concentration and the binding function of **plasma proteins**.

Red Blood Cells

Structure, Metabolism and Functions of Red Cells

- A mature red cell is a flexible, anucleate **biconcave** disc about 7–8 micrometres in diameter.
    - Its thin centre shortens the diffusion distance, while the biconcave shape provides a large surface area relative to volume.
    - Membrane proteins and the cytoskeleton permit deformation in narrow capillaries.
- Adult **red cell** counts are commonly around 4–6 million cells/μL, with a higher average in men than in women.
    - The precise interval depends on the laboratory and population.
- **Red cells** normally survive for about 120 days before macrophages remove ageing or damaged cells.

Metabolic Pathways in Mature Red Cells

- Mature **red cells** lack mitochondria and obtain ATP by anaerobic glycolysis.
    - This preserves the oxygen they carry for other tissues.
- The **pentose phosphate pathway** supplies NADPH to maintain reduced glutathione, which protects haemoglobin and the membrane against oxidant damage.

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Contribution to Gas Transport and Buffering

- The red cell contains **carbonic anhydrase**, which accelerates the reversible conversion of carbon dioxide and water to carbonic acid.
    - **Haemoglobin** buffers the hydrogen ions produced.
    - **Chloride** exchange with bicarbonate helps maintain electrical neutrality during carbon dioxide transport.

Haemoglobin

Structure, Synthesis and Physiological Functions

Molecular Structure of Haemoglobin

- **Haemoglobin** contains four globin chains, each associated with one haem group.
    - Each haem contains ferrous **iron**, which binds one oxygen molecule reversibly.
    - One **haemoglobin** molecule can therefore bind four oxygen molecules, and fully oxygenated haemoglobin carries about 1.34 mL oxygen per gram under physiological conditions.

Synthesis of Haem and Globin

- **Haem synthesis** occurs partly in mitochondria and partly in the cytoplasm of developing erythroid cells.
    - **Glycine and succinyl-CoA** begin the pathway, which requires vitamin B6.
- The first step forms delta-aminolaevulinic acid through the enzyme ALA synthase.
- Cytoplasmic reactions build the porphyrin ring, and the final mitochondrial step uses ferrochelatase to insert ferrous iron.
    - **Iron** is inserted into protoporphyrin IX to form haem.
- **Globin chains** are synthesised on ribosomes and combine with haem.

Normal Haemoglobin Types

A. Adult Haemoglobin A

- Adult haemoglobin is predominantly **HbA**, which contains two alpha and two beta chains.

B. Adult Haemoglobin A2

- **HbA2** contains two alpha and two delta chains and usually forms about 2–3.5% of adult haemoglobin.

C. Fetal Haemoglobin

- **HbF** contains two alpha and two gamma chains; it predominates during fetal life and normally forms less than about 1% in adults.

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