Composition of Blood

- Blood is the body's only fluid tissue
- It is composed of liquid plasma and formed elements
- Formed elements include:
  - Erythrocytes, or red blood cells (RBCs)
  - Leukocytes, or white blood cells (WBCs)
  - Platelets
- Hematocrit – the percentage of RBCs out of the total blood volume

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Components of Whole Blood

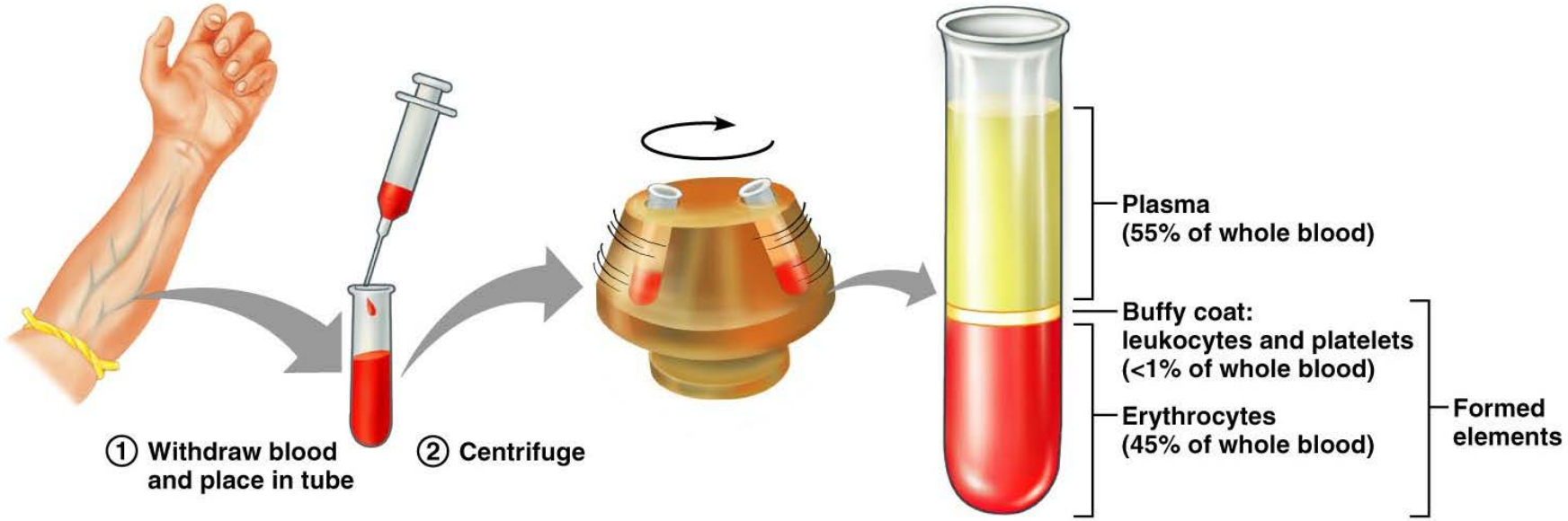

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Figure 17.1

Physical Characteristics and Volume

- Blood is a sticky, opaque fluid with a metallic taste
- Color varies from scarlet to dark red
- The pH of blood is 7.35–7.45
- Temperature is 38°C
- Blood accounts for approximately 8% of body weight
- Average volume: 5–6 L for males, and 4–5 L for females

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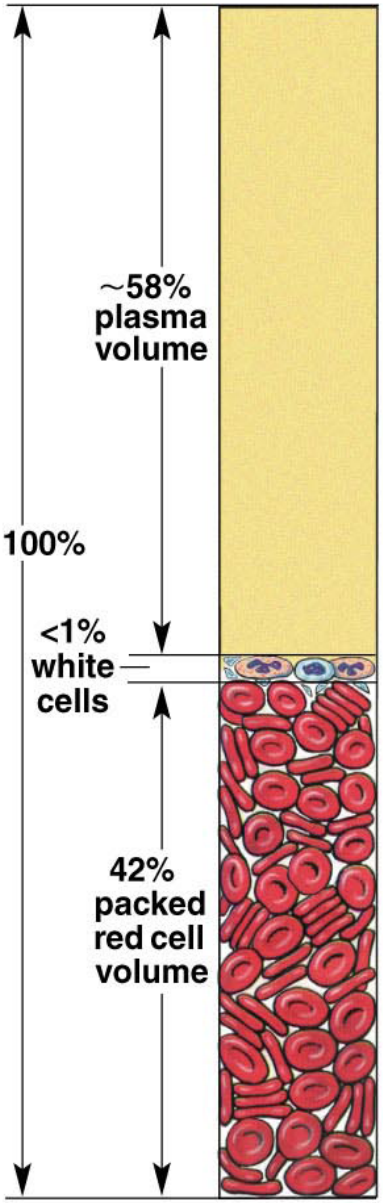

	Males	Females
Hematocrit	40–54%	37–47%
Hemoglobin (g Hb/dL* blood)	14–17	12–16
Red cell count (cells/μL)	$4.5–6.5 \times 10^6$	$3.9–5.6 \times 10^6$
Total white cell count (cells/μL)	$4–11 \times 10^3$	$4–11 \times 10^3$
Differential white cell count		
Neutrophils	50-70%	50-70%
Eosinophils	1-4%	1-4%
Basophils	<1%	<1%
Lymphocytes	20–40%	20–40%
Monocytes	2–8%	2–8%
Platelets (per μL)	$200–500 \times 10^3$	$200–500 \times 10^3$
* 1 deciliter (dL) = 100 mL		

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Functions of Blood

- Blood performs a number of functions dealing with:
  - Substance distribution
  - Regulation of blood levels of particular substances
  - Body protection

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Distribution

- Blood transports:
  - Oxygen from the lungs and nutrients from the digestive tract
  - Metabolic wastes from cells to the lungs and kidneys for elimination
  - Hormones from endocrine glands to target organs

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Regulation

- Blood maintains:
  - Appropriate body temperature by absorbing and distributing heat
  - Normal pH in body tissues using buffer systems
  - Adequate fluid volume in the circulatory system

