Cardiovascular System:
Blood (Chapter 19)
Lecture Materials
for
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Primary Sources for figures and content:

Cardiovascular system = blood, heart and blood vessels (anatomical division)
Circulatory system = cardiovascular system and lymphatic system (clinical)

Blood – a fluid connective tissue
Functions of blood:
1. Distribution
   a. deliver O₂ and nutrients to cells
   b. remove metabolic waste
   c. transport hormones to targets
2. Regulation
   a. maintain body temp →
      distribute heat from muscles
   b. maintain pH
   c. maintain fluid volume
3. Protection
   a. restrict loss at injury (clotting)
   b. prevent infection (leukocytes)

Characteristics of blood
- pH 7.4
- temperature 38°C / 100.4°F
- total volume 4-6 L (9-11 pints)

Fun fact:
to estimate your own blood volume:
  7% body weight in kg = blood in L
  (1 kg = 2.2 lb)
  (weight lb / 2.2) X 0.07

Composition of blood:
(CT = cells in matrix)
Blood matrix = plasma: ~55%
  water + soluble proteins
Blood cells = formed elements:
  - Erythrocytes: ~45%
    transport O₂
  - Leukocytes: < 1%
    defense
  - Platelets: < 1%
    cell fragments,
    for clotting
Plasma:
-90% water + dissolved solutes (nutrients, gasses, hormones, wastes, ions, proteins)

Plasma Proteins (~8% of total plasma)
-7.6g/100ml
(5X more proteins than interstitial fluid)
-These proteins remain in plasma, not absorbed by cells for nutrients

1. Albumins (60% of plasma proteins)
   Produced by the liver
   Functions:
   -act as pH buffer for blood
   -contribute to osmotic pressure of blood (keep water in blood)
   -transport fatty acids and hormones

2. Globulins (35% of plasma proteins)
   A. Gamma globulins / Antibodies / Immunoglobulins:
   -produced by plasma cells in the lymphatic system
   -function to attack foreign substances
   B. Alpha and Beta globulins / Transport globulins:
   -produced by the liver
   -function to transport small or insoluble compounds to prevent filtration loss by kidney

3. Clotting Factors (4% of plasma proteins)
   -produced by the liver
   -11 total, fibrinogen most abundant
   -all function to promote or form a clot
   (serum = plasma – fibrinogen)

4. Other (1% of plasma proteins)
   -From liver:
     -metabolic enzymes and antibacterial proteins
   -From endocrine organs:
     -hormones

*liver disease can lead to a variety of blood disorders (many plasma proteins produced by liver)

Hematopoiesis
blood cell production
-all formed elements arise from the same progenitor cell: the hemocytoblast, located in the red bone marrow
(follow lineages on handout)
**Erythrocytes (RBCs)**  
- 99.9% of the formed elements of blood  
- 1/3 of total body cells  
  (average human = ~75 trillion cells)  
- Average RBC count = 4.2-6.3 million/μl

Hematocrit = % of whole blood occupied by formed elements  
  (mostly erythrocytes: 99.9%)  
  - male = 46%  
  - female = 42%

*Polycythemia* = excess erythrocytes but normal blood volume, usually due to bone marrow cancer  
  ↑ hematocrit = ↑ viscosity = ↑ heart strain and stroke

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**Erythrocyte structure**  
- biconcave disc  
  - 7.8μm diameter  
  - large surface area for gas exchange  
  - can fold and stack to pass narrow vessels

**Hemoglobin Molecule (Hb)**  
- 2 α chains  
- 2 β chains  
- each chain has one heme group with iron in center:  
  - iron binds O₂  

Oxyhemoglobin = O₂ bound, bright red  
Deoxyhemoglobin = no O₂, burgundy  
-fetal Hb binds O₂ more strongly than adult:  
  - insures transfer of O₂ from mom  

280 million Hb/ RBC  
  - 4 hemes/Hb, each heme binds 1 O₂ =  
    >1 billion O₂ per RBC  
    (25 trillion RBC per person)  

- most O₂ is carried in blood bound to Hb  
  (some in plasma)  
- only 20% CO₂ carried by Hb:  
  Carbaminohemoglobin - CO₂ bound to amino acids on α/β chains, not on heme

- when plasma O₂ is low, Hb releases O₂ and binds CO₂  
  - at lungs CO₂ exchanged for O₂ by diffusion  

*Anemia* = O₂ starvation, due to:  
  1. insufficient # RBCs  
  2. low Hb  
  3. abnormal Hb

  **Thalassemia** = inability to produce α or β chains, slow RBC production, cells fragile and short lived  
  **Sickle-cell anemia** = single amino acid mutation in β chain  
  high O₂, cells normal  
  low O₂, Hb misfolds, RBCs deform into crescent shape:  
  fragile, blocks capillaries
Erythropoiesis = red blood cell formation
-2 million/sec (1 oz new blood per day)
-occurs in reticular CT in red bone marrow,
in spongy bone

