The Blood

Extracellular Fluids
- Include blood plasma, interstitial fluid, and lymph
- Blood plasma similar to others because of osmosis, diffusion & bulk transport except:
  - Proteins too large to pass through capillary walls
  - Red blood cells (while WBC move freely & are more concentrated in lymph)

Function of Blood
- Transport of gases, nutrients, heat, wastes, & hormones
- Regulation of pH (7.35-7.45), temperature (38º C or 100.4 ºF) and water content (more viscous)
- Protection
  - Against blood loss through clotting
  - Combats toxins and microbes

Components of Blood
- About 8% of body weight, 4-5 liters in females, 5-6 liters in males
- 55% plasma
- 45% formed elements
  - 99% RBC
  - 1% WBC
  - Plus platelets

Plasma
- 91.5% water and 8.5 % solute by weight
- Solutes include:
  - Proteins (7%) that are largely produced by liver
    - Albumins (54%) smallest of plasma proteins, essential osmotic components
    - Globulins (38%) include transport proteins, that move non-water soluble molecules (lipids, vitamins, iron, & hormones) and immunoglobins that are antibodies
  - Nutrients including glucose, amino acids, and fatty acids
  - Enzymes and hormones for regulation
  - Respiratory gases
  - Electrolytes including Na⁺, Cl⁻, K⁺, PO₄²⁻
  - Waste products including ammonia, urea, uric acid

Formed Elements
- Erythrocytes (RBCs)
- Leucocytes (WBCs)
  - Granular - neutrophils, eosinophils, basophils
- Agranular - lymphocytes (B, T, natural killer), monocytes
- Platelets

- Number of RBCs relatively constant due to negative feedback system
- Number of WBCs variable depending on type and intensity of infection

**Hemopoiesis**

- All derived from hemopoietic (or pluripotent) stem cells
- Myeloid stem cells - develop in red bone marrow and produce all but lymphocytes
- Lymphoid stem cells - partial development in bone marrow and complete development in lymphoid tissue, produce lymphocytes
- Formation of “-blast” cells
  - Proerythroblasts → erythrocytes
  - Myeloblasts → eosinophils, neutrophils, basophils (granular)
  - Monoblasts → monocytes
  - Megakaryoblasts → platelets
  - Lymphoblasts form pre-B cells and prothymocytes respectively → B & T lymphocytes
- Occurs in red bone marrow in long bones, pelvis, cranium, vertebrae, sternum, & ribs
  - except lymphocytes (form in lymphoid tissue)

**Hemopoietic Growth Factors**

- Stimulate differentiation and proliferation of progenitor cells
- Erythropoietin (EPO) from kidneys (liver in newborns) → erythrocyte precursors - stimulated by testosterone
- Colony-stimulating factors and interleukins → leucocyte formation and function
  - These are cytokines (a class of small glycoproteins) produced by red marrow, other leucocytes and macrophages, and fibroblasts
- Thrombopoietin (TPO) from liver → platelet formation

**Erythrocytes**

- Numerous - 4.8 million per mm³ for females & 5.4 for males
- Replacement 2 million per second
- Efficient structure for oxygen transfer
  - No nuclei or organelles (e.g. mitochondria), anaerobic
  - Biconcave - increased surface area for diffusion and flexible
  - 33% hemoglobin
    - alpha and beta globin units plus 4 heme molecules
    - carries 23% of CO₂ bound to proteins as carbaminohemoglobin
- Blood pressure regulation
  - Nitrous oxide (NO) produced by endothelial cells - causes vasoconstriction
  - Super NO produced by lung cells - causes vasodilation
Both appear to be transported by hemoglobin

**RBC Life Cycle**
- Live about 120 days
- Hemoglobin is recycled
  - Globin broken down to amino acids for further use
  - Iron separated and carried via transferrin to storage sites in liver, muscle, and spleen
    - Reused in erythropoiesis
  - Remaining heme ultimately converted to bilirubin, carried to liver and excreted via bile
    - Further converted to urobilinogen and departs via feces or urine
- Hypoxia sensed by kidney cells which stimulate release of erythropoietin and RBC replacement

**Anemia**
- Iron-deficiency anemia - due to insufficient absorption or excessive loss of iron
- Pernicious anemia - lack of ability to produce intrinsic factor, critical to the absorption of Vit B₁₂
- Hemorrhagic anemia - loss of RBCs due to loss of blood
- Hemolytic anemia - ruptured RBCs causing distorted shape
  - Due to abnormal hemoglobin, RBC enzymes, or membranes
  - May be caused by parasites, toxins, or Rh incompatibility with fetus
- Aplastic anemia - reduced bone marrow
  - May be caused by toxins, gamma radiation, or medication
- Sickle cell anemia - abnormal hemoglobin causes misshapened cells
  - Provides resistance to malaria - sickling of cell causes increase membrane permeability to potassium, potassium leaves cell, low level of potassium kills malaria causing parasite
  - Co-dominant expression of inherited gene

**Tests for Anemia**
- Hematocrit - percentage RBCs per volume of blood
  - Normal - females 38-46%, males 40-54% (higher due to testosterone levels)
- Reticulocyte count in blood - measure of level of erythropoiesis
  - Normal - 0.5-1.5% of all RBCs

**Leukocytes**
- Various types with varying size, structure and staining
- Primary function is combat inflammation and infection through phagocytosis and immune response (the latter related to self cell recognition - histocompatibility)
- 5-10K per mm³ but number varies as required
  - High number - leucocytosis, low number - leukopenia
**WBC Protection**
- “Emigration” from vessels to site of inflammation or infection
- Process slows WBC by adhesion proteins (e.g. selectins displayed due to injury that stick to carbohydrates on neutrophil)
- WBC passes between capillary endothelial cells
- WBCs perform different tasks (Exhibit 19.2)

**WBC Protection Examples**
- Neutrophils respond to tissue damage, phagocytize bacteria or kill them with a variety of toxic substances (strong oxidants and defensins)
- B-lymphocytes responsible for the creation of antibodies to foreign antigens
- Differential WBC count - since WBCs have different protective responsibilities, proportional numbers of each aid diagnosis

**Platelets**
- Partial cells from megakaryoblasts
- Involved in forming the platelet plug to stop bleeding and chemically promote clotting
- 250-400K per mm³
- Production controlled by thrombopoietin
- Platelets contain variety of active molecules
  - Alpha granules - clotting factors and platelet-derived growth factors (important for growth of endothelia, smooth muscle, and fibroblast cells)
  - Dense granules - ADP, ATP, Ca²⁺, serotonin, thromboxane A2, fibrin-stabilizing factor

**Hemostasis**
- Three steps
  - Vascular spasm - smooth muscle response
  - Platelet plug formation
    - Platelet adhesion - collecting of platelets on endothelial surface of vessel
    - Platelet release response
      - Activation of nearby platelets with ADP & thromboxane A2
      - Vasoconstriction with serotonin & thromboxane A2
    - Platelet aggregation
      - Enhanced by ADP forming platelet plug
  - Clotting or coagulation - network of plasma proteins, fibrin
    - Clotting factors - variety of active molecules
    - Formation of prothrombinase
    - Formation of thrombin
    - Conversion of fibrinogen to fibrin

**Blood Groups**
- ABO
- Rh factor