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 $O_2$
- 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
Erythrocyte structure
- biconcave disc
- 7.8µm diameter
- large surface area for gas exchange
- can fold and stack to pass narrow vessels

- mature erythrocytes lack all organelles
  - no division, no repair
  - low metabolic demands
  - life span < 120 days
- cell is 97% hemoglobin protein (red color)
- hemoglobin transports O₂ and some CO₂
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
280million Hb/ RBC  X
  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 $O_2$)
- stimulate RBC production:
  - $\uparrow$ cell division rates (up to 30 million/sec)
  - $\uparrow$ Hb synthesis = $\downarrow$ maturation time
“blood doping” = injecting EPO or RBCs to enhance athletic performance: $\uparrow$ $O_2$ to tissues, but also $\uparrow$ 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
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 10h

**Functions:**
- Respiratory burst: \( \text{H}_2\text{O}_2 \) & \( \text{O}_2^- \), 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
- 12 µm 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
Lymphocyte

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

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)
Lymphoid stem cells $\rightarrow$ Lymphocytes
production involves immune response
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)
**Thrombopoiesis** = 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)
Hemostasis

Vascular Phase

Vessel lumen

Endothelium

Basal lamina

Vessel wall

Concentric smooth muscle

Platelet adhesion

Platelet aggregation

Release of chemicals (ADP, thromboxane A₂, Ca²⁺, platelet factors)

Blood

Platelet plug

Contracted smooth muscle cells

Cut edge of vessel wall

Interstitial fluid

Platelet Phase
(a) The coagulation phase

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(b) A blood clot

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Bleeding Disorders:

Thrombosis = clotting in undamaged vessels, slow or prevent flow (intrinsic pathway)
Embolus = free floating thrombosis, blocks small vessels → tissue damage, heart attack, stroke

Disseminated Intravascular Coagulation:
  widespread clotting followed by systemic bleeding, rare: complication of pregnancy, septicemia or mismatched transfusion

Hemophilia = inadequate production of clotting factors
  Type A → Factor VIII (X linked)
  Type B → Factor IX
  Type C → Factor XI
Other blood disorders:

Dietary:
- Calcium required for clotting cascade
- Vitamin K required for liver to synthesize clotting factors
- Iron required for hemoglobin production
- Vitamin B12 required for RBC stem cell division

Organ health:
- Impaired liver = ↓ clotting (↓ clotting factors)
- Impaired kidney = ↓ RBC (↓ EPO)
  ↓ platelets (↓ thrombopoietin)