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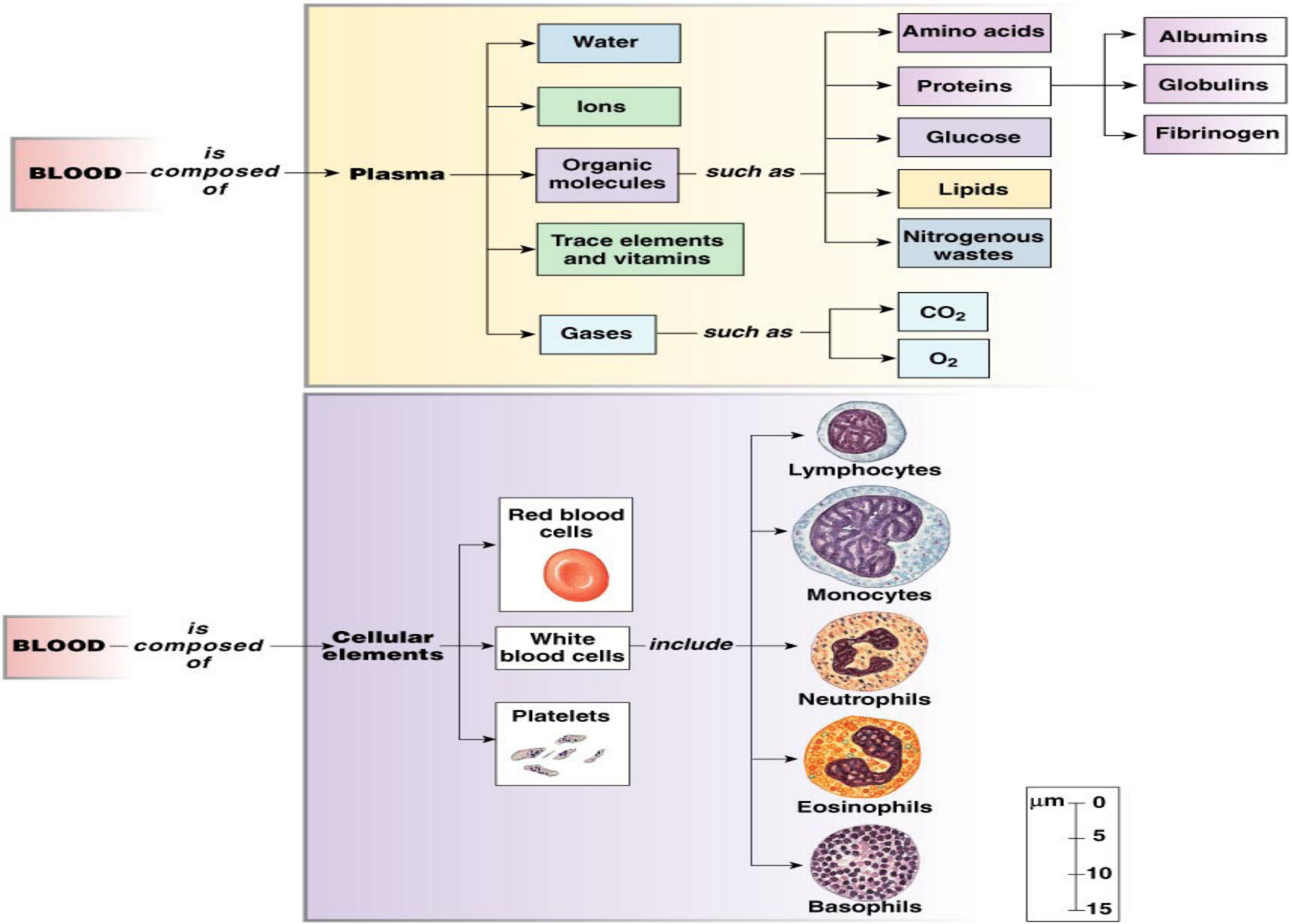

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Protection

- Blood prevents blood loss by:
  - Activating plasma proteins and platelets
  - Initiating clot formation when a vessel is broken
- Blood prevents infection by:
  - Synthesizing and utilizing antibodies
  - Activating complement proteins
  - Activating WBCs to defend the body against foreign invaders

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Blood Plasma

- Blood plasma contains over 100 solutes, including:
  - Proteins – albumin, globulins, clotting proteins, and others
  - Lactic acid, urea, creatinine
  - Organic nutrients – glucose, carbohydrates, amino acids
  - Electrolytes – sodium, potassium, calcium, chloride, bicarbonate
  - Respiratory gases – oxygen and carbon dioxide

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Formed Elements

- Erythrocytes, leukocytes, and platelets make up the formed elements
  - Only WBCs are complete cells
  - RBCs have no nuclei or organelles, and platelets are just cell fragments
- Most formed elements survive in the bloodstream for only a few days
- Most blood cells do not divide but are renewed by cells in bone marrow

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Erythrocytes (RBCs)

- Biconcave discs, anucleate, essentially no organelles
- Filled with hemoglobin (Hb), a protein that functions in gas transport
- Contain the plasma membrane protein spectrin and other proteins that:
  - Give erythrocytes their flexibility
  - Allow them to change shape as necessary

