Circulatory System (also called the cardiovascular system)

1. **Blood, blood vessels, and heart** (the lymphatic system is also part of the circulatory system)
2. Heart pumps about 1.3 gal/min (5L/min). 1900 gals (7200 L) of blood are pumped through **62,000 miles** of blood vessels each day (700,000 gal/yr). If all blood vessels placed end-to-end, they would extend 2.5x around the equator. Blood moves through the vessels at an average rate of 2 mph.
3. About **2 to 3 million new RBC’s** form in the red marrow of bone every second. There are about **25 trillion RBC’s** in the body (they account for 1 of 3 cells since there are an estimated 75 trillion cells in the body)

**Major Functions**
1. **Transport** (dissolved gases, nutrients, hormones, and metabolic wastes)
   a. Move **nutrients** from the digestive system to the cells of the body
   b. Transport **blood gases**: O₂ from the lungs to cells and CO₂ from the cells to the lung
   c. Move cell **waste** products like urea, uric acid, and creatinine to the kidney for incorporation into urine
   d. Transport **hormones** like insulin, calcitonin, PTH, GH and testosterone from the glands that produce them to their target cells
2. Regulation of **body temperature** by distributing heat generated mostly by skeletal muscle cells as they undergo cellular respiration (40-45% of body mass; over 600 skeletal muscles); even at rest, muscle tone or low levels of contraction to maintain muscle rigidity generates heat.

3. **Protect** the body against disease-causing organisms (pathogens) and poisons. WBC’s attack and kill viruses, bacteria, fungi, parasitic worms and cancer cells. WBC’s protect the body against non-self.

4. Chemicals in the blood buffer acids and bases to **maintain a stable pH** that ranges from 7.35 to 7.45 (avg 7.4) within all the fluid compartments of body (plasma, interstitial fluid, and cytosol).

**The Nature of Blood** (hematology is the study of blood)

1. Specialized type of **connective** tissue in which cells are suspended in a **liquid matrix** called plasma **without insoluble fibers** (no collagen or elastic fibers in matrix).

2. Blood is **5x thicker** (viscous) than water and can be stored for 40 days at 4°C (refrigerated); red cells are the densest component of blood.

3. Body contains about **5L or 1.5 gallons of blood**. Male: 5-6 L, Female: 4-5L. The differences in volume between the sexes is due to body size (5’9” male, 5’6” female)(3.8L = Gallon).

4. Blood makes up about **8% of total body mass**.

5. Blood consists of
   a. **Formed Elements (cellular components)**: RBC’s (erythrocytes), WBC’s (leucocytes), and platelets (cell fragments involved with clotting).
   b. **Plasma** (fluid component) – watery solution filled with dissolved chemicals (solute).

6. **Hematocrit (HCT)**: %age of whole blood volume that consists of red blood cells which represent the bulk of all of the formed elements (99.9% of the formed element fraction is made of red cells). The hematocrit of blood is about 40-45%. Hematocrit is also called the **packed cell volume** (PCV). Since the blood cell population is mostly RBCs, the hematocrit is equivalent to the RBC volume.

7. **Centrifuge Test Tube of Whole Blood to separate out its components** (3,000 revolutions/min for 30 min)
   a. **RBC** (around 40%-female and 45%-male) – **hematocrit** or packed cell volume (Red Cross ranges: male: 41-50, female: 36-44).
   b. **Buffy Layer** = WBC and platelets (<1%) (buffy as a color is light brownish-yellow).
   c. **Plasma** (around 55%).

Centrifugal forces in a spinning centrifuge cause heavy materials to settle to the bottom of a tube.
8. **Serum** – blood plasma without the clotting factors; when blood clots and the solids are removed, the remaining fluid is called serum; serum is the same as plasma except that it doesn’t contain clotting factors like the protein fibrinogen

9. Blood temperature is roughly **100.4°F (38°C)**, whereas body temperature measured at or near the surface is around **98.6°F (37°C)**

10. **Arterial Blood pH = 7.4** (slightly alkaline; varies from 7.35 to 7.45)(pH<7.35 – acidosis; pH>7.45 - alkalosis); fatal if < 6.8 or > 7.8; symptoms of acidosis include headaches, drowsiness, arrhythmias, nausea, sleepiness, confusion, loss of consciousness

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**Plasma** – pale yellow liquid portion of blood; water is the solvent with solute dissolved in it

1. **90-92% water (aqueous solvent), 7-9% plasma proteins, 1% other dissolved solutes**; aqueous solution (water is the solvent; dissolved chemicals are the solute)
2. **mineral ions** (sodium, potassium, chloride, magnesium, calcium) (e.g., Na+, K+, Cl-); salts are ionic compounds, hence in aqueous solution exist as ions
3. **organic nutrients** (amino acids, glucose, fatty acids, vitamins) (glucose is blood sugar)
4. **plasma proteins** – the liver synthesizes and releases more than 90% of the plasma proteins including all albumins and blood clotting proteins like fibrinogen
   a. **albumins** (55% of plasma proteins) – contribute to osmotic pressure of the blood and transport fatty acids and steroid hormones; albumin is the most abundant plasma protein
   b. **antibodies** or immunoglobulins (Ig)
   c. **fibrinogen** and **prothrombin** – involved with blood clotting
   d. **peptide hormones** (FSH, GH, insulin)
5. **waste products**: e.g., urea, CO2
**Formed Elements** – cellular portion of blood

**Hemopoiesis** (Gk; “to make blood”) – process by which the formed elements are produced in the red marrow of certain adult bones

1. undifferentiated **stem cells** called hemocytoblasts (multipotent stem cells) are found in the red marrow inside spongy bone of certain adult bones.
   a. Hemocytoblasts divide by mitosis to produce the formed elements of blood (RBC, WBC, platelets).
   b. each day an adult typically produces 200 billion tiny platelets, 175 billion red cells, and about 10 billion white cells

2. **primary hemopoietic bones in adults**: heads of humerus and femur, ribs, sternum, flat bones of skull, centra of vertebrae, coxal (hip) bones

**Hemocytoblasts in red marrow of bones divide by mitosis**

**Myeloid stem cells**
- Erythroblast (lose nucleus) -> RBC (anucleate)
- Megakaryocytes (fragment into cell fragments) -> platelets
- Myeloblasts (WBC's): Neutrophils, Basophils, Eosinophils, Monocytes -> macrophages

