1. Circulatory system has 3 basic components that work to maintain tissue homeostasis by distributing essential nutrients, signals, electrolytes, gases, wastes, etc.:
   a. Heart – the pump.
   c. Blood – the fluid transport medium

2. Blood
   a. Fluid connective tissue
      i. Cells suspended in a liquid fibrous matrix.
      ii. Blood cells = formed elements
      iii. Liquid matrix = plasma.
   b. Formed elements = erythrocytes (red blood cells), leukocytes (white blood cells) and platelets.

3. Centrifuged blood divides into 3 portions
   a. Plasma
   b. Packed RBCs (42-56% in ♂ and 38-46% in ♀. This % = hematocrit.)
   c. Buffy layer containing WBCs and platelets. (<1%)

4. Physical characteristics
   a. Color = scarlet (oxygen-rich) to dark red (oxygen-poor).
   b. 5x the viscosity of water. Due primarily to the formed elements.
   c. pH = 7.35-7.45 (slightly alkaline).
   d. Temperature = 100°F.
   e. Volume = 4-5 L ♀ and 5-6 L ♂.

5. Transportation functions
   a. Carries O₂ (from lungs) and nutrients (from GI tract and body stores) to all cells
   b. Carries wastes from all cells to elimination sites (lungs for CO₂; kidneys for nitrogenous wastes)
   c. Carries hormones (chemical signals) from endocrine organs to target tissues.

6. Regulatory functions
   a. Regulates body T° by absorbing and distributing heat, maintains body fluid pH by virtue of its buffers, and maintains adequate body fluid volumes.

7. 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.

8. Blood plasma
   a. 44-58% of blood volume in ♂ and 54-62% of blood volume in ♀.
   b. 90% water. Water acts as a solvent and suspending medium.
   c. Dissolved solutes = plasma proteins, nutrients, electrolytes, respiratory gases, hormones, 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 produced in the liver
         2. Alpha and beta globulins transport lipids, metal ions, and fat-soluble vitamins.
         3. Gamma globulins are antibodies produced during the immune response.
      iii. Clotting proteins = E.g. prothrombin and fibrinogen. Most produced in the liver.
   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).

9. Red blood cells
   a. Small (7.5μm diam.), biconcave discs. 4-6 million RBCs per μL of blood.
b. Primary function is O$_2$ transport. Play a minor role in CO$_2$ transport.
c. Biconcave shape gives
   i. high surface area to volume ratio (good for O$_2$ entry/exit)
   ii. increased flexibility (good for squeezing thru tight capillaries)
   iii. ability to stack single file (forming a rouleau) which facilitates passage thru capillaries.
d. Anucleate and lack organelles. Increases storage space w/i the cell allowing it to be filled with hemoglobin (an O$_2$ binding protein).

10. Hemoglobin
       the weakness of the binding allows for quick pickup and easy release of oxygen.
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. Each Hb can thus transport four O$_2$ molecules.
c. In lungs, Hb binds O$_2$ and is oxyhemoglobin. In tissues, Hb releases O$_2$ and is deoxyhemoglobin.
d. 20% of blood’s CO$_2$ is transported by combining with Hb’s amino acids. (carbaminohemoglobin).

11. Hemopoiesis (or Hematopoiesis) = Blood cell formation.

   a. Occurs in red bone marrow. Adult RBM is found in skull, ribs, vertebrae, sternum, pelvis, proximal humeri, and proximal femurs.
b. All blood cells arise from a hemopoietic stem cell (hemocytoblast).

12. Erythropoiesis = RBC formation. (3 million RBCs produced per second.)

   a. Hemocytoblast divides and differentiates. Its nucleus and organelles are discarded while Hb stores are built up to tremendous levels. Requires roughly 5 days. Requires Fe and vitamin B$_{12}$.

13. 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 kidneys always release the hormone erythropoietin which controls the rate of erythropoiesis.
d. If blood O$_2$ content ↓, the kidneys ↑ EPO release, which stimulates RBC synthesis to↑.

e. Kidney O$_2$ levels can change due to: ΔRBC #, altitudeΔ, ↑aerobic activity, lung or CV disease.

14. RBC removal/recycling – 1% of circulating RBCs are removed daily.

   a. The lack of a nucleus and organelles precludes replication or self-repair.
b. Macrophages phagocytize old (120d) and damaged RBCs in the spleen and liver.
c. Hb in 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 into the blood stream for reuse elsewhere.
f. Iron is removed from heme and carried to the liver by a plasma protein, transferrin. In the liver, iron is attached to storage proteins (ferritin or hemosiderin).

g. Remainder of the heme turns into a pigment called bilirubin which 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 (stercobilin and urobilin) that are excreted in feces and urine.

15. White blood cells

   a. Only formed elements with nuclei and normal organelles – thus they’re the only “true cells.”
b. Protect the body from pathogens, toxins, and cancerous cells.

c. Normal range is 4500-11,000 per \( \mu \text{L} \) of blood.

d. Leukopenia=low WBC count. Leukocytosis=high WBC count.

e. 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.

f. Their flexibility allows them to perform diapedesis (i.e., leave the bloodstream) and enter connective or lymphatic tissue where they mount an immune response.

g. Capable of flowing thru the tissue spaces with an amoeboid-like motion.

h. Attracted to chemicals released by pathogens, damaged cells, or WBCs. (Positive chemotaxis.)

i. 5 types: neutrophils, lymphocytes, monocytes, eosinophils, and basophils.

j. “Never let monkeys eat bananas” specifies the 5 types in order of abundance.

k. Divided into 2 large classes: granulocytes and agranulocytes.


m. Granulocytes include neutrophils, eosinophils, and basophils. All are spherical, larger than RBCs, have lobed nuclei, and stain specifically with Wright’s stain.

n. Agranulocytes include lymphocytes and monocytes.