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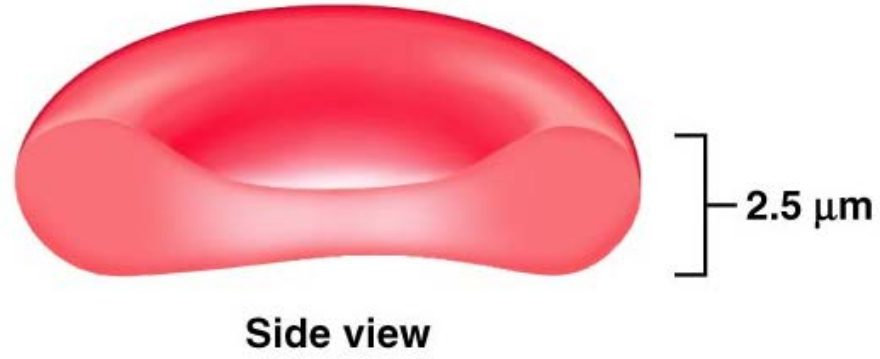
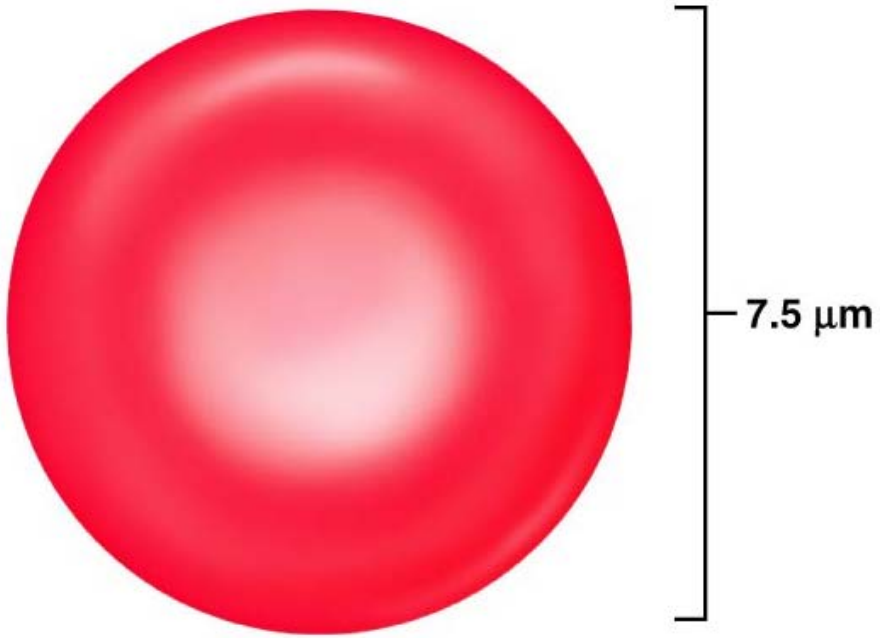
Erythrocytes (RBCs)



Side view



Top view

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Figure 17.3

Components of Whole Blood

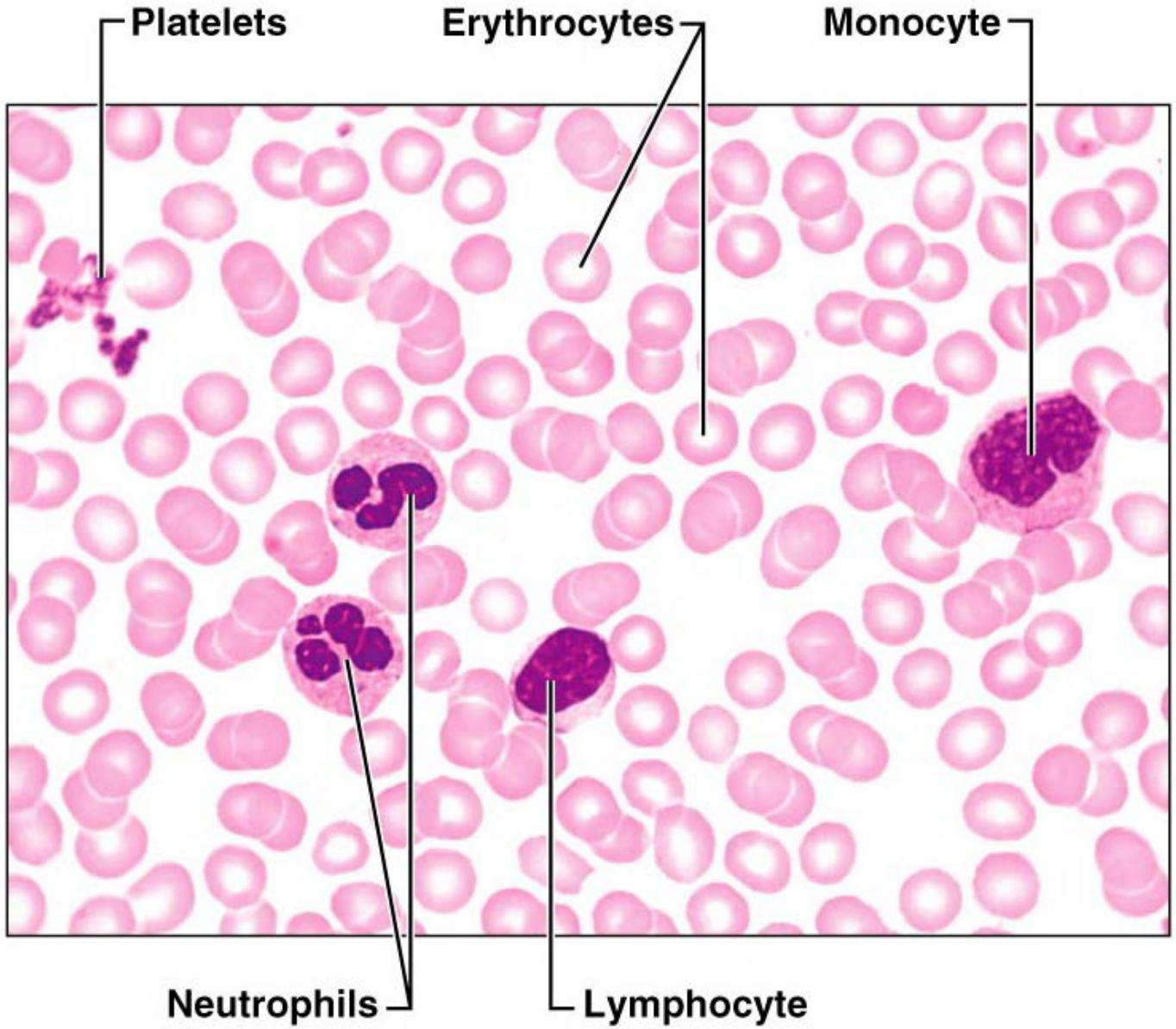

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Figure 17.2

Erythrocytes (RBCs)

