FUNCTIONS OF BLOOD
1. Transportation of gases, nutrients, and waste products.
   A. Gas exchange. Oxygen enters the lungs and is carried to cells. Carbon dioxide is carried from cells to the lungs and expelled.
   B. Nutrients are ingested and transported from the gastrointestinal tract to cells.
   C. Waste products are produced by cells and carried to the kidneys, lungs, skin, or gastrointestinal tract and eliminated.
2. Transport of processed molecules (e.g., lactic acid in the Cori cycle and vitamin D).
3. Transport of regulatory molecules (e.g., hormones and enzymes).
4. Regulation of pH and osmosis.
   A. Buffers are chemicals in the blood that prevent a change in blood pH.
   B. The osmotic composition of blood affects tissue fluid and electrolyte balance.
5. Maintenance of body temperature. Increasing or decreasing blood flow to the skin can increase or decrease heat loss.
6. Protection against foreign substances. Cells and chemicals of the blood are part of the immune system.
7. Clot formation prevents excessive fluid and cell loss and is the first step in tissue repair.

BLOOD COMPONENTS

1. Blood accounts for about 8% of total body weight. Males have 5-6 liters of blood and females have 4-5 liters.
2. Blood consists of a liquid called plasma (55% of blood) and formed elements (45%).
PLASMA
1. Plasma is a colloidal solution, i.e., a liquid containing fine particles that stay suspended in the solution.

2. Plasma consists of water (91%), proteins (7%), and other substances (2%).
   A. Proteins.
      1) Albumins are involved in osmotic pressure.
      2) Globulins. **Alpha and beta globulins** are transport molecules, clotting factors, and immune system chemicals. **Gamma globulins** include antibodies, which are part of the immune system.
      3) **Fibrinogen** is involved in blood clotting.

   B. Other substances.
      1) **Ions** such as sodium, potassium, calcium, chlorine, and bicarbonate.
      2) **Nutrients** such as glucose, amino acids, triglycerides, and cholesterol.
      3) **Waste products** such as urea (a product of protein metabolism) and bilirubin (breakdown product from red blood cells).
      4) **Gases.** Three percent of transported oxygen and eight percent of transported carbon dioxide is dissolved in plasma.
      5) **Regulatory substances** such as hormones and enzymes.

FORMED ELEMENTS

| TABLE 19.2 |

1. **Red blood cells** or erythrocytes transport oxygen and carbon dioxide. Red blood cells makeup about 95% of the volume of the formed elements.

2. **White blood cells** or leukocytes are involved in immunity. White blood cells makeup about 5% of the volume of the formed elements.

3. **Platelets** or thrombocytes are cell fragments involved in clot formation. Platelets are so small they makeup a negligible portion of the volume of formed elements.

**Production of Formed Elements**
1. **Hematopoiesis** or hemopoiesis is the formation of the formed elements of blood.

2. Hematopoiesis occurs in red bone marrow located in the epiphyses of long bones, the sternum, ribs, clavicle, vertebrae, and pelvis.
3. The process begins with a stem cell which divides to form two cells. One of the new cells formed by this division undergoes further divisions to become a red blood cell, a white blood cell, or a platelet. The other cell acts as a new stem cell.

**Red Blood Cells**

**Structure**

1. The shape of red blood cells.
   A. Red blood cells are flat, round cells with a depression in the center (biconcave disk).
   
   B. The shape increases the amount of surface area relative to the volume of the cell, which allows better exchange of gases. The shape also makes it possible for the cell to bend and pass through small capillaries.

2. Red blood cells lose their nucleus and most other cellular organelles during their development. They contain the pigmented protein **hemoglobin**, which accounts for the red color of red blood cells.

**Function**

1. Hemoglobin is responsible for transporting oxygen and carbon dioxide. Hemoglobin only functions inside red blood cells. If **hemolysis** or rupture of the red blood cell occurs, the hemoglobin is denatured.
2. **Carbonic anhydrase (CA)** is an enzyme within red blood cells involved with the transport of carbon dioxide. Carbonic anhydrase catalyzes the reaction between carbon dioxide and water to form carbonic acid. The carbonic acid dissociates to form bicarbonate ions that "contain" the carbon dioxide. Bicarbonate ions transport about 72% of the carbon dioxide in blood.

\[
\text{CO}_2 + \text{H}_2\text{O} \xrightarrow{\text{CA}} \text{H}_2\text{CO}_3 \xrightarrow{} \text{H}^+ + \text{HCO}_3^- \\
\text{Carbon Dioxide} \quad \text{Water} \quad \text{Carbonic Acid} \quad \text{Hydrogen Ion} \quad \text{Bicarbonate Ion}
\]

**Hemoglobin**

1. **Hemoglobin** consists of 4 heme molecules, each of which is attached to a different globin (protein) molecule. Each heme group has an iron atom (Fe).

