1. Blood
    a. Fluid connective tissue
        i. Consists of cells suspended in a liquid fibrous matrix.
        ii. Blood cells = formed elements
        iii. Liquid matrix = plasma.
    b. Formed elements consist of erythrocytes (red blood cells), leukocytes (white blood cells) and platelets.
2. Centrifuged blood divides into 3 portions
    a. Plasma
    b. Packed RBCs (42-52% in ♂ and 37-47% in ♀. This % = hematocrit.)
    c. Buffy layer containing WBCs and platelets. (<1%)
3. Physical characteristics
    a. Color ranges from scarlet (oxygen-rich) to dark red (oxygen poor).
    b. Viscosity is 5x that of water, due primarily to the presence of formed elements.
    c. pH normally ranges from 7.35-7.45 (slightly alkaline).
    d. Temperature is typically 100°F.
    e. Volume is 4-5 L for females and 5-6 L for males.
4. Distribution functions
    a. Carries O_2 (from lungs) and nutrients (from GI tract and body stores) to all cells
    b. Carries wastes from all cells to elimination sites (lungs for CO_2; kidneys for nitrogenous wastes
    c. Carries hormones (chemical signals) from endocrine organs to target tissues.
5. Regulatory functions
    a. Regulates body T° by absorbing and distributing heat
    b. Maintains body fluid pH by virtue of its many buffers
    c. Maintains adequate body fluid volumes.
6. Protective functions
    a. Prevents blood loss by initiating clotting mechanisms in response to blood vessel damage
    b. Prevents infection via WBCs and plasma immune proteins.
7. Blood plasma
    a. 48-58% of blood volume in ♂ and 53-63% of blood volume in ♀.
    b. 90% water. Water acts as a solvent and suspending medium.
    c. Solutes dissolved in plasma include: plasma proteins, nutrients, electrolytes, respiratory gases, hormones and wastes.
    d. Plasma proteins
        i. Albumin = most abundant plasma protein
            1. Produced by the liver
            2. Maintains plasma osmotic pressure.
            3. Acts as a buffer and is involved in the transport of steroids and bilirubin.
        ii. Globulins are another major type of plasma protein.
            1. Many are produced in the liver and act as transport proteins for lipids, metal ions, and fat-soluble vitamins.
            2. Other globulins, known as antibodies are produced during the immune response.
        iii. Clotting proteins.
            1. Most are produced in the liver, e.g., prothrombin and fibrinogen.
    e. Nutrients
        i. Absorbed from the GI tract or body reserves and distributed throughout the body.
        ii. E.g., amino acids, glucose, fatty acids, triglycerides, vitamins, and cholesterol.
    f. Electrolytes (ions, such as Ca^{2+}, Na^{+}, and K^{+}, etc.)
    g. Respiratory gases (dissolved CO_2, O_2, and N_2)
    h. Wastes (byproducts of cell metabolism, e.g., urea, uric acid, ammonia, creatinine, and lactic acid)
    i. Buffers (chemicals that function to prevent fluctuations in plasma pH)
    j. Hormones (chemical messengers such as insulin or epinephrine).
8. Red blood cells
    a. Small (7.5μm diam.), biconcave discs.
    b. Biconcave shape gives them a high surface area to volume ration (good for O_2 entry/exit) and increased flexibility (good for squeezing thru tight capillaries).

   c. Anucleate and lack organelles.
   d. Stuffed with hemoglobin proteins.
   e. 4-6 million RBCs per μL of blood.
   f. Primary function is O_2 transport. Play a minor role in CO_2 transport.
9. Hemoglobin
   a. Abundant within RBCs. Small amount is also dissolved in plasma. reversibly binds and releases O_2.
   b. Protein (globin) bound to red heme pigments. Globin consists of four polypeptide chains (2 alpha chains and 2 beta chains), each with their own heme. Each heme contains one Fe atom that can reversibly bind one O_2 molecule.
   c. Each can transport four O_2 molecules.
   d. In lungs, Hb binds O_2 and is oxyhemoglobin.
   e. In tissues, Hb releases O_2 and is then deoxyhemoglobin or reduced hemoglobin.
   f. 20% of blood's CO_2 is transported by combining with Hb's amino acids. (Carbaminohemoglobin).
10. Hemopoiesis (or Hematopoiesis) = Blood cell formation.
   a. Occurs in red bone marrow. Adult red marrow is found in ribs, vertebrae, sternum, pelvis, proximal humeri, and proximal femurs.
   b. All blood cells arise from a hemopoietic stem cell (hemocytoblast).