**Lymphoid stem cell** -(WBC): lymphocytes (B and T), NK cells
**Erythrocytes** (Red blood cells, red cells, RBC’s)

1. **most numerous** blood cell accounting for >99% of all the formed elements (male: 5.5 mil RBC’s/mm³, female: 4.5 mil RBC’s/mm³) (1 űl = 1 mm³)(1 űl = 1x10⁻⁶L)(1 ml = cc = 1 cm³)(1 mL = 1x10⁻³L)
   a. estimated **20-25 trillion RBC’s** in circulation at any given moment (this is nearly 70% of the 37 or so trillion cells in the human body)
   b. **800-1000 RBC for every 1 WBC (slide of a blood smear)**
   c. the body produces upwards of 2-3 million RBC’s each second and makes about **175 billion RBC’s per day** (if produce 2 mil RBC/sec, then produce 1.73 x 10¹¹ RBC’s/day = 173 billion). RBC’s are produced at the same rate at which old ones are cleared from the circulation so that the numbers of red cells stays constant over time
   d. A **drop** of blood contains about 250 mil RBC’s
   e. endurance athletes may have up to 15% more blood volume and a higher density of RBC’s
   f. red cells contribute the most to the thickness or viscosity of the blood

2. **RBC’s are anucleate when they enter the circulation**
   a. hemocytoblastic stem cells divide by mitosis and produce **nucleated cells in the red marrow** (erythroblasts)
   b. nucleus is **extruded as erythroblast becomes a erythrocyte (RBC)**, then the RBC enters into the general circulation by squeezing through capillary walls within the red marrow. The ejected nuclei are phagocytized in the marrow by white blood cells called macrophages. Red cells are incapable of protein synthesis and mitosis (erythroblast without nucleus becomes erythrocyte)
c. RBC’s also lack mitochondria and ribosomes. They generate ATP anaerobically so that they do not consume the oxygen they carry
d. nucleus is ejected to
   1. make more room for hemoglobin
   2. allow cell to assume a biconcave shape that deforms (stretch, bend, and fold) more easily so the cells can better squeeze through small capillaries; the diameter of a red cell is greater than that of the capillary. It takes a red cell about 1 to 2 seconds to get through a capillary bed
   3. a biconcave shape also has 30% more surface area for the diffusion of gases across it then a spherical cell

3. Lifespan of a RBC
   a. RBC’s live for about 120 days (about 4 months)
   b. RBC’s cannot repair themselves without a nucleus or ribosomes. Circulating RBC’s travel about 60 miles in 120 days.
   c. RBC’s lose their flexibility and they damage their plasma membranes over time as they distort their shape to squeeze through small blood vessels (diameter of a RBC at 7 um is larger than that of a small capillary)
   d. Damaged RBC’s are detected by macrophages in the liver and spleen and phagocytized
   e. Every 120 days, the body must make 25 trillion new RBC’s to keep pace with the rate at which they are removed from the circulatory system

4. Function of RBC
   a. Transport Blood Gases: RBC’s transport 99% of the O2 and 23% of the CO2 (most of the CO2 is transported as HCO₃⁻ in plasma). O₂ and CO₂ bind to hemoglobin within RBC’s.
   b. Hb acts as a buffer to control pH: the hemoglobin in RBC’s binds and releases H⁺
5. **Hemoglobin** (Hb) – protein (575 aa) with a quaternary structure (2 alpha and 2 beta subunits)
   a. **iron-containing protein** found in RBC’s (mix powdered Hb with water and get a red solution); Hb is a red pigment since its presence will turn a water-based solution red. This is due to the way the Fe-O2 bond reflects light
   b. if removed water from RBC, then Hb would make up 97% of what is left
   c. Each RBC contains about 270 million Hb molecules
   d. each Hb consists of a globular protein and 4 iron-containing heme groups. RBC’s contain about 65% of the body’s iron (Fe).
   e. Each of the heme groups contains 1 iron atom and each iron atom reversibly binds to 1 O2. Thus, one Hb molecule with 4 heme groups can bind to 4 O2
   f. RBC’s can carry about 1 billion O2 when fully saturated with O2. The adult body has about 20-25 trillion RBC’s
   g. the amino acids of the globin portion of Hb bind to CO2 and H^+
   h. Hb and its breakdown products create the color sequence of a bruised area of the skin. The bruise is initially red (RBC’s and oxyHb as they rupture escape into the interstitial fluid), then black and blue (deoxyHb), then yellowish (bilirubin) – can see through thin and relatively transparent epidermis (can see ink designs of tattoo in dermis)

<table>
<thead>
<tr>
<th>Blood</th>
<th>O2 Saturation of Hb (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood draining off the lungs</td>
<td>100 (4 O2/Hb)</td>
</tr>
<tr>
<td>Blood in systemic veins (resting)</td>
<td>75 (3 O2/Hb)</td>
</tr>
<tr>
<td>Blood in systemic veins (exercise)</td>
<td>25-50 (1-2 O2/Hb)</td>
</tr>
</tbody>
</table>

**Erythropoietin Mechanism**

6. **Erythropoietin** (EPO)
   a. EPO is a **protein hormone** that is released by **kidney** cells (peritubular interstitial cells) when **blood O2 levels are low** (hypoxemia).
      1. This can occur after **blood loss or at high altitudes** where the air is thin (low in O2).
         Kidneys are endocrine glands
2. **hypoxemia** – low O2 in arterial blood (normal resting value between 80-100 mmHg)
3. **hypoxia** - pathological condition in which the body or a region of the body is deprived of an adequate oxygen supply. hypoxia can be caused by low levels of O2 in arterial blood (hypoxemia) due to low numbers of RBC’s or RBC’s without normal amounts of Hb, or atherosclerosis, etc.

b. EPO **stimulates** cells (proerythrocytoblasts) in the red marrow to make RBC’s (erythropoiesis). EPO can boost the hematocrit (% RBC in whole blood) to more than 60% (normal is around 45%)

c. **Effects of altitude**
   1. Altitude is inversely proportional to Atm P (effect of gravity decreases as get further from the center of the earth)
   2. Atm P is proportional to the density of air molecules
   3. increase in altitude causes a decrease in the density of air molecules (decrease availability of O2 in the air that one inhales)
   4. takes a while to acclimate to the thinner air in Vail, CO at 8100’

d. **Testosterone** (steroid hormone from leydig cells of testes) stimulates EPO production by kidney cells. Males have higher circulating numbers of RBC’s)(normal RBC count: 5.5 mil/ul in males; 4.5 mil/ul in females)

d. maximal stimulation by EPO can increase RBC production by 10-fold to 20 million cells/sec.

7. **Blood Doping** – boosts the number of RBC’s to increase athletic performance

a. Induces **artificial polycythemia**.
   1. Prior to an event, athlete withdraws their blood which triggers RBC production.
   2. The athlete then reinfuses their blood to boost RBC density.
   3. more RBC’s will increase O2 delivery to cells to increase stamina and endurance

b. **Illegal**
   1. normal HCT: male – 41-50%; female – 36-44%
   2. blood doping can increase HCT to > 50%. If HCT exceeds 50%, then competitive cyclists receive a suspension from cycling
   3. bicycling is all about getting a lot of O2 to exercising skeletal muscle
   4. blood doping with EPO; competitive cyclists must have their blood tested for EPO. If test EPO positive, then banned from cycling for 1-2 years.

