CHAPTER 8: CIRCULATORY SYSTEM

At the end of this chapter, student will be able to:

a) Describe the composition and explain the functions of blood plasma.
b) State the function of red blood cells, including the protein and the mineral involved.
c) Name the nutrients necessary for red blood cell production, and state the function of each.
d) Explain how hypoxia may change the rate of red blood cell production.
e) Describe what happens to red blood cells that have reached the end of their life span; what happens to the hemoglobin?
f) Explain the ABO and Rh blood types.
g) State what platelets are, and explain how they are involved in hemostasis.
h) Describe the stages of chemical blood clotting.
i) Explain how abnormal clotting is prevented in the vascular system.
j) State the normal values in a complete blood count.
k) Describe the location of the heart, the pericardial membranes, and the endocardium.
l) Name the chambers of the heart and the vessels that enter or leave each.
m) Name the valves of the heart, and explain their functions.
n) Describe coronary circulation, and explain its purpose.
o) Describe the cardiac cycle.
p) Explain how heart sounds are created.
q) Name the parts of the cardiac conduction pathway, and explain why it is the sinoatrial node that initiates each beat.
r) Explain stroke volume, cardiac output, and Starling's law of the heart.
s) Explain how the nervous system regulates heart rate and force of contraction.
t) Describe the structure of arteries and veins, and relate their structure to function.
u) Explain the purpose of arterial and venous anastomoses.
v) Describe the structure of capillaries, and explain the exchange processes that take place in capillaries.
w) Describe the pathway and purpose of pulmonary circulation.
x) Name the branches of the aorta and their distributions.
y) Name the major systemic veins, and the parts of the body they drain of blood.

z) Describe the pathway and purpose of hepatic portal circulation.

aa) Define blood pressure, and state the normal ranges for systemic and pulmonary blood pressure.

bb) Explain the factors that maintain systemic blood pressure.

cc) Explain how the heart and kidneys are involved in the regulation of blood pressure.

dd) Explain how the medulla and the autonomic nervous system regulate the diameter of blood vessels.

ee) Describe the functions of the lymphatic system.

ff) Describe how lymph is formed.

gg) Describe the system of lymph vessels, and explain how lymph is returned to the blood.

hh) State the locations and functions of the lymph nodes and nodules.

ii) State the location and functions of the spleen and thymus.

jj) Explain what is meant by immunity.

kk) Describe the aspects of innate immunity.

ll) Describe adaptive immunity: cell-mediated and antibody-mediated.

mm) Describe the responses to a first and second exposure to a pathogen.

nn) Explain the difference between genetic immunity and acquired immunity.

oo) Explain the difference between passive acquired immunity and active acquired immunity.

pp) Explain how vaccines work.

9.1 . CARDIOVASCULAR SYSTEM

8.1.0 Introduction to cardiovascular system

The cardiovascular system is sometimes called the blood-vascular or simply the circulatory system. It consists of the heart, which is a muscular pumping device, and a closed system of vessels called arteries, veins, and capillaries. As the name implies, blood contained in the circulatory system is pumped by the heart around a closed circle or circuit of vessels as it passes again and again through the various "circulations" of the body.

As in the adult, survival of the developing embryo depends on the circulation of blood to maintain homeostasis and a favorable cellular environment. In response to this need, the cardiovascular system makes its appearance early in development and reaches a functional state long before any other major organ system. Incredible as it seems, the primitive heart begins to beat regularly early in the fourth week following fertilization.

The vital role of the cardiovascular system in maintaining homeostasis depends on the continuous and controlled movement of blood through the thousands of miles of capillaries that permeate every tissue and reach every cell in the body. It is in the microscopic capillaries that blood performs its ultimate transport function. Nutrients and other essential materials pass from capillary blood into fluids surrounding the cells as waste products are removed.

Numerous control mechanisms help to regulate and integrate the diverse functions and component parts of the cardiovascular system in order to supply blood to specific body areas according to need. These mechanisms ensure a constant internal environment surrounding each body cell regardless of differing demands for nutrients or production of waste products.

8.1.1 Structure of cardiovascular system

It consists of Heart, blood and a closed system of vessels called arteries, veins, and capillaries.

a. Heart

The heart is a muscular pump that provides the force necessary to circulate the blood to all the tissues in the body. Its function is vital because, to survive, the tissues need a continuous supply of oxygen and nutrients, and metabolic waste products have to be removed. Deprived of these necessities, cells soon undergo irreversible changes that lead to death. While blood is the transport medium, the heart is the organ that keeps the blood moving through the vessels. The normal adult heart pumps about 5 liters of blood every minute throughout life. If it loses its pumping effectiveness for even a few minutes, the individual's life is jeopardized.

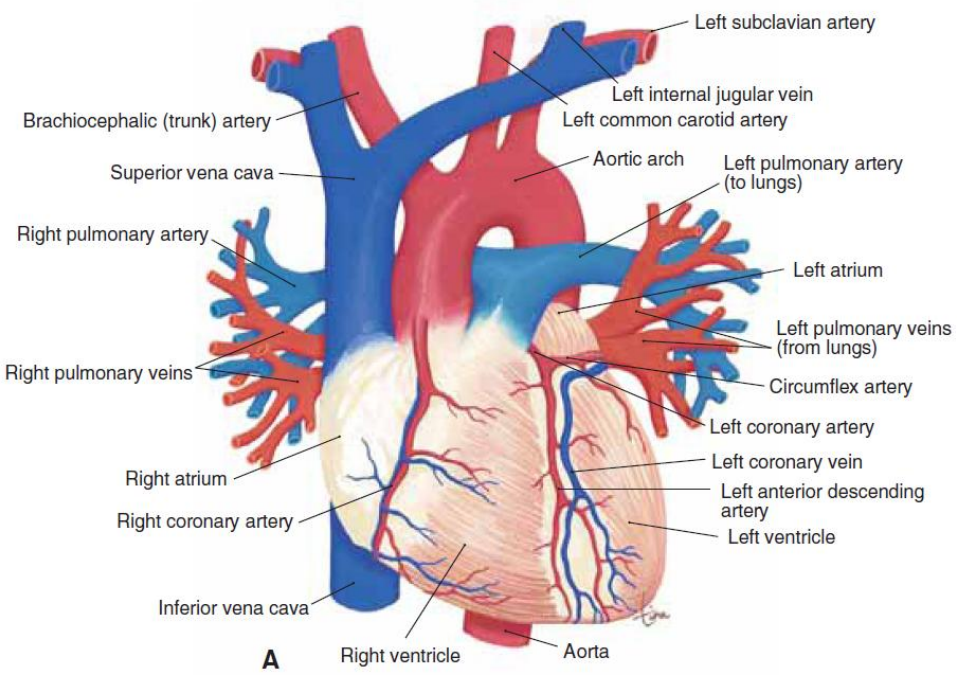


Figure*:* Anterior view of the heart and major blood vessels.

Structure of the Heart

The human heart is a four-chambered muscular organ, shaped and sized roughly like a man's closed fist with two-thirds of the mass to the left of midline. The heart is enclosed in a pericardial sac that is lined with the parietal layers of a serous membrane. The visceral layer of the serous membrane forms the epicardium. Three layers of tissue form the heart wall: The outer layer of the heart wall is the epicardium, the middle layer is the myocardium, and the inner layer is the endocardium.

Chambers, big vessels and valves of heart

The walls of the four chambers of the heart are made of cardiac muscle called the **myocardium**. The chambers are lined with **endocardium**, simple squamous epithelium that also covers the valves of the heart and continues into the vessels as their lining (endothelium). The important physical characteristic of the endocardium is not its thinness, but rather its smoothness.This very smooth tissue prevents abnormal blood clotting, because clotting would be initiated by contact of blood with a rough surface.

The upper chambers of the heart are the right and left **atria** (singular: **atrium**), which have relatively thinwalls and are separated by a common wall of myocardium called the **interatrial septum**. The lower chambers are the right and left **ventricles**, which have thicker walls and are separated by the **interventricular septum**. As you will see, the atria receive blood, either from the body or the lungs, and the ventricles pump blood to either the lungs or the body.

Right atrium

The two large **caval veins** return blood from the body to the right atrium. The **superior vena cava** carries blood from the upper body, and the **inferior vena cava** carries blood from the lower body. From the right atrium, blood will flow through the **right atrioventricular (AV) valve**, or **tricuspid valve**, into the right ventricle. The tricuspid valve is made of three flaps (or cusps) of endocardium reinforced with connective tissue. The general purpose of all valves in the circulatory system is to prevent backflow of blood. The specific purpose of the tricuspid valve is to prevent backflow of blood from the right ventricle to the right atrium when the right ventricle contracts. As the ventricle contracts, blood is forced behind the three valve flaps, forcing them upward and together to close the valve.

Left atrium

The left atrium receives blood from the lungs, by way of four **pulmonary veins**. This blood will then flow into the left ventricle through the left atrioventricular (AV) valve, also called the **mitral valve** or **bicuspid** (two flaps) valve. The mitral valve prevents backflow of blood from the left ventricle to the left atrium when the left ventricle contracts. Another function of the atria is the production of a hormone involved in blood pressure maintenance. When the walls of the atria are stretched by increased blood volume or blood pressure, the cells produce **atrial natriuretic peptide (ANP)**, also called **atrial natriuretic hormone (ANH)**. (The ventricles of the heart produce a similar hormone called B-type natriuretic peptide, or BNP, but we will use ANP as the representative cardiac hormone.) ANP decreases the reabsorption of sodium ions by the kidneys, so that more sodium ions are excreted in urine, which in turn increases the elimination of water. The loss of water lowers blood volume and blood pressure. You may have noticed that ANP is an antagonist to the hormone aldosterone, which raises blood pressure.

Right ventricle

When the right ventricle contracts, the tricuspid valve closes and the blood is pumped to the lungs through the pulmonary artery (or trunk). At the junction of this large artery and the right ventricle is the **pulmonary semilunar valve** (or more simply, pulmonary valve).Its three flaps are forced open when the right ventricle contracts and pumps blood into the pulmonary artery. When the right ventricle relaxes, blood tends to come back, but this fills the valve flaps and closes the pulmonary valve to prevent backflow of blood into the right ventricle. Projecting into the lower part of the right ventricle are columns of myocardium called **papillary muscles**. Strands of fibrous connective tissue, the **chordae tendineae**, extend from the papillary muscles to the flaps of the tricuspid valve. When the right ventricle contracts, the papillary muscles also contract and pull on the chordae tendineae to prevent inversion of the tricuspid valve. If you have ever had your umbrella blown inside out by a strong wind, you can see what would happen if the flaps of the tricuspid valve were not anchored by the chordae tendineae and papillary muscles.

Left ventricle

The walls of the left ventricle are thicker than those of the right ventricle, which enables the left ventricle to contract more forcefully. The left ventricle pumps blood to the body through the **aorta**, the largest artery of the body. At the junction of the aorta and the left ventricle is the **aortic semilunar valve** (or aortic valve). This valve is opened by the force of contraction of the left ventricle, which also closes the mitral valve. The aortic valve closes when the left ventricle relaxes, to prevent backflow of blood from the aorta to the left ventricle. When the mitral (left AV) valve closes, it prevents backflow of blood to the left atrium; the flaps of the mitral valve are also anchored by chordae tendineae and papillary muscles. **Fibrous skeleton of the heart** is fibrous connective tissue that anchors the outer edges of the valve flaps and keeps the valve openings from stretching. It also separates the myocardium of the atria and ventricles and prevents the contraction of the atria from reaching the ventricles except by way of the normal conduction pathway.

As you can see from this description of the chambers and their vessels, the heart is really a double, or two-sided, pump. The right side of the heart receives deoxygenated blood from the body

and pumps it to the lungs to pick up oxygen and release carbon dioxide. The left side of the heart receives oxygenated blood from the lungs and pumps it to the body. Both pumps work simultaneously; that is, both atria contract together, followed by the contraction of both ventricles.

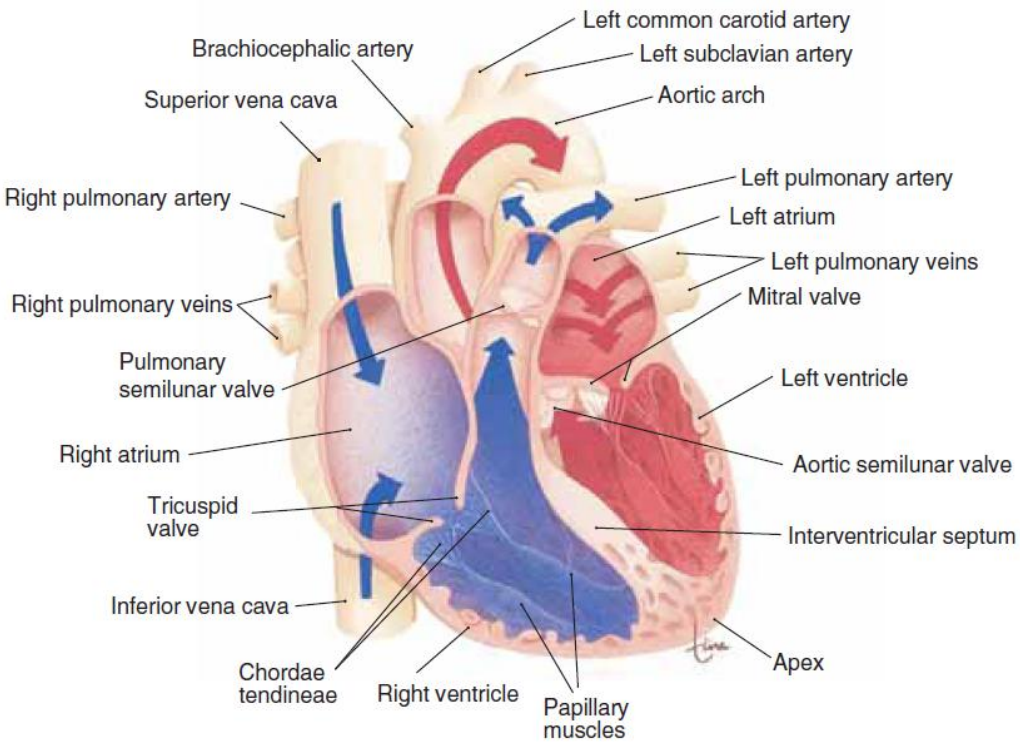


Figure: Frontal section of the heart in anterior view, showing internal structures.

Coronary vessels

The right and left **coronary arteries** are the first branches of the ascending aorta, just beyond the aortic semilunar valve. The two arteries branch into smaller arteries and arterioles, then to capillaries.The coronary capillaries merge to form coronary veins, which empty blood into a large coronary sinus that returns blood to the right atrium. The purpose of the coronary vessels is to supply blood to the myocardium itself, because oxygen is essential for normal myocardial contraction.

