Biomedicine: Human Sciences

Lecture 5:
Cardiovascular System
Part One
In today’s topic you will learn:

- The different components of the blood and their function in the human body.

- The signs, symptoms, investigation procedures & some orthodox treatments of common blood pathologies.
Parts of the Cardiovascular System

1. Heart
2. Blood vessels
3. Blood

Cardi(o)- is Greek, pertaining to the heart
Vas(o)- is Latin for duct
Blood

- Blood is a **fluid type of connective tissue**.
- Composed of **plasma** (55%) & **cells** (45%).
  
  - 7% of body weight.
  - 5.6 L in an adult male, 4.5 L in an adult female.

**FUNCTIONS:**

- Contributes to homeostasis by **transporting** oxygen, carbon dioxide, nutrients, wastes and hormones to and from body cells

- Helps regulate pH and **temperature**

- **Immune function** with antibodies, phagocytes, clotting factors etc.

*Plasma:* 

*the fluid portion of the blood in which the components are suspended.*

*Homeo = sameness
Stasis = still*
Blood plasma

- Pale yellow coloured liquid (if cells removed from blood)

**Consists of:**
- Water (91%)
- Proteins (7%)
- Mineral salts (0.9%)
- Nutrients
- Organic waste materials
- Hormones
- Enzymes
- Gases.

**Serum** = plasma with clotting factors removed

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Blood Plasma Proteins

- All synthesised by liver cells (hepatocytes)

- The following three account for the majority of plasma proteins:

1. **Albumin:**
   - Smallest & most numerous. 12g produced per day
   - Carrier of substances (lipids & steroid hormones).
   - Maintains osmotic pressure.

2. **Globulins:** (38%)
   - Immunity – Immunoglobulins
   - Transport iron. Lipids and vitamins

3. **Fibrinogen:** (7%)
   - Also called clotting factor 1. Essential for blood clotting

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Blood Plasma Nutrients

- Products of digestion pass into the blood for distribution to all body cells.

- **Carbohydrates** (sugars) – mostly glucose.

- Amino acids.

- **Fats / oils** - carried by proteins (HDL, LDL, VLDL).

- Vitamins.

- **The main mineral components are:**
  - **Cations** (positively charged ion): Sodium, potassium, calcium, magnesium
  - **Anions** (Negatively charged ions): Chlorides, bicarbonates, phosphates

A salt is a compound with two or more ions held together by opposite charges.

Na⁺= sodium  
Ca⁺²= calcium  
K⁺= potassium  
Mg⁺²= magnesium  
Cl⁻= chlorine  
HCO₃⁻= bicarbonate  
PO₄⁻³= phosphate  
SO₄⁻²= sulphate
Blood plasma

ORGANIC WASTE
• Urea – produced from the breakdown of proteins
• Creatinine – produced from the breakdown of proteins
• Uric acid – produced from the breakdown of proteins
• Carbon dioxide - produced from respiratory metabolism.

HORMONES
• Chemical messengers carried by the blood to the target cells/tissues.

ENZYMES
• Catalysts for biochemical reactions in the body.

GASES
• Oxygen (O₂) & carbon dioxide (CO₂).

Recap: How is carbon dioxide transported in the blood?
Blood Cells

Erythrocytes (Red blood cells)

Leukocytes (White blood cells)

Thrombocytes (Platelets)

erthro- = Greek for red
-cyte = cell

leuko = Greek for white
-cyte = cell

thrombo = Greek for clot
-cyte = cell
Haematopoiesis

“The production of all blood cells”

- All blood cells originate from **pluripotent stem cells** in the red bone marrow.

- During the first 2 months of gestation, the embryonic yolk sac performs haematopoiesis. Between months 2 and 9 of foetal life, the **liver** and spleen carry out this function.

- In first few years of life all bone marrow is **red** and produces blood cells.

- In adults, haematopoiesis occurs in **vertebrae, ribs, sternum, skull, sacrum, pelvis and proximal long bones** (mostly femur)
Blood Cells

**Blast**: Greek germ or bud.
**Cyte** = cell.
Erythrocytes

- Biconcave & non-nucleated giving the cells a larger surface area to transport more oxygen
- Life span of 90 to 120 days.
- Approx. 6-8 µm (micrometres) in diameter
- Strong & flexible plasma membrane
- The percentage of total blood volume occupied by erythrocytes is called the haematocrit (Females = 42%, Males = 47%)

Why might this value differ between genders?
Erythrocyte Structure

- Made up of **haemoglobin** molecules which carry mostly oxygen & some carbon dioxide
- Each erythrocyte has 280 Million haemoglobin molecules
- One haemoglobin molecule consists of 4 polypeptide chains (‘globin’). Each chain is bound to a pigment called ‘haem’, which contains iron.
- Each haem group in haemoglobin can carry an oxygen molecule, thus each haemoglobin can carry up to 4 oxygen molecules.