8. **Destruction of RBC’s**

a. **Lifespan = 120 days** (4 months)

b. the **worn-out plasma membranes of old and damaged RBC’s** are detected by **macrophages** as RBC’s circulate through the **spleen and liver**. RBC membranes are damaged as they squeeze through capillaries in single file.
   1. Most RBC’s are broken down by macrophages primarily in the **spleen, but also in the liver and bone marrow**. The spleen contains large vascular sinuses (special veins) that are lined by fixed macrophages.
   2. Macrophages engulf (“eat”) RBC’s and **phagocytize** them with the help of lysosomes

c. **Almost 1% of all RBC’s are replaced each day** equaling the rate at which they form (2 million/sec) so their numbers stay constant. Body makes around 175 billion new RBC’s/day
d. Hemoglobin breakdown in spleen and liver

1. Globin is broken down into amino acids that diffuse out of the macrophages into the blood and become part of the body's free pool of amino acids for reuse by cells.

2. Heme is degraded to iron and bilirubin.
   a. Fe can be recycled into the blood and used by erythroblasts as they form in the red marrow to make new RBC's. The body still needs replacement iron in the diet, since some iron is always lost each day in the urine, feces and some in sweat as well. In females, menstruation also results in the loss of iron.
b. the rest of the heme is converted to **bilirubin** (yellow-green pigment)
c. **bilirubin** is taken to the **liver** and incorporated by **hepatocytes** into a liver secretion called **bile** (the dark green color of bile is due to the bilirubin)
d. the liver excretes bile into ducts that lead to the gall bladder. **Bile moves from the gall bladder through ducts into the small intestine** where it is eliminated with the feces (bilirubin is converted to a yellowish-brown pigment by bacteria and gives color to feces)

9. **Jaundice** (high levels of bilirubin in the blood)
   a. **Abnormal increase in bilirubin** in the blood. Some of the bilirubin leaks (diffuses) out of capillaries into peripheral tissues giving them a yellow color that is most apparent in the dermis of the **skin** as seen through the thin epidermis and over the **sclera** of the eyes. High levels of bilirubin can cause **brain damage**.
   b. **Types of Jaundice**
      1. **Obstructive** – block bile secretion by obstructing the ducts that carry bile from the liver to the small intestine. This can occur with gallstones in the bile duct. Gallstones are usually crystals of cholesterol.
      2. **Hemolytic** – abnormal rate of RBC destruction (hemolysis means to rupture) which leads to an increase in the amount of bilirubin carried by the blood
      3. Hemolytic Jaundice in many **newborns**
         a. **fetus has a high RBC/ul count in order to maximally extract O₂ across the placenta**
<table>
<thead>
<tr>
<th>Age group</th>
<th>RBC Count (mil/ul)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult male</td>
<td>4.6-6.1</td>
</tr>
<tr>
<td>Adult female</td>
<td>4.2-5.4</td>
</tr>
<tr>
<td>Fetus/newborn</td>
<td>5.5-6</td>
</tr>
<tr>
<td>children</td>
<td>4.7</td>
</tr>
</tbody>
</table>

b. **at birth**, high rate of RBC breakdown in newborn to get rid of the extra RBC’s that circulate in fetal blood resulting in jaundice (common in newborns).
   1. The rate of breakdown exceeds the ability of the liver to process all of the bilirubin into bile.
   2. the liver is still maturing at birth
   c. **green and blue lights** break down bilirubin in the skin blood vessels to a more soluble form that is easier to secrete with the bile
   d. jaundice appears about day 2 after birth and disappears by 1-2 weeks of age

10. **Anemia** – decrease in O2-carrying capacity of blood
   a. anemia is a **decrease in the blood’s ability to carry oxygen** due to 2 causes (1) **decr # RBC’s/ul** or (2) **decr Hb in RBC’s**
      1. **Decrease in RBC numbers**: usually caused by low numbers of circulating RBC’s that results in O2-deprivation to the tissues (causes fatigue, headaches, dizziness, shortness of breath)
      2. **Decrease in #Hb/RBC**: anemia can also be caused by reduced amounts of hemoglobin inside RBC’s
      3. decreased O2 leads to a decrease in ATP production by cellular respiration. This leads to a decrease in the number of critical ATP-dependent reactions within cells and a decrease in metabolic activity. Neurons can die off if deprived of O2 for more than 5 minutes leading to brain death or a persistent vegetative coma.
   b. **Decrease in # of RBC’s**
      1. **Hemorrhagic** – excessive bleeding due to injury (usually acute) leads to decrease RBC count
      2. **Aplastic** – failure of hematopoietic stem cells in red bone marrow to function properly thus leading to a decrease in the red cell count.
         a. This can be caused by overexposure to X-rays or effects of chemotherapeutic drugs.
         b. The 1986 nuclear accident in Chernobyl (in the former USSR) caused a number of cases of aplastic anemia
      3. **Hemolytic** – increased rate of RBC destruction that leads to decreased number of RBC’s (e.g., malaria parasite, adverse reaction to drug, hereditary disorders like sickle-cell anemia)
      4. **Pernicious** – Vitamin B$_{12}$ deficiency.
         a. Vit B$_{12}$ is necessary for stem cells in red marrow to make RBC’s.
         b. Also caused by autoimmune disease that destroys the parietal cells of the gastric glands that make intrinsic factor. Intrinsic factor is a protein that is necessary for the absorption of Vit B$_{12}$ from the small intestine
         c. Vit B$_{12}$ contains cobalt (Co). It is one of the 8 B vitamins that humans need and comes from meat, poultry, fish, eggs, milk, and cheese (meat and dairy products). Vegetarians sometimes take B12 supplements or foods fortified with B12
         d. decreases RBC count
c. **Decrease in # Hb molecules in RBC’s**

1. **Iron-deficiency anemia** – caused by a diet low in iron or blood loss
   a. lack of iron results in a decrease in the ability to make enough hemoglobin for RBC production.
   b. In iron deficiency anemia RBCs cannot synthesize enough functional Hb and RBCs end up being unusually small as they enter the bloodstream. The hematocrit declines and the Hb content and oxygen-carrying capacity of the blood are substantially reduced.
   c. Symptoms include weakness and fatigue. Good dietary sources of iron include liver, red meats, kidney beans, egg yolks, spinach and carrots.
   d. decrease in Hb and RBC’s