1. Hemocytoblast differentiates into myeloid stem cell
2. followed by many stages of differentiation, all involve ↑ protein synthesis
3. cell fills with Hb, loses organelles (nucleus too)
4. 3-5 days reticulocytes are formed (Hb + some ribosomes), released into blood, 1-2% of total blood RBCs
5. 2 days in circulation lose ribosomes (no more protein synthesis) = mature erythrocyte

-Vitamin B12 necessary for erythropoiesis for stem cell division
Lack B12 = pernicious anemia

Erythropoietin (EPO)
-hormone, released by kidney during hypoxia (low O₂)
-stimulate RBC production:
- ↑ cell division rates (up to 30million/sec)
- ↑ Hb synthesis = ↓ maturation time
“blood doping” = injecting EPO or RBCs to enhance athletic performance: ↑ O₂ to tissues, but also ↑ hematocrit/viscosity = clots, stroke, heart strain
Kidney failure often = low RBCs due to lack of EPO

Erythrocyte Recycling
-old/damaged RBCs removed by phagocytes in spleen
-replaced by new, ~1% turnover per day

-phagocytosed cells broken down:
-protein → amino acids, released for use
-heme →
1. iron removed, bound to transferrin in blood for recycling back to bone marrow (new RBCs)
2. pigment → biliverdin (green)
biliverdin → bilirubin (yellow-green), released into blood, filtered by liver, excreted in bile
Jaundice = failure of bilirubin to be excreted in bile, collects in peripheral tissues → yellow skin & eyes
3. in gut, bilirubin → urobilins (yellow) & stercobilins (brown) via bacteria urobilins absorbed, excreted in urine stercobilins remain in feces
Hemolysis = RBC rupture in blood →
Hemoglobinuria = red/brown urine due to kidney filtering intact α & β chains of hemoglobin

Blood Types
-all cell membranes have surface antigens:
indicate “self” (antigen = substance that triggers immune response)
-RBCs have 50+, 3 important for transfusion: agglutinogens: A, B, D

Type A blood = surface antigen A (40%)
Type B blood = surface antigen B (10%)
Type AB blood = both A + B antigens (4%)
Type O blood = neither A nor B antigen (46%)
Rh+ = surface antigen D (85%)
Rh- = no D antigen (15%)
-at birth, blood contains antibodies against A or B antigens that are not present
-the antibodies will cause agglutination (clumping) of antigen (agglutinogen)
**Type A blood** = antibodies against B antigen  
**Type B blood** = antibodies against A antigen  
**Type AB blood** = neither antibody  
**Type O blood** = antibodies against both A & B

- antibodies against D antigen only form upon exposure and are small enough to cross placenta

Hemolytic disease of the newborn/

*Erythroblastosis fetalis:*

Rh- mom pregnant with Rh+ baby, gets exposed to D antigen during birth, makes anti-D antibodies, pregnant with second Rh+ baby, antibodies cross placenta, causes agglutination and lysis of fetal RBCs = anemia and death

Prevention: treat mom with RhoCAM during first birth to prevent antibody formation

- blood typing always done before transfusion to prevent body wide agglutination
- if blood type unknown: type O- = universal donor: it lacks all 3 agglutinogens (A, B, D) so no risk of agglutination by antibodies in anyone

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Leukocytes (WBCs)

- < 1% total blood volume
- 5 types
- functions:
  - defend against pathogens
  - remove toxins and wastes
  - remove abnormal/damaged cells
  - all have nuclei & organelles, no hemoglobin
  - 6000-9000 leukocytes/µl blood
  - use blood to travel to tissues, not permanent residents of blood
- characteristics:
  1. ameboid movement
  2. diapedesis (move out of blood):
     a. margination = adhere to vessel
     b. emigration = pass between endothelial cells

3. exhibit positive chemotaxis
4. phagocytosis (3 of 5)
   - engulf pathogens and debris

**Types of Leukocytes:**
(on handout)
Granulocytes vs. Agranulocytes
**Neutrophil** (a.k.a PMNs) (polymorphonuclear leukocytes)

- Non-specific defense
- Phagocytic
- 50-70% of WBCs
- 3-5 lobed nucleus
- 12µm diameter
- Granules contain enzymes and defensins
- Very mobile: first at injury
- Life span less than 10 h

**Functions:**
- Respiratory burst: H₂O₂, O₂⁻, kill phagocytosed things
- Degranulation: release defensins, lyse bacteria
- Prostaglandins: induce inflammation to stop spread of injury
- Leukotrienes: attract phagocytes