11. Erythropoiesis = RBC formation.
   a. Hemocytoblast divides and differentiates. Its nucleus and organelles are discarded while Hb stores are built up to tremendous levels.
   b. Requires iron and vitamin B_{12}.
12. RBC levels
   a. # of RBCs in blood is remarkably constant and maintained via negative feedback.
   b. Too few RBCs compromises O_2 transport. Too many causes a detrimental ↑ in blood viscosity.
   c. The hormone erythropoietin (EPO) controls the rate of erythropoiesis.
   d. The kidneys always release EPO.
   e. If blood O_2 content ↓, the kidneys ↑ EPO release, which stimulates RBC synthesis to↑.
   f. O_2 delivery to the kidney could change due to RBC count, altitude, increased aerobic activity, lung disease, or CV disease.
13. RBC removal/recycling
   a. After 120d RBCs become old/damaged. The lack of a nucleus and organelles precludes replication or self-repair.
   b. Old/damaged RBCs are engulfed by scavenger cells, known as macrophages, in the spleen, liver, and red bone marrow.
   c. Hb within the phagocytosed RBC will be broken down and partially recycled and partially excreted.
   d. Hb is broken down into its globin and heme portions.
   e. Globin is reduced to amino acids, which are released from the macrophage into the blood stream for reuse elsewhere.
   f. Iron is removed from heme and then transported to the liver by a plasma protein, transferrin. In the liver, iron is stored as ferritin or hemosiderin.
   g. The remainder of the heme is converted into a pigment called bilirubin. Bilirubin is released from the macrophage and transported to the liver by albumin. The liver then modifies bilirubin and secretes it into the small intestine as part of bile. In the intestine, bilirubin is metabolized by resident bacteria producing metabolites that are ultimately excreted in the feces and urine.
14. White blood cells
   a. Only formed elements with nuclei and normal organelles – thus they're the only "true cells."
   b. Account for far less than 1% of total blood volume.
   c. Protect the body from pathogens, toxins, and cancerous cells.
   d. Formed in red bone marrow from hemocytoblasts.
   e. Normal range is 5000-10,000 per μL of blood.
   f. Only a small fraction of the body's total WBCs are found in the blood at any one time. Most are in lymphatic organs (e.g., lymph nodes, spleen, tonsils, and appendix) and within the loose connective tissue that underlies the reproductive, respiratory, digestive, and urinary tracts.

g. Perform diapedesis (i.e., leave the blood stream) and enter connective or lymphatic tissue where they mount an immune response.
h. Capable of flowing thru the tissue spaces with an amoeboid-like motion.
i. Attracted to chemicals by pathogens, damaged cells, or activated WBCs. (Positive chemotaxis.)
j. 5 types: neutrophils, lymphocytes, monocytes, eosinophils, and basophils.
k. *"Never let monkeys eat bananas"* specifies the 5 types in order of abundance.
l. Divided into 2 large classes: granulocytes and agranulocytes.
m. Granulocytes contain membrane-bound granules that are dyed by Wright's stain.
n. Agranulocytes lack stainable granules.
o. Granulocytes include neutrophils, eosinophils, and basophils. All are spherical, larger than RBCs, have lobed nuclei, and stain specifically with Wright's stain.
p. Agranulocytes include lymphocytes and monocytes.

15. Neutrophils
    a. Most numerous circulating WBC.
    b. Constitute 50-70% of circulating WBC population.
    c. Contain fine lilac colored granules that take up acidic and basic dyes,
    d. Nucleus consist of 3-6 lobes (Polymorphonuclear).
    e. Count increases during acute bacterial infections.
16. Eosinophils
    a. Make up 2-4% of the circ. WBC pop.
    b. Bilobed nuclei.
    c. Take up acidic dyes, which cause their granules to turn reddish orange.
    d. Attack parasitic worms.
    e. Engulf immune complexes involved in allergic rxns. (Lessening their severity.)
17. Basophils
    a. Make up <1% of the circ. WBC pop.
    b. Take up basic dyes, which cause their granules to turn a dark purple. Granules contain a vasodilator (histamine) and an anticoagulant (heparin). Released during inflammation.
18. Lymphocytes
    a. Comprise 30% of the circ. WBC pop.
    b. Large, round, purple nuclei taking up most of the cell volume.
    c. Trillions of lymphocytes in the body, but only a relatively small # in the blood. Most are found w/i lymphatic tissues (e.g., lymph nodes, spleen).
    d. 2 main types
        i. T lymphocytes defend against virus-infected and tumor cells, and control and manage the immune response.
        ii. B lymphocytes differentiate into plasma cells, which produce antibodies.