Haemoglobin is often referred to as Hb
A haemoglobin molecule is made up of four polypeptide chains:

- Adult haemoglobin (HbA) is composed of two α (alpha) and two β (beta) subunits.
- Foetal Haemoglobin (HbF) is composed of two α (alpha) and two γ (gamma) subunits.
Why is blood red?

Blood appears red due to the interaction of iron and oxygen within haem units.

More specifically because of the way the chemical bonds between iron and oxygen reflect light.
Erythropoiesis

- The formation of erythrocytes occurs in the red bone marrow.

- Immature erythrocytes have nuclei & organelles which they lose as they mature (loss of nucleus causes indent in cell)

- **Nutrients:** vitamin $B_{12}$, folic acid and iron are all required for RBC formation.
Erythropoiesis

- Hypoxia stimulates the secretion of the hormone erythropoietin (EPO) which stimulates erythropoiesis in the bone marrow via negative feedback.
- Causes include high altitude, haemolysis, excessive blood loss, pregnancy.
- Premature new-born's often exhibit anaemia, partly due to inadequate EPO.
- During first weeks after birth, the liver (not kidneys) produces EPO. The liver is less sensitive to hypoxia so smaller response to anaemia.

Hypo = below normal / Oxy = oxygen
Haem = blood / Lysis = destruction
Haemolysis

• The destruction of RBCs to release haemoglobin into plasma.

• An erythrocyte normally **survives 90 to 120 days.** About 1% of erythrocytes break down each day.

• Carried out by specialised **macrophages** (phagocytic cells) found in many tissues, especially the **spleen**, bone marrow & liver.

• Haemoglobin splits into haem and globin. Globin amino acids and iron are recycled.

• **Bilirubin** is a yellow coloured pigment formed from haem catabolism. It is excreted in bile and urine.
Haemolysis & Bilirubin
Erythrocyte Life Cycle

1. **Stimulus:** Low $O_2$ levels detected by Kidneys
2. Kidneys release EPO into bloodstream
3. EPO stimulates Erythropoiesis – RBC maturation and release from bone marrow
4. NFB: RBCs increase $O_2$ carrying capacity of blood, relieving stimulus. RBCs live for about 120 days – worn out from bending to fit through capillaries.
5. Aged and damaged RBCs are phagocytized by macrophages in liver, spleen, and bone marrow.
6. Globin protein from Hemoglobin is broken down into amino acids and recycled into new proteins.
7. Heme Groups from Hemoglobin are broken down into Fe$^{3+}$ and Biliverdin.
8. Fe$^{2+}$ is recycled into new Hemoglobin.
9. Bilirubin is excreted via bile in feces.

Raw materials are made available in blood for erythropoiesis.

Iron (Fe$^{3+}$) stored in liver and released in blood.

Heme

Iron (Fe$^{2+}$) is recycled for erythropoiesis.

Bilirubin is collected by liver, secreted into intestine in bile and excreted in feces.

Amino acids are recycled for protein synthesis.

Bilirubin is excreted in bile in feces.

Aged and damaged red blood cells are engulfed by macrophages of liver, spleen, and bone marrow; the hemoglobin is broken down.

Heme

Globin

Amino acids

Iron (Fe$^{2+}$) is recycled for erythropoiesis.

Raw materials are made available in blood for erythropoiesis.

Food nutrients (amino acids, Fe, B12, folic acid) are absorbed from intestine.

Bilirubin is collected by liver, secreted into intestine in bile and excreted in feces.

Heme

Iron (Fe$^{2+}$) is recycled for erythropoiesis.

Raw materials are made available in blood for erythropoiesis.

Iron (Fe$^{2+}$) is recycled for erythropoiesis.

Raw materials are made available in blood for erythropoiesis.
Blood Groups

• Antigens are located on the surface of erythrocytes and are composed of glycoproteins and glycolipids. There are two major blood groups.

ABO System

• Based on two glycolipid antigens called A and B
• Those whose erythrocytes display antigen A have blood group A. etc.
• Blood plasma contains antibodies that react with A or B antigens if the two are mixed. Anti-A antibody reacts with antigen A etc
• Antibodies are large IgM type

YOU DO NOT HAVE ANTIBODIES THAT REACT WITH YOUR OWN ANTIGENS
ABO Blood Group

- In a **transfusion reaction**, the antigen-antibody complex activates an immune response that causes erythrocyte membranes to become leaky and rupture.