If a coronary artery becomes obstructed, by a blood clot for example, part of the myocardium becomes **ischemic**, that is, deprived of its blood supply. Prolonged ischemia will create an **infarct**, an area of necrotic (dead) tissue. This is a myocardial infarction, commonly called a heart attack: Coronary Artery Disease.

LOCATION AND PERICARDIAL MEMBRANES

The heart is located in the thoracic cavity between the lungs. This area is called the **mediastinum**. The base of the cone-shaped heart is uppermost, behind the sternum, and the great vessels enter or leave here. The apex (tip) of the heart points downward and is just above the diaphragm to the left of the midline. This is why we may think of the heart as being on the left side, because the strongest beat can be heard or felt here. The heart is enclosed in the **pericardial membranes**, of which there are three layers.

The outermost is the **fibrous pericardium**, a loosefitting sac of strong fibrous connective tissue that extends inferiorly over the diaphragm and superiorly over the bases of the large vessels that enter and leave the heart. The serous pericardium is a folded membrane; the fold gives it two layers, parietal and visceral. Lining the fibrous pericardium is the **parietal pericardium**. On the surface of the heart muscle is the **visceral pericardium**, often called the **epicardium**. Between the parietal and visceral pericardial membranes is **serous fluid**, which prevents friction as the heart beats.

CARDIAC CYCLE AND HEART SOUNDS

The **cardiac cycle** is the sequence of events in one heartbeat. In its simplest form, the cardiac cycle is the simultaneous contraction of the two atria, followed a fraction of a second later by the simultaneous contraction of the two ventricles. **Systole** is another term for contraction. The term for relaxation is **diastole**. You are probably familiar with these terms as they apply to blood pressure readings.

If we apply them to the cardiac cycle, we can say that atrial systole is followed by ventricular systole.

There is, however, a significant difference between the movement of blood from the atria to the ventricles and the movement of blood from the ventricles to the arteries.

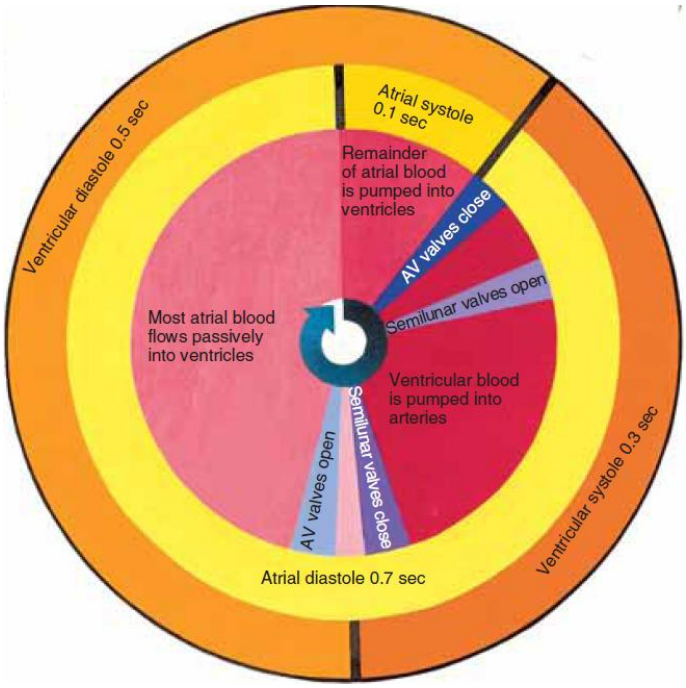


Figure: The cardiac cycle depicted in one heartbeat (pulse: 75). The outer circle represents the ventricles, the middle circle the atria, and the inner circle the movement of blood and its effect on the heart valves.

In this traditional representation, the cardiac cycle is depicted in a circle, because one heartbeat follows another, and the beginning of atrial systole is at the top (12 o'clock). The size of the segment or arc of the circle indicates how long it takes. Find the segment for atrial systole and the one for ventricular systole, and notice how much larger (meaning "longer") ventricular systole is. Do you think this might mean that ventricular contraction is more important than atrial contraction? It does, as you will see. We will begin at the bottom (6 o'clock) where the atria are in the midst of diastole and the ventricles have just completed their systole.

The entire heart is relaxed and the atria are filling with blood. Blood is constantly flowing from the veins into both atria. As more blood accumulates, its pressure forces open the right and left AV valves. Two-thirds of the atrial blood flows passively into the ventricles (which brings us to 12 o'clock); the atria then contract to pump the remaining blood into the ventricles. Following their contraction, the atria relax and the ventricles begin to contract.

Ventricular contraction forces blood against the flaps of the right and left AV valves and closes them; the force of blood also opens the aortic and pulmonary semilunar valves. As the ventricles continue to contract, they pump blood into the arteries.

Notice that blood that enters the arteries must all be pumped. The ventricles then relax, and at the same time blood continues to flow into the atria, and the cycle begins again.

The important distinction here is that most blood flows passively from atria to ventricles, but *all* blood to the arteries is actively pumped by the ventricles.For this reason, the proper functioning of the ventricles is much more crucial to survival than is atrial functioning. You may be asking "All this in one heartbeat?" The answer is yes. The cardiac cycle is this precise sequence of events that keeps blood moving from the veins, through the heart, and into the arteries.

The cardiac cycle also creates the **heart sounds**: Each heartbeat produces two sounds, often called *lubdup*, that can be heard with a stethoscope. The first sound, the loudest and longest, is caused by ventricular systole closing the AV valves. The second sound is caused by the closure of the aortic and pulmonary semilunar valves. If any of the valves do not close properly, an extra sound called a **heart murmur** may be heard.

CARDIAC CONDUCTION PATHWAY

The cardiac cycle is a sequence of mechanical events that is regulated by the electrical activity of the myocardium. Cardiac muscle cells have the ability to contract spontaneously; that is, nerve impulses are not required to cause contraction. The heart generates its own beat, and the electrical impulses follow a very specific route throughout the myocardium. The natural pacemaker of the heart is the **sinoatrial (SA) node**, a specialized group of cardiac muscle cells located in the wall of the right atrium just below the opening of the superior vena cava. The SA node is considered specialized because it has the most rapid rate of contraction, that is, it depolarizes more rapidly than any other part of the myocardium (60 to 80 times per minute). As you may recall, depolarization is the rapid entry of Na_ ions and the reversal of charges on either side of the cell membrane.

The cells of the SA node are more permeable to Na_ ions than are other cardiac muscle cells. Therefore, they depolarize more rapidly, then contract and initiate each heartbeat.From the SA node, impulses for contraction travel to the **atrioventricular (AV) node**, located in the lower interatrial septum. The transmission of impulses from the SA node to the AV node and to the rest of the atrial myocardium brings about atrial systole. Recall that the fibrous skeleton of the heart separates the atrial myocardium from the ventricular myocardium; the fibrous connective

tissue acts as electrical insulation between the two sets of chambers. Ventricles, therefore, is the **atrioventricular bundle (AV bundle)**, also called the **bundle of His**.

The AV bundle is within the upper interventricular septum; it receives impulses from the AV node and transmits them to the right and left **bundle branches**. From the bundle branches, impulses travel along **Purkinje fibers** to the rest of the ventricular myocardium and bring about ventricular systole. The electrical activity of the atria and ventricles is depicted by an electrocardiogram (ECG). If the SA node does not function properly, the AV node will initiate the heartbeat, but at a slower rate (50 to 60 beats per minute).

The AV bundle is also capable of generating the beat of the ventricles, but at abut at a much slower rate (15 to 40 beats per minute). This may occur in certain kinds of heart disease in which transmission of impulses from the atria to the ventricles is blocked. **Arrhythmias** are irregular heartbeats; their effects range from harmless to life-threatening. Nearly everyone experiences heart **palpitations** (becoming aware of an irregular beat) from time to time. These are usually not serious and may be the result of too much caffeine, nicotine, or alcohol. Much more serious is ventricular **fibrillation**, a very rapid and uncoordinated ventricular beat that is totally ineffective for pumping blood.

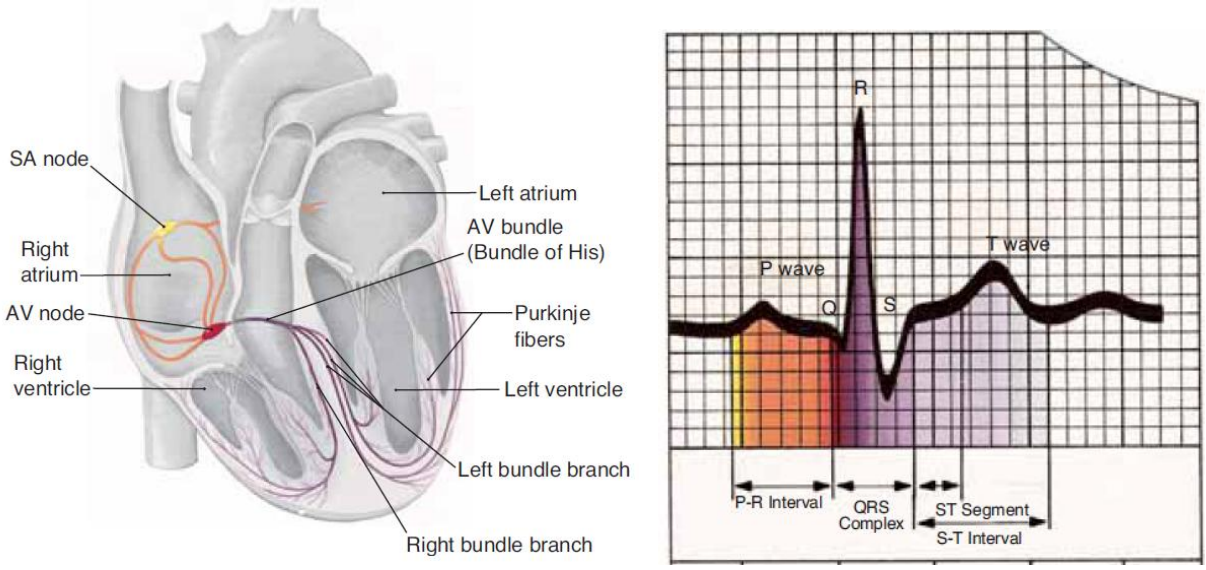


Figure: Conduction pathway of the heart. Anterior view of the interior of the heart. The electrocardiogram tracing is of one normal heartbeat.

Heart rate

A healthy adult has a resting heart rate (**pulse**) of 60 to 80 beats per minute, which is the rate of depolarization of the SA node. (The SA node actually has a slightly faster rate, closer to 100 beats per minute, but is slowed by parasympathetic nerve impulses to what we consider a normal resting rate.) A rate less than 60 (except for athletes) is called **bradycardia**; a prolonged or consistent rate greater than 100 beats per minute is called **tachycardia**.

A child's normal heart rate may be as high as 100 beats per minute, that of an infant as high as 120, and that of a near-term fetus as high as 140 beats per minute. These higher rates are not related to age, but rather to size: the smaller the individual, the higher the metabolic rate and the faster the heart rate. Parallels may be found among animals of different sizes; the heart rate of a mouse is about 200 beats per minute and that of an elephant about 30 beats per minute.

Let us return to the adult heart rate and consider the person who is in excellent physical condition. As you may know, well-conditioned athletes have low resting pulse rates. Those of basketball players are often around 50 beats per minute, and the pulse of a marathon runner often ranges from 35 to 40 beats per minute. To understand why this is so, remember that the heart is a muscle. When our skeletal muscles are exercised, they become stronger and more efficient. The same is true for the heart; consistent exercise makes it a more efficient pump, as you will see in the next section.

Cardiac output

Cardiac output is the amount of blood pumped by a ventricle in 1 minute. A certain level of cardiac output is needed at all times to transport oxygen to tissues and to remove waste products. During exercise, cardiac output must increase to meet the body's need for more oxygen. We will return to exercise after first considering resting cardiac output. To calculate cardiac output, we must know the pulse rate and how much blood is pumped per beat. **Stroke volume** is the term for the amount of blood pumped by a ventricle per beat; an average resting stroke volume is 60 to 80 mL per beat. A simple formula then enables us to determine cardiac output:

Cardiac output =stroke volume × pulse (heart rate)

Let us put into this formula an average resting stroke volume, 70 mL, and an average resting pulse, 70 beats per minute (bpm): Cardiac output = 70 mL × 70 bpm Cardiac output =4900 mL per minute (approximately 5 liters) Naturally, cardiac output varies with the size of the person, but the average resting cardiac output is 5 to 6 liters per minute.

Notice that this amount is just about the same as a person's average volume of blood. At rest, the heart pumps all of the blood in the body within about a minute. Changes are possible, depending on circumstances and extent of physical activity. If we now reconsider the athlete, you will be able to see precisely why the athlete has a low resting pulse. In our formula, we will use an average resting cardiac output (5 liters) and an athlete's pulse rate (50):

Cardiac output = stroke volume× pulse

5000 mL= stroke volume × 50 bpm

5000/50 = stroke volume

100 mL = stroke volume

Notice that the athlete's resting stroke volume is significantly higher than the average. The athlete's more efficient heart pumps more blood with each beat and so can maintain a normal resting cardiac output with fewer beats.Now let us see how the heart responds to exercise. Heart rate (pulse) increases during exercise, and so does stroke volume. The increase in stroke volume is the result of **Starling's law of the heart**, which states that the more the cardiac muscle fibers are stretched, the more forcefully they contract.

During exercise, more blood returns to the heart; this is called **venous return**. Increased venous return stretches the myocardium of the ventricles, which contract more forcefully and pump more blood, thereby increasing stroke volume. Therefore, during exercise, our formula might be the following:

Cardiac output = stroke volume ×pulse

Cardiac output = 100 mL × 100 bpm

Cardiac output =10,000 mL (10 liters)

This exercise cardiac output is twice the resting cardiac output we first calculated, which should not be considered unusual. The cardiac output of a healthy young person may increase up to four times the resting level during strenuous exercise.

This difference is the **cardiac reserve**, the extra volume the heart can pump when necessary. If resting cardiac output is 5 liters and exercise cardiac output is 20 liters, the cardiac reserve is 15 liters. The marathon runner's cardiac output may increase six times or more compared to the resting level and cardiac reserve is even greater than for the average young person; this is the result of the marathoner's extremely efficient heart. Because of Starling's law, it is almost impossible to overwork a healthy heart.

No matter how much the volume of venous return increases, the ventricles simply pump more forcefully and increase the stroke volume and cardiac output.Also related to cardiac output, and another measure of the health of the heart, is the **ejection fraction**. This is the percent of the blood in a ventricle that is pumped during systole. A ventricle does not empty completely when it contracts, but should pump out 60% to 70% of the blood within it. A lower percentage would indicate that the ventricle is weakening.