- Erythrocytes are an example of the complementarity of structure and function
- Structural characteristics contribute to its gas transport function
  - Biconcave shape has a huge surface area relative to volume
  - Erythrocytes are more than 97% hemoglobin
  - ATP is generated anaerobically, so the erythrocytes do not consume the oxygen they transport

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Erythrocyte Function

- RBCs are dedicated to respiratory gas transport
- Hb reversibly binds with oxygen and most oxygen in the blood is bound to Hb
- Hb is composed of the protein globin, made up of two alpha and two beta chains, each bound to a heme group
- Each heme group bears an atom of iron, which can bind to one oxygen molecule
- Each Hb molecule can transport four molecules of oxygen

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Structure of Hemoglobin

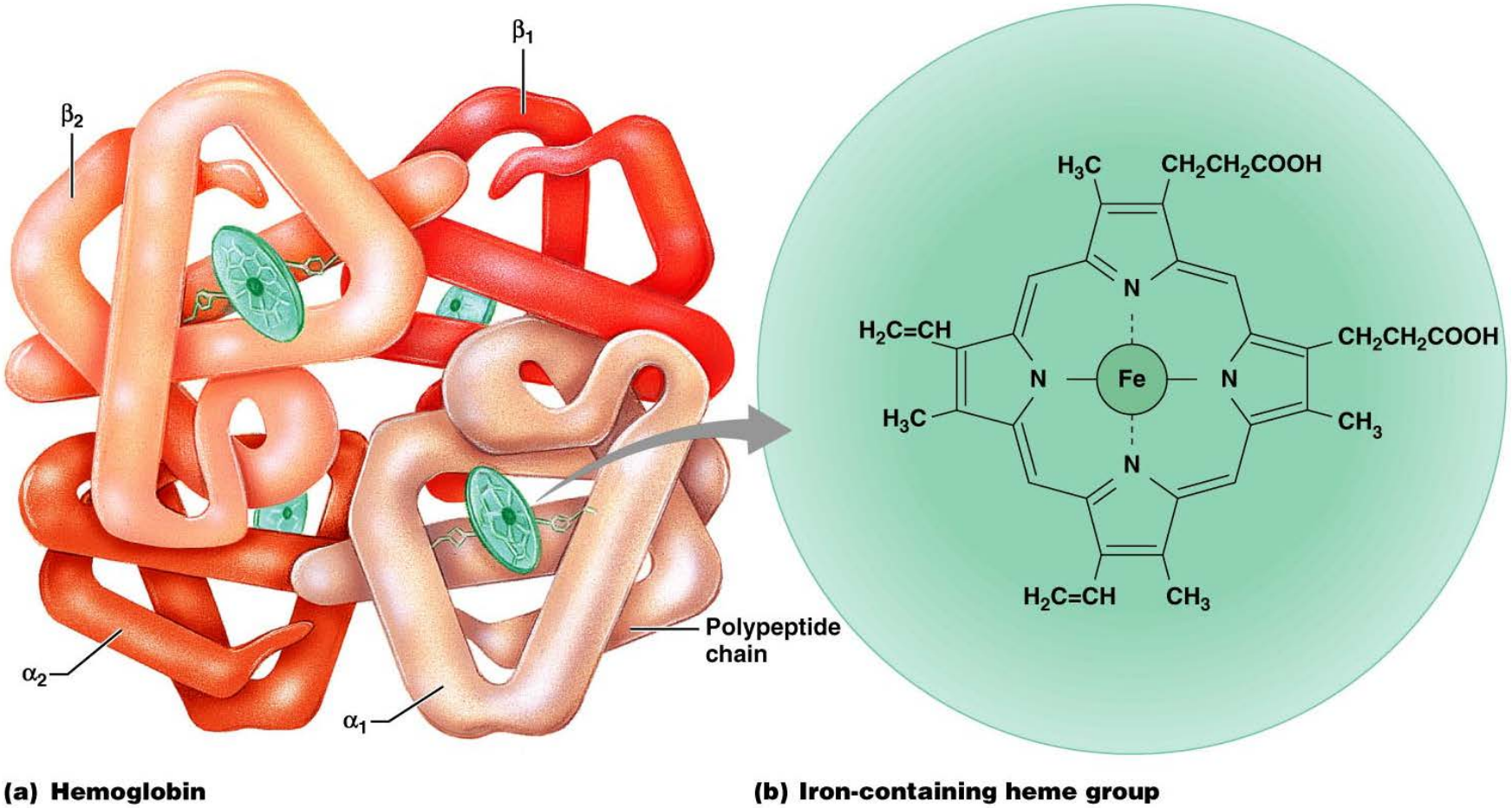

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Figure 17.4

Hemoglobin (Hb)

- Oxyhemoglobin – Hb bound to oxygen
  - Oxygen loading takes place in the lungs
- Deoxyhemoglobin – Hb after oxygen diffuses into tissues (reduced Hb)
- Carbaminohemoglobin – Hb bound to carbon dioxide
  - Carbon dioxide loading takes place in the tissues

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Regulation and Requirements for Erythropoiesis

- Circulating erythrocytes – the number remains constant and reflects a balance between RBC production and destruction
  - Too few RBCs leads to tissue hypoxia
  - Too many RBCs causes undesirable blood viscosity
- Erythropoiesis is hormonally controlled and depends on adequate supplies of iron, amino acids, and B vitamins

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Hormonal Control of Erythropoiesis

- Erythropoietin (EPO) release by the kidneys is triggered by:
  - Hypoxia due to decreased RBCs
  - Decreased oxygen availability
  - Increased tissue demand for oxygen
- Enhanced erythropoiesis increases the:
  - RBC count in circulating blood
  - Oxygen carrying ability of the blood

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Dietary Requirements of Erythropoiesis

- Erythropoiesis requires:
  - Proteins, lipids, and carbohydrates
  - Iron, vitamin B_{12}, and folic acid
- The body stores iron in Hb (65%), the liver, spleen, and bone marrow
- Intracellular iron is stored in protein-iron complexes such as ferritin and hemosiderin
- Circulating iron is loosely bound to the transport protein transferrin

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Fate and Destruction of Erythrocytes