- **Blood group O** = **Universal donor** because erythrocytes have neither A or B antigens for antibodies to attach too.

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So what group is the universal recipient?
ABO Blood Group

<table>
<thead>
<tr>
<th>Antigen (on RBC)</th>
<th>Antigen A</th>
<th>Antigen B</th>
<th>Antigens A + B</th>
<th>Neither A or B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibody (in plasma)</td>
<td>Anti-B Antibody</td>
<td>Anti-A Antibody</td>
<td>Neither Antibody</td>
<td>Both Antibodies</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Blood Type</th>
<th>Type A</th>
<th>Type B</th>
<th>Type AB</th>
<th>Type O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannot have B or AB blood</td>
<td>Cannot have A or AB blood</td>
<td>Can have any type of blood</td>
<td>Can only have O blood</td>
<td></td>
</tr>
<tr>
<td>Can have A or O blood</td>
<td>Can have B or O blood</td>
<td>Is the universal recipient</td>
<td>Is the universal donor</td>
<td></td>
</tr>
</tbody>
</table>

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Rhesus Blood Group

- **Rhesus antigen** (rhesus factor) is another surface antigen found on erythrocytes.

- Those that have Rhesus (Rh) antigens are designated Rh positive, those who lack Rh antigen are Rh negative (*can also say D +ve/-ve*).

- Inheritance of the rhesus factor is via a rhesus dominant gene (85% of people are rhesus positive).

- **Anti-Rhesus Antibodies** are produced in rhesus negative individuals only if they come in to contact with the rhesus antigen (not normally in blood plasma).

- Can come into contact in pregnancy or incompatible blood transfusion.

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Named ‘Rhesus’ because the antigen was first discovered in the blood of rhesus monkeys.
Rhesus Blood Group

- **In Pregnancy**: The only way antibodies are developed against the Rh antigen are through placental sensitisation or transfusion. This only occurs if the mother is Rh- and the unborn baby is Rh+ (inheriting the father's rhesus antigen).

- Normally maternal and foetal blood cells do not mix, but this can occur at delivery or if ante partum haemorrhage or in subsequent pregnancies.

- The most common problem with Rh incompatibility is **haemolytic disease of the newborn** (see later)

- An **Injection of anti-Rh antibodies** bind to and inactivate foetal Rh antigens
Rhesus Blood Group

1. Rh\(^+\) father.
2. Rh\(^-\) mother carrying her first Rh\(^+\) fetus. Rh antigens from the developing fetus can enter the mother’s blood during delivery.
3. In response to the fetal Rh antigens, the mother will produce anti-Rh antibodies.
4. If the woman becomes pregnant with another Rh\(^+\) fetus, her anti-Rh antibodies will cross the placenta and damage fetal red blood cells.
The 8 blood groups:

<table>
<thead>
<tr>
<th></th>
<th>O +ve</th>
<th>O -ve</th>
</tr>
</thead>
<tbody>
<tr>
<td>A +ve</td>
<td></td>
<td>A -ve</td>
</tr>
<tr>
<td>B +ve</td>
<td></td>
<td>B -ve</td>
</tr>
<tr>
<td>AB +ve</td>
<td></td>
<td>AB -ve</td>
</tr>
</tbody>
</table>

The + and- indicate the presence/absence of the rhesus antigen

Video: Blood Groups
www.youtube.com/watch?v=KXTF7WehgM8

RED BLOOD CELL COMPATIBILITY TABLE

<table>
<thead>
<tr>
<th>Recipient</th>
<th>O-</th>
<th>O+</th>
<th>A-</th>
<th>A+</th>
<th>B-</th>
<th>B+</th>
<th>AB-</th>
<th>AB+</th>
</tr>
</thead>
<tbody>
<tr>
<td>O-</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>O+</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>A-</td>
<td>✓</td>
<td>✓</td>
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<td>✓</td>
<td>✓</td>
<td>✓</td>
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</tr>
<tr>
<td>A+</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>B-</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>B+</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>AB-</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
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<tr>
<td>AB+</td>
<td>✓</td>
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<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
Summary Questions

1. What is the most common plasma protein in blood? What is its function?
2. What is meant by ‘Blood plasma’?
3. List three functions of blood
4. What is meant by erythropoiesis? After birth, where does this take place?
5. How many polypeptide chains form the globin part of haemoglobin?
6. What stimulates erythropoiesis: Tissue _________-ia?
7. Where does most haemolysis of RBCs occur? By what cell?
8. When the iron portion of the haem is removed during haemolysis, it produces ____________?
9. Where are blood group antigens present?
10. What blood group is considered the universal donor and why? What blood group is the universal recipient?
Leukocytes

• Play an important function in **defending the body from microbes** (ie. bacteria, viruses, fungi) & foreign particles.