Regulation of heart rate

Although the heart generates and maintains its own beat, the rate of contraction can be changed to adapt to different situations. The nervous system can and does bring about necessary changes in heart rate as well as in force of contraction. The **medulla** of the brain contains the two cardiac centers, the **accelerator center** and the **inhibitory center**.

These centers send impulses to the heart along autonomic nerves. Recall that the autonomic nervous system has two divisions: sympathetic and parasympathetic. Sympathetic impulses from the accelerator center along sympathetic nerves increase heart rate and force of contraction during exercise and stressful situations. Parasympathetic impulses from the inhibitory center along the vagus nerves decrease the heart rate. At rest these impulses slow down the depolarization of the SA node to what we consider a normal resting rate, and they also slow the heart after exercise is over.

Our next question might be: What information is received by the medulla to initiate changes? Because the heart pumps blood, it is essential to maintain normal blood pressure. Blood contains oxygen, which all tissues must receive continuously. Therefore, changes in blood pressure and oxygen level of the blood are stimuli for changes in heart rate. You may also recall that pressoreceptors and chemoreceptors are located in the carotid arteries and aortic arch.

Pressoreceptors in the carotid sinuses and aortic sinus detect changes in blood pressure. **Chemoreceptors** in the carotid bodies and aortic body detect changes in the oxygen content of the blood. The sensory nerves for the carotid receptors are the glossopharyngeal (9th cranial) nerves; the sensory nerves for the aortic arch receptors are the vagus (10th cranial) nerves.

If we now put all of these facts together in a specific example, you will see that the regulation of heart rate is a reflex. A person who stands up suddenly from a lying position may feel light-headed or dizzy for a few moments, because blood pressure to the brain has decreased abruptly. The drop in blood pressure is detected by pressoreceptors in the carotid sinuses—notice that they are "on the way" to the brain, a very strategic location. The drop in blood pressure causes fewer impulses to be generated by the pressoreceptors.

These impulses travel along the glossopharyngeal nerves to the medulla, and the decrease in the frequency of impulses stimulates the accelerator center. The accelerator center generates impulses that are carried by sympathetic nerves to the SA node, AV node, and ventricular myocardium. As heart rate and force increase, blood pressure to the brain is raised to normal, and the sensation of light-headedness passes.

When blood pressure to the brain is restored to normal, the heart receives more parasympathetic impulses from the inhibitory center along the vagus nerves to the SA node and AV node. These parasympathetic impulses slow the heart rate to a normal resting pace. The heart will also be the effector in a reflex stimulated by a decrease in the oxygen content of the blood.

The aortic receptors are strategically located so as to detect such an important change as soon as blood leaves the heart. The reflex arc in this situation would be (1) aortic chemoreceptors, (2) vagus nerves (sensory), (3) accelerator center in the medulla, (4) sympathetic nerves, and (5) the heart muscle, which will increase its rate and force of contraction to circulate more oxygen to correct the hypoxia.

Recall also that the hormone epinephrine is secreted by the adrenal medulla in stressful situations. One of the many functions of epinephrine is to increase heart rate and force of contraction. This will help supply more blood to tissues in need of more oxygen.

AGING AND THE HEART

The heart muscle becomes less efficient with age, and there is a decrease in both maximum cardiac output and heart rate, although resting levels may be more than adequate. The health of the myocardium depends on its blood supply, and with age there is greater likelihood that atherosclerosis will narrow the coronary arteries. Atherosclerosis is the deposition of cholesterol on and in the walls of the arteries, which decreases blood flow and forms rough surfaces that may cause intravascular clot formation. High blood pressure (hypertension) causes the left ventricle to work harder; it may enlarge and outgrow its blood supply, thus becoming weaker.

A weak ventricle is not an efficient pump, and such weakness may progress to congestive heart failure; such a progression may be slow, or may be rapid. The heart valves may become thickened by fibrosis, leading to heart murmurs and less efficient pumping. Arrhythmias are also more common with age, as the cells of the conduction pathway become less efficient.

- **Applications to the nursing care**

1. CORONARY ARTERY DISEASE

Coronary artery disease results in decreased blood flow to the myocardium. If blood flow is diminished but not completely obstructed, the person may experience difficulty breathing and angina, which is chest pain caused by lack of oxygen to part of the heart muscle. If blood flow is completely blocked, however, the result is a myocardial infarction (necrosis of cardiac muscle). The most common cause of coronary artery disease is **atherosclerosis**. Plaques of cholesterol form in the walls of a coronary artery; this narrows the lumen (cavity) and creates a rough surface where a clot (thrombus) may form. A predisposing factor for such clot formation, one that cannot be changed, is a family history of coronary artery disease.

There is no "gene for heart attacks," but we do have genes for the enzymes involved in cholesterol metabolism. Many of these are liver enzymes that regulate the transport of cholesterol in the blood in the form of lipoproteins and regulate the liver's excretion of excess cholesterol in bile. Some people, therefore, have a greater tendency than others to have higher blood levels of cholesterol and certain lipoproteins. In women before menopause, estrogen is believed to exert a

protective effect by lowering blood lipid levels. This is why heart attacks in the 30- to 50-year-old age range are less frequent in women than in men. Other predisposing factors for atherosclerosis include cigarette smoking, diabetes mellitus, and high blood pressure. Any one of these may cause damage to the lining of coronary arteries, which is the first step in the abnormal deposition of cholesterol. A diet high in cholesterol and saturated fats and high blood levels of these lipids will increase the rate of cholesterol deposition.

A possible chemical marker of risk is a high blood level of homocysteine. Homocysteine is a metabolic product of the essential amino acid methionine, and may be converted back to methionine or further changed and excreted by the kidneys. A high blood level of homocysteine may indicate inflammation of the walls of arteries. Yet another chemical marker of inflammation is C-reactive protein (CRP). There is still much to learn about the role of inflammation in atherosclerosis, but simple blood tests for chemical markers may someday provide a diagnosis before heart damage occurs. When coronary artery disease becomes lifethreatening, coronary artery bypass surgery may be performed. In this procedure, a synthetic vessel or a vein (such as the saphenous vein of the leg) is grafted around the obstructed coronary vessel to restore blood flow to the myocardium. This is not a cure, for atherosclerosis may occur in a grafted vein or at other sites in the coronary arteries.

2. HEART MURMUR

A heart murmur is an abnormal or extra heart sound caused by a malfunctioning heart valve. The function of heart valves is to prevent backflow of blood, and when a valve does not close properly, blood will regurgitate (go backward), creating turbulence that may be heard with a stethoscope. Rheumatic heart disease is now uncommon complication of a streptococcal infection. In rheumatic fever, the heart valves are damaged by an abnormal response by the immune system. Erosion of the valves makes them "leaky" and inefficient, and a murmur of backflowing blood will be heard.

Mitral valve regurgitation, for example, will be heard as a systolic murmur, because this valve is meant to close and prevent backflow during ventricular systole. Some valve defects involve a narrowing (**stenosis**) and are congenital; that is, the child is born with an abnormally narrow

valve. In aortic stenosis, for example, blood cannot easily pass from the left ventricle to the aorta. The ventricle must then work harder to pump blood through the narrow valve to the arteries, and the turbulence created is also heard as a systolic murmur. Children sometimes have heart murmurs that are called "functional" because no structural cause can be found. These murmurs usually disappear with no adverse effects on the child.

3. ELECTROCARDIOGRAM

Heartbeat is a series of electrical events, and the electrical changes generated by the myocardium can be recorded by placing electrodes on the body surface. Such a recording is called an **electrocardiogram (ECG)**. A typical ECG consists of three distinguishable waves or deflections: the P wave, the QRS complex, and the T wave. Each represents a specific electrical event. The P wave represents depolarization of the atria, that is, the transmission of electrical impulses from the SA node throughout the atrial myocardium.

The QRS complex represents depolarization of the ventricles as the electrical impulses spread throughout the ventricular myocardium. The T wave represents repolarization of the ventricles (atrial repolarization does not appear as a separate wave because it is masked by the QRS complex). In general, the length of each wave and the time intervals between waves are noted. An ECG may be helpful in the diagnosis of coronary atherosclerosis, which deprives the myocardium of oxygen, or of rheumatic fever or other valve disorders that result in enlargement of a chamber of the heart and prolong a specific wave of an ECG. For example, the enlargement of the left ventricle that is often a consequence of hypertension may be indicated by an abnormal QRS complex.

4. ARRHYTHMIAS

Arrhythmias (also called dysrhythmias) are irregular heartbeats caused by damage to part of the conduction pathway, or by an **ectopic focus**, which is a beat generated in part of the myocardium other than the SA node. **Flutter** is a very rapid but fairly regular heartbeat. In atrial flutter, the atria may contract up to 300 times per minute.

Because atrial pumping is not crucial, however, blood flow to the ventricles may be maintained for a time, and flutter may not be immediately life-threatening.

Ventricular flutter is usually only a brief transition between ventricular tachycardia and fibrillation. **Fibrillation** is very rapid and uncoordinated contractions. Ventricular fibrillation is a medical emergency that must be quickly corrected to prevent death. Normal contraction of the ventricles is necessary to pump blood into the arteries, but fibrillating ventricles are not pumping, and cardiac output decreases sharply.

Ventricular fibrillation may follow a non-fatal heart attack (myocardial infarction). Damaged cardiac muscle cells may not be able to maintain a normal state of polarization, and they depolarize spontaneously and rapidly. From this ectopic focus, impulses spread to other parts of the ventricular myocardium in a rapid and haphazard pattern, and the ventricles quiver rather than contract as a unit. It is often possible to correct ventricular fibrillation with the use of an electrical defibrillator. This instrument delivers an electric shock to the heart, which causes the entire myocardium to depolarize and contract, then relax.

If the first part of the heart to recover is the SA node (which usually has the most rapid rate of contraction), a normal heartbeat may be restored.

b. The vascular system

The role of blood vessels in the circulation of blood has been known since 1628, when William Harvey, an English anatomist, demonstrated that blood in veins always flowed toward the heart. Before that time, it was believed that blood was static or stationary, some of it within the vessels but the rest sort of in puddles throughout the body.

Harvey showed that blood indeed does move, and only in the blood vessels (though he did not know of the existence of capillaries). In the centuries that followed, the active (rather than merely passive) roles of the vascular system were discovered, and all contribute to homeostasis.

The vascular system consists of the arteries, capillaries, and veins through which the heart pumps blood throughout the body. As you will see, the major "business" of the vascular system, which is the exchange of materials between the blood and tissues, takes place in the capillaries. The arteries and veins, however, are just as important, transporting blood between the capillaries and the heart. Another important topic of this chapter will be blood pressure (BP), which is the force the blood exerts against the walls of the vessels. Normal blood pressure is essential for circulation and for some of the material exchanges that take place in capillaries.

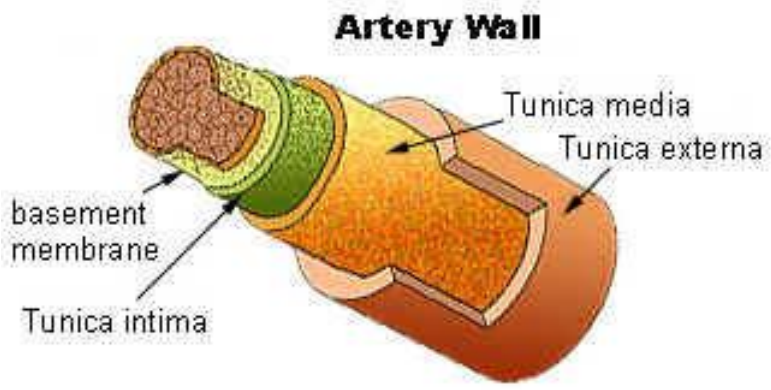
Arteries

Arteries carry blood from the heart to capillaries; smaller arteries are called **arterioles**. If we look at an artery in cross-section, we find three layers (or tunics) of tissues, each with different functions. The innermost layer, the **tunica intima**, is the only part of a vessel that is in contact with blood. It is made of simple squamous epithelium called **endothelium**. This lining is the same type of tissue that forms the endocardium, the lining of the chambers of the heart.

As you might guess, its function is also the same: Its extreme smoothness prevents abnormal blood clotting. The endothelium of vessels, however, also produces nitric oxide (NO), which is a vasodilator. The **tunica media**, or middle layer, is made of smooth muscle and elastic connective tissue. Both of these tissues are involved in the maintenance of normal blood pressure, especially diastolic blood pressure when the heart is relaxed.

The smooth muscle is the tissue affected by the vasodilator NO; relaxation of this muscle tissue brings about dilation of the vessel. Smooth muscle also has a nerve supply; sympathetic nerve impulses bring about vasoconstriction. Fibrous connective tissue forms the outer layer, the **tunica externa**. This tissue is very strong, which is important to prevent the rupture or bursting of the larger arteries that carry blood under high pressure.

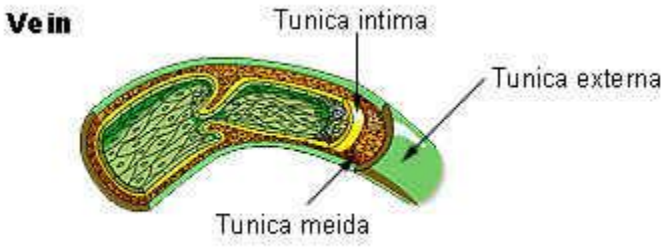
The outer and middle layers of large arteries are quite thick. In the smallest arterioles, only individual smooth muscle cells encircle the tunica intima. As mentioned, the smooth muscle layer enables arteries to constrict or dilate. Such changes in diameter are regulated by the medulla and autonomic nervous system, and will be discussed in a later section on blood pressure.



Veins

Veins carry blood from capillaries back to the heart; the smaller veins are called **venules**. The same three tissue layers are present in veins as in the walls of arteries, but there are some differences when compared to the arterial layers. The inner layer of veins is smooth endothelium, but at intervals this lining is folded to form **valves**.

Valves prevent backflow of blood and are most numerous in veins of the legs, where blood must often return to the heart against the force of gravity. The middle layer of veins is a thin layer of smooth muscle. It is thin because veins do not regulate blood pressure and blood flow into capillaries as arteries do.Veins can constrict extensively, however, and this function becomes very important in certain situations such as severe hemorrhage. The outer layer of veins is also thin; not as much fibrous connective tissue is necessary because blood pressure in veins is very low.



Anastomoses

An **anastomosis** is a connection, or joining, of vessels, that is, artery to artery or vein to vein. The general purpose of these connections is to provide alternate pathways for the flow of blood if one vessel becomes obstructed. An arterial anastomosis helps ensure that blood will get to the capillaries of an organ to deliver oxygen and nutrients and to remove waste products.

There are arterial anastomoses, for example, between some of the coronary arteries that supply blood to the myocardium.