- The life span of an erythrocyte is 100–120 days
- Old RBCs become rigid and fragile, and their Hb begins to degenerate
- Dying RBCs are engulfed by macrophages
- Heme and globin are separated and the iron is salvaged for reuse

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Fate and Destruction of Erythrocytes

- Heme is degraded to a yellow pigment called bilirubin
- The liver secretes bilirubin into the intestines as bile
- The intestines metabolize it into urobilinogen
- This degraded pigment leaves the body in feces, in a pigment called stercobilin

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Fate and Destruction of Erythrocytes

- Globin is metabolized into amino acids and is released into the circulation
- Hb released into the blood is captured by haptoglobin and phgocytized

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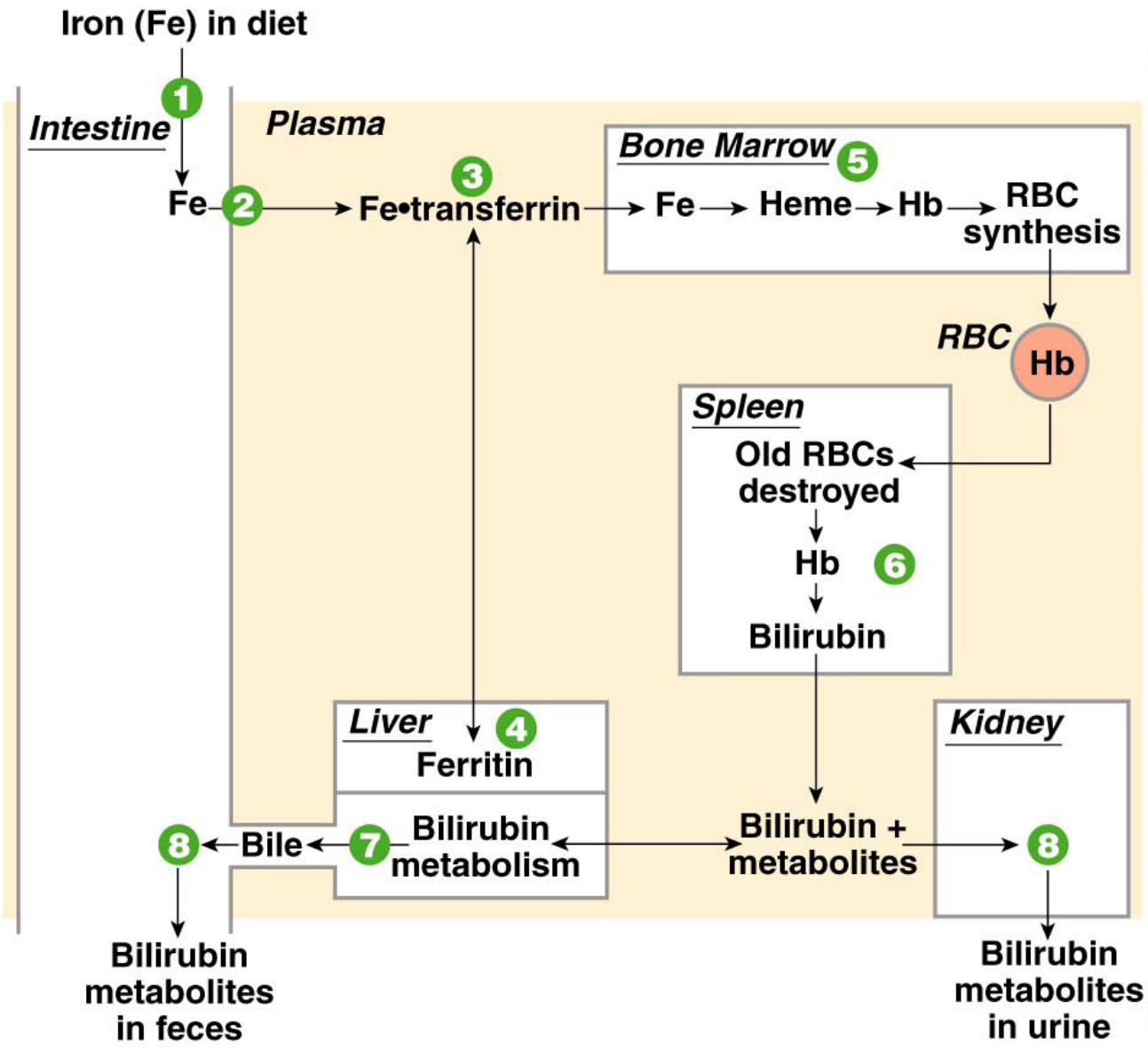

1. Iron comes from the diet.
2. Fe is absorbed by active transport.
3. Transferrin protein transports Fe in plasma.
4. Liver stores excess Fe as ferritin.
5. Bone marrow uses Fe to make hemoglobin (Hb).
6. Spleen converts Hb to bilirubin.
7. Liver metabolizes bilirubin and excretes it in bile.
8. Bilirubin metabolites are excreted in urine and feces.

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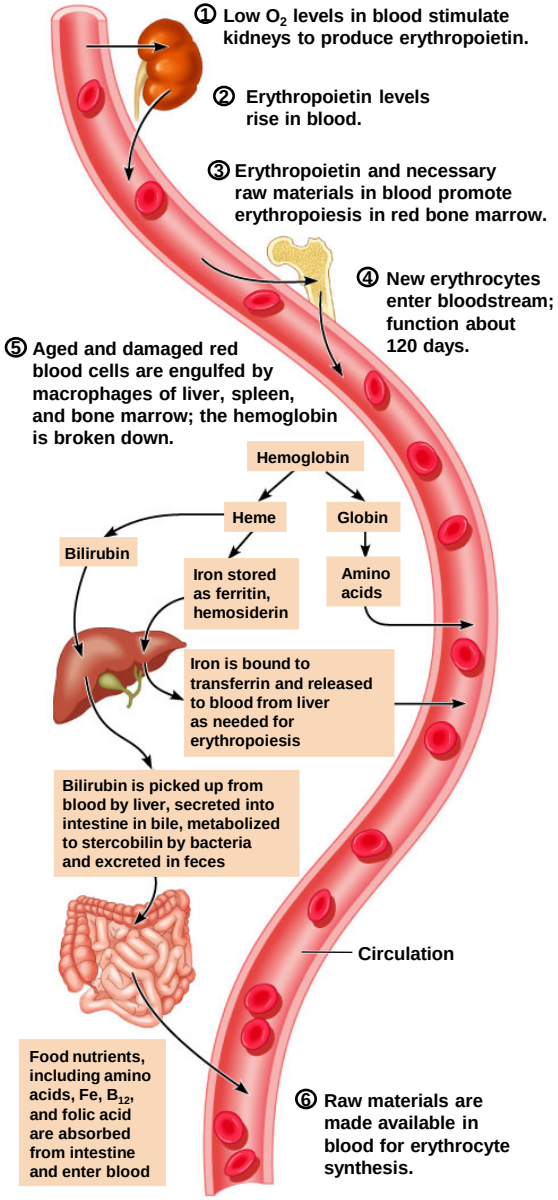