• They account for 1% of the blood volume.

• Contain nuclei.

**Divided into:**
1. **Granulocytes** – have granules in their cytoplasm.

2. **Agranulocytes** – no granules in their cytoplasm.

Leuco = white -cyte = cell.
# Granulocytes

<table>
<thead>
<tr>
<th>PRIMARY FUNCTION</th>
<th>BASOPHILS / MAST CELLS (1%)</th>
<th>NEUTROPHILS (60%)</th>
<th>EOSINOPHILS (2-4%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MODE OF ACTION</strong></td>
<td>• Release histamine &amp; heparin from granules. Histamine dilates blood vessel</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• NOT phagocytic</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• NOT chemotaxic</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>PRIMARY FUNCTION</strong></td>
<td>• In blood = basophils</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• In tissue = mast cells</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Contain inflammatory mediators: heparin &amp; histamine which cause inflammation.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Phagocytosis:</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Lysosomes used to digest microbes</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Chemotaxic</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• 1&lt;sup&gt;st&lt;/sup&gt; to migrate to site of infection (within the hour)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>MODE OF ACTION</strong></td>
<td>• Phagocytosis - ingest &amp; destroy bacteria &amp; fungi</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Multi-lobed nucleus</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• These cells die forming part of the pus</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Eliminate parasites</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Promote inflammation - predominant inflammatory cells in allergic reactions</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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## Granulocytes

<table>
<thead>
<tr>
<th>BASOPHILS / MAST CELLS</th>
<th>NEUTROPHILS</th>
<th>EOSINOPHILS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulcerative colitis</td>
<td>Strenuous exercise</td>
<td>Allergic / atopic asthma,</td>
</tr>
<tr>
<td>Drug / food hypersensitivity</td>
<td>Microbial infection</td>
<td>Hay fever &amp; hives</td>
</tr>
<tr>
<td>Diabetes mellitus &amp; hypothyroidism</td>
<td>Tissue damage</td>
<td>Drug allergy</td>
</tr>
<tr>
<td>Infection e.g. chicken pox, smallpox, TB</td>
<td>Metabolic disorders</td>
<td>Atopic eczema, pemphigus &amp; dermatitis herpetiformis</td>
</tr>
<tr>
<td>Allergy</td>
<td>Leukaemia</td>
<td>Parasitic infections.</td>
</tr>
<tr>
<td>Some forms of leukaemia &amp; lymphoma</td>
<td>Heavy smoking</td>
<td>Systemic autoimmune conditions e.g. SLE</td>
</tr>
<tr>
<td>Parasitic infections</td>
<td>Rheumatoid arthritis</td>
<td>Hodgkin's &amp; non-hodgkin's lymphoma</td>
</tr>
</tbody>
</table>

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# Agranulocytes

<table>
<thead>
<tr>
<th>PRIMARY FUNCTION</th>
<th>MONOCYTES / MACROPHAGES</th>
<th>LYMPHOCYTES</th>
</tr>
</thead>
<tbody>
<tr>
<td>In blood = monocytes</td>
<td>B- lymphocytes, T- lymphocytes &amp; natural killer cells (NK cells)</td>
<td></td>
</tr>
<tr>
<td>In tissue = macrophages</td>
<td>Abundant in blood &amp; lymphatic tissue where B and T lymphocytes are critical for antigen specific immunity to pathogenic antigens.</td>
<td></td>
</tr>
</tbody>
</table>

Inflammation & repair
- **Phagocytosis** - ingest & destroy cellular debris & pathogens
- Activate other immune cells via antigen presentation

MODE OF ACTION
- Phagocytosis & chemotaxis
- Secrete cytokines e.g. Interleukin 1 – promotes fever, Produces globulins & activates T- lymphocytes

| B- lymphocytes activate immune response via antibody formation |
| T- lymphocytes & NK cells kill abnormal / invading pathogens (NK cells do this directly) |
Video: Mast Cell Degranulation
www.youtube.com/watch?v=VT7knZ6_8rk

Neutrophil

Eosinophil

Basophil
Leukocytes

Neutrophil

Eosinophil

Basophil

Lymphocytes

Monocyte

RBC for size comparison
Thrombocytes

• **Small, non-nucleated discs** produced in the red bone marrow

• Thrombocytes develop from megakaryoblasts that transform into megakaryocytes. These huge cells break down unto 2000-3000 fragments, enclosed by a piece of plasma membrane

• Produced under influence of **thrombopoietin** (mostly from liver). Life span of 10 days.