A venous anastomosis helps ensure that blood will be able to return to the heart in order to be pumped again. Venous anastomoses are most numerous among the veins of the legs, where the possibility of obstruction increases as a person gets older.

Capillaries

Capillaries carry blood from arterioles to venules. Their walls are only one cell in thickness; capillaries are actually the extension of the endothelium, the simple squamous lining, of arteries and veins. Some tissues do not have capillaries; these are the epidermis, cartilage, and the lens and cornea of the Eye.Most tissues, however, have extensive capillary networks.The quantity or volume of capillary networks in an organ reflects the metabolic activity of the organ. The functioning of the kidneys, for example, depends upon a good blood supply. In contrast, a tendon such as the Achilles tendon at the heel or the patellar tendon at the knee would have far fewer vessels, because fibrous connective tissue is far less metabolically active.

Blood flow into capillary networks is regulated by smooth muscle cells called **precapillary sphincters**, found at the beginning of each network. Precapillary sphincters are not regulated by the nervous system but rather constrict or dilate depending on the needs of the tissues. Because there is not enough blood in the body to fill all of the capillaries at once, precapillary sphincters are usually slightly constricted. In an active tissue that requires more oxygen, such as exercising muscle, the precapillary sphincters dilate to increase blood flow.

These automatic responses ensure that blood, the volume of which is constant, will circulate where it is needed most. Some organs have another type of capillary called **sinusoids**, which are larger and more permeable than are other capillaries. The permeability of sinusoids permits large substances such as proteins and blood cells to enter or leave the blood. Sinusoids are found in the red bone marrow and spleen, where blood cells enter or leave the blood, and in organs such as the liver and pituitary gland, which produce and secrete proteins into the blood.

Exchanges in capillaries

Capillaries are the sites of exchanges of materials between the blood and the tissue fluid surrounding cells. Some of these substances move from the blood to tissue fluid, and others move from tissue fluid to the blood. Gases move by **diffusion**, that is, from their area of greater concentration to their area of lesser concentration. Oxygen, therefore, diffuses from the blood in systemic capillaries to the tissue fluid, and carbon dioxide diffuses from tissue fluid to the blood to be brought to the lungs and exhaled.

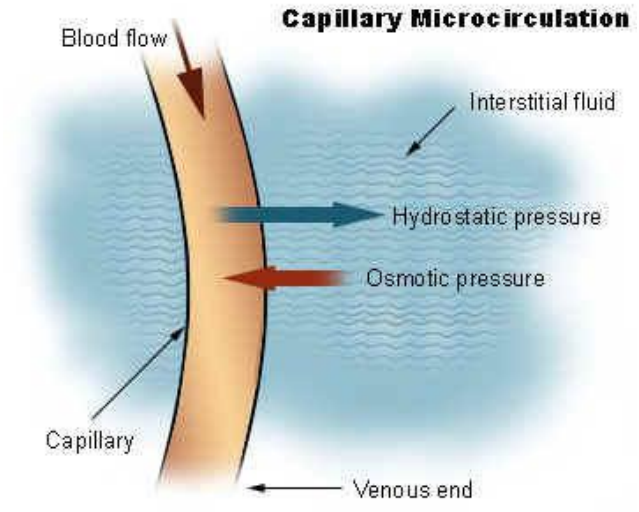
Let us now look at the blood pressure as blood enters capillaries from the arterioles. Blood pressure here is about 30 to 35 mmHg, and the pressure of the surrounding tissue fluid is much lower, about 2 mmHg. Because the capillary blood pressure is higher, the process of **filtration** occurs, which forces plasma and dissolved nutrients out of the capillaries and into tissue fluid. This is how nutrients such as glucose, amino acids, and vitamins are brought to cells.

Blood pressure decreases as blood reaches the venous end of capillaries, but notice that proteins such as albumin have remained in the blood. Albumin contributes to the **colloid osmotic pressure** (COP) of blood; this is an "attracting" pressure, a "pulling" rather than a "pushing" pressure. At the venous end of capillaries, the presence of albumin in the blood pulls tissue fluid into the capillaries, which also brings into the blood the waste products produced by cells.

The tissue fluid that returns to the blood also helps maintain normal blood volume and blood pressure.

The amount of tissue fluid formed is slightly greater than the amount returned to the capillaries. If this were to continue, blood volume would be gradually depleted.

The excess tissue fluid, however, enters lymph capillaries. Now called lymph, it will be returned to the blood to be recycled again as plasma, thus maintaining blood volume.

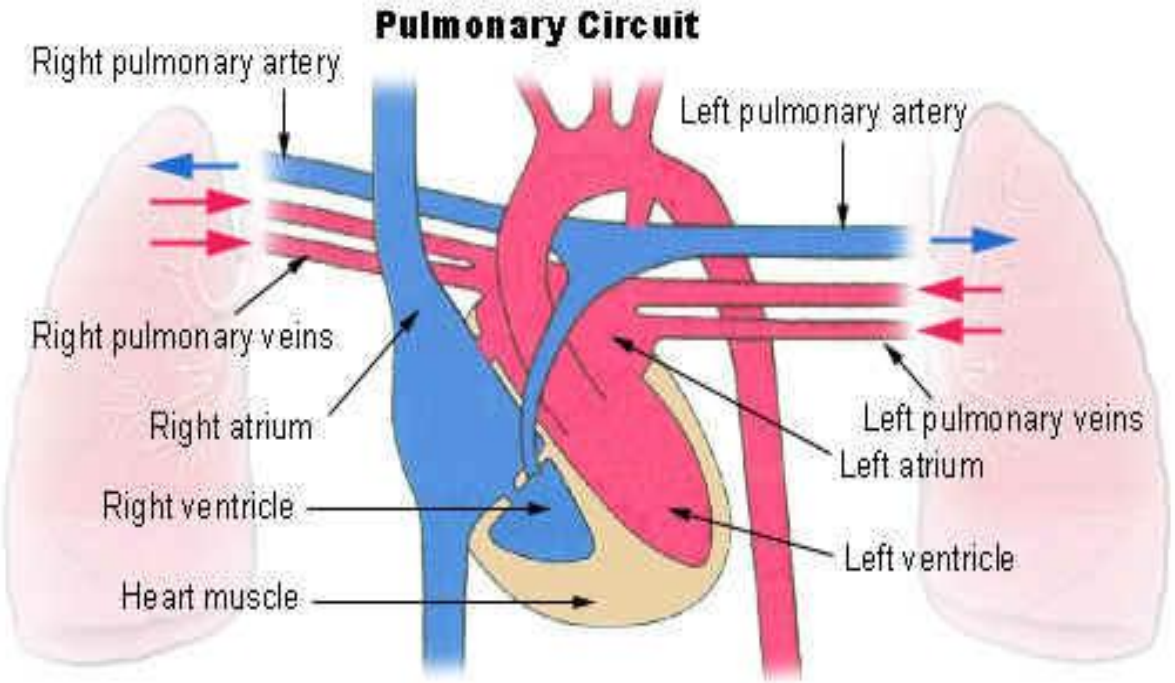


8.1.2 Pathways of circulation

The two major pathways of circulation are pulmonary and systemic. Pulmonary circulation begins at the right ventricle, and systemic circulation begins at the left ventricle. Hepatic portal circulation is a special segment of systemic circulation that will be covered separately. Fetal circulation involves pathways that are present only before birth and will also be discussed separately.

1. Pulmonary circulation

The right ventricle pumps blood into the pulmonary artery (or trunk), which divides into the right and left pulmonary arteries, one going to each lung. Within the lungs each artery branches extensively into smaller arteries and arterioles, then to capillaries. The pulmonary capillaries surround the alveoli of the lungs; it is here that exchanges of oxygen and carbon dioxide take place. The capillaries unite to form venules, which merge into veins, and finally into the two pulmonary veins from each lung that return blood to the left atrium. This oxygenated blood will then travel through the systemic circulation. (Notice that the pulmonary veins contain oxygenated blood; these are the only veins that carry blood with a high oxygen content. The blood in systemic veins has a low oxygen content; it is systemic arteries that carry oxygenated blood.)



2. Systemic circulation

The left ventricle pumps blood into the aorta, the largest artery of the body. We will return to the aorta and its branches in a moment, but first we will summarize the rest of systemic circulation. The branches of the aorta take blood into arterioles and capillary networks throughout the body. Capillaries merge to form venules and veins. The veins from the lower body take blood to the inferior vena cava; veins from the upper body take blood to the superior vena cava. These two caval veins return blood to the right atrium. The aorta is a continuous vessel, but for the sake of precise description it is divided into sections that are named anatomically: ascending aorta, aortic arch, thoracic aorta, and abdominal aorta. The ascending aorta is the first inch that emerges from the top of the left ventricle.

The arch of the aorta curves posteriorly over the heart and turns downward. The thoracic aorta continues down through the chest cavity and through the diaphragm. Below the level of the diaphragm, the abdominal aorta continues to the level of the 4th lumbar vertebra, where it divides into the two common iliac arteries. Along its course, the aorta has many branches through which blood travels to specific organs and parts of the body. The ascending aorta has only two branches: the right and left coronary arteries, which supply blood to the myocardium.The aortic arch has three branches that supply blood to the head and arms: the brachiocephalic artery, left common carotid artery, and left subclavian artery.

The brachiocephalic (literally, "arm-head") artery is very short and divides into the right common carotid artery and right subclavian artery. The right and left common carotid arteries extend into the neck, where each divides into an internal carotid artery and external carotid artery, which supply the head. The right and left subclavian arteries are in the shoulders behind the clavicles and continue into the arms. As the artery enters another body area (it may not "branch," simply continue), its name changes: The subclavian artery becomes the axillary artery, which becomes the brachial artery. Keep in mind that the name of the vessel often tells us where it is. The facial artery, for example, is found in the face. Some of the arteries in the head contribute to an important arterial anastomosis, the **circle of Willis** (or cerebral arterial circle), which is a "circle" of arteries around the pituitary.

The circle of Willis is formed by the right and left internal carotid arteries and the basilar artery, which is the union of the right and left vertebral arteries (branches of the subclavian arteries).

The brain is always active, even during sleep, and must have a constant flow of blood to supply oxygen and remove waste products. For this reason there are four vessels that bring blood to the circle of Willis. From this anastomosis, several paired arteries (the cerebral arteries) extend into the brain itself. The thoracic aorta and its branches supply the chest wall and the organs within the thoracic cavity. The abdominal aorta gives rise to arteries that supply the abdominal wall and organs and to the common iliac arteries, which continue into the legs. Notice in that the common iliac artery becomes the external iliac artery, which becomes the femoral artery, which becomes the popliteal artery; the same vessel has different names based on location. The systemic veins drain blood from organs or parts of the body and often parallel their corresponding arteries.

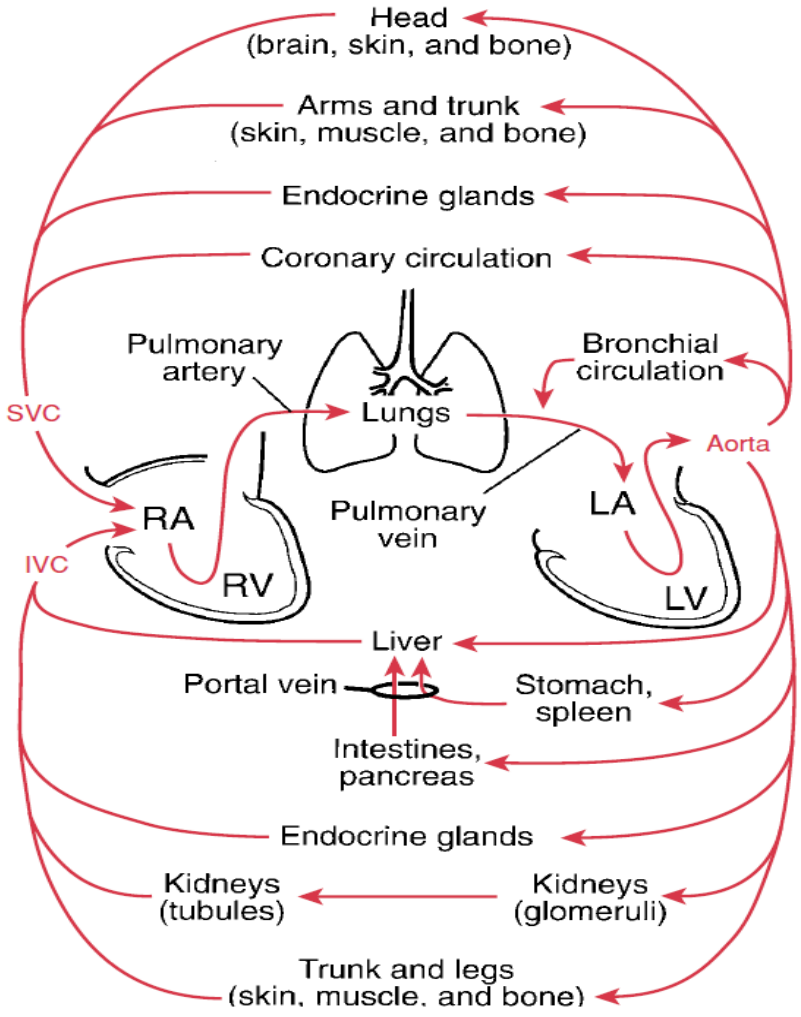


Figure: Systemic circulation

HEPATIC PORTAL CIRCULATION

Hepatic portal circulation is a subdivision of systemic circulation in which blood from the abdominal digestive organs and spleen circulates through the liver before returning to the heart. Blood from the capillaries of the stomach, small intestine, colon, pancreas, and spleen flows into two large veins, the superior mesenteric vein and the splenic vein, which unite to form the portal vein. The portal vein takes blood into the liver, where it branches extensively and empties blood into the sinusoids, the capillaries of the liver. From the sinusoids, blood flows into hepatic veins, to the inferior vena cava and back to the right atrium.

Notice that in this pathway there are two sets of capillaries, and keep in mind that it is in capillaries that exchanges take place. Let us use some specific examples to show the purpose and importance of portal circulation. Glucose from carbohydrate digestion is absorbed into the capillaries of the small intestine; after a big meal this may greatly increase the blood glucose level.