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Figure 17.7

Bacterial or Viral infection from CBC

- Neutrophils are by far the most common form of white blood cell that you have in your body (pus is simply dead neutrophils). Neutrophils are infection fighters that increase during bacterial infections (neutrophils are also known as granulocytes)
- Lymphocytes, on the other hand, can increase in cases of viral infections.

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Erythrocyte Disorders

- Anemia – blood has abnormally low oxygen-carrying capacity
  - It is a symptom rather than a disease itself
  - Blood oxygen levels cannot support normal metabolism
  - Signs/symptoms include fatigue, paleness, shortness of breath, and chills

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Anemia: Insufficient Erythrocytes

- Hemorrhagic anemia – result of acute or chronic loss of blood
- Hemolytic anemia – prematurely ruptured RBCs
- Aplastic anemia – destruction or inhibition of red bone marrow

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Anemia: Decreased Hemoglobin Content

- **Iron-deficiency anemia** results from:
  - A secondary result of hemorrhagic anemia
  - Inadequate intake of iron-containing foods
  - Impaired iron absorption
- **Pernicious anemia** results from:
  - Deficiency of vitamin B_{12}
  - Lack of intrinsic factor needed for absorption of B_{12}
- Treatment is intramuscular injection of B_{12}; application of Nascobal

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Anemia: Abnormal Hemoglobin

- **Thalassemias** – absent or faulty globin chain in Hb
  - RBCs are thin, delicate, and deficient in Hb
- **Sickle-cell anemia** – results from a defective gene coding for an abnormal Hb called hemoglobin S (HbS)
  - HbS has a single amino acid substitution in the beta chain
  - This defect causes RBCs to become sickle-shaped in low oxygen situations

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Polycythemia

- Polycythemia – excess RBCs that increase blood viscosity

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White Blood cells (WBC)

1. Granulocytes:
    1. Neutrophils (active phagocytes)
    2. Eosinophils (kill parasitic worms, play a complex role in allergy attack).
    3. Basophils (release histamine, at sites of inflammation; contain heparin).
2. Agranulocytes:
    1. Lymphocytes (B and T lymphocytes, fight tumors and viruses via cell attack)
    2. Monocytes (active phagocytes that become macrophages in the tissues; increase in number during infections such TB)

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White Blood cells (WBC)

- Are able to slip into and out of the blood vessels. (diapedesis).
- Can locate area of tissue damage and infection in the body by responding to certain chemicals that diffuse from the damaged cells (positive chemotaxis)

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Platelets

- Platelets are fragments of megakaryocytes with a blue-staining outer region and a purple granular center
- Their granules contain serotonin, Ca^{2+}, enzymes, ADP, and platelet-derived growth factor (PDGF)
- Platelets function in the clotting mechanism by forming a temporary plug that helps seal breaks in blood vessels
- Platelets not involved in clotting are kept inactive by NO and prostacyclin

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Hemostasis

- A series of reactions for stoppage of bleeding
- During hemostasis, three phases occur in rapid sequence
  - Vascular spasms – immediate vasoconstriction in response to injury
  - Platelet plug formation
  - Coagulation (blood clotting)

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Platelet Plug Formation

- Platelets do not stick to each other or to blood vessels
- Upon damage to blood vessel endothelium platelets:
  - With the help of von Willebrand factor (VWF) adhere to collagen
  - Are stimulated by thromboxane A2
  - Stick to exposed collagen fibers and form a platelet plug
  - Release serotonin and ADP, which attract still more platelets
- The platelet plug is limited to the immediate area of injury by prostacyclin

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Coagulation

- A set of reactions in which blood is transformed from a liquid to a gel
- Coagulation follows intrinsic and extrinsic pathways
- The final three steps of this series of reactions are:
  - Prothrombin activator is formed
  - Prothrombin is converted into thrombin
  - Thrombin catalyzes the joining of fibrinogen into a fibrin mesh