• Involved in **blood clotting** (haemostasis) and **prevent blood loss** from damaged blood vessels by forming a platelet plug

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Haem = blood / -stasis = stop
Thrombo = blood clot / cyto = cell
-poietin = to make
Mega = large / -blasts = immature cell
Thrombocytes

Stem cell → Developmental pathway → Platelets

Hemocytoblast → Megakaryoblast → Promegakaryocyte → Megakaryocyte → Platelets

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Thrombocytes

- Platelets contain ‘storage’ granules. These are tiny sacs that release proteins & adhesion molecules such as clotting factors (eg. von Willebrand factor).

- When activated, platelets release the contents of these granules in order to initiate clotting and eventually, healing.

- Platelet activation also initiates the production of thromboxane which is a vasoconstrictor that helps to strengthen a blood clot.

\[\text{vaso} = \text{duct} \quad \text{Constrict} = \text{to make narrower}\]
Stages of Blood Clotting

<table>
<thead>
<tr>
<th>Stages</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Vasoconstriction</td>
<td>When arterioles are damaged, the smooth muscle contracts immediately. When collagen is exposed in vascular endothelium, thromboxane is released which causes vascular spasm and attracts platelets.</td>
</tr>
<tr>
<td>2) Platelet Plug Formation:</td>
<td>Platelets contact and stick to the damaged wall, they are activated and release binding proteins. vWF is needed for this stage. These changes lead to platelet aggregation and causes platelets to become sticky. (positive feedback)</td>
</tr>
<tr>
<td>3) Coagulation:</td>
<td>Clotting factors form clot thereby reinforcing the plug. The enzyme ‘Thrombin’ is produced which converts fibrinogen into fibrin. Fibrin forms long, sticky threads that produce a mesh in the clot. Erythrocytes become caught up in the web and a clot forms.</td>
</tr>
<tr>
<td>4) Fibrinolysis:</td>
<td>Breakdown of a clot. The enzyme plasmin can dissolve a clot by digesting fibrin threads and inactivating fibrinogen and thrombin.</td>
</tr>
</tbody>
</table>

*Fibra = fibre / lysis = dissolution*
Video: Blood Clotting
www.youtube.com/watch?v=cy3a__OOa2M

A good animation of the process (you don’t need to remember all of the clotting factors).
Anticoagulants

- **Heparin** – a natural anti-coagulant produced by the body, produced by mast cells and basophils

**Drugs:**
- **Warfarin** (vitamin K antagonist and hence blocks synthesis of 4 clotting factors)
- **Aspirin** - anti-coagulant.

**Anti-coagulant Herbs:**
- Ginkgo, Garlic, Ginger, Turmeric

**Nutrients:**
- Vitamin E - anti-coagulant.
- Essential fatty acids (EFAs) - anti-coagulant.
- **Vitamin K** - a fat soluble vitamin responsible for making four clotting factors (does not cause clotting itself). Found in dark green vegetables & tomatoes. Produced by gut bacteria
Key Suffixes to remember:

- **blast** = immature cell (only partially differentiated)

- **cytosis** = more than normal cell numbers

- **penia** = lack of cells
Erythrocyte Pathologies: Anaemia

• A deficiency in haemoglobin given the persons age, sex and geographical location

Normal Haemoglobin ranges:

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>13-18 g/dL</td>
</tr>
<tr>
<td>Females</td>
<td>11.5-16.5 g/dL</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>&gt;11 g/dL</td>
</tr>
</tbody>
</table>

SIGNS & SYMPTOMS:

• (Often asymptomatic)
• Fatigue, shortness of breath on exertion, palpitations, irritability, fainting

• Signs: Tachycardia, thin/thready pulse, pallor (skin/conjunctiva)
Iron-Deficiency Anaemia

- Most common cause of anaemia worldwide.