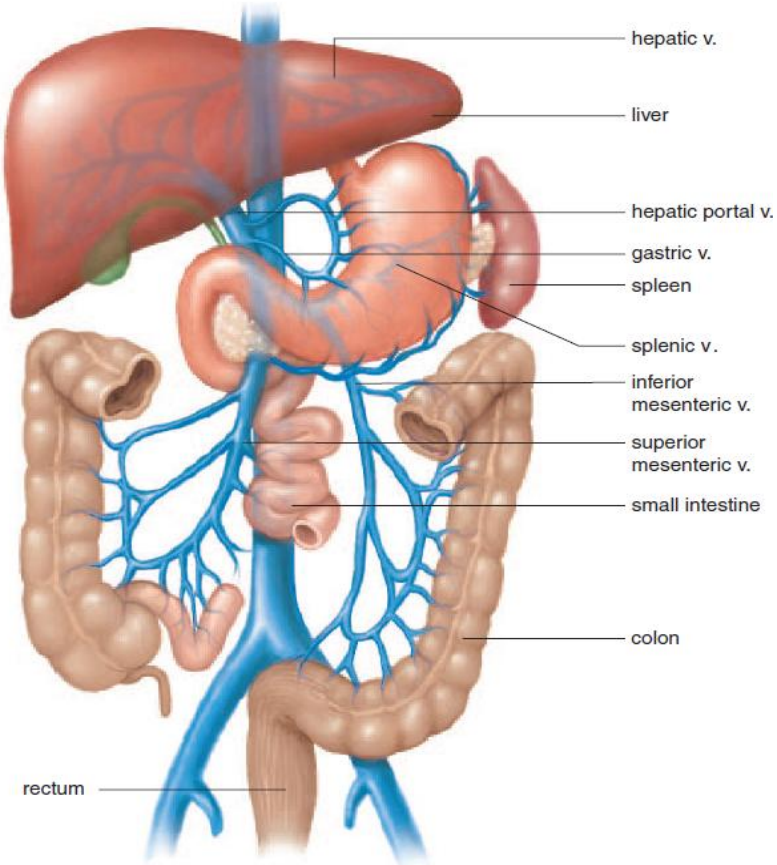


Figure: Hepatic portal circulation

If this blood were to go directly back to the heart and then circulate through the kidneys, some of the glucose might be lost in urine. However, blood from the small intestine passes first through the liver sinusoids, and the liver cells remove the excess glucose and store it as glycogen. The blood that returns to the heart will then have a blood glucose level in the normal range. Another example: Alcohol is absorbed into the capillaries of the stomach. If it were to circulate directly throughout the body, the alcohol would rapidly impair the functioning of the brain.

Portal circulation, however, takes blood from the stomach to the liver, the organ that can detoxify the alcohol and prevent its detrimental effects on the brain. Of course, if alcohol consumption continues, the blood alcohol level rises faster than the liver's capacity to detoxify, and the well known signs of alcohol intoxication appear. As you can see, this portal circulation pathway enables the liver to modify the blood from the digestive organs and spleen. Some nutrients may be stored or changed, bilirubin from the spleen is excreted into bile, and potential poisons are detoxified before the blood returns to the heart and the rest of the body.

FETAL CIRCULATION

The fetus depends upon the mother for oxygen and nutrients and for the removal of carbon dioxide and other waste products. The site of exchange between fetus and mother is the **placenta**, which contains fetal and maternal blood vessels that are very close to one another. The blood of the fetus does not mix with the blood of the mother; substances are exchanged by diffusion and active transport mechanisms.

The fetus is connected to the placenta by the umbilical cord, which contains two umbilical arteries and one umbilical vein. The **umbilical arteries** are branches of the fetal internal iliac arteries; they carry blood from the fetus to the placenta. In the placenta, carbon dioxide and waste products in the fetal blood enter maternal circulation, and oxygen and nutrients from the mother's blood enter fetal circulation. The **umbilical vein** carries this oxygenated blood from the placenta to the fetus. Within the body of the fetus, the umbilical vein branches: One branch takes some blood to the fetal liver, but most of the blood passes through the **ductus venosus** to the inferior vena cava, to the right atrium.

After birth, when the umbilical cord is cut, the remnants of these fetal vessels constrict and become nonfunctional. The other modifications of fetal circulation concern the fetal heart and

large arteries.Because the fetal lungs are deflated and do not provide for gas exchange, blood is shunted away from the lungs and to the body. The **foramen ovale** is an opening in the interatrial septum that permits some blood to flow from the right atrium to the left atrium, not, as usual, to the right ventricle. The blood that does enter the right ventricle is pumped into the pulmonary artery. The **ductus arteriosus** is a short vessel that diverts most of the blood in the pulmonary artery to the aorta, to the body. Both the foramen ovale and the ductus arteriosus permit blood to bypass the fetal lungs. Just after birth, the baby breathes and expands its lungs, which pulls more blood into the pulmonary circulation. More blood then returns to the left atrium, and a flap on the left side of the foramen ovale is closed.

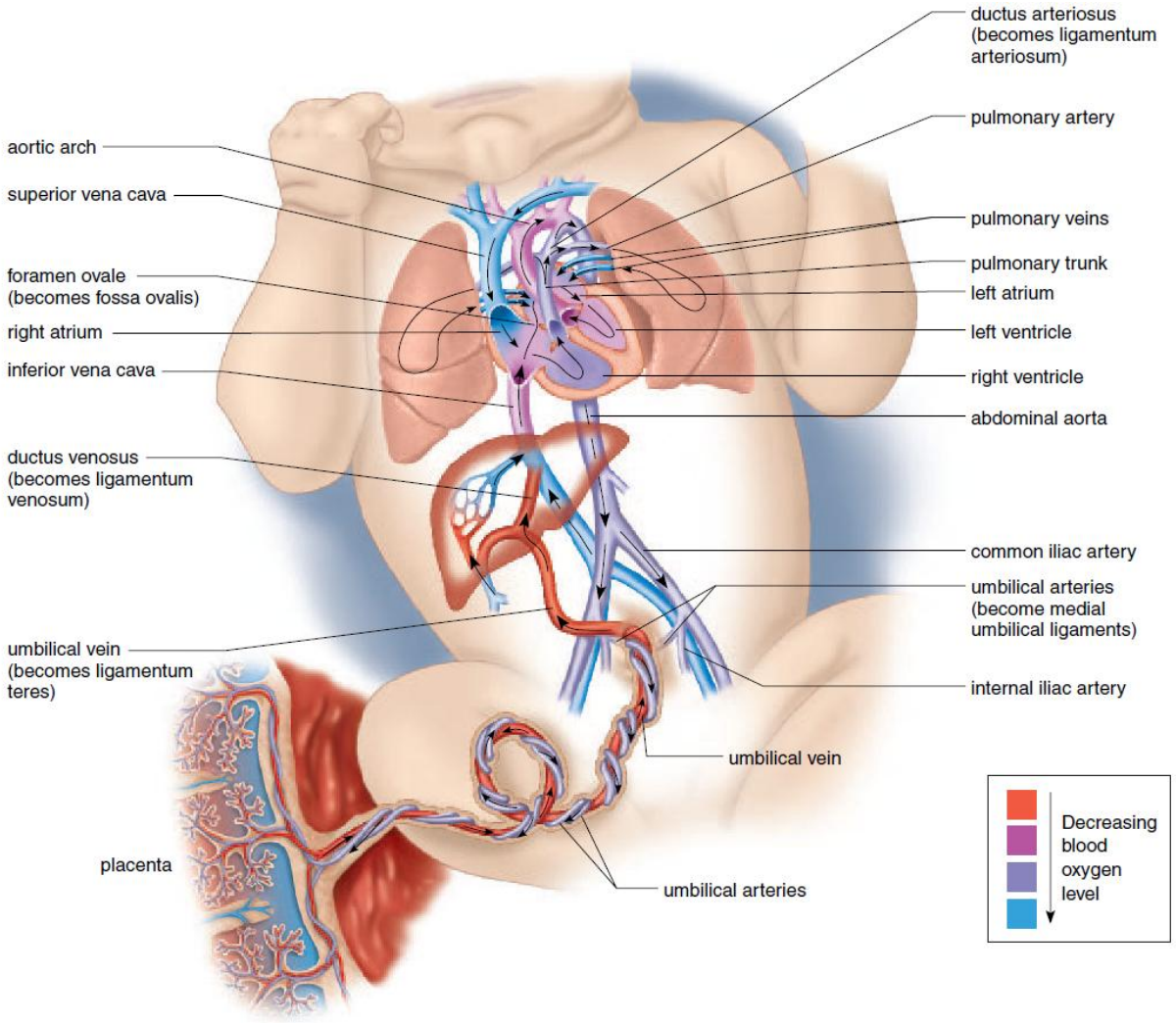


Figure: Fetal circulation

The ductus arteriosus constricts, probably in response to the higher oxygen content of the blood, and pulmonary circulation becomes fully functional within a few days.

VELOCITY OF BLOOD FLOW

The velocity, or speed, with which blood flows, differs in the various parts of the vascular system. Velocity is inversely related (meaning as one value goes up, the other goes down) to the cross-sectional area of the particular segment of the vascular system. The aorta receives all the blood from the left ventricle, its cross-sectional area is small, about 3 cm2, and the blood moves very rapidly, at least 30 cm per second (about 12 inches). Each time the aorta or any artery branches, the total cross-sectional area becomes larger, and the speed of blood flow decreases. Think of a river that begins in a narrow bed and is flowing rapidly.

If the river bed widens, the water spreads out to fill it and flows more slowly. If the river were to narrow again, the water would flow faster. This is just what happens in the vascular system. The capillaries in total have the greatest crosssectional area, and blood velocity there is slowest, less than 0.1 cm per second. When capillaries unite to form venules, and then veins, the cross-sectional area decreases and blood flow speeds up. Recall that it is in capillary networks that exchanges of nutrients, wastes, and gases take place between the blood and tissue fluid.

The slow rate of blood flow in capillaries permits sufficient time for these essential exchanges. Think of a train slowing down (not actually stopping) at stations to allow people to jump on and off, then speeding up again to get to the next station. The capillaries are the "stations" of the vascular system. The more rapid blood velocity in other vessels makes circulation time quite short. This is the time it takes for blood to go from the right ventricle to the lungs, back to the heart to be pumped by the left ventricle to the body, and return to the heart again. Circulation time is about 1 minute or less, and ensures an adequate exchange of gases.

8.1.3 Blood

One of the simplest and most familiar life-saving medical procedures is a blood transfusion. As you know, however, the blood of one individual is not always compatible with that of another person. The ABO blood types were discovered in the early 1900s by Karl Landsteiner, an Austrian-American. He also contributed to the discovery of the Rh factor in 1940.

In the early 1940s, Charles Drew, an African- American, developed techniques for processing and storing blood plasma, which could then be used in transfusions for people with any blood type. When we donate blood today, our blood may be given to a recipient as whole blood, or it may be separated into its component parts, and recipients will then receive only those parts they need, such as red cells, plasma, factor 8, or platelets. Each of these parts has a specific function, and all of the functions of blood are essential to our survival. The general functions of blood are transportation, regulation, and protection. Materials transported by the blood include nutrients, waste products, gases, and hormones. The blood helps regulate fluid–electrolyte balance, acid–base balance, and the body temperature. Protection against pathogens is provided by white blood cells, and the blood clotting mechanism prevents excessive loss of blood after injuries.

Characteristics of blood

Blood has distinctive physical characteristics:

Amount: a person has 4 to 6 liters of blood, depending on his or her size. Of the total blood volume in the human body, 38% to 48% is composed of the various blood cells, also called *formed elements*. The remaining 52% to 62% of the blood volume is plasma, the liquid portion of blood.

Color: you're probably saying to yourself, "Of course, it's red!" Mention is made of this obvious fact, however, because the color does vary. Arterial blood is bright red because it contains high levels of oxygen. Venous blood has given up much of its oxygen in tissues, and has a darker, dull red color. This may be important in the assessment of the source of bleeding. If blood is bright red, it is probably from a severed artery, and dark red blood is probably venous blood.

pH: the normal pH range of blood is 7.35 to 7.45, which is slightly alkaline. Venous blood normally has a lower pH than does arterial blood because of the presence of more carbon dioxide.

Viscosity: this means thickness or resistance to flow. Blood is about three to five times thicker than water. Viscosity is increased by the presence of blood cells and the plasma proteins, and this thickness contributes to normal blood pressure.

Plasma

Plasma is the liquid part of blood and is approximately 91% water. The solvent ability of water enables the plasma to transport many types of substances.

Nutrients absorbed in the digestive tract, such as glucose, amino acids, and minerals, are circulated to all body tissues. Waste products of the tissues, such as urea and creatinine, circulate through the kidneys and are excreted in urine. Hormones produced by endocrine glands are carried in the plasma to their target organs, and antibodies are also transported in plasma. Most of the carbon dioxide produced by cells is carried in the plasma in the form of bicarbonate ions (HCO_3^-). When the blood reaches the lungs, the CO_2 is re-formed, diffuses into the alveoli, and is exhaled. Also in the plasma are the **plasma proteins**. The clotting factors **prothrombin**, **fibrinogen**, and others are synthesized by the liver and circulate until activated to form a clot in a ruptured or damaged blood vessel.

Albumin is the most abundant plasma protein. It too is synthesized by the liver. Albumin contributes to the colloid osmotic pressure of blood, which pulls tissue fluid into capillaries. This is important to maintain normal blood volume and blood pressure. Other plasma proteins are called **globulins**. Alpha and beta globulins are synthesized by the liver and act as carriers for molecules such as fats. The gamma globulins are antibodies produced by lymphocytes. Antibodies initiate the destruction of pathogens and provide us with immunity. Plasma also carries body heat. Heat is one of the by-products of cell respiration (the production of ATP in cells). Blood is warmed by flowing through active organs such as the liver and muscles. This heat is distributed to cooler parts of the body as blood continues to circulate.

Blood cells

There are three kinds of blood cells: red blood cells, white blood cells, and platelets. Blood cells are produced from stem cells in **hemopoietic tissue**. After birth this is primarily the **red bone marrow**, found in flat and irregular bones such as the sternum, hip bone, and vertebrae. Lymphocytes mature and divide in **lymphatic tissue**, found in the spleen, lymph nodes, and thymus gland. The thymus contains stem cells that produce T lymphocytes, and the stem cells in other lymphatic tissue also produce lymphocytes.

a) Red blood cells

Also called **erythrocytes**, red blood cells (RBCs) are biconcave discs, which mean their centers are thinner than their edges. You may recall that red blood cells are the only human cells without nuclei. Their nuclei disintegrate as the red blood cells mature and are not needed for normal functioning. A normal RBC count ranges from 4.5 to 6.0 million cells per microliter (μL) of blood (1 microliter =1 mm3= one millionth of a liter, a very small volume).

RBC counts for men are often toward the high end of this range; those for women are often toward the low end. Another way to measure the amount of RBCs is the **hematocrit**. This test involves drawing blood into a thin glass tube called a capillary tube, and centrifuging the tube to force all the cells to one end. The percentages of cells and plasma can then be determined.

Because RBCs are by far the most abundant of the blood cells, a normal hematocrit range is just like that of the total blood cells: 38% to 48%. Both RBC count and hematocrit (Hct) are part of a complete blood count (CBC).