   ![FIGURE 19.4](image)

2. Iron is necessary for hemoglobin to transport oxygen because oxygen binds to the iron.
   A. Stomach acid and vitamin C increase the solubility and absorption of ingested iron.
   B. The mucosa (epithelial lining) of the small intestine regulates total iron levels in the body by controlling the amount of iron absorbed into the blood.
   C. Most of the absorbed iron becomes part of hemoglobin. Small amounts of iron are lost in urine and feces. Women lose an additional amount in menstrual fluid and therefore require more dietary iron than men. Most of the iron in the body is recycled.

3. Oxygen can combine with the iron in the heme group. Each hemoglobin can carry 4 oxygen molecules.
   A. **Oxyhemoglobin** is hemoglobin with oxygen and it is responsible for 98.5% of the oxygen transport in blood (1.5% is dissolved in plasma). Oxyhemoglobin is bright red in color.
Red Packer, a physical education major, wanted to improve his performance in an upcoming marathon race. Six weeks before the race 1 pint of blood was removed from his body, and the formed elements were separated from the plasma. The formed elements were frozen, and the plasma was reinfused into his body. Just before the competition, the formed elements were thawed and injected into his body. Explain why this procedure, called blood doping, would help Red’s performance.

B. **Deoxyhemoglobin** is hemoglobin without oxygen. It is dark red in color.

C. Carbon monoxide (found in cigarette smoke and car exhaust) binds almost irreversibly to the iron in hemoglobin and prevents oxygen transport. Nitrate poisons also prevent oxygen attachment.

Explain the cause of death when a person commits suicide by locking his or her self in a garage with a car engine running.

4. Carbon dioxide can combine with the globin part of hemoglobin to form **carbaminohemoglobin**. Approximately 20% of the carbon dioxide in blood is transported bound to hemoglobin or other proteins. The rest of the carbon dioxide is transported as bicarbonate ions (72%) or is dissolved in plasma (8%).
Life History of Red Blood Cells

1. **Erythropoiesis** is the production of new red blood cells. The process takes 3 to 5 days.
   A. *Stem cells* give rise to **proerythroblasts**.

   B. Proerythroblasts become **early erythroblasts**, which contain many ribosomes (site of protein synthesis, e.g., hemoglobin synthesis).

   C. Early erythroblasts become **intermediate erythroblasts** as they produce hemoglobin.

   D. Intermediate erythroblasts become **late erythroblasts** as their ribosomes degenerate and hemoglobin production stops. Approximately 34% of the cell volume is hemoglobin.

   E. A late erythroblast becomes a **reticulocyte** when it loses its nucleus. The **reticulocyte count**, which is the percent of red blood cells that are reticulocytes, is sometimes used as a measure of the rate of red blood cell production. When the production rate is high, reticulocytes are released into the blood at a faster rate and the reticulocyte count is higher than normal. A normal reticulocyte count is around 1% to 3%.

   F. Within 1 - 2 days the reticulocytes lose their remaining ribosomes and becomes mature red blood cells. Note that red blood cells do **NOT** have a nucleus.

   G. **Hematocrit** is the percent of total blood volume composed of red blood cells. For example, a woman could have a hematocrit measurement of 43%, which means 43% of the blood volume is red blood cells, and 57% is plasma and white blood cells. What effect would a decreased intake of iron have on a person's hematocrit?

2. The role of folic acid and vitamin B$_{12}$ in erythropoiesis.
   A. **Folic acid** and **vitamin B$_{12}$** are necessary for DNA duplication. Because red blood cells are formed by several divisions, a deficiency of these vitamins inhibits red blood cell production.

   B. Absorption.
      1) Folic acid is absorbed by active transport in the small intestine. Alcohol interferes with normal folic acid absorption and metabolism. Consequently, many alcoholics form inadequate numbers of red blood cells (alcoholics also often have poor diets that are deficient in folic acid).
2) Vitamin B₃₂ combines with **intrinsic factor** produced by parietal cells in the stomach. When the B₃₂-intrinsic factor complex binds to receptors in the small intestine, the B₃₂ is absorbed.

3. Regulation of erythropoiesis.

**FIGURE 19.5**

A. In response to decreased blood oxygen, **erythropoietin** (a glycoprotein hormone) is produced by the kidneys and released into the plasma.

B. Erythropoietin is carried to red bone marrow and stimulates red blood cell production.

C. The amount of oxygen delivered to the kidneys determines the amount of erythropoietin produced.
   1) If oxygen levels are low, erythropoietin production increases, red blood cell production increases, and oxygen delivery increases.
   2) If oxygen levels are high, erythropoietin production decreases, red blood cell production decreases, and oxygen delivery decreases.
   3) Factors that decrease oxygen delivery include hemorrhage (wounds, menstruation), high altitude, inadequate gas exchange in the lungs (emphysema), or inadequate blood delivery (heart failure).