11. **Polycythemia** (abnormal excess of RBC’s) – higher than normal number of RBC’s/ul. 2 Types (1) incr in #RBC’s/ul in a normal blood vol, (2) decr in blood vol that causes incr in RBC’s/ul in a normal blood volume

   a. Abnormal excess of **RBC relative to plasma.** Associated with HCT values >= 55%
      1. The hematocrit (HCT) can climb to more than 60-80% where the RBC density is 8-11 mil/ul.
      2. An elevated hematocrit with a normal blood volume is polycythemia.
      3. then the hematocrit reaches 80%, the tissues become starved for oxygen because RBC’s are so thick they block smaller vessels and one runs a high risk of abnormal blood clots (thrombus). Blood becomes thick and gloppy. This can cause clots that block blood vessels. This can lead to heart failure, problems breathing and kidney failure.

b. **Causes**
   1. overproduction of RBC’s – problem with hemopoiesis
   2. blood-doping
   3. reaction to chronically low O2 levels (heart disease, lung problems)
   4. too much illegal EPO

   c. blood becomes very **viscous** (thick) like molasses and does not flow easily. Blood can become up to 3x thicker then normal. Over time this can overwork the heart and result in **heart failure** (also get abnormal clotting, stroke in brain)

   d. **Excessive sweating** (evaporative cooling) and loss of fluids due to **burns** can cause dehydration (loss of blood volume) that leads to polycythemia – high school athletes (or college or pro etc.) during spring training on hot days can sweat profusely. If they fail to replace the water that they lose, it can cause polycythemia. Occasionally, an athlete dies as a result of heart failure. The effects of dehydration can accumulate over a several-day period.
   1. Dehydration leads to viscous blood, heat stroke and cardiac arrest
   2. What happens when people get extremely dehydrated from heat isn’t well-documented because scientists can’t ethically overheat people. But evidence suggests that when people lose 8% to 10% of their weight in water, their temperature shoots up to around 102, their blood gets thicker, resting heart rate goes up and blood flow to the kidneys decreases. People become disoriented and lose the ability to salivate. Water loss in excess of 10% can lead to dangerously high body temperatures in excess of 105 F and death.
   3. Heat stroke: This medical condition is life-threatening. The person's cooling system, which is controlled by the brain, stops working and the internal body temperature rises
to the point where brain damage or damage to other internal organs may result (temperature may reach 105°F).

e. **Other causes**: cancer, **high altitudes** (thin air can boost RBC’s to 6-8 mil/mm³), artificial blood doping, use of EPO. **Emphysema** can also cause hypoxemia which induces an increase in RBC count. The Olympic training camp is in Colorado Springs, CO in part to take advantage of the effect of high altitude (over 6,000’) on the production of extra RBCs.

**Blood Doping**
1. The practice of blood doping has occurred among competitive athletes involved in endurance sports, such as cycling and cross-country skiing.
2. **the procedure involves removing whole blood from the athlete in the weeks before an event.** The packed red cells are separated from the plasma and stored. By the time of the race, the athlete’s bone marrow will have replaced the lost blood. Immediately before the event, the packed red cells are reinfused increasing the hematocrit. The objective is to elevate the oxygen-carrying capacity of the blood and thereby increase endurance.
3. **the consequence of blood doping can be a lot of strain on the heart from having to pump the thickened blood and the thicker blood can clog small arteries causing strokes, kidney damage, or heart attacks.**
4. EPO has the same effect as blood doping.
5. Athletes have died as a result of blood doping.
6. A safer, milder form of erythrocytosis occurs in athletes who train at high altitudes
7. athletes who train at high altitudes will increase EPO production and increase their RBC count and simulate the effects of blood doping.

**White Blood Cells (leucocytes)**
1. **< 1% of formed elements.**
   a. 999 (99.9%) RBC to 1 (0.1%) WBC (25 trillion RBC/5L and around 35 billion WBC/5L)
   b. Nevertheless, there are tens of billions of WBC’s in the body, both in and out of blood vessels.
   c. Many WBC’s live outside of blood vessels in **loose CT spaces, the spleen, and lymph nodes**
2. **Normal range** of WBC’s - about 4,500 – 11,000 WBC’s/ul
   a. **Avg WBC’s around 8000/ul** (mm³ = 1 ul)(during an infection the WBC count can double temporarily). Blood: 5 mil RBC/ul, 8000 WBC/ul, 200,000 platelets/ul (25 trillion RBC/5 L; 35 billion WBC/SL)
   b. WBC’s fluctuate as they are **produced in response to need** (i.e., fight infection or repair tissue damage)
   c. A WBC count **over 11,000 WBC’s/ul** indicates a response to bacterial or viral invasion
3. **Typical lifespan of WBC:** **about 5 to 10 days**, although some last a lifetime (RBC lives for about 120 days)
4. **Function of WBC’s**
   a. **kill pathogens** (non-self)
      1. bacteria, viruses, fungi, and parasitic worms (pinworms, tapeworms, nematodes)
      2. pathogens are disease-causing organisms (flu, osteomyelitis, athlete’s foot, malaria, eye infection, infected wounds)
   b. **detoxify poisons** (e.g., bee venom)
c. clear **allergens** like pollen grains from the lungs that come in with inhaled air; alveolar macrophages live in the air sacs of the lung
d. move to the site of tissue damage and **phagocytize cell debris** (e.g., dead and dying cells)

5. Most of the work of WBC’s is performed **outside of the blood vessels**.
   a. **blood carries WBC’s** to site of infection or tissue damage to help repair the damage
   b. WBC’s then **squeeze through capillary walls** (emigration) to enter the tissue spaces
c. circulating white cells do not stay in the blood for very long.
   1. Granulocytes like neutrophils circulate for 4 to 8 hours and then migrate through capillary walls and into the tissues, where they live for another 3 days.
   2. monocytes travel in the blood for 10 to 20 hours, then migrate into the tissues and transform into a variety of macrophages. Macrophages can live as long as a few years.
   3. lymphocytes survive for a few weeks to decades. Lymphocytes leave the bloodstream and eventually enter the lymphatic system which empties them back into the blood. Thus, they are continually recycled from blood to tissue fluid to lymph and then back to blood.

6. **Macrophages secrete pyrogens** in response to bacterial and viral infections
   a. pyrogens (e.g., interleukin-1) travel to the hypothalamus and reset the body’s thermostat to a higher setting to **induce a fever** (“pyro” means fire)
   b. pyrogens stimulate the hypothalamus to **release TSH-Releasing Hormone** that in turn stimulates the anterior pituitary to release TSH. TSH then travels by way of the blood to stimulate the thyroid gland to release thyroxine.
   c. thyroxine **raises the BMR** of cells resulting in an increase in body heat production
   d. elevated body temperatures **inhibit bacterial and viral reproduction**. This helps the body fight off the infection.