- Reduced concentration of haemoglobin in erythrocytes causing them to appear paler and thus **hypochromic microcytic anaemia**

**CAUSES:**
- Deficient dietary intake
- Malabsorption
- Excessive blood loss (GIT/gynae)
- Excess requirements eg. Pregnancy/rapid child growth

**hypo = less**
**chromic = colour**
**micro = small**
Iron-Deficiency Anaemia

SIGNS & SYMPTOMS:
• General anaemia signs & symptoms

• Spoon shaped nails (koilonychia), angular stomatitis, glossitis, brittle hair, tachycardia

• Blood tests: Low RBCs and Hb, low ferritin (correlates with total body iron stores), blood film

TREATMENT:
• Treat cause! Also: Iron rich foods, iron supplementation, herbs (Withania), beetroot, dark green leafy veges, red meat.
Megaloblastic Anaemia

- Characterised by large, immature and dysfunctional red blood cells.

- Folic acid (folate) & vitamin $B_{12}$ are required for DNA synthesis in all proliferating cells, hence affecting rapidly dividing cells (erythrocytes).

- DNA replication is slowed down and cell growth continues without division and maturation, resulting in large RBC’s (may have nucleus and has shorter life span) – macrocytic cells.

- Diagnosis by blood test: **Mean Corpuscular Volume** (MCV) $>97$

$Mega = large$
$-blastic = immature cells$

$Macro = large$
cytic = cells
Megaloblastic Anaemia

CAUSES:

• **Deficient dietary intake** of folic acid &/or vitamin B₁₂ (rare except in vegans)

• **Lack of intrinsic factor** due to autoimmune disease (pernicious anaemia), gastrectomy, chronic gastritis, bariatric surgery, stomach tumours, coeliac disease

• **Malabsorption** in crohn’s disease, surgical excision

• **Drugs** – methotrexate is a folate antagonist

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Megaloblastic Anaemia: B$_{12}$

- The liver has abundant stores so if absorption is impaired it takes 2-4 years to develop. (folic acid only 4 months)

**SIGNS & SYMPTOMS:**
- General anaemia signs & symptoms
- Enlarged red sore shiny tongue
- Neurological symptoms: Tingling, numbness, weakness, loss of co-ordination (loss of co-ordination) burning sensations, tinnitus, depression

**TREATMENT:**
- Intramuscular Vitamin B12 Injections

Vitamin B$_{12}$ is also essential for the production and maintenance of the myelin sheath (surrounds nerve fibres)
Megaloblastic Anaemia: Folate

SIGNS & SYMPTOMS:
• Same as for B₁₂ deficiency (but no neurological damage)

TREATMENT:
• Folate supplementation.

Folic acid is also required for the development of a healthy foetal nervous system.
Hypo/Aplastic Anaemias

- Rare, potentially life-threatening failure of haemopoiesis (blood cell production)
- Pancytopenia and hypocellular bone marrow (few or no cells)

**Pancytopenia = Absence of all three cell types**

**CAUSES:**
- Congenital (“fanconi’s”)
- Idiopathic (unknown cause)
- Can be secondary to drugs (naproxen, diclofenac etc.), chemicals, radiation, cancer, hepatitis/EBV

**hypo– = low**
**a– = without**
**-plastic = formation**
SIGNS & SYMPTOMS:
• Anaemia (pallor, headache, dyspnoea, palpitations)
• Multiple infections (low white blood cell count)
• Easy bleeding (low thrombocyte count).

TREATMENT:
• Bone marrow stem cell transplant. Platelet transfusion/blood transfusion. Treat cause

The most common cause of death is sepsis, then bleeding.
Haemolytic Anaemias

• Anaemia resulting from excessive breakdown of RBCs, when bone marrow activity cannot compensate for the loss of RBC’s

• Erythrocyte life span can become as low as 5 days

CAUSES:
• Genetic (e.g. sickle cell, thalassemia)
• Some drugs, chemicals, autoimmune, rhesus factor incompatibility, malaria, radiation.

SIGNS & SYMPTOMS:
• Fatigue, shortness of breath on exertion, palpitations, irritability, fainting, tachycardia
• Jaundice, splenomegaly, gallstones, frequent infections, vascular occlusions.

Haem = blood
-lytic = destruction

Plasmodium parasites in malaria enter and mature within human erythrocytes and cause them to rupture.
Haemolytic Anaemias:

Sickle Cell Anaemia

- Sickle cell anaemia causes a deficiency of the 2-alpha/2-beta formation of haemoglobin and causes it to sickle up. Haemoglobin is called HbS.

- When HbS gives up oxygen to interstitial fluid, it causes the erythrocyte to sickle up.

- These cells rupture easily. Even though erythropoiesis is stimulated, it cannot keep up with the rate of haemolysis.