Suppose a nonsmoker smoked a pack of cigarettes a day for two weeks. What would happen to his reticulocyte count? Explain.

D. Testosterone stimulates erythropoietin production, and this may account for the greater number of red blood cells in males.
4. Fate of red blood cells.

A. The average red blood cell lives 120 days. Red blood cells do not have nuclei and are not able to synthesis the molecules necessary to maintain the cells.

B. Red blood cells come to their end by rupturing as they squeeze through small spaces or rub against a rough surface. The spleen (most important), liver, and bone marrow function to remove and process red blood cells.

C. After rupturing, the red blood cells’ hemoglobin is ingested by macrophages primarily in the spleen.

D. Fate of hemoglobin.
   1) Globin is broken down into amino acids that are used as a source of energy or are made into new proteins.

   2) The iron in heme is released into the blood. It is transported to the liver and stored, or it is transported to red marrow and made into new hemoglobin.

   3) The heme is converted to biliverdin and then to bilirubin. These substances are often called bile pigments.
      a. The bilirubin is released into the blood as free bilirubin, which is transported to the liver bound to albumin.

      b. Free bilirubin is taken up by liver cells and bound to glucuronic acid to form conjugated bilirubin, which is more water soluble than free bilirubin.

      c. Most of the conjugated bilirubin is secreted as part of bile. Some reenters the blood and is secreted by the kidneys as part of urine.

      d. If bilirubin builds up in the blood jaundice results. Jaundice (Fr. yellow) is a yellowish staining of the skin, sclerae (white of the eyes), and other tissues with bile pigments.

      e. Bilirubin is converted by bacteria in the intestine into other pigments that give feces its characteristic brown color.

      f. Some of these pigments are absorbed into the blood and travel to the kidneys. The kidneys modify the pigments, which are excreted in the urine, giving urine its yellowish color.
In hereditary hemolytic anemia, the plasma membranes of red blood cells are more fragile than normal. Explain how jaundice and bilirubin gallstones can develop in this condition.

In 1910, it was discovered that removal of the spleen “cures” hereditary hemolytic anemia. Explain.

White Blood Cells
1. **Immunity** is the ability to resist damage from foreign substances, such as microorganisms and harmful chemicals.

2. White blood cells, and the cells derived from white blood cells, form the cellular component of the immune system.
   A. White blood cells are transported by the blood and can leave the blood by a process called **diapedesis**, in which they squeeze between the epithelial cells lining blood vessels.

   B. **Chemotaxis** is the ability of white blood cells to move toward foreign materials or dead cells by detecting chemical gradients.

   C. At sites of infection, white blood cells aggregate and phagocytize bacteria, etc.; then they die. The accumulation of dead white blood cells, cell debris, and fluid is called **pus**.
3. There are five types of white blood cells named according to their appearance when stained.

**FIGURE 19.8**

A. White blood cells containing large cytoplasmic granules that are easily seen with a light microscope when stained.
   1) Neutrophils stain with both basic and acidic dyes.
   2) Basophils stain with basic dyes.
   3) Eosinophils stain with acidic dyes.

B. White blood cells containing small cytoplasmic granules that are not easily seen with a light microscope when stained.
   1) Monocytes
   2) Lymphocytes

**Neutrophils**

1. Neutrophils are the most common type of white blood cell. Because their nuclei are commonly trilobed, they are sometimes called polymorphonuclear neutrophils (PMNs).

2. Neutrophils are usually the first cells to leave the blood and enter infected tissues.
   A. Neutrophils phagocytize bacteria and other foreign substances
   B. Neutrophils often die after a single phagocytic event. Pus is an accumulation of mostly dead neutrophils.
   C. Neutrophils release lysosomes (their granules), which can kill microbes. These chemicals can also damage "innocent bystander" cells and cause inflammation.
**Basophils and Eosinophils**

1. Basophils and eosinophils leave the blood and enter tissues.

2. Basophils release chemicals, such as **histamine**, that promote inflammation. They also release **heparin**, which inhibits blood clotting.

3. Eosinophils release enzymes that counteract inflammation, for example, by destroying histamine.

4. A balance between the activities of these cells regulates the amount of inflammation produced.

- **Basophil**, too much = hypersensitivity reaction
- **Inflammation** right amount = beneficial
- **Eosinophil** too little = more susceptible to disease

**Lymphocytes**

1. The two major types of lymphocytes are B cells and T cells.

2. **B cells.** B cells produce specific proteins, called **antibodies**. The antibodies bind to foreign substances, such as bacteria or toxins, and activate mechanism that result in the destruction of the foreign substances.