7. **Emigration (Diapedesis)** – all WBC’s can migrate out of the bloodstream
   a. process by which WBC’s **squeeze between the epithelial lining of a capillary** and move into the tissue spaces (mostly loose CT’s)
   b. WBC’s move by **pseudopodial or amoeboid locomotion**; **all white cells** are capable of moving through openings in capillary walls and into the connective tissue spaces of body
   c. billions of WBC’s live in loose CT, spleen (vascular sinuses), and lymph nodes (500-700)
Emigration of WBCs

- WBCs roll along endothelium, stick to it & squeeze between cells.
  - adhesion molecules (selectins) help WBCs stick to endothelium
    - displayed near site of injury
  - molecules (integrins) found on neutrophils assist in movement through wall
- Neutrophils & macrophages phagocytize bacteria & debris
  - chemotaxis of both
    - kinins from injury site & toxins
**Lymphatic System**

1. **All RBC’s circulate in blood vessels** without leaving. If RBC’s are outside of blood vessels then a vessel has broken.

2. **WBC’s form in red marrow by hemopoiesis**, then *emigrate* through capillary walls into the loose CT’s within organs throughout the body. WBC’s will move into lymph capillaries and from there into lymph nodes. WBC’s also congregate inside the spleen.

3. There are **500-600 lymph nodes** in the body

4. **Lymph** is the fluid within lymph vessels

5. **Interstitial fluid flows into lymph capillaries and becomes lymph.**

6. Lymph flows through lymph vessels and eventually **flows into the subclavian veins** where it becomes plasma via either the **thoracic duct or the right lymphatic duct**.
Types of WBC’s (5 types in 2 major groups)

1. All WBC’s are initially produced by **stem cells in the red marrow**. Once produced, WBC’s circulate in the blood for several hours, then move out of blood vessels and travel into the tissue spaces within organs, as well as lymph tissues (e.g., spleen, lymph nodes, and tonsils) where they can produce additional white cells; the red marrow of bone stores granulocytes and monocytes until they are needed and contains 10 to 20 times more of these cells than found in circulating blood

2. **Granulocytes** (N, E, B) – possess lysosomes that show up as cytoplasmic granules when stained (grainy appearance under the microscope).
   a. **neutrophils** (60%, range of 40-70%)
      1. most **numerous** WBC
      2. short life span of **6 hours** to **3 days**
      3. **Phagocytize bacteria**. Neutrophils are potent killers of bacteria and their populations increase explosively during a bacterial infection
      4. **arrive at sites of tissue damage and clean up cellular debris**; phagocytize dead and dying cells (garbage collectors)
      5. **phagocytes**
         a. Phagocytes are cells that protect the body by ingesting by phagocytosis harmful foreign particles, bacteria, and dead or dying cells.
         b. phagocytes include neutrophils, macrophages, dendritic cells and other cells like fibroblasts
b. **eosinophils (2%)** – phagocytic WBC’s that live 8-12 hours
   1. **kill parasitic worms** (tapeworms, flukes, pinworms, hookworms)
   2. phagocytize or **eat antigen-antibody complexes and allergens**

c. **basophils (<1%)** – live for a few days
   1. release **histamines** at the site of tissue damage (injury and/or infection) that promote blood flow to tissues when damaged.
      a. Histamines increase the diameter of arterioles (**vasodilation**) and **increase the permeability of capillaries** causing blood flow to the site to increase.
      b. This can cause **swelling** in the affected tissues as plasma leaks out into the interstitial spaces (contributes to edema).
      c. Swelling **helps to move WBC’s into the injured area** that can fight against infectious bacteria if they are present and clean up cell debris
   2. tonically release **heparin** (anticoagulant) – helps to prevent blood from forming abnormal clots in unbroken blood vessels
   3. basophils leave the blood and increase in number at the site of an infection. They also play a major role in some allergic responses.

3. **Agranulocytes (L, M)**
   a. **2 major types** of agranulocytes: lymphocytes and monocytes
      1. **lymphocytes**
         a. **B cells** that become **plasma cells** when stimulated by foreign chemicals called antigens (Ag)
         b. **T cells** (3 types: cytotoxic, helper, suppressor)
      2. **monocytes** become **macrophages** when they emigrate out of capillaries into the tissues where they live out the rest of their life
   b. **lymphocytes (30% WBC’s)** (neutrophils make up 60%)
      1. occur mostly as **B and T cells**
      2. most lymphocytes are found in **lymph nodes and vascular sinuses in the spleen; only a small percentage of** lymphocytes circulate in the blood
A bacterial Ag binds to a B cell receptor (BCR) and activates the B cell. Helper T cells are involved in this process. The activated B cell proliferates by mitosis and their clonal daughter cells differentiate into Ab-secreting plasma cells. Plasma cells are terminally differentiated and non-dividing cells. B cell activation by exposure to Ag’s and their transformation into plasma cells usually occurs in lymph nodes or the spleen. Ab’s secreted by plasma cells are distributed throughout the body in lymph and blood. Ab’s bind to Ag’s to form Ag-Ab complexes that promote phagocytic destruction of the bacteria. Long-lived memory B-cells can be stimulated at a later time by the same Ag to differentiate into plasma cells.
c. **B cells** (also called B lymphocytes)
   1. normally found in lymph nodes (500-600)
   2. B cells are **stimulated by antigens (Ag) to transform into plasma cells that secrete antibodies (Ab)**. Each plasma cell can secrete up to 2,000 antibodies per second (170 mil/day)
   3. **Antigen (Ag)**
      a. Ag = non-self or foreign chemical that is not normally found in the body
      b. Ag’s are mostly proteins or polysaccharide molecules. They are associated with bacteria and foreign material like pollen grains
      c. Ag’s are chemicals associated with the following foreign or “non-self” chemicals
         1. **pathogens** (e.g., bacteria, viruses, fungi, parasitic worms)
            a. antigens may be part of their cell walls or plasma membranes or viral capsids
            b. bacterial cell wall may have over 100 Ag’s associated with it. These are molecules that are not found in our bodies, hence they are non-self
         2. exotoxins secreted by bacteria
         3. various **allergens** like pollen grains coming in with inhaled air, flecks of dead skin flaking off an animal, feces of dust mites that live in rugs
      4. WBC’s can attack and destroy or neutralize Ag’s or anything associated with an Ag (bacteria or virus)
   d. **Antibodies (Ab)** are glycoproteins made by plasma cells. The plasma cells are derived from B cells. Ab’s circulating in the blood are also known as immunoglobulins (Ig’s)
      1. Ag’s bind to receptors on the plasma membrane of a B cell. This might occur in a lymph node where many B cells live. This stimulates the B cells to divide by mitosis and produce clonal daughter B cells.
      2. Ag binding to a B cell stimulates that B cell to change into a plasma cell
      3. plasma cell starts to make antibodies (Ab) that will bind to the antigen (Ag)
         a. This dorms antigen-antibody complexes (Ag-Ab complexes).
         b. Plasma cells can make around 2,000 Ab molecules per second for days to weeks (around 170 mil/day)
      4. The Ab’s made by plasma cells are released to the outside of the plasma cell and enter into the general blood circulation
         a. Ab’s circulate within the blood to all parts of the body. Ab’s are plasma proteins called immunoglobulins (Ig) when they circulate in plasma
         b. Ab’s move out of the blood through capillary walls and bind to Ag’s wherever they might be found
         c. WBC’s like neutrophils and macrophages attack and kill anything that has an Ag-Ab complex associated with it
         d. Ag-AB complexes are tags or markers that identify non-self in the body for rapid destruction by phagocytes
         e. Ag-Ab complexes also activate a system of proteins in the blood called complement.
         f. complement proteins attack and kill bacteria with Ag-Ab complexes on their surface by “punching holes” in their plasma membranes
1. water is osmotically taken up by the hypertonic bacterial cells through the holes made by complement proteins
2. this causes the cell to swell and burst (lyse). This kills the bacterial cell