Function

Red blood cells contain the protein **hemoglobin** (Hb), which gives them the ability to carry oxygen. Each red blood cell contains approximately 300 million hemoglobin molecules, each of which can bond to four oxygen molecules. In the pulmonary capillaries, RBCs pick up oxygen and oxyhemoglobin is formed. In the systemic capillaries, hemoglobin gives up much of its oxygen and becomes reduced hemoglobin.

A determination of hemoglobin level is also part of a CBC; the normal range is 12 to 18 grams per 100 mL of blood. Essential to the formation of hemoglobin is the mineral iron; there are four atoms of iron in each molecule of hemoglobin. It is the iron that actually bonds to the oxygen and also makes RBCs red.

Hemoglobin is also able to bond to carbon dioxide (CO_2), and does transport some CO_2 from the tissues to the lungs. But hemoglobin accounts for only about 10% of total CO2 transport (most is carried in the plasma as bicarbonate ions).

Production and Maturation

Red blood cells are formed in red bone marrow (RBM) in flat and irregular bones. Within red bone marrow are precursor cells called **stem cells**. Recall that stem cells are unspecialized cells that may develop, or differentiate, in several ways. The stem cells of the red bone marrow may also be called **hemocytoblasts** (hemo _ "blood," cyto _ "cell," blast _ "producing"), and they constantly undergo mitosis to produce all the kinds of blood cells, many of which are RBCs . The rate of production is very rapid (estimated at several million new RBCs per second), and a major regulating factor is oxygen. If the body is in a state of **hypoxia**, or lack of oxygen, the kidneys produce a hormone called **erythropoietin**, which stimulates the red bone marrow to increase the rate of RBC production (that is, the rate of stem cell mitosis). This will occur following hemorrhage or if a person stays for a time at a higher altitude.

As a result of the action of erythropoietin, more RBCs will be available to carry oxygen and correct the hypoxic state. The stem cells that will become RBCs go through a number of developmental stages, only the last two of which we will mention. The **normoblast** is the last stage with a nucleus, which then disintegrates. The **reticulocyte** has fragments of the endoplasmic reticulum, which are visible when blood smears are stained for microscopic evaluation. These immature cells are usually found in the red bone marrow, although a small number of reticulocytes in the peripheral circulation is considered normal (up to 1.5% of the total RBCs).

Large numbers of reticulocytes or normoblasts in the circulating blood mean that the number of mature RBCs is not sufficient to carry the oxygen needed by the body. Such situations include hemorrhage, or when mature RBCs have been destroyed, as in Rh disease of the newborn, and malaria. The maturation of red blood cells requires many nutrients. Protein and iron are necessary for the synthesis of hemoglobin and become part of hemoglobin molecules. Copper is part of some enzymes involved in hemoglobin synthesis. The vitamins folic acid and B12 are required for DNA synthesis in the stem cells of the red bone marrow.

As these cells undergo mitosis, they must continually produce new sets of chromosomes. Vitamin B12 is also called the **extrinsic factor** because its source is external, our food. Parietal cells of the stomach lining produce the **intrinsic factor**, a chemical that combines with the vitamin B12 in food to prevent its digestion and promote its absorption in the small intestine. A deficiency of either vitamin B12 or the intrinsic factor results in **pernicious anemia.**

Life Span

Red blood cells live for approximately 120 days. As they reach this age they become fragile and are removed from circulation by cells of the **tissue macrophage system** (formerly called the reticuloendothelial or RE system). The organs that contain macrophages (literally, "big eaters") are the liver, spleen, and red bone marrow. The old RBCs are phagocytized and digested by macrophages, and the iron they contained is put into the blood to be returned to the red bone marrow to be used for the synthesis of new hemoglobin. If not needed immediately for this purpose, excess iron is stored in the liver. The iron of RBCs is actually recycled over and over again. The globin or protein portion of the hemoglobin molecule is also recycled.

It is digested to its amino acids, which may then be used for the synthesis of new proteins. Another part of the hemoglobin molecule is the heme portion, which cannot be recycled and is a waste product. The heme is converted to **bilirubin** by macrophages. The liver removes bilirubin from circulation and excretes it into bile; bilirubin is a bile pigment. Bile is secreted by the liver into the duodenum and passes through the small intestine and colon, so bilirubin is eliminated in feces, and gives feces their characteristic brown color.

In the colon some bilirubin is changed to urobilinogen by the colon bacteria. Some urobilinogen may be absorbed into the blood, but it is changed to urobilin and excreted by the kidneys in urine. If bilirubin is not excreted properly, perhaps because of liver disease such as hepatitis, it remains in the blood. This may cause **jaundice**, a condition in which the whites of the eyes appear yellow. This yellow color may also be seen in the skin of lightskinned people.

Blood Types

Our blood types are genetic; that is, we inherit genes from our parents that determine our own types. There are many red blood cell factors or types; we will discuss the two most important ones: the **ABO group** and the **Rh factor**. The **ABO group** contains four blood types: A, B, AB, and O. The letters A and B represent antigens (protein-oligosaccharides) on the red blood cell membrane. A person with type A blood has the A antigen on the RBCs, and someone with type B blood has the B antigen. Type AB means that both A and B antigens are present, and type O means that neither the A nor the B antigen is present.

Circulating in the plasma of each person are natural antibodies for those antigens *not* present on the RBCs. Therefore, a type A person has anti-B antibodies in the plasma; a type B person has anti-A antibodies; a type AB person has neither anti-A nor anti-B antibodies; and a type O person has both anti-A and anti-B antibodies . These natural antibodies are of great importance for transfusions. If possible, a person should receive blood of his or her own type; only if this type is not available should another type be given. For example, let us say that a type A person needs a transfusion to replace blood lost in hemorrhage. If this person were to receive type B blood, what would happen? The type A recipient has anti-B antibodies that would bind to the type B antigens of the RBCs of the donated blood. The type B RBCs would first clump (**agglutination**) then rupture (**hemolysis**), thus defeating the purpose of the transfusion.

An even more serious consequence is that the hemoglobin of the ruptured RBCs, now called free hemoglobin, may clog the capillaries of the kidneys and lead to renal damage or renal failure. You can see why **typing** and **cross-matching** of donor and recipient blood in the hospital laboratory is so important before any transfusion is given. This procedure helps ensure that donated blood will not bring about a hemolytic transfusion reaction in the recipient. You may have heard of the concept that a person with type O blood is a "universal donor." Usually, a unit of type O negative blood may be given to people with any other blood type. This is so because type O RBCs have neither the A nor the B antigens and will not react with whatever antibodies the recipient may have. If only one unit (1 pint) of blood is given, the anti-A and anti-B antibodies in the type O blood plasma will be diluted in the recipient's blood plasma and will not have a harmful effect on the recipient's RBCs. The term *negative*, in O negative, the universal donor, refers to the Rh factor, which we will now consider.

The **Rh factor** is another antigen (often called D) that may be present on RBCs. People whose RBCs have the Rh antigen are Rh positive; those without the antigen are Rh negative. Rh-negative people do not have natural antibodies to the Rh antigen, and for them this antigen is foreign. If an Rh-negative person receives Rh-positive blood by mistake, antibodies will be formed just as they would be to bacteria or viruses. A first mistaken transfusion often does not cause problems, because antibody production is slow upon the first exposure to Rh-positive RBCs. A second transfusion, however, when anti-Rh antibodies are already present, will bring about a transfusion reaction, with hemolysis and possible kidney damage.

b) White blood cells

White blood cells (WBCs) are also called **leukocytes**. There are five kinds of WBCs; all are larger than RBCs and have nuclei when mature. The nucleus may be in one piece or appear as several lobes or segments. Special staining for microscopic examination gives each kind of WBC a distinctive appearance. A normal WBC count (part of a CBC) is 5,000 to 10,000 per μL. Notice that this number is quite small compared to a normal RBC count. Many of our WBCs are not circulating within blood vessels but are carrying out their functions in tissue fluid or in lymphatic tissue.

Classification

The five kinds of white blood cells, all produced in the red bone marrow (and some lymphocytes in lymphatic tissue), may be classified in two groups: granular and agranular. The granular leukocytes are the **neutrophils**, **eosinophils**, and **basophils**, which usually have nuclei in two or more lobes or segments, and have distinctly colored granules when stained. Neutrophils have light blue granules, eosinophils have red granules, and basophils have dark blue granules.The agranular leukocytes are **lymphocytes** and **monocytes**, which have nuclei in one piece. Monocytes are usually quite a bit larger than lymphocytes. A **differential WBC count** (part of a CBC) is the percentage of each kind of leukocyte.

Functions

White blood cells all contribute to the same general function, which is to protect the body from infectious disease and to provide **immunity** to certain diseases. Each kind of leukocyte makes a contribution to this very important aspect of homeostasis. Neutrophils and monocytes are capable of the **phagocytosis** of pathogens. Neutrophils are the more abundant phagocytes, but the monocytes are the more efficient phagocytes, because they differentiate into **macrophages**, which also phagocytize dead or damaged tissue at the site of any injury, helping to make tissue repair possible. During an infection, neutrophils are produced more rapidly, and the immature forms, called **band**, may appear in greater numbers in peripheral circulation (band cells are usually less than 10% of the total neutrophils).

The term "band" refers to the nucleus that has not yet become segmented, and may look somewhat like a dumbbell. Eosinophils are believed to detoxify foreign proteins and will phagocytize anything labeled with antibodies. This is especially important in allergic reactions and parasitic infections such as trichinosis (a worm parasite). Basophils contain granules of heparin and histamine.

Heparin is an anticoagulant that helps prevent abnormal clotting within blood vessels. **Histamine**, you may recall, is released as part of the inflammation process, and it makes capillaries more permeable, allowing tissue fluid, proteins, and white blood cells to accumulate in the damaged area. There are two major kinds of lymphocytes, T cells and B cells, and a less numerous third kind called natural killer cells. For now we will say that **T cells** (or T lymphocytes) help recognize foreign antigens and may directly destroy some foreign antigens. **B cells** (or B lymphocytes) become plasma cells that produce antibodies to foreign antigens. Both T cells and B cells provide memory for immunity. **Natural killer cells** (NK cells) destroy foreign cells by chemically rupturing their membranes. As mentioned earlier, leukocytes function in tissue fluid as well as in the blood. Many WBCs are capable of self-locomotion (ameboid movement) and are able to squeeze between the cells of capillary walls and out into tissue spaces.

Macrophages provide a good example of the dual locations of leukocytes. Some macrophages are "fixed," that is, stationary in organs such as the liver, spleen, and red bone marrow (part of the tissue macrophage or RE system—the same macrophages that phagocytize old RBCs) and in the lymph nodes. They phagocytize pathogens that circulate in blood or lymph through these organs. Other "wandering" macrophages move about in tissue fluid, especially in the areolar connective tissue of mucous membranes and below the skin.

Pathogens that gain entry into the body through natural openings or through breaks in the skin are usually destroyed by the macrophages and other leukocytes in connective tissue before they can cause serious disease. The alveoli of the lungs, for example, have macrophages that very efficiently destroy pathogens that enter with inhaled air. A high WBC count, called **leukocytosis**, is often an indication of infection. **Leukopenia** is a low WBC count, which may be present in the early stages of diseases such as tuberculosis. Exposure to radiation or to chemicals such as benzene may destroy WBCs and lower the total count.

Such a person is then very susceptible to infection. The white blood cell types (analogous to RBC types such as the ABO group) are called **human leukocyte antigens (HLA).**

c) Platelets

The more formal name for platelets is **thrombocytes**, which are not whole cells but rather fragments or pieces of cells. Some of the stem cells in the red bone marrow differentiate into large cells called **megakaryocytes**, which break up into small pieces that enter circulation. These small, oval, circulating pieces are platelets, which may last for 5 to 9 days, if not utilized before that. **Thrombopoietin** is a hormone produced by the liver that increases the rate of platelet production.A normal platelet count (part of a CBC) is 150,000 to 300,000/μL (the high end of the range may be extended to 500,000). **Thrombocytopenia** is the term for a low platelet count.

Function

Platelets are necessary for **hemostasis**, which means prevention of blood loss. There are three mechanisms and platelets are involved in each.

1. Vascular spasm: when a large vessel such as an artery or vein is severed, the smooth muscle in its wall contracts in response to the damage (called the myogenic response). Platelets in the area of the rupture release serotonin, which also brings about vasoconstriction. The diameter of the vessel is thereby made smaller, and the smaller opening may then be blocked by a blood clot. If the vessel did not constrict first, the clot that forms would quickly be washed out by the force of the blood pressure.

2. Platelet plugs: when capillaries rupture, the damage is too slight to initiate the formation of a blood clot. The rough surface, however, causes platelets to change shape (become spiky) and become sticky. These activated platelets stick to the edges of the break and to each other. The platelets form a mechanical barrier or wall to close off the break in the capillary. Capillary ruptures are quite frequent, and platelet plugs, although small, are all that is needed to seal them. Would platelet plugs be effective for breaks in larger vessels? No, they are too small, and though they do form, they are washed away (until a clot begins to form that can contain them).

Would vascular spasm be effective for capillaries? Again, the answer is no, because capillaries have no smooth muscle and cannot constrict at all.

3. Chemical clotting: The stimulus for clotting is a rough surface within a vessel, or a break in the vessel, which also creates a rough surface. The more damage there is, the faster clotting begins, usually within 15 to 120 seconds. The clotting mechanism is a series of reactions involving chemicals that normally circulate in the blood and others that are released when a vessel is damaged. The chemicals involved in clotting include platelet factors, chemicals released by damaged tissues, calcium ions, and the plasma proteins prothrombin, fibrinogen, Factor 8, and others synthesized by the liver. (These clotting factors are also designated by Roman numerals; Factor 8 would be Factor VIII.)

Vitamin K is necessary for the liver to synthesize prothrombin and several other clotting factors (Factors 7, 9, and 10). Most of our vitamin K is produced by the bacteria that live in the colon; the vitamin is absorbed as the colon absorbs water and may be stored in the liver. Chemical clotting is usually described in three stages. Stage 1 begins when a vessel is cut or damaged internally, and includes all of the factors shown. As you follow the pathway, notice that the product of stage 1 is prothrombin activator, which may also be called prothrombinase. Each name tells us something.The first name suggests that this chemical activates prothrombin, and that is true. The second name ends in "ase," which indicates that this is an enzyme.

The traditional names for enzymes use the substrate of the enzyme as the first part of the name, and add "ase." So this chemical must be an enzyme whose substrate is prothrombin, and that is also true. The stages of clotting may be called a cascade, where one leads to the next, as inevitable as water flowing downhill. Prothrombin activator, the product of stage 1, brings about the stage 2 reaction: converting prothrombin to thrombin. The product of stage 2, thrombin, brings about the stage 3 reaction: converting fibrinogen to fibrin. The clot itself is made of **fibrin**, the product of stage 3. Fibrin is a thread-like protein. Many strands of fibrin form a mesh that traps RBCs and platelets, and creates a wall across the break in the vessel.