- **B cell** Antibody **Antibody attaches** Bacteria destroyed to bacteria

3. **T cells.** T cells have the ability to recognize cells that are infected with viruses. The T cell then causes the infected cell to lyse (rupture). T cells are also involved with the destruction of tumor cells and graft rejections.

- **T cell** Virus infected cell
Monocytes
1. Monocytes are the largest white blood cells. In the blood, monocytes are phagocytic.

2. Monocytes leave the blood, enter tissues, enlarge, and become **macrophages**.
   A. Macrophages can phagocytize many items and large items. They clean up dead neutrophils and other cellular debris.
   B. Macrophages release chemicals that promote inflammation.
   C. Macrophages process foreign substances and present them to lymphocytes, which then respond.
   D. Monocyte numbers increase in chronic infections.

Platelets

**FIGURE 19.2**

1. Stem cells give rise (eventually) to megakaryocytes. Platelets, or thrombocytes, are small pieces of cytoplasm surrounded by cell membrane that pinch off from the megakaryocyte.

2. Platelet functions.
   A. Formation of platelet plugs.
   B. Formation of clots.

HEMOSTASIS
1. General remarks.
   A. All animals with a vascular system must be able to minimize blood loss when blood vessels are damaged.
   B. In medium to large sized vessels, bleeding is not usually controllable by the body. Pressure on the vessel or ligature of the vessel may be necessary to stop blood loss.
   C. Bleeding from veins is less dangerous than bleeding from arteries because arteries have higher blood pressure which prevents closure of the damaged vessel.
   D. Although the events in preventing blood loss do not occur in a neat orderly fashion, but overlap in time and are closely interrelated, a general sequence of events can be described.
2. **Hemostasis**, the arrest of bleeding, involves the processes of vascular spasm, platelet plug formation, and coagulation.

Vascular Spasm
1. When a blood vessel is damaged, the smooth muscles in the vessel constrict. In small vessels, this can completely close off the vessel.

2. Constriction is mediated through neural responses to pain, and by thromboxane released by platelets and endothelin released by the endothelial (epithelial) cells lining blood vessels.
Platelet Plug Formation

1. Platelets do not adhere to the endothelium lining blood vessels. When the vessel is damaged, collagen in the tissue under the endothelium is exposed.

2. In platelet adhesion, platelets attach to the collagen. Von Willebrand factor is produced by endothelial cells. It binds to collagen and its receptor on platelets.

3. In the platelet release reaction, platelets attached to collagen become activated and release ADP and thromboxane. ADP and thromboxane bind to their receptors on platelets, which activates them. The activated platelets release more ADP and thromboxane, and so on. Thus many platelets are activated.

4. In platelet aggregation, the activated platelets bind to fibrinogen, forming a platelet plug.

5. Important point: Activation of platelets exposes phospholipid sites on the platelet surface that are involved in the formation of clots (see discussion of coagulation).

Thromboxanes are derived from prostaglandins. Aspirin inhibits prostaglandin synthesis. What effect does aspirin have on platelet plug formation and clot formation? Explain.

Why is aspirin effective in preventing heart attacks and strokes? Explain.
Coagulation
1. Except for minor damage, coagulation or clot formation is the dominant factor in preventing blood loss.

2. In the plasma are a group of proteins, called coagulation factors, that are involved in clot formation. The proteins are produced in the liver, and many of them require vitamin K for their production.

3. Normally the clotting proteins are in an inactive state. Activation of the proteins results in the formation of a blood clot. There are three stages in this process.

   FIGURE 19.10 and 19.11

   A. Clotting can begin with the extrinsic or intrinsic pathways.
   
   B. The extrinsic and intrinsic pathways converge into the common pathway.
   
   C. The phospholipid sites on platelets, as well as Ca^{2+}, are necessary for these reactions to proceed.

Extrinsic Pathway
1. The extrinsic pathway involves (initially) chemicals released by damaged tissues.

2. Damaged tissue releases thromboplastin or tissue factor (factor III).
   
   A. Thromboplastin, in conjunction with other chemicals, activates proteins in the plasma.
   
   B. Reactions in the plasma result in the production of activated factor X, which is the beginning of the common pathway.

Intrinsic Pathway
1. The intrinsic pathway of clot formation involves clotting factors and platelets found in the plasma.

2. When a vessel is damaged, factor XII (Hageman factor) comes into contact with collagen and becomes activated.
   
   A. Activated factor XII activates another clotting protein, which in turn activates another clotting protein, and so on.
   
   B. Eventually activated factor X is formed.

Common Pathway
1. On the surface of platelets, activated factor X, factor V, platelet phospholipids, and Ca^{2+} combine to form prothrombinase.

2. Prothrombinase converts prothrombin to thrombin. Thrombin converts fibrinogen into fibrin, which forms the clot.
**Control of Clot Formation**

1. **Anticoagulants** are chemicals that prevent the blood from clotting. They function to prevent unwanted clotting.