4. T cells (3 types: cytotoxic, helper and suppressor)
   a. Cytotoxic T cells attack and kill
      1. viral-infected cells which kills the virus and prevents it from replicating
      2. cancer cells that arise in the body to decrease risk of developing cancer
   b. Helper T cells help B cells change to Ab-secreting plasma cells
   c. Declines in Helper T cell populations leave the body susceptible to a wide range of infections from bacteria (pneumonia), viruses, and fungi (fungal meningitis), as well as certain rare cancers such as Kaposi’s sarcoma (cancer of the lining of blood vessels)
   d. Suppressor T cells help to “turn off” or suppress the action of B cells and other T cells to prevent the immune system from becoming over-active

5. Natural Killer Cells (NK Cells) – play a major role in rejecting tumors and killing cells infected by viruses. NK lymphocytes are phagocytic cells that attack and kill bacteria and viral-infected cells
   a. NK cells are cytotoxic lymphocytes. They play a major role in killing viral-infected cells. NK cells kill by releasing perforin and granzymes that kill target cells.
   b. Perforins form pores in the cell membrane of the target cell through which the granzymes enter. The granzymes then kill the target cell which causes the destruction of the virus inside.
   
   b. monocytes (6%, 3-8%) – live for several months in tissue spaces, spleen, liver, and lymph nodes as macrophages
   1. Function: very active phagocytic cells. They arrive at the site of injury along with neutrophils and eat dead and dying cells and phagocytize bacteria
   2. monocytes typically leave the circulatory system by moving through capillary walls (emigration), then live in the tissue spaces as macrophages. Macrophages phagocytize
pathogens (e.g., bacteria) and the debris of dead cells. They are the “scavengers” of the body.
3. macrophages are abundant in the intestine, liver, spleen, skin, lung, and epididymis
4. macrophages are given special names depending on where they are found (e.g., Dust cells in the lung alveoli, Kupffer Cells in the liver, osteoclasts in bone, Langerhans or dendritic cells in the epidermis of the skin, microglial cells in the brain, alveolar macrophages in the lung, etc.)

Leukocytosis and Leukopenia
1. **Leukocytosis** is an abnormally high WBC count (> 11,000 WBC/ul) that may indicate bacterial or viral infection, metabolic diseases, hemorrhage or leukemia
2. **Leukopenia** is a decrease in the WBC count below 4000 WBC/ul and may indicate X-ray therapy, TB, or hepatitis
Leukemia

1. **Cancer of the red bone marrow that involves the production of cancerous non-functional WBC’s**
   a. There are several types of leukemias. They are named after the cell in which they first arise. Cancerous WBC’s are all descendants of a single abnormal cell.
   b. **Leukemias do not begin with hemocytoblasts**, but with their daughter cells that go on to form WBC’s.
   c. **Myelocytic leukemia** involves myeloblast descendants, whereas **lymphocytic leukemia** involves the lymphoid stem cell line. Leukemias that involve abnormal granulocytes are called myeloid, whereas those that involve abnormal lymphocytes are called lymphoid.

2. The first symptoms appear as immature and abnormal white blood cells enter the bloodstream. As the number of abnormal white cells increases, they **travel through the circulation, invading tissues and organs throughout the body**. Over time leukemic cells replace normal white cells.

3. Characterized by an **uncontrolled production of abnormally large numbers of non-functional WBC’s circulating in the bloodstream. There is no tumor.**
   a. The bone marrow becomes filled with cancerous WBC’s and immature WBC’s flood the bloodstream. The high number of abnormal WBC’s in the marrow, crowd out the other formed elements leading to **anemia** and a **low platelet count**.
   b. Unlike other cancers, **leukemia doesn’t form a tumor**

4. **WBC count** (mm$^3$ = ul)
   a. **Normal**: around 8000 WBC/ul
   b. **Leukemia**: 200,000 to 1 mil non-functional WBC’s/ul

5. **Non-functional WBC’s are ineffective** and do not wage a proper fight against bacteria and viral infections

6. **Non-functional WBC’s fill up marrow spaces and crowd out hemopoietic cells.**

7. Over time, **fewer RBC’s and platelets are made leading to anemia and problems clotting blood** (low platelet count)

8. **Without treatment, all leukemias are fatal**. Death usually results from **bacterial infections** or excessive **internal bleeding** (internal hemorrhaging). If untreated, leukemias kill within 3 months to 3 years from the time of onset.

9. **Bone marrow transplant** (for some patients with leukemia)
   a. Large doses of chemotherapy and/or radiation are used to destroy the abnormal stem cells and abnormal blood cells in the bone marrow of the patient. This requires the replacement of functioning stem cells for the patient
   b. These therapies kill abnormal and normal cells, thus have side effects
   c. **Donor**
      1. Under general anesthesia, needle inserted into the center of both coxal bones and red marrow cells withdrawn
      2. Healthy marrow from both the hip bones of a donor (usually a family member) is then infused into the patient’s bloodstream where the healthy marrow cells migrate into the cavities of the large bones and start producing normal blood cells. Within 2 months, WBC’s reach normal levels.
      3. Need a donor with few HLA’s (human leucocyte antigens) on WBC’s to protect against rejection
d. there is no guarantee of success or that the disease will not recur, but the transplant increases the likelihood of a cure or at least a long period where the individual is disease-free

Platelets (thrombocytes)
1. Tiny fragments of cells (about 1/4th the diameter of a lymphocyte) that form as megakaryocytes in red bone marrow split apart (as if one broke a porcelain or china plate). Each megakaryocyte is a huge cell that can fragment into 1000’s of platelets. Megakaryocytes form from hemocytoblasts. Platelets are released into the blood at the rate of 200 billion per day. They circulate for 10 to 12 days before dying.