CAUSES:
- Inherited recessive condition (substitution chromosome 21)
- Afro-Caribbean
- The sickle trait protects against malaria because it causes sickle formation and potassium leakage out of erythrocytes
Sickle Cell Anaemia

SIGNS & SYMPTOMS:
- Usually begins 3-6 months of age as HbF falls.
- Signs/symptoms as for Anaemia
- **Splenomegaly** and jaundice.
- Can also occlude vessels and cause ischaemic pain, placental infarction, strokes, renal colic, mesenteric ischaemia

BLOOD TEST:
- FBC and blood film. Hb = 6-8g/dL

TREATMENT:
- Analgesics (pain relief), fluid therapy, blood transfusion, bone marrow transplant
Thalassaemia

- Thalassaemia is associated with a defect in synthesis of either the alpha or beta haemoglobin chains
- An Inherited disease (recessive)

**SIGNS & SYMPTOMS:**
- If **B-Thalassaemia** = Starts when HbA production begins/gamma chain ceases (usually later part of first year). Causes ‘failure to thrive’ and anaemia.
- If **A-Thalassaemia** = Can be lethal in utero in severe cases (‘major’). Signs/symptoms of anaemia, jaundice, splenomegaly, hepatomegaly, exercise intolerance. To compensate haemolysis, bone marrow proliferation (mostly skull/ribs)

Recap:
- HbA = 2 Alpha/2 Beta chains
- HbF = 2 Alpha/2 Gamma chains
Haemolytic Disease of the Newborn

- Occurs when the mother produces anti-rhesus antibodies that cross the placenta.

- The antibodies bind to the foetal rhesus antigens and cause agglutination and haemolysis.

- Sensitisation occurs with the first baby producing maternal antibodies against rhesus.

- The greatest possibility of sensitisation occurs at delivery, so the first born child is normally unaffected.
Polycythaemia

• Also known as erythrocytosis. A myeloproliferative disorder

• Excess production of erythrocytes resulting in increased blood viscosity, reduced blood flow, increased risk of thrombosis.

CAUSES:
• Physiological: high altitude
• Pathological: unknown/genetic

Poly = many
-aemia = blood
Erythrocyt- = red blood cell
-cytosis = increase cell numbers
Myelo = bone marrow
Polycythaemia

SIGNS & SYMPTOMS:
• Mild cases may cause no problems.

• Arterial thrombosis: MI, pulmonary embolism, stroke

• Venous thrombosis: DVT

• Hypertension, red skin, headaches, dizziness, pruritus

TREATMENT:
• Treat underlying cause, prevent blood clots.
Leukocyte Pathologies: Granulocytopenia

Granulocytes = Neutrophils, eosinophils, basophils

- Marked reduction in the number of granulocyte leukocytes
- I.e. Neutropenia: Normally 2.5-7.5x10^9/L. Severe if <0.5.

CAUSES:
- Drug toxicity
- Radiation
- Bone marrow diseases
- Severe infections
- HIV / AIDS

Granulo = granulocytes
Cyt = cell
Penia = Greek for deficiency
Neutro- = neutrophil
Leukocyte Pathologies: Granulocytopenia

Granulocytes = Neutrophils, eosinophils, basophils

SIGNS & SYMPTOMS:
• Severe illness
• Malaise
• Chills
• Necrosis of mucous tissues

TREATMENT:
• Treat the cause
• Support immunity through herbs (Echinacea, Andrographis) and nutrients (vitamin C, zinc, vitamin A, vitamin D) as well as life-style to support immunity and support healing (avoid stress!)

Necrosis = death
Leukocytosis

• Marked increase in the number of all leukocytes

CAUSES:

• Response to infections.

• Leukaemia (uncontrolled production of leukocytes in bone marrow due to cancer).

Leuko = white
-cyto = cell
-cytosis = increase cell numbers
Leukaemia

- A group of cancers of the bone marrow, characterised by an abnormal over production of leukocytes

- This uncontrolled proliferation results in suppressed production of erythrocytes (=anaemia) and thrombocytes (=thrombocytopenia)

Divided into:
- **Acute leukaemia's**: Rapid onset, more aggressive course. Immature cells (>20% blast cells in bone marrow)
- **Chronic leukaemia's**: Insidious onset. More differentiated cells.
## Leukaemia