Once the clot has formed and bleeding has stopped, **clot retraction** and **fibrinolysis** occur. Clot retraction requires platelets, ATP, and Factor 13 and involves folding of the fibrin threads to pull the edges of the rupture in the vessel wall closer together. This will make the area to be

repaired smaller. The platelets contribute in yet another way, because as they disintegrate they release platelet-derived growth factor (PDGF), which stimulates the repair of blood vessels (growth of their tissues). As repair begins, the clot is dissolved, a process called fibrinolysis. It is important that the clot be dissolved, because it is a rough surface, and if it were inside a vessel it would stimulate more and unnecessary clotting, which might eventually obstruct blood flow.

Prevention of Abnormal Clotting

Clotting should take place to stop bleeding, but too much clotting would obstruct vessels and interfere with normal circulation of blood. Clots do not usually form in intact vessels because the **endothelium** (simple squamous epithelial lining) is very smooth and repels the platelets and clotting factors. If the lining becomes roughened, as happens with the lipid deposits of atherosclerosis, a clot will form. Heparin, produced by basophils, is a natural anticoagulant that inhibits the clotting process (althoughheparin is called a "blood thinner," it does not "thin" or dilute the blood in any way; rather it prevents a chemical reaction from taking place).

The liver produces a globulin called **antithrombin**, which combines with and inactivates excess thrombin. Excess thrombin would exert a positive feedback effect on the clotting cascade, and result in the splitting of more prothrombin to thrombin, more clotting, more thrombin formed, and so on. Antithrombin helps to prevent this, as does the fibrin of the clot, which adsorbs excess thrombin and renders it inactive. All of these factors are the external brake for this positive feedback mechanism.Together they usually limit the fibrin formed to what is needed to create a useful clot but not an obstructive one.

Thrombosis refers to clotting in an intact vessel; the clot itself is called a **thrombus**. Coronary thrombosis, for example, is abnormal clotting in a coronary artery, which will decrease the blood (oxygen) supply to part of the heart muscle. An **embolism** is a clot or other tissue transported from elsewhere that lodges in and obstructs a vessel.

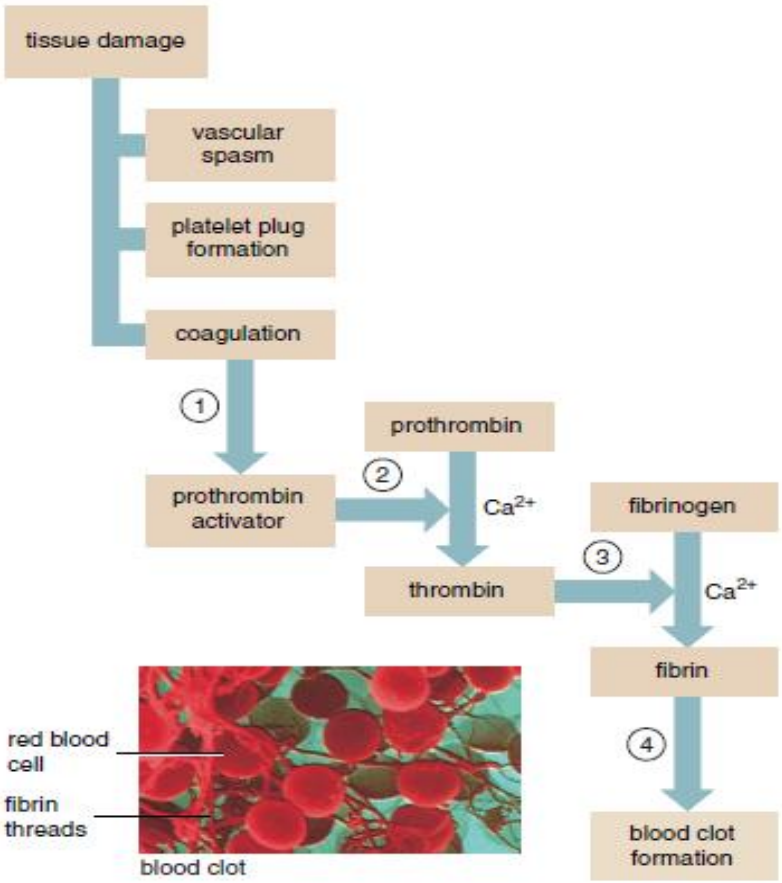
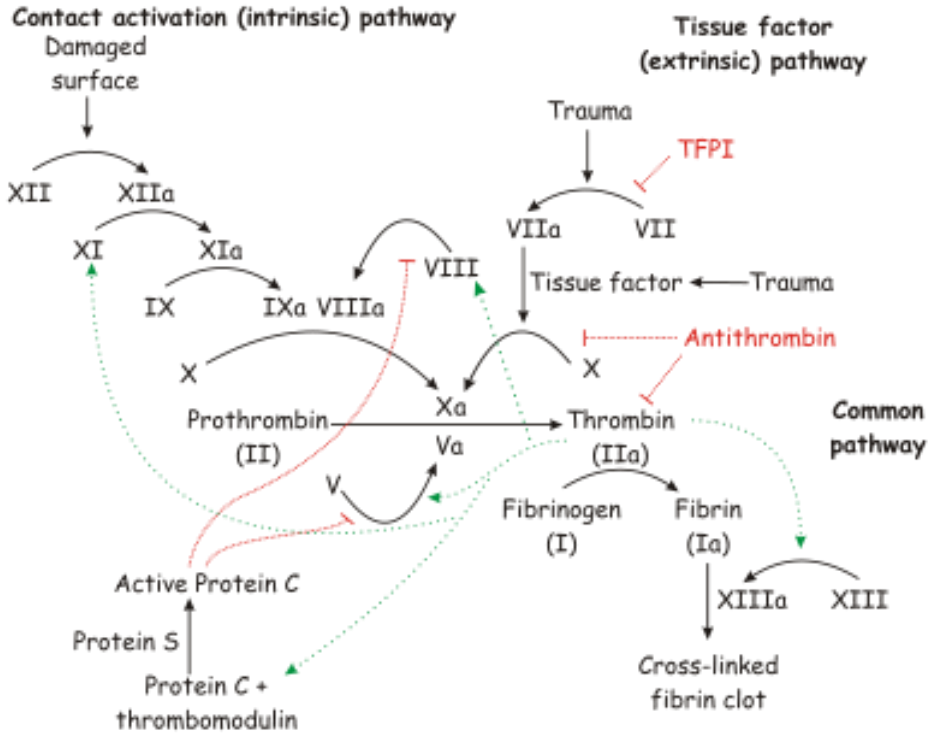


Figure: Three events and hemostasis. Coagulation is further broken down into four steps.

The coagulation cascade

The coagulation cascade of secondary hemostasis has two pathways which lead to *fibrin* formation. These are the *contact activation pathway* (the intrinsic pathway), and the *tissue factor pathway* (the extrinsic pathway). The pathways are a series of reactions, in which a *zymogen* (inactive enzyme precursor) of a *serine protease* and its *glycoprotein* co-factor are activated to become active components that then catalyze the next reaction in the cascade, ultimately resulting in cross-linked fibrin. Coagulation factors are generally indicated by *Roman numerals*, with a lowercase ***a*** appended to indicate an active form.



Coagulation factors and related substances

NUMBER AND/OR NAME	*FUNCTION*
I (*fibrinogen*)	Forms clot (fibrin)
II (**prothrombin**)	Its active form (IIa) activates **I, V, VII, VIII, XI, XIII**, **protein C**, **platelets**
Tissue factor	Co-factor of VIIa (formerly known as factor **III**)
Calcium	Required for coagulation factors to bind to phospholipid (formerly known as factor IV)
V (**proaccelerin, labile factor**)	Co-factor of **X** with which it forms the *prothrombinase* complex
VI	*Unassigned* – old name of Factor Va
VII (**stable factor, proconvertin**)	Activates **IX**, **X**
VIII (**Antihemophilic factor A**)	Co-factor of **IX** with which it forms the **tenase** complex
IX (**Antihemophilic factor B** or **Christmas factor**)	Activates X: forms **tenase** complex with factor **VIII**
X (**Stuart-Prower factor**)	Activates II: forms **prothrombinase** complex with factor V

XI (**plasma thromboplastin antecedent**)	Activates IX
XII (**Hageman factor**)	Activates factor XI, VII and prekallikrein
XIII (**fibrin-stabilizing factor**)	Crosslinks fibrin
von Willebrand factor	Binds to VIII, mediates platelet adhesion
prekallikrein (**Fletcher factor**)	Activates XII and prekallikrein; cleaves HMWK
high-molecular-weight kininogen (HMWK) (**Fitzgerald factor**)	Supports reciprocal activation of XII, XI, and prekallikrein
fibronectin	Mediates cell adhesion
antithrombin III	Inhibits IIa, Xa, and other proteases;
heparin cofactor II	Inhibits IIa, cofactor for heparin and **dermatan sulfate** ("minor antithrombin")
protein C	Inactivates Va and VIIIa
protein S	Cofactor for activated protein C (APC, inactive when bound to C4b-binding protein)
protein Z	Mediates thrombin adhesion to phospholipids and stimulates degradation of factor X by ZPI
Protein Z-related protease inhibitor (ZPI)	Degrades factors X (in presence of protein Z) and XI (independently)
plasminogen	Converts to plasmin, lyses fibrin and other proteins
alpha 2-antiplasmin	Inhibits plasmin
tissue plasminogen activator (tPA)	Activates plasminogen
urokinase	Activates plasminogen
plasminogen activator inhibitor-1 (PAI1)	Inactivates tPA & urokinase (endothelial PAI)
plasminogen activator inhibitor-2 (PAI2)	Inactivates tPA & urokinase (**placental** PAI)
cancer procoagulant	Pathological **factor X** activator linked to thrombosis in **cancer**

- **Applications to the nursing care**

1. ANEMIA

Anemia is a deficiency of red blood cells, or insufficient hemoglobin within the red blood cells. There are many different types of anemia.

Iron-deficiency anemia is caused by a lack of dietary iron, and there is not enough of this mineral to form sufficient hemoglobin. A person with this type of anemia may have a normal RBC count and a normal hematocrit, but the hemoglobin level will be below normal. A deficiency of vitamin B12, which is found only in animal foods, leads to ***pernicious anemia***, in which the RBCs are large, misshapen, and fragile. Another cause of this form of anemia is lack of the intrinsic factor due to autoimmune destruction of the parietal cells of the stomach lining.

Sickle-cell anemia is a genetic disorder of hemoglobin, which causes RBCs to sickle, clog capillaries, and rupture.

Aplastic anemia is suppression of the red bone marrow, with decreased production of RBCs, WBCs, and platelets. This is a very serious disorder that may be caused by exposure to radiation, certain chemicals such as benzene, or some medications. There are several antibiotics that must be used with caution since they may have this potentially fatal side effect.

Hemolytic anemia is any disorder that causes rupture of RBCs before the end of their normal life span. Sickle-cell anemia and Rh disease of the newborn are examples.

Another example is malaria, in which a protozoan parasite reproduces in RBCs and destroys them. Hemolytic anemias are often characterized by jaundice because of the increased production of bilirubin.

2. JAUNDICE

Jaundice is not a disease, but rather a sign caused by excessive accumulation of bilirubin in the blood. Because one of the liver's many functions is the excretion of bilirubin, jaundice may be a sign of liver disease such as hepatitis or cirrhosis.

This may be called **hepatic jaundice**, because the problem is with the liver. Other types of jaundice are prehepatic jaundice and posthepatic jaundice: The name of each tells us where the

problem is. Recall that bilirubin is the waste product formed from the heme portion of the hemoglobin of old RBCs.

Prehepatic jaundice means that the problem is "before" the liver; that is, hemolysis of RBCs is taking place at a more rapid rate. Rapid hemolysis is characteristic of sickle cell anemia, malaria, and Rh disease of the new- born; these are hemolytic anemias. As excessive numbers of RBCs are destroyed, bilirubin is formed at a faster rate than the liver can excrete it. The bilirubin that the liver cannot excrete remains in the blood and causes jaundice. Another name for this type is **hemolytic jaundice**.

Posthepatic jaundice means that the problem is "after" the liver. The liver excretes bilirubin into bile, which is stored in the gallbladder and then moved to the small intestine. If the bile ducts are obstructed, perhaps by gallstones or inflammation of the gallbladder, bile cannot pass to the small intestine and backs up in the liver. Bilirubin may then be reabsorbed back into the blood and cause jaundice. Another name for this type is **obstructive jaundice**.

3. Rh disease of the newborn

Rh disease of the newborn may also be called **erythroblastosis fetalis** and is the result of an Rh incompatibility between mother and fetus. During a normal pregnancy, maternal blood and fetal blood do not mix in the placenta. However, during delivery of the placenta (the "afterbirth" that follows the birth of the baby), some fetal blood may enter maternal circulation. If the woman is Rh negative and her baby is Rh positive, this exposes the woman to Rh-positive RBCs. In response, her immune system will now produce anti-Rh antibodies following this first delivery. In a subsequent pregnancy, these maternal antibodies will cross the placenta and enter fetal circulation.

If this next fetus is also Rh positive, the maternal antibodies will cause destruction (hemolysis) of the fetal RBCs. In severe cases this may result in the death of the fetus. In less severe cases, the baby will be born anemic and jaundiced from the loss of RBCs. Such an infant may require a gradual exchange transfusion to remove the blood with the maternal antibodies and replace it with Rh-negative blood. The baby will continue to produce its own Rh-positive RBCs, which will not be destroyed once the maternal antibodies have been removed. Much better than treatment, however, is prevention.

If an Rh-negative woman delivers an Rh positive baby, she should be given **RhoGAM** within 72 hours after delivery. RhoGAM is an anti-Rh antibody that will destroy any fetal RBCs that have entered the mother's circulation *before* her immune system can respond and produce antibodies. The RhoGAM antibodies themselves break down within a few months. The woman's next pregnancy will be like the first, as if she had never been exposed to Rh-positive RBCs.

4. LEUKEMIA

Leukemia is the term for malignancy of the blood forming tissue. There are many types of leukemia, which are classified as acute or chronic, by the types of abnormal cells produced, and by either childhood or adult onset. In general, leukemia is characterized by an overproduction of immature white blood cells. These immature cells cannot perform their normal functions, and the person becomes very susceptible to infection.

As a greater proportion of the body's nutrients are used by malignant cells, the production of other blood cells decreases. Severe anemia is a consequence of decreased red blood cell production, and the tendency to hemorrhage is the result of decreased platelets.

Chemotherapy may bring about cure or remission for some forms of leukemia, but other forms remain resistant to treatment and may be fatal within a few months of diagnosis. In such cases, the cause of death is often pneumonia or some other serious infection, because the abnormal white blood cells cannot prevent the growth and spread of pathogens within the body.