2. Only live for about 10 days in the bloodstream before they degenerate
   a. About 25-40% of the platelets are stored in the spleen and released as needed
   b. the remainder circulate in the blood and live for about 10 days before they degenerate and die

3. Normal number of platelets in blood: 200,000/mm$^3$ (mm$^3$ or ul also holds 5 mil RBC’s and around 8000 WBC’s)

4. Form platelet plugs when a blood vessel breaks

5. Function Associated with Plugging Up a Broken Blood Vessel
   a. secrete vasoconstrictors that contract smooth muscle in walls of broken blood vessels and help to reduce blood loss
   b. they stick together and to collagen fibers to form temporary platelet plugs to seal small breaks in blood vessels
   c. secrete procoagulants to promote clotting
   d. secrete chemicals that attract neutrophils and monocytes to the site of injury
   e. secrete growth factors that stimulate mitosis in fibroblasts and smooth muscle that help to repair broken blood vessels

Hemostasis
1. Process by which breaks in a damaged blood vessel are plugged up to stop the bleeding
2. involves 2 processes
   a. platelet plug formation (10-15 seconds)
   b. coagulation (around 5 minutes) – formation of the blood clot
Platelet Plug Formation

1. platelets form a platelet plug prior to the formation of a blood clot; the process of platelet plug formation takes about **10 to 15 seconds** and the **plug fully forms within 1 minute**; 
2. platelets are highly **effective at plugging up a hole in a small blood vessel**; the platelet plug is the **first defense** against blood loss. 
3. A platelet plug **can stop blood loss completely if the hole in the blood vessel is not too large**. 
4. **Steps in platelet plug formation**
   a. platelets do not adhere to the endothelial lining of undamaged blood vessels 
   b. when a vessel breaks as the result of an injury a hole forms that allows blood to spill through 
   c. **when a vessel breaks, collagen fibers in its wall are exposed** since the walls of blood vessels contain collagen fibers in their connective tissues 
   d. upon contact with **collagen, platelets grow spiny pseudopods** (spiky projections) out from their plasma membrane and **become sticky**. 
   e. As a result, **platelets adhere to one another (interlock) and tightly to the collagen fibers sticking out of a damaged blood vessel wall**. Platelets will stick to each other, to collagen fibers and to the basal lamina 
   f. this forms the **platelet plug** 
   g. platelet plug initially plugs up a hole in a blood vessel 
   h. the platelet plug is an essential first step in the clotting process within 10-15 seconds of the break 
   i. **once the platelet plug forms, then coagulation occurs**
Coagulation (Blood Clotting)

1. **Coagulation** is the clotting of blood; it is the last but most effective defense against blood loss.

2. Blood starts to clot within **10 to 15 seconds after an injury to a vessel** and is finished within **3 to 7 minutes**; it is important that blood clots quickly when a vessel breaks, but not to clot at any other time.

3. Blood clot consists of a **mesh of fibrin strands** (fibrin mesh), trapped **RBC’s, platelets, and WBC’s** (RBC’s give clots their red color).

4. **Goal of Coagulation**
   a. Convert fibrinogen to fibrin, a sticky protein that adheres to the walls of broken blood vessels and forms a fibrin mesh.
   b. The mesh then traps mostly red cells as well as some WBC’s and platelets to make the clot — plasma becomes thick and gel-like.

5. **Mechanism** (extrinsic mechanism)
   a. Damaged endothelial cells associated with blood vessels release **Tissue Factor** (TF). TF triggers the activation of **prothrombinase** (also called Factor X or prothrombin activator).
   b. **Prothrombinase** converts an inactive plasma protein called **prothrombin (made in liver from Vit K)** to **thrombin**.
   c. Thrombin converts a soluble plasma protein called **fibrinogen (made in liver)** to **fibrin**, an insoluble thread-life protein (polymerization reaction).
   d. **Fibrin strands cross-link to form a mesh** of long hair-like fibers (structural framework of the clot). The fibrin strand mesh **sticks to the broken surfaces** of the broken blood vessel.
   e. The mesh of fibrin strands **trap platelets and RBC’s** to form a clot; the mesh of cross-linked fibrin is the structural framework for the clot (analogous to a spider web trapping flying insects).
   f. Blood clot **seals off the broken blood vessel** and allows the healing process to begin.
Summary of Blood Clotting Extrinsic Mechanism

1. Prothrombin, and fibrinogen and an inactive form of prothrombinase are plasma proteins made by the liver that circulate in blood plasma at all times.

2. This process begins 10-15 seconds after the break and is over in 3-5 minutes

3. Damaged cells release chemicals (Tissue Factor or TF) that convert an inactive plasma protein to prothrombinase

4. Cascade of Events that Form Clot
   a. Activate Prothrombinase
      Damaged endothelial cells release Tissue Factor (TF) that converts the inactive form of prothrombinase to the active form
   b. Formation of Fibrin
      Prothrombin (liver, vitamin K, plasma protein) ↓ prothrombinase ← Tissue Factor (damaged cells)
      Thrombin (enzyme) ↓ (polymerization)
      Fibrinogen (liver, plasma protein) → Fibrin strands cross-link to form a fibrin mesh (traps RBC’s and platelets) to form CLOT

5. Molecules of fibrinogen polymerize into fibrin strands. The fibrin strands then cross-link with one another to form the fibrin mesh

6. The clot consists primarily of the fibrin mesh, RBC’s and platelets

7. eventually tissue repair of the broken vessel is completed and the clot is broken down as the fibrin mesh is dissolved away by a process called fibrinolysis
Types of Abnormal Clots

1. **thrombus** – blood clot; it is the final product of hemostasis.
   a. **thrombosis** – process by which an abnormal thrombus or clot forms in an unbroken blood vessel
      1. more likely to occur in deep leg veins (tibial, fibular, popliteal) then arteries because the blood flows more slowly in veins. DVT – deep vein thrombosis
      2. **thrombosis is common in the leg veins** of inactive older people who are bedridden or wheelchair-bound, but it can occur in anyone who goes for a long time without moving much (long car or plane ride or sitting in chair for hours working on a project)
      3. **causes**
         a. endothelial cell injury as a result of hypertension, trauma, surgery, infection, dehydration
         b. stagnation of blood flow from sitting too long or lying in bed for long periods
         c. idiopathic – unknown cause
   b. A blood clot attached to a vessel wall begins to form as platelets stick to the wall of an intact blood vessel.
      1. Often the platelets are attracted to areas called plaques
      2. The thrombus gradually enlarges, projecting into the lumen of the vessel and decreasing its diameter. Eventually, smaller vessels (usually arteries) may be completely blocked, creating an infarct, or a large chunk may break off, creating a dangerous embolus.
      3. infarct – area of dead cells caused by lack of nutrients and O2 by blocking a blood vessel (e.g., stroke in brain, myocardial infarct in heart)
   c. most CVA strokes and heart attacks are due to thrombosis. A thrombus (clot) may grow large enough to obstruct a small vessel or a piece of it may break loose and travel downstream as an embolus where it lodges in a small vessel and obstructs flow from that point onward.
   d. if blood flow to vital cells of the heart, brain, lungs, or kidney is impaired, then tissue death (infarction) can occur.