<table>
<thead>
<tr>
<th></th>
<th>Acute Leukaemias</th>
<th>Chronic Leukaemias</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>All ages</td>
<td>Usually adults</td>
</tr>
<tr>
<td><strong>Onset</strong></td>
<td>Sudden</td>
<td>Insidious</td>
</tr>
<tr>
<td><strong>Leukaemic cells</strong></td>
<td>Immature (-blasts)</td>
<td>Mature</td>
</tr>
<tr>
<td><strong>Anaemia</strong></td>
<td>Prominent</td>
<td>Mild</td>
</tr>
<tr>
<td><strong>Thrombocytopenia</strong></td>
<td>Prominent</td>
<td>Mild</td>
</tr>
<tr>
<td><strong>Leukocyte count</strong></td>
<td>Variable</td>
<td>Increased</td>
</tr>
<tr>
<td><strong>Lymph node enlargement</strong></td>
<td>Mild</td>
<td>Prominent</td>
</tr>
<tr>
<td><strong>Splenomegaly</strong></td>
<td>Mild</td>
<td>Prominent</td>
</tr>
</tbody>
</table>
Blood Cell Lines

Myeloid

Lymphoid
Leukaemia

Four types of Leukaemia:
1. Acute myelogenous leukaemia (AML)
2. Acute lymphocytic leukaemia (ALL)
3. Chronic myeloid leukaemia (CML)
4. Chronic lymphocytic leukaemia (CLL)

SIGNS & SYMPTOMS:
- Malaise, anaemia (fatigue, pallor etc), frequent infections, easy bleeding/bruising
- Fever, weight loss
- Splenomegaly (abdominal swelling/discomfort)
- Lymph node enlargement
Leukaemia

DIAGNOSIS:
• FBC: anaemia, low thrombocytes, variable leukocyte count
• Blood film
• Bone marrow biopsy

ALLOPATHIC TREATMENT:
• Chemotherapy, bone marrow transplant, radiotherapy, immunotherapy
• Relapse is common

ALTERNATIVE THERAPIES:
• Cancer support using herbal medicines, nutrition & nutritional supplements, homeopathy.

PROGNOSIS:
• Depends on type, treatment & age.
Thrombocytopenia

- Reduction in the thrombocyte count

**SIGNS & SYMPTOMS:**
- **Excessive bleeding**, prolonged bleeding times (spontaneous bleeding occurs when count is less than 30), excessive bruising
- **Petechiae** (micro-haemorrhages underneath the skin)
- Haematuria, haematemesis, bleeding gums, PPH.

**CAUSES:**
- Leukaemia, congenital (eg. Fanconi’s syndrome), radiation, drugs, chemotherapy, viral infections (EBV, hepatitis, HIV, MMR), autoimmune destruction.

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**Thrombocyte Pathologies:**

- *penia* = deficiency

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Haemophilbia

• A Deficiency of clotting factors

• Haemophilia A:
  Deficiency of clotting factor VIII (8)

• Haemophilia B:
  Deficiency of clotting factor IX (9)

CAUSES:
• Genetic: X-Linked recessive disorder
  (usually affects males. Females normally carriers. 1 in 5000 males)
Haemophilia

SIGNS & SYMPTOMS:
- **Severe disease**: Excessive and easy bleeding, GIT/mucosal haemorrhage, haematuria, haemarthrosis (causing inflammation and pain)
- **Moderate disease**: Easy bleeding
- **Mild disease**: Bleeding after major trauma/injury

TREATMENT:
- No cure. Replacement of clotting factors/blood transfusion.
- Avoid contact sports
von Willebrand Disease (vWD)

• A blood coagulation disorder, resulting from **deficiency or abnormal function of a coagulation factor (vWF)**.

• The factor **normally assists in platelet plug formation** by attracting circulating platelets. It also binds factor VIII and prevents it being rapidly broken down.

**SIGNS & SYMPTOMS:**
• **Usually asymptomatic**, detected more in women with very **heavy menses** & excessive blood loss during childbirth
• Spontaneous bleeding (eg. haemarthrosis), easy bruising, nose bleeds, gums

**CAUSES:**
• **Genetic** disease - autosomal dominant (affects males & females equally)

**TREATMENT:**
• Education and desmopressin (stimulates release of vWF from endothelium)
Summary Questions

1) Name two granulocytes and state their function
2) What is meant by ‘haemostasis’?
3) When arterioles are damaged and collagen is exposed, what chemical is released that triggers vasoconstriction?
4) What is the function of vitamin K?
5) List three causes of iron deficiency anaemia
6) What are the classic signs and symptoms of anaemia?
7) What is meant by megaloblastic anaemia? List possible causes
8) What is the average life span of a RBC? How low can this be in sickle cell anaemia?
9) What is meant by: A) Thalassaemia. B) Haemophilia A
10) Explain what is meant by Leukaemia. State any medical investigations performed to assist in the diagnosis of leukaemia