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Coagulation

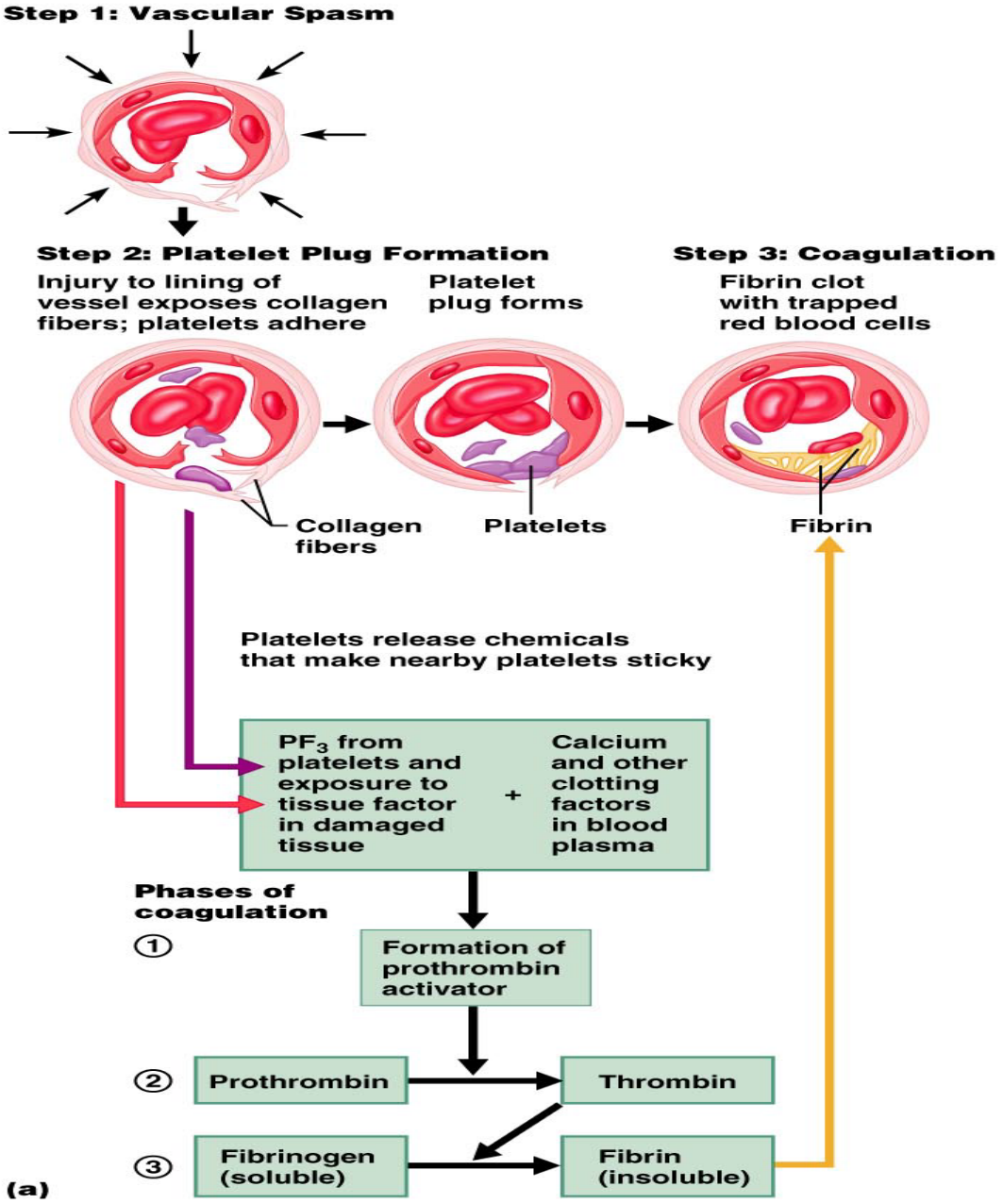

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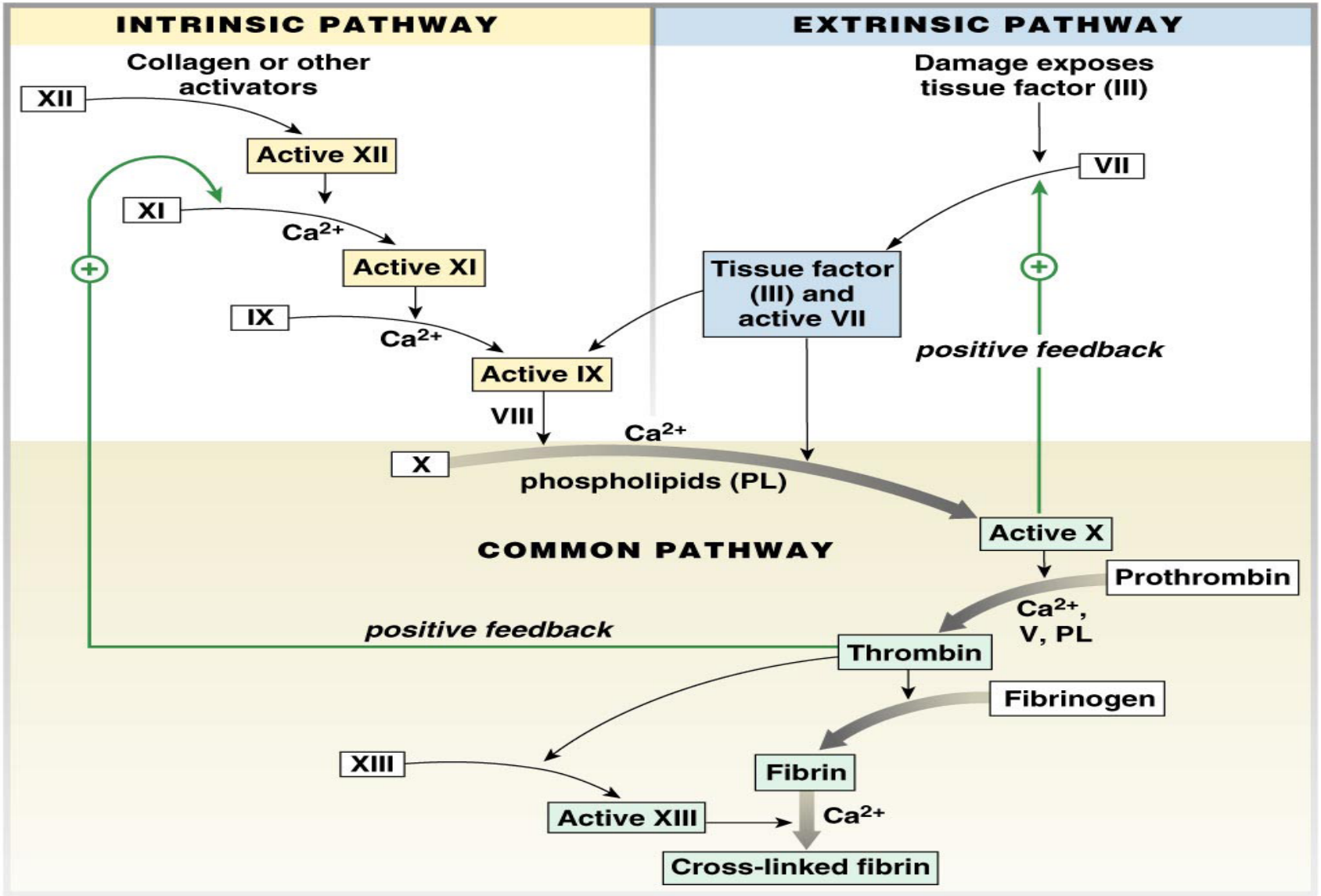
Figure 17.13a