2. **Antithrombin**, a plasma protein, has the ability to destroy thrombin. Without thrombin, fibrinogen is not converted to fibrin and there is no clot formation.  
   A. At the site of injury there is strong stimulation of the clotting mechanism and more thrombin is formed than can be inactivated by antithrombin.
   B. Away from the site of injury antithrombin neutralizes any thrombin in the blood, preventing clot formation.

3. **Heparin**, released by basophils, increase the effectiveness of antithrombin.

4. **Prostacyclin** is a prostaglandin derivative produced by endothelial cells that inhibits coagulation. [ ]

5. Other anticoagulants.  
   A. **Dicumarol** interferes with vitamin K which is required for the formation of plasma clotting factors. Dicumarol is used to prevent clotting in the body.
   B. In the laboratory.  
      1) Substances than interfere with calcium activity in the clotting process are used to prevent blood from clotting. Examples are CPD (citrate phosphate dextrose), ACD (acid citrate dextrose), and EDTA (ethylenediaminetetraacetic acid).
      2) Heparin is used on glassware to prevent clotting, e.g., capillary tubes for collecting blood.
**Clot Retraction and Dissolution**

1. Following clot formation (within 30 minutes), the clot actually gets smaller, a process called **clot retraction**.
   A. The clot becomes denser and therefore stronger.
   
   B. As the clot retracts it pulls damaged tissue closer together.
   
   C. Serum can be observed on a recently retracted clot. **Serum** is a clear watery solution that is plasma minus blood cells and clotting factors.

2. Clot retraction is caused by platelets caught within the fibrin of the clot.
   A. The platelets send out small projections that attach to the fibrin.
   
   B. The projections contain actin and myosin contractile proteins that use ATP. Contraction of the projections results in clot retraction.

3. **Clot dissolution** is the breakdown of the clot. The clot is dissolved in a process called **fibrinolysis**. After clots are formed they are eventually dissolved and tissue repair takes place.

   ![FIGURE 19.12](image)

   A. Activated factor XII converts **plasminogen** (an inactive plasma protein produced by the liver) to plasmin. **Plasmin** is an enzyme than can break down fibrin. At the same time that the clot is formed, plasmin is trapped in the clot and will later cause the clot to dissolve.

   B. **Tissue plasminogen activator (t-PA)**, release by cells around the clot, also cause the production of plasmin.

   C. Clinically, genetic engineered t-PA is used to break down clots. Other substances, such as **streptokinase**, a bacterial enzyme, are also used.

**Clotting Abnormalities**

1. **Thrombocytopenia** is a reduced number of platelets caused by excess platelet destruction (autoimmune disease) or depression of platelet production (pernicious anemia, drugs, radiation). Thrombocytopenia results in blood loss through the capillaries because of reduced platelet plug formation [can result in petechiae (pE-tE′kE-E)].

2. **Von Willebrand’s disease** is the most common inherited bleeding disorder. It is treated by administering von Willebrand factor or drugs that increase the production of von Willebrand factor.

3. **Hemophilia** is a genetic trait (sex linked recessive) that results in the absence of some of the clotting plasma factors and therefore difficulty in stopping bleeding.

4. A **thrombus** is a clot that forms in a blood vessel, adheres to the wall of the vessel, and eventually can cause blockage of the vessel. Blockage leads to tissue death. In the heart this is called a **coronary thrombosis** and in the brain it is a **stroke**.
5. An embolus is a clot that breaks free and moves through the circulatory system. It can eventually become lodged in a small vessel (often in the lungs) and produce the same results as a thrombus.

A patient is taking large doses of an oral antibiotic. What effect could this have on the ability of her blood to clot? Explain.

An alcoholic is admitted to the hospital because of bleeding from his urinary tract. He was treated with injections of vitamin K. Why wasn’t he given vitamin K orally?

BLOOD GROUPING
1. When blood is lost, blood volume decreases, resulting in a drop in blood pressure. In addition, the loss of red blood cells results in a decreased ability to transport oxygen.

2. A transfusion is the transfer of blood or blood components from one person to another. An infusion is the injection of fluids that function as a blood substitute (e.g., physiological saline restores blood volume). Transfusions and infusions can prevent tissue damage, shock, and death.

3. The donor is the person giving blood, and the recipient is the person receiving blood. When blood is transferred between individuals a transfusion reaction in the recipient can result.
   A. Transfusion reactions occur when antigens (substances recognized by the immune system) on the surface of the donor’s red blood cells react with antibodies (proteins produced by lymphocytes) in the recipient’s plasma.
   B. When antibody and antigen combine, a transfusion reaction results in agglutination (clumping) and hemolysis (rupture) of red blood cells.
**ABO Blood Group**

1. There are many different antigens on the surface of red blood cells. These have been categorized into **blood groups**, of which the **ABO blood group** is one of the most important.