19. Monocytes
    a. Comprise 3-8% of the circ. WBC pop.
    b. Largest leukocyte – up to 3x the size of an RBC.
    c. Pale blue cytoplasm and a dark U or kidney-shaped nucleus.
    d. Leave the bloodstream to become macrophages – cells specialized in phagocytosis of foreign particles and debris.
20. Leukopoiesis = WBC formation
    a. Occurs primarily within the red marrow but also w/i lymphatic tissues.
    b. Stem cell for all WBCs is the hemocytoblast.
21. Platelets
    a. Fragments (2-4 μm diam.) of extremely large bone marrow cells (megakaryocytes) that are derived from hemocytoblasts.
    b. Contain membrane-bound granules filled with chemicals involved in blood clotting.
    c. Help form blood clots and temporary patches (platelet plugs) for torn blood vessels.
    d. 150,000-400,000 platelets per μL of blood.
    e. Platelet formation (thrombopoiesis) occurs in the red marrow, begins with hemocytoblasts, and is stimulated by a hormone called thrombopoietin.
22. Hemostasis
    a. Set of processes that stop bleeding and help heal damaged blood vessel walls.

   b. Consists of 3 events: vascular spasm, platelet plug formation, and coagulation.
23. Vascular spasm
   a. Damaged vessels release chemicals that cause the smooth muscle in their walls to contract. This ↓ vessel diameter, which will ↓ blood loss and ↓ local BP (thus facilitating patching and repair).
24. Platelet plug formation
   a. Platelets are activated when the tearing of a blood vessel wall exposes the collagen that underlies the vessel's endothelium (i.e., its simple squamous epithelial lining).
   b. Activated platelets then aggregate at the injury site.
   c. Aggregated, activated platelets release chemicals that: enhance vascular spasm; are involved in coagulation; and facilitate the activation and aggregation of more platelets at the injury site (a +feedback process).
   d. Aggregation of platelets is a platelet plug and is a temporary seal to the break in the vessel wall.
   e. Platelet plug is restricted to the injury site b/c intact endothelial cells release the chemical prostacyclin, which inhibits platelet aggregation.
25. Procoagulants vs. anticoagulants
   a. Procoagulants initiate and stimulate the formation of a blood clot
   b. Anticoagulants inhibit and impede the formation of a blood clot.
   c. When vessels are intact, the anticoagulants "win" and clotting does not occur. However, blood vessel damage sets off a chain of events whereby the procoagulants dominate and coagulation occurs.
26. Coagulation
   a. Complicated multi-step process that results in the formation of a sturdy clot that seals the tear until repairs are complete.
   b. In response to vessel damage, prothrombin activator (PTA) is formed.
   c. PTA converts the inactive plasma protein prothrombin into the active thrombin.
   d. Thrombin converts the insoluble plasma protein fibrinogen into the insoluble fibrin.
   e. Fibrin molecules then link to one another and form a meshwork of strands on the platelet plug. RBCs, WBCs, and plasma are trapped w/i the fibrin mesh. This is a blood clot.
   f. 2 pathways by which PTA is formed: extrinsic and intrinsic.
   g. Extrinsic path
      i. Begins when blood is exposed to a chemical released by damaged tissue cells outside the blood vessel.
      ii. Has few steps and thus PTA can be formed quickly.
   h. Intrinsic path
      i. Begins in response to the release of certain chemicals by damaged blood vessel cells.
      ii. Has many steps, which makes it slower, but allows for amplification, which yields tremendous amounts of PTA.
   i. In the body, both pathways typically occur in response to the same event. Having 2 pathways allows for PTA to be formed quickly (extrinsic) as well as in large amounts (intrinsic).
   j. Multiple clotting factors are involved in the coagulation process. Many of these are formed in the liver. Vitamin K is required for their synthesis. Calcium is also required for coagulation.
27. Cot retraction
   a. Following clot formation the actin/myosin in platelets contract, compacting the clot and pulling the vessel edges together (facilitating repair).
   b. Squeezes serum (plasma minus clotting factors) from the clot.
28. Fibrinolysis
   a. Breakdown of the clot
   b. Following vessel repair the inactive plasma protein plasminogen is converted to plasmin by tissue plasminogen activator. Plasmin digests fibrin once repairs have taken place.
29. Clot restriction/promotion
   a. Clots are restricted from growing too large by the removal of clotting factors as well as the presence of normal anticoagulant chemicals.
   b. Coagulation can be promoted by:
      i. Roughened vessel lining, which attracts/activates platelets.
      ii. Pooling of blood w/i vessels can result in the activation of clotting factors and the initiation of the coagulation process.