Detailed Events of Coagulation



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Coagulation Phase 1: Two Pathways to Prothrombin Activator

- May be initiated by either the intrinsic or extrinsic pathway
  - Triggered by tissue-damaging events
  - Involves a series of procoagulants
  - Each pathway cascades toward factor X
- Once factor X has been activated, it complexes with calcium ions, PF_3, and factor V to form prothrombin activator

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Coagulation Phase 2: Pathway to Thrombin

- Prothrombin activator catalyzes the transformation of prothrombin to the active enzyme thrombin

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Coagulation Phase 3: Common Pathways to the Fibrin Mesh

- Thrombin catalyzes the polymerization of fibrinogen into fibrin
- Insoluble fibrin strands form the structural basis of a clot
- Fibrin causes plasma to become a gel-like trap
- Fibrin in the presence of calcium ions activates factor XIII that:
  - Cross-links fibrin
  - Strengthens and stabilizes the clot

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Clot Retraction and Repair

- Clot retraction – stabilization of the clot by squeezing serum from the fibrin strands
- Repair
  - Platelet-derived growth factor (PDGF) stimulates rebuilding of blood vessel wall
  - Fibroblasts form a connective tissue patch
  - Stimulated by vascular endothelial growth factor (VEGF), endothelial cells multiply and restore the endothelial lining

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Hemostasis Disorders: Thromboembolytic Conditions

- Thrombus – a clot that develops and persists in an unbroken blood vessel
  - Thrombi can block circulation, resulting in tissue death
  - Coronary thrombosis – thrombus in blood vessel of the heart

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Hemostasis Disorders: Thromboembolytic Conditions

- Embolus – a thrombus freely floating in the blood stream
  - Pulmonary emboli can impair the ability of the body to obtain oxygen
  - Cerebral emboli can cause strokes

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Prevention of Undesirable Clots

- Substances used to prevent undesirable clots:
  - Aspirin – an antiprostaglandin that inhibits thromboxane A_2
  - Heparin – an anticoagulant used clinically for pre- and postoperative cardiac care
  - Warfarin – used for those prone to atrial fibrillation

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Human Blood Groups

- RBC membranes have glycoprotein antigens on their external surfaces
- These antigens are:
  - Unique to the individual
  - Recognized as foreign if transfused into another individual
  - Promoters of agglutination and are referred to as agglutinogens
- Presence or absence of these antigens is used to classify blood groups

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Blood Groups

- Humans have 30 varieties of naturally occurring RBC antigens
- The antigens of the ABO and Rh blood groups cause vigorous transfusion reactions when they are improperly transfused
- Other blood groups (M, N, Dufy, Kell, and Lewis) are mainly used for legalities

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ABO Blood Groups

- The ABO blood groups consists of:
  - Two antigens (A and B) on the surface of the RBCs
  - Two antibodies in the plasma (anti-A and anti-B)
- ABO blood groups may have various types of antigens and preformed antibodies
- Agglutinogens and their corresponding antibodies cannot be mixed without serious hemolytic reactions

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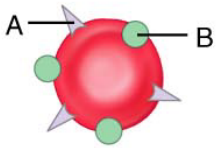
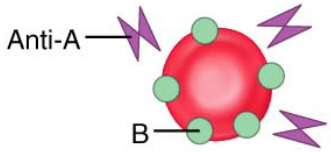
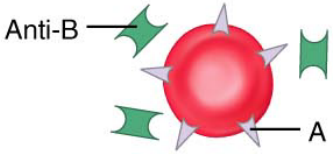
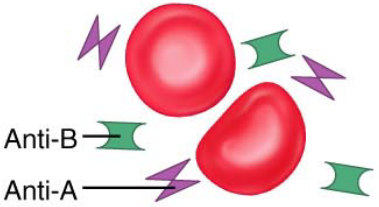
ABO Blood Groups

TABLE 17.4 ABO Blood Groups

BLOOD GROUP	FREQUENCY (% U.S. POPULATION) WHITE	BLACK	ASIAN	NATIVE AMERICAN	RBC ANTIGENS (AGGLUTINOGENS)	ILLUSTRATION	PLASMA ANTIBODIES (AGGLUTININS)	BLOOD THAT CAN BE RECEIVED
AB	4	4	5	<1	A B		None	A, B, AB, O (Universal recipient)
B	11	20	27	4	B		Anti-A (a)	B, O
A	40	27	28	16	A		Anti-B (b)	A, O
O	45	49	40	79	None		Anti-A (a) Anti-B (b)	O (Universal donor)

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Rh Blood Groups

- There are eight different Rh agglutinogens, three of which (C, D, and E) are common
- Presence of the Rh agglutinogens on RBCs is indicated as Rh^+
- Anti-Rh antibodies are not spontaneously formed in Rh^- individuals
- However, if an Rh^- individual receives Rh^+ blood, anti-Rh antibodies form
- A second exposure to Rh^+ blood will result in a typical transfusion reaction

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Hemolytic Disease of the Newborn

- Hemolytic disease of the newborn – Rh^+ antibodies of a sensitized Rh^- mother cross the placenta and attack and destroy the RBCs of an Rh^+ baby
- Rh^- mother becomes sensitized when exposure to Rh^+ blood causes her body to synthesize Rh^+ antibodies

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Hemolytic Disease of the Newborn

- The drug RhoGAM can prevent the Rh^- mother from becoming sensitized
- Treatment of hemolytic disease of the newborn involves pre-birth transfusions and exchange transfusions after birth

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- High hemoglobin often occurs in cigarette smokers. Carbon monoxide in the smoke blocks oxygen attachment to the red cells' empty hemoglobin slots. The body panics, interpreting low hemoglobin as a signal to increase red cell production. Hemoglobin rises, and so do red cells.

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