2. Type A blood has type A antigen, type B blood has type B antigen, type AB blood has both type A and type B antigen, and type O blood has neither type A nor type B antigen.

3. Type A blood has anti-B antibodies, which act against type B antigens; type B blood has anti-A antibodies, which act against type A antigens; type AB blood has neither anti-A nor anti-B antibodies; and type O blood has both anti-A and anti-B antibodies.

   A transfusion of type A blood into a recipient with type A blood does not result in a transfusion reaction. Explain.

   A transfusion of type A blood into a recipient with type B blood result in a transfusion reaction? Explain.

4. Normally blood is transferred between people with the same blood type. This avoids transfusion reactions. Under emergency situations (e.g., the patient will die without a transfusion) blood of one type may be transfused into a person with a different blood type.

   A person with type ______ blood is considered to be a **universal donor**. That is, the blood of a universal donor does not cause a transfusion reaction when given to a person who is any of the other ABO blood types. Explain.
A person with type ______ blood is considered to be a **universal recipient**. That is, a universal recipient can receive any of the other ABO blood types and not have a transfusion reaction. Explain.

5. The presence of anti-A and anti-B antibodies in blood is not clearly understood.
   A. Normally, antibodies do not develop against an antigen unless the body is exposed to the antigen. How can a person with type A blood have anti-B antibodies if they have never been exposed to type B blood?

   B. Up to two months of age a person does not have anti-A or anti-B antibodies. It is hypothesized that these antibodies develop as a result of exposure to A or B antigens found in food or bacteria that are ingested. This is called a **cross reaction**.

   If a person was type A blood, why would they develop anti-B antibodies, but not anti-A antibodies?

**Rh Blood Group**

1. People are **Rh-positive** if they have certain Rh antigens on their red blood cells. They are **Rh-negative** if they don't have these Rh antigens. Normally there are no anti-Rh antibodies in the blood. However, Rh-negative people can make anti-Rh antibodies if they are exposed to Rh antigens. Rh positive people do not make anti-Rh antibodies because they would be making antibodies against themselves.

2. **Hemolytic disease of the newborn (HDN)**, occurs when Rh antibodies (produced by a Rh-negative mother) cause the red blood cells of an Rh-positive fetus to agglutinate and/or undergo hemolysis.

   A. HDN is not usually a problem during the first pregnancy because exchange of blood between mother and fetus does not occur until late in the pregnancy or until delivery.
B. If Rh-positive blood from the fetus enters the mother's blood, the mother's immune system recognizes the Rh antigen as a foreign substance and produces anti-Rh antibodies. Once the mother's immune system is "sensitized" to the Rh-positive antigen, she can very rapidly make large amounts of anti-Rh antibodies.

C. In the second pregnancy, if any Rh-positive blood from the fetus enters the mother's blood, large amounts of antibodies are rapidly produced. These antibodies cross the placenta and damage the blood of the fetus.

D. HDN can usually be prevented with anti-Rho (D) immune globulin (RhoGam), given before or after delivery. These antibodies bind to any Rh antigens in the mother's blood and inactivate them. Thus, the mother's immune system never "sees" the Rh antigens and therefore does not "learn" to produce anti-Rh antibodies.

3. Fetal responses during HDN.
   A. Anti-Rh antibodies bind to Rh antigens on fetal red blood cells and they undergo hemolysis and agglutination.

   B. Bilirubin resulting from the lysed red blood cells crosses the placenta and is eliminated by the mother. The fetal liver is mostly inactive before birth. Blood bypasses the liver and only a small amount of bile is released into the intestine (meconium).

   C. The fetus produces new red blood cells to replace those that were lysed, but does not produce enough, so anemia (reduced number of red blood cells) results. The stimulus for red blood cell production in the fetus is the low oxygen level in the fetal blood resulting from the low number of red blood cells.

   D. After birth, red blood cells are still destroyed by the remaining antibodies (it takes several months to naturally eliminate the antibodies). There is no placenta to remove the bilirubin, which builds up because the infant's liver is overloaded. Jaundice results and the high levels of bilirubin are toxic to brain tissue.

Would you expect the rate of red blood cell production in the newborn to be higher than or lower than the rate in the fetus. Explain.
4. Treatment.
   A. Transfusion exchange is the removal of the baby's blood and replacement with donor blood.

   Explain why transfusion exchange would be an effective treatment.

   Would you give the Rh-positive newborn a transfusion of Rh-positive blood or Rh-negative blood? Explain.