2. **embolus**
   a. anything abnormal (e.g., piece of a blood clot or atherosclerotic plaque) that is carried within the blood that is capable of blocking small blood vessels like an arteriole
      1. The sudden blockage is called an **embolism** and the area of tissue damage caused by the blockage is one form of an **infarct**. Infarctions in the brain are known as strokes
      2. infarctions in the heart are called myocardial infarctions or heart attacks
      3. emboli probably drift for less than a minute before they clog up small blood vessels
   b. may be a **thrombus that breaks off** and drifts downstream. DVT’s can break off as emboli and float with the blood through the right side of the heart into the pulmonary arteries. The emboli can clog up pulmonary arteries and reduce blood flow into the pulmonary circuit of the lungs. This can make the heart hypertrophy and decrease the amount of O2 the blood can pick up in the lungs
   c. **pulmonary** embolism – may cause damage to the lungs and difficulty breathing
   d. **cerebral** embolism – may cause a stroke in the brain
Substances that Influence Clotting
1. **Vitamin K** – necessary for the formation of **prothrombin** by the liver;
   a. Vit K is produced by **intestinal bacteria** and released into the lumen when they die. Vit K is absorbed across the gut wall and used by liver cells for the synthesis of prothrombin. Bacteria in this respect are beneficial to humans as a supplier of essential vitamins.
   b. Vit K is also found in **green leafy vegetables** like spinach and lettuce
2. **Heparin**
   a. tonically secreted by basophils, mast cells, and endothelial cells that line blood vessels
   b. **anticoagulant** that helps prevent abnormal clots in the blood
   c. works by blocking the action of **thrombin on fibrinogen** (heparin actually prevents the formation of prothrombinase which in turn prevents thrombin formation)
3. **Warfarin (Coumadin)**
   a. Vitamin K antagonists, hence anticoagulants
   b. these drugs block the activity of vitamin K, thus prevent the production of clotting factors like prothrombin.
   c. low doses of these drugs are taken by patients at risk of thrombosis
   d. warfarin is typically incorporated into pellets that are used to kill rats and mice. When warfarin-laced foods are eaten by mice and rats they internally bleed to death within a few days
4. **Xarelto** is a blood-thinner drug that inhibits the formation of Factor Xa, hence the prothrombinase complex. Xarelto prevents the formation of abnormal blood clots.

Inflammation
1. **Physiological response of the body to tissue damage in an attempt to heal itself**
2. **4 classical symptoms: heat, pain, redness, and swelling**
   a. **Redness and heat** due to increased blood flow to the damaged area. Circulating blood is 100.4°F (38°C) which is slightly higher than body temperature as measured with a thermometer (98.6°F)
   b. localized **swelling** as the result of vasodilation and increased capillary permeability
   c. **Pain** occurs as tissue-damaged cells release chemicals (e.g., kinins) that stimulate pain endings. Swelling can also cause pain by putting pressure on pain endings (nociceptors)
<table>
<thead>
<tr>
<th>Cell Type</th>
<th>Illustration</th>
<th>Description*</th>
<th>Cells/mm$^3$ (µl) of Blood</th>
<th>Duration of Development (D) and Life Span (LS)</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrocytes (red blood cells, RBCs)</td>
<td><img src="Image" alt="Erythrocyte" /></td>
<td>Biconcave, anucleate disc; salmon-colored; diameter 7–8 µm</td>
<td>4–6 million</td>
<td>D: 5–7 days LS: 100–120 days</td>
<td>Transport oxygen and carbon dioxide</td>
</tr>
<tr>
<td>Leukocytes (white blood cells, WBCs)</td>
<td><img src="Image" alt="Leukocyte" /></td>
<td>Spherical, nucleated cells</td>
<td>4800–10,800</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Granulocytes</td>
<td></td>
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</tr>
<tr>
<td>Neutrophil</td>
<td><img src="Image" alt="Neutrophil" /></td>
<td>Nucleus multilobed; inconspicuous cytoplasmic granules; diameter 10–12 µm</td>
<td>3000–7000</td>
<td>D: 6–9 days LS: 6 hours to a few days</td>
<td>Phagocytize bacteria</td>
</tr>
<tr>
<td>Eosinophil</td>
<td><img src="Image" alt="Eosinophil" /></td>
<td>Nucleus bilobed; red cytoplasmic granules; diameter 10–14 µm</td>
<td>100–400</td>
<td>D: 6–9 days LS: 8–12 days</td>
<td>Kill parasitic worms; destroy antigen-antibody complexes; inactivate some inflammatory chemicals of allergy</td>
</tr>
<tr>
<td>Basophil</td>
<td><img src="Image" alt="Basophil" /></td>
<td>Nucleus lobed; large blue-purple cytoplasmic granules; diameter 8–10 µm</td>
<td>20–50</td>
<td>D: 3–7 days LS: 7 (a few hours to a few days)</td>
<td>Release histamine and other mediators of inflammation; contain heparin, an anticoagulant</td>
</tr>
<tr>
<td>Agranulocytes</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Lymphocyte</td>
<td><img src="Image" alt="Lymphocyte" /></td>
<td>Nucleus spherical or indented; pale blue cytoplasm; diameter 5–17 µm</td>
<td>1500–3000</td>
<td>D: days to weeks LS: hours to 10 years</td>
<td>Mount immune response by direct cell attack or via antibodies</td>
</tr>
<tr>
<td>Monocyte</td>
<td><img src="Image" alt="Monocyte" /></td>
<td>Nucleus U or kidney shaped; gray-blue cytoplasm; diameter 14–24 µm</td>
<td>100–700</td>
<td>D: 2–3 days LS: months</td>
<td>Phagocytosis; develop into macrophages in tissues</td>
</tr>
<tr>
<td>Platelets</td>
<td><img src="Image" alt="Platelets" /></td>
<td>Discoid cytoplasmic fragments containing granules; stain deep purple; diameter 2–4 µm</td>
<td>150,000–400,000</td>
<td>D: 4–5 days LS: 5–10 days</td>
<td>Seal small tears in blood vessels; instrumental in blood clotting</td>
</tr>
</tbody>
</table>

*Appearance when stained with Wright's stain.