16. Neutrophils – Most numerous circulating WBC. Constitute 50-70% of circulating WBC population.

a. Polymorphonuclear cells that contain fine lilac colored granules.

b. Count increases during acute bacterial infections (Neutrophilia).

c. Spend 10-12hrs in blood then enter tissues to phagocytize bacteria.

d. Neutropenia = low neutrophil count.

17. Eosinophils – Make up 1-4% of the circ. WBC pop.

a. Contain bilobed nuclei and have granules that take up acidic dyes, turning them reddish orange.

b. Attack parasitic worms and engulf immune complexes involved in allergic rxns.

c. Count increases during allergic rxns and parasitic worm infections (eosinophilia).

18. Basophils – Make up <1% of the circ. WBC pop.

a. 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.

19. Lymphocytes – Comprise 20-40% of the circ. WBC pop.

a. Large, round, purple nuclei taking up most of the cell volume.

b. 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).

c. Count increases in viral infections (lymphocytosis).

d. 3 main types
   i. T lymphocytes attack virus-infected and tumor cells, and control the immune response.
   ii. B lymphocytes differentiate into plasma cells, which produce antibodies.
   iii. Natural killer cells (NK cells) also kill virus-infected and tumor cells.

20. Monocytes – Comprise 2-8% of the circ. WBC pop.

a. Largest WBC (3x an RBC) w/ pale blue cytoplasm and a dark U or kidney-shaped nucleus.

b. Leave the bloodstream to become macrophages.

21. Leukopoiesis = WBC formation

a. Occurs within the red marrow but also w/i lymphatic tissues. Stem cell is the hemocytoblast.

22. Platelets - Fragments (2-4 \( \mu \)m diam.) of extremely large bone marrow cells (megakaryocytes) that are derived from hemocytoblasts. (150,000-400,000 platelets per \( \mu \text{L} \) of blood.)

a. Contain membrane-bound granules filled with chemicals involved in blood clotting.

b. Help form blood clots and temporary patches (platelet plugs) for torn blood vessels.
c. Platelet formation (thrombopoiesis) occurs in the red marrow, begins with hemocytoblasts, and is stimulated by a hormone called thrombopoietin.

d. About 30% of platelets are stored in the spleen.

23. Hemostasis = Set of processes that stop bleeding and help heal damaged blood vessel walls.
   a. Consists of 3 events: vascular spasm, platelet plug formation, and coagulation.

24. Vascular spasm = Damaged vessels release chemicals that cause smooth muscle in their walls to contract. This ↓ vessel diameter, which will ↓ blood loss and ↓ local BP (thus facilitating patching and repair).

25. Platelet plug formation
   a. Platelets are activated when the tearing of a blood vessel wall exposes the collagen within.
   b. Activated platelets then aggregate at the injury site and 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).
   c. Aggregation of platelets is a platelet plug and is a temporary seal to the break in the vessel wall.
   d. Platelet plug is restricted to the injury site b/c intact endothelial cells release the chemical prostacyclin, which inhibits platelet aggregation.

26. 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 procoagulants dominate and coagulation occurs.

27. Coagulation = Multi-step process that forms a sturdy clot that seals the tear until repairs are complete.
   a. A clot is formed by fibrin molecules that 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.
   b. Fibrin is formed from the inactive plasma protein fibrinogen. This is catalyzed by thrombin.
   c. Thrombin is formed from the inactive plasma protein prothrombin. This is catalyzed by prothrombin activator, which is formed in response to vessel damage.
   d. There are 2 pathways by which PTA is formed: extrinsic and intrinsic.
   e. Extrinsic path = starts w/ exposure of blood to chemicals released by damaged perivascular tissue.
      i. Has few steps and thus PTA can be formed quickly.
   f. Intrinsic path = starts w/ the release of chemicals by platelets in response to vessel damage.
      i. Has many steps, which makes it slower, but allows for amplification, which yields tremendous amounts of PTA.
   g. In the body, both pathways 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).
   h. 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.

28. Cot retraction = After formation the actinomyosin in platelets contracts, compacting the clot and pulling the vessel edges together (facilitating repair). This squeezes serum (plasma w/o clotting factors) from the clot.

29. Fibrinolysis = Breakdown of the clot
   a. Following vessel repair the inactive plasma protein plasminogen is converted to plasmin (a.k.a. fibrinolysin) by tissue plasminogen activator. Plasmin digests fibrin following vessel repair.

30. 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 a roughened vessel lining (attracts/activates platelets) and by pooling of blood w/i vessels (activates clotting factors).

31. Response to blood loss (>10% of BV) = Activates the sympathetic NS causing vasoconstriction, increased HR, increased force of cardiac contraction, and increased BP. This maintains blood flow to the brain.