   B. Phototherapy. Fluorescent lights break down bilirubin to less toxic compounds.
Anemias

1. **Anemia** is a reduced number of red blood cells and/or reduced hemoglobin. It is a symptom that has many causes. General symptoms include the following:
   A. Reduce oxygen transport results in decreased ATP synthesis. The decreased energy availability results in fatigue and a lower metabolism, less heat production, and increased sensitivity to the cold.
   B. Reduce hemoglobin, which is a red-pigment molecule, results in paleness.

2. **Aplastic anemia** results from red bone marrow destruction (radiation, chemicals, drugs) leading to reduced production of red blood cells, platelets, and white blood cells.

3. **Maturation failure anemia**
   A. **Folic acid deficiency**. Impairs cell division.
   B. **Pernicious anemia** (lack of vitamin B₁₂). Impairs cell division.
   C. **Iron deficiency anemia** Cells appear pale in color and are smaller than normal because of a lack of hemoglobin.
   D. **Thalassemia** is a hereditary disease characterized by an abnormally low rate of hemoglobin production because of decrease synthesis of the globin part of the molecule.

4. **Hemorrhagic anemia** is the loss of blood by bleeding.
   A. Rapid hemorrhage. Plasma levels are replaced in 1-3 days while red blood cell replacement takes 3-4 weeks.
   B. Chronic hemorrhage (usually due to gastrointestinal bleeding). Loss of red blood cells leads to iron deficiency anemia (recall that iron is normally recycled).

5. **Hemolytic anemia** occurs when red blood cells rupture or are destroyed at an excessive rate.
   A. **Hemolytic disease of the new born HDN**, also called **erythroblastosis fetalis**. Rh antibodies produced by the mother cause agglutination and hemolysis of fetal and newborn red blood cells.
   B. **Sickle cell anemia** is an inherited disorder that results from an abnormal hemoglobin structure. When oxygen levels are low (as in tissues), the cells assume a sickle shape. This can result in clogging of small blood vessels and rupture of the red blood cells.
   C. Weak, abnormal cell membranes (spherocytosis).
   D. Drug-induced damaged to red blood cells.
Erythrocytosis
1. Erythrocytosis is an overabundance of red blood cells. It makes it harder for blood to circulate (increased viscosity), causing an increase in blood pressure and makes the heart work harder than normal. There is also blockage of blood vessels as the red blood cells pile up, and bleeding as the extra blood is forced out of vessels.

2. Types of erythrocytosis.
   A. **Relative erythrocytosis** results from decreased blood volume, such as that caused by dehydration, diuretics, and burns.

   B. **Primary erythrocytosis (polycythemia vera)** is a stem cell defect of unknown cause that results in the overproduction of normal red blood cells, granulocytes, and platelets. Erythropoietin levels are decreased.

   B. **Secondary erythrocytosis (polycythemia).** An increase in red blood cell production due to decreased oxygen delivery to tissues. Erythropoietin levels are increased.
Type and Crossmatch
1. **Blood-typing** determines the ABO and Rh blood groups of a blood sample.

2. Even if ABO and Rh groups are compatible, a crossmatch is performed because there are other blood groups that could cause a transfusion reaction. The donor’s cells are mixed with the recipient’s serum (contains the antibodies) and the donor’s serum is mixed with the recipient’s cells. If no agglutination occurs the blood is safe for transfusion.

Complete Blood Count
The **complete blood count (CBC)** is an overview of the blood that provides much information. It consists of a red blood cell count, hemoglobin and hematocrit measurements, and a white blood cell count.

1. **Red Blood Count**
   A. Blood cell counts are usually done electronically with a machine, but they can be done manually with a microscope. A normal red blood count for a male is 4.2 to 5.8 million red blood cells per µL of blood and for a female it is 3.6 to 5.2 million per µL of blood.

   B. **Erythrocytosis** is an overabundance of red blood cells. It can result from red bone marrow tumors (primary erythrocytosis) or a decreased oxygen supply (secondary erythrocytosis), which stimulates erythropoietin formation. Erythrocytosis makes it harder for the blood to flow through blood vessels and increases the work load of the heart. It can reduce blood flow through tissues, and if severe, plugging of small blood vessels (capillaries) occurs.

2. **Hemoglobin Measurement**
   A. Hemoglobin is a measure of the amount of hemoglobin in a given volume of blood, usually expressed as grams of hemoglobin per 100 milliliters of blood. The normal hemoglobin for a male is 14 to 18 grams per 100 milliliters of blood, and for a female it is 12 to 16 grams per 100 milliliters of blood.

   B. Abnormally low hemoglobin is an indication of **anemia**.

3. **Hematocrit**

   A. The percentage of total blood volume composed of red blood cells is the hematocrit. One way to determine hematocrit is to place blood in a tube and spin the tube in a centrifuge. The formed elements are heavier than the plasma and are forced to the end of the tube. Red blood cells account for 44% to 54% of the total blood volume in males and 38% to 48% in females.