**Eosinophil**

- Non-specific defense
- Phagocytic
- 2-4% of WBCs
- Bilobed nucleus
- 12µm diameter
- Granules contain toxins
- Life span 9 d

**Functions:**
- Phagocytosis of antibody covered objects
- Defense against parasites: exocytose toxins on large pathogens
- Reduce inflammation: anti-inflammatory chemicals/enzymes

**Basophil**

In tissues = Mast cell

- Non-specific defense
- Not phagocytic
- Less than 1% of WBCs
- “U” shaped nucleus
- 8-10µm diameter
- Granules contain histamine: dilate blood vessels
- Heparin: prevents clotting
- Life span 9 d

**Functions:**
- Inflammation
- Allergic response (via histamine)

**Monocyte**

In tissues = Macrophage

- Non-specific defense
- Phagocytic
- 2-8% of WBCs
- Kidney shaped nucleus
- 15µm + diameter
- Circulate 24 h, exit to tissues = macrophage
- Life span several months

**Functions:**
- Phagocytosis: virus & bacteria
- Attract phagocytes
- Attract fibroblasts for scar formation
- Activate lymphocytes to mount immune response
**Lymphoid Stem Cells**

- Immune response
- 20-30% of WBCs
- Large round nucleus
- 5-17µm diameter
- Migratory between blood and tissues
- Most in lymphatic system
- Life span days to lifetime

**Lymphocytes**

Function depends on type, 3 types:

- B cells: humoral immunity (secrete antibodies)
- T cells: cell-mediated immunity (attack foreign cells)
- NK cells: immune surveillance (destroy abnormal tissue)

**Leukopoiesis** = WBC production

Myeloid stem cells → Basophils, Eosinophils, Neutrophils, Macrophages as directed by specific colony stimulating factors (CSF) produced by Macrophages and T cells (different CSF (hormone) results in different cell)

Leukopenia = too few WBCs
Leukocytosis = excessive WBCs in normal blood volume

- Normal infection ↑ WBCs from 7,500 to 11,000/µl
- >100,000/µl → leukemia, cancerous stem cells, WBCs produced are immature and abnormal

Infectious Mononucleosis:

- Epstein Bar virus infection causes production of excess agranulocytes that are abnormal, self limiting
Platelets (Thrombocytes)
-flattened discs, 2-4μm diameter, 1μm thick
-cell fragments, no nucleus
-constantly replaced, 9-12 d in circulation, then phagocytosed by cells in spleen
-350,000 / μl blood
-1/3 of total platelets held in reserve in spleen, mobilized for crisis
Functions:
-transport clotting chemicals, release when activated
-form patch (platelet plug) over damaged vessel
-contract wound after clotting (contain actin and myosin)

Thrombocytopoiesis = platelet production
-Megakaryocyte in bone marrow breaks off membrane enclosed cytoplasm to blood
-Each megakaryocyte can produce ~4000 platelets
-Induced by thrombopoietin from kidney and CSF from leukocytes
Thrombocytopenia = too few platelets < 80,000/μl, results in bleeding and petechia
Thrombocytosis = too many platelets > 1 million/μl, due to cancer or infection, clotting risk

Hemostasis
(on handout)
**Bleeding Disorders:**

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Thrombosis</td>
<td>Clotting in undamaged vessels, slow or prevent flow (intrinsic pathway)</td>
</tr>
<tr>
<td>Embolus</td>
<td>Free floating thrombosis, blocks small vessels → tissue damage, heart attack, stroke</td>
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<tr>
<td>Disseminated Intravascular Coagulation:</td>
<td>Widespread clotting followed by systemic bleeding, rare: complication of pregnancy, septicemia or mismatched transfusion</td>
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<tr>
<td>Hemophilia</td>
<td>Inadequate production of clotting factors</td>
</tr>
<tr>
<td>Type A</td>
<td>Factor VIII (X linked)</td>
</tr>
<tr>
<td>Type B</td>
<td>Factor IX</td>
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<tr>
<td>Type C</td>
<td>Factor XI</td>
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**Other blood disorders:**

<table>
<thead>
<tr>
<th>Dietary</th>
<th>Requirements</th>
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<tbody>
<tr>
<td>-Calcium required for clotting cascade</td>
<td></td>
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<tr>
<td>-Vitamin K required for liver to synthesize clotting factors</td>
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<tr>
<td>-Iron required for hemoglobin production</td>
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<tr>
<td>-Vitamin B12 required for RBC stem cell division</td>
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<tr>
<td>Organ health</td>
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<tr>
<td>-Impaired liver = ↓clotting (↓ clotting factors)</td>
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<tr>
<td>-Impaired kidney = ↓RBC (↓ EPO)</td>
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</tr>
<tr>
<td></td>
<td>↓platelets (↓thrombopoietin)</td>
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