   B. The hematocrit reflects the number and the size (volume) of the red blood cells. If the hematocrit is below normal, for example, it can indicate that red blood cells are smaller than normal. This can occur when there is inadequate iron in the diet and the production of hemoglobin is impaired. Consequently, during their formation, red blood cells do not fill up with hemoglobin.
4. **White Blood Count**
   A. A white blood count (WBC) measures the total number of white blood cells in the blood. There are normally between 5000 to 10,000 white blood cells per µL of blood.

   B. **Leukopenia** is a lower than normal white blood count and often indicates depression or destruction of the red marrow (e.g., radiation, drugs, tumor, or a deficiency of vitamin B₁₂ or folic acid). **Leukocytosis** is an abnormally high white blood count. **Leukemia**, a tumor of the red marrow, and bacterial infections often cause leukocytosis.

**Differential White Blood Count**
1. A white blood count provides information about the numbers of white blood cells. A differential white blood count determines the percentage of each of the five kinds of white blood cells in the white blood cell count. Normally neutrophils account for 60% to 70%, lymphocytes 20% to 30%, monocytes 2% to 8%, eosinophils 1% to 4%, and basophils 0.5% to 1%.

2. Much insight about a patient's condition can be obtained from a differential white blood count. For example, in bacterial infections, the neutrophil count is often greatly increased, whereas in allergic reactions the eosinophil and basophil counts are elevated.

**Clotting**
Two measurements that test the ability of the blood to clot are the platelet count and the prothrombin time.
1. **Platelet Count**
   A. A normal platelet count is 250,000 to 400,000 platelets per µL of blood.

   B. **Thrombocytopenia** is a condition in which the platelet count is greatly reduced, resulting in chronic bleeding through small vessels and capillaries. It can be caused by decreased platelet production due to hereditary disorders, pernicious anemia, drug therapy, or radiation therapy.

2. **Prothrombin Time**
   A. Prothrombin time is a measure of how long it takes for the blood to start clotting, which is normally 9 to 12 seconds.

   B. Because many clotting factors have to be activated before prothrombin is activated, a deficiency of any one of them can cause an abnormal prothrombin time. Vitamin K deficiency, certain liver diseases, and drug therapy can cause a reduced prothrombin time.

**Blood Chemistry**
1. The composition of materials dissolved or suspended in the plasma can be used to assess the functioning of many of the body's systems.

2. For example, high blood glucose levels can indicate that the pancreas is not producing enough insulin, high blood urea nitrogen (BUN) is a measure of reduced kidney function, increased bilirubin can indicate liver dysfunction, and high cholesterol levels can indicate an increased risk of developing cardiovascular disease. A number of blood chemistry tests are routinely done when a blood sample is taken, and additional tests are available.
Described on the next page are 5 blood disorders labeled 1-5. Also provided is a table that gives the normal blood values for some routine laboratory measurements of blood. Also in the table, labeled A-F, are some abnormal blood values. Match each of the disorders with their blood values from the table and explain your choices.

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Blood Value</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3.</td>
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</tr>
<tr>
<td>4.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1. **Pernicious anemia.** As a result of insufficient vitamin B₁₂, the synthesis of DNA is inhibited. Many cells are produced but few complete all the divisions necessary to form red blood cells. The immature cells that do not develop are destroyed in the red marrow.

2. **Spherocytosis.** A hereditary disorder in which the red blood cells are spherical instead of biconcave disks. As a result, the cells cannot fold and pass through small capillaries. Instead, they rupture. Thus, in this disease red blood cells are destroyed faster than they can be produced.

3. **Primary erythrocytosis (polycythemia vera).** The overproduction of normal red blood cells. The cause is unknown.

4. **Aplastic anemia.** Few red blood cells are produced because of the destruction of red bone marrow by radiation, chemicals, or drugs.

5. **Iron deficiency anemia.** Red blood cells are formed with a reduced amount of hemoglobin due to an inadequate supply of iron to the red marrow.

### TABLE OF BLOOD VALUES

<table>
<thead>
<tr>
<th></th>
<th>RBC</th>
<th>Hgb</th>
<th>Hct</th>
<th>Reticulocyte Count</th>
<th>Bilirubin Level</th>
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</thead>
<tbody>
<tr>
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<td>45</td>
<td>1.3</td>
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<td>2</td>
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<tr>
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<tr>
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<td>9</td>
<td>10</td>
<td>70</td>
<td>6.0</td>
<td>4</td>
</tr>
</tbody>
</table>

where

- RBC = number (times 1 million) of red blood cells/mm³ of blood
- Hgb = hemoglobin (grams/100 ml of blood)
- Hct = hematocrit (percent volume of red blood cells)
- Reticulocyte count = % of red blood cells that are reticulocytes
- Bilirubin level = bilirubin (mg/100 ml of blood)