5. HEMOPHILIA

There are several forms of **hemophilia**; all are genetic and are characterized by the inability of the blood to clot properly. Hemophilia A is the most common form and involves a deficiency of clotting Factor 8. The gene for hemophilia A is located on the X chromosome, so this is a **sex linked trait**, with the same pattern of inheritance as red-green color blindness and Duchenne's muscular dystrophy. Without factor 8, the first stage of chemical clotting cannot be completed, and prothrombin activator is not formed. Without treatment, a hemophiliac experiences prolonged bleeding after even minor injuries and extensive internal bleeding, especially in joints subjected to the stresses of weight-bearing.

In recent years, treatment (but not cure) has become possible with factor 8 obtained from blood donors. The Factor 8 is extracted from the plasma of donated blood and administered in concentrated form to hemophiliacs, enabling them to live normal lives.

In what is perhaps the most tragic irony of medical progress, many hemophiliacs were inadvertently infected with HIV, the virus that causes AIDS. Before 1985, there was no test to detect HIV in donated blood, and the virus was passed to hemophiliacs in the very blood product that was meant to control their disease and prolong their lives. Today, all donated blood and blood products are tested for HIV, and the risk of AIDS transmission to hemophiliacs, or anyone receiving donated blood, is now very small.

6. DISSOLVING CLOTS

Abnormal clots may cause serious problems in coronary arteries, pulmonary arteries, cerebral vessels, and even veins in the legs. However, if clots can be dissolved before they cause death of tissue, normal circulation and tissue functioning may be restored.

One of the first substances used to dissolve clots in coronary arteries was **streptokinase**, which is actually a bacterial toxin produced by some members of the genus *Streptococcus*. Streptokinase did indeed dissolve clots, but its use created the possibility of clot destruction throughout the body, with serious hemorrhage a potential consequence. Safer chemicals called third-generation thrombolytics are now used (thrombo _ "clot" and lytic _ "to lyse" or "split").

In a case of coronary thrombosis, if a thrombolytic can be administered within a few hours, the clot may be dissolved and permanent heart damage prevented. The same procedure is also used to prevent permanent brain damage after strokes (CVAs) caused by blood clots.

8.1.4 Blood pressure

Blood pressure is the force the blood exerts against the walls of the blood vessels. Filtration in capillaries depends upon blood pressure; filtration brings nutrients to tissues, and is the first step in the formation of urine. Blood pressure is one of the "vital signs" often measured, and indeed a normal blood pressure is essential to life. The pumping of the ventricles creates blood pressure, which is measured in mmHg (millimeters of mercury).

When a systemic blood pressure reading is taken, two numbers are obtained: systolic and diastolic, as in 110/70 mmHg. **Systolic** pressure is always the higher of the two and represents the blood pressure when the left ventricle is contracting. The lower number is the **diastolic** pressure, when the left ventricle is relaxed and does not exert force. Diastolic pressure is maintained by the arteries and arterioles and is discussed in a later section. Systemic blood pressure is highest in the aorta, which receives all of the blood pumped by the left ventricle. As blood travels farther away from the heart, blood pressure decreases.

The brachial artery is most often used to take a blood pressure reading; here a normal systolic range is 90 to 120 mmHg, and a normal diastolic range is 60 to 80 mmHg. In the arterioles, blood pressure decreases further, and systolic and diastolic pressures merge into one pressure. At the arterial end of capillary networks, blood pressure is about 30 to 35 mmHg, decreasing to 12 to 15 mmHg at the venous end of capillaries. This is high enough to permit filtration but low enough to prevent rupture of the capillaries.

As blood flows through veins, the pressure decreases further, and in the caval veins, blood pressure approaches zero as blood enters the right atrium. The upper limit of the normal blood pressure range is now 120/80 mmHg. The levels of 125 to 139/85 to 89 mmHg, once considered high-normal, are now called "prehypertension," that is, with the potential to become even higher. A systemic blood pressure consistently higher than the normal range is called **hypertension**. A lower than normal blood pressure is called **hypotension**. Pulmonary blood pressure is created by the right ventricle, which has relatively thin walls and thus exerts about one-sixth the force of the left ventricle.

The result is that pulmonary arterial pressure is always low: 20 to 25 /8 to 10 mmHg and in pulmonary capillaries is lower still. This is important to *prevent* filtration in pulmonary capillaries, which in turn prevents tissue fluid from accumulating in the alveoli of the lungs.

Maintenance of systemic blood pressure

Because blood pressure is so important, many physiological factors and processes interact to keep blood pressure within normal limits:

1. Venous return: the amount of blood that returns to the heart by way of the veins. Venous return is important because the heart can pump only the blood it receives. If venous return decreases, the cardiac muscle fibers will not be stretched, the force of ventricular systole will decrease (Starling's law), and blood pressure will decrease. This is what might happen following a severe hemorrhage. When the body is horizontal, venous return can be maintained fairly easily, but when the body is vertical, gravity must be overcome to return blood from the lower body to the heart. Three mechanisms help promote venous return: constriction of veins, the skeletal muscle pump, and the respiratory pump.Veins contain smooth muscle, which enables them to constrict and force blood toward the heart; the valves prevent backflow of blood. The second mechanism is the **skeletal muscle pump**, which is especially effective for the deep veins of the legs. These veins are surrounded by skeletal muscles that contract and relax during normal activities such as walking. Contractions of the leg muscles squeeze the veins to force blood toward the heart. The third mechanism is the **respiratory pump**, which affects veins that pass through the chest cavity. The pressure changes of inhalation and exhalation alternately expand and compress the veins, and blood is returned to the heart.

2. Heart rate and force: in general, if heart rate and force increase, blood pressure increases; this is what happens during exercise. However, if the heart is beating extremely rapidly, the ventricles may not fill completely between beats, and cardiac output and blood pressure will decrease.

3. Peripheral resistance: this term refers to the resistance the vessels offer to the flow of blood. The arteries and veins are usually slightly constricted, which maintains normal diastolic blood pressure. It may be helpful to think of the vessels as the "container" for the blood. If a person's body has 5 liters of blood, the "container" must be smaller in order for the blood to exert a pressure against its walls.

This is what normal vasoconstriction does: It makes the container (the vessels) smaller than the volume of blood so that the blood will exert pressure even when the left ventricle is relaxed. If more vasoconstriction occurs, blood pressure will increase (the container has become even smaller). This is what happens in a stress situation, when greater vasoconstriction is brought about by sympathetic impulses. If vasodilation occurs, blood pressure will decrease (the con-

tainer is larger). After eating a large meal, for example, there is extensive vasodilation in the digestive tract to supply more oxygenated blood for digestive activities. To keep blood pressure within the normal range, vasoconstriction must, and does, occur elsewhere in the body. This is why strenuous exercise should be avoided right after eating; there is not enough blood to completely supply oxygen to exercising muscles and an active digestive tract at the same time.

4. Elasticity of the large arteries: when the left ventricle contracts, the blood that enters the large arteries stretches their walls. The arterial walls are elastic and absorb some of the force. When the left ventricle relaxes, the arterial walls recoil or snap back, which helps keep diastolic pressure within the normal range. Normal elasticity, therefore, lowers systolic pressure, raises diastolic pressure, and maintains a normal pulse pressure. (Pulse pressure is the difference between systolic and diastolic pressure. The usual ratio of systolic to diastolic to pulse pressure is approximately 3:2:1. For example, with a blood pressure of 120/80 mmHg, the pulse pressure is 40, and the ratio is 120:80:40, or 3:2:1.)

5. Viscosity of the blood: normal blood viscosity depends upon the presence of red blood cells and plasma proteins, especially albumin. Having too many red blood cells is rare but does occur in the disorder called polycythemia vera and in people who are heavy smokers. This will increase blood viscosity and blood pressure. A decreased number of red blood cells, as is seen with severe anemia, or decreased albumin, as may occur in liver disease or kidney disease, will decrease blood viscosity and blood pressure. In these situations, other mechanisms such as vasoconstriction will maintain blood pressure as close to normal as is possible.

6. Loss of blood: a small loss of blood, as when donating a pint of blood, will cause a temporary drop in blood pressure followed by rapid compensation in the form of a more rapid heart rate and greater vasoconstriction. After a severe hemorrhage, however, these compensating mechanisms may not be sufficient to maintain normal blood pressure and blood flow to the brain. Although a person may survive loss of 50% of the body's total blood, the possibility of brain damage increases as more blood is lost and not rapidly replaced.

7. Hormones: several hormones have effects on blood pressure. The adrenal medulla secretes norepinephrine and epinephrine in stress situations. Norepinephrine stimulates vasoconstriction,

which raises blood pressure. Epinephrine also causes vasoconstriction, and increases heart rate and force of contraction, both of which increase blood pressure. Antidiuretic hormone (ADH) is secreted by the posterior pituitary gland when the water content of the body decreases. ADH increases the reabsorption of water by the kidneys to prevent further loss of water in urine and a further decrease in blood pressure. Aldosterone, a hormone from the adrenal cortex, has a similar effect on blood volume.

When blood pressure decreases, secretion of aldosterone stimulates the reabsorption of Na_ ions by the kidneys. Water follows sodium back to the blood, which maintains blood volume to prevent a further drop in blood pressure. Atrial natriuretic peptide (ANP), secreted by the atria of the heart, functions in opposition to aldosterone. ANP increases the excretion of Na_ ions and water by the kidneys, which decreases blood volume and lowers blood pressure.

Distribution of blood flow

An individual's blood volume remains relatively constant within the normal range appropriate to the size of the person. Active tissues, however, require more blood, that is, more oxygen, than do less active tissues. As active tissues and organs receive a greater proportion of the total blood flow, less active organs must receive less, or blood pressure will decrease markedly.

As mentioned previously, precapillary sphincters dilate in active tissues and constrict in less active ones. The arterioles also constrict to reduce blood flow to less active organs. This ensures that metabolically active organs will receive enough oxygen to function properly and that blood pressure for the body as a whole will be maintained within normal limits. An example will be helpful here; let us use the body at rest and the body during exercise. Resting cardiac output is approximately 5000 mL per minute.

Exercise cardiac output is three times that, about 15,000 mL per minute. Keep in mind that the volume of blood is the same in both cases, but that during exercise the blood is being circulated more rapidly. Compare the amounts of blood flowing to various organs and tissues during exercise and at rest. During exercise, the heart receives about three times as much blood as it does when the body is at rest. The very active skeletal muscles receive about ten times as much blood. The skin, as an organ of heat loss, receives about four times as much blood.

Other organs, however, can function adequately with less blood. Blood flow is reduced to the digestive tract, to the kidneys, and to other parts of the body such as bones. When the exercise ceases, cardiac output will gradually return to the resting level, as will blood flow to the various organs. These changes in the distribution of blood ensure sufficient oxygen for active tissues and an appropriate blood pressure for the body as a whole.

Regulation of blood pressure

The mechanisms that regulate systemic blood pressure may be divided into two types: intrinsic mechanisms and nervous mechanisms. The nervous mechanisms involve the nervous system, and the intrinsic mechanisms do not require nerve impulses.

- **Intrinsic mechanisms**

The term *intrinsic* means "within." Intrinsic mechanisms work because of the internal characteristics of certain organs. The first such organ is the heart. When venous return increases, cardiac muscle fibers are stretched, and the ventricles pump more forcefully (Starling's law). Thus, cardiac output and blood pressure increase. This is what happens during exercise, when a higher blood pressure is needed. When exercise ends and venous return decreases, the heart pumps less forcefully, which helps return blood pressure to a normal resting level.

The second intrinsic mechanism involves the kidneys. When blood flow through the kidneys decreases, the process of filtration decreases and less urine is formed. This decrease in urinary output preserves blood volume so that it does not decrease further. Following severe hemorrhage or any other type of dehydration, this is very important to maintain blood pressure. The kidneys are also involved in the **renin- angiotensin mechanism**.

When blood pressure decreases, the kidneys secrete the enzyme **renin**, which initiates a series of reactions that result in the formation of **angiotensin II**. Angiotensin II causes vasoconstriction and stimulates secretion of aldosterone by the adrenal cortex, both of which will increase blood pressure.

- **Nervous mechanisms**

The medulla and the autonomic nervous system are directly involved in the regulation of blood pressure. The first of these nervous mechanisms concerns the heart; the second nervous mechanism involves peripheral resistance, that is, the degree of constriction of the arteries and arterioles and, to a lesser extent, the veins.The medulla contains the **vasomotor center**, which consists of a vasoconstrictor area and a vasodilator area. The vasodilator area may depress the vasoconstrictor area to bring about vasodilation, which will decrease blood pressure.

The vasoconstrictor area may bring about more vasoconstriction by way of the sympathetic division of the autonomic nervous system. Sympathetic vasoconstrictor fibers innervate the smooth muscle of all arteries and veins, and several impulses per second along these fibers maintain normal vasoconstriction. More impulses per second bring about greater vasoconstriction, and fewer impulses per second cause vasodilation. The medulla receives the information to make such changes from the pressoreceptors in the carotid sinuses and the aortic sinus. The inability to maintain normal blood pressure is one aspect of circulatory shock.

AGING AND THE VASCULAR SYSTEM

It is believed that the aging of blood vessels, especially arteries, begins in childhood, although the effects are not apparent for decades. The cholesterol deposits of atherosclerosis are to be expected with advancing age, with the most serious consequences in the coronary arteries. A certain degree of arteriosclerosis is to be expected, and average resting blood pressure may increase, which further damages arterial walls.

Consequences include stroke and left-sided heart failure.The veins also deteriorate with age; their thin walls weaken and stretch, making their valves incompetent. This is most likely to occur in the veins of the legs; their walls are subject to great pressure as blood is returned to the heart against the force of gravity. Varicose veins and phlebitis are more likely to occur among elderly people.

- **Applications to the nursing care**

1) Disorders of arteries

- ***Arteriosclerosis:*** although commonly called "hardening of the arteries," arteriosclerosis really means that the arteries lose their elasticity, and their walls become weakened. Arteries carry blood under high pressure, so deterioration of their walls is part of the aging process.
- ***Aneurysm:*** a weak portion of an arterial wall may bulge out, forming a sac or bubble called an aneurysm. Arteriosclerosis is a possible cause, but some aneurysms are congenital. An aneurysm may be present for many years without any symptoms and may only be discovered during diagnostic procedures for some other purpose. The most common sites for aneurysm formation are the cerebral arteries and the aorta, especially the abdominal aorta. Rupture of a cerebral aneurysm is a possible cause of a cerebrovascular accident (CVA). Rupture of an aortic aneurysm is life-threatening and requires immediate corrective surgery. The damaged portion of the artery is removed and replaced with a graft. Such surgery may also be performed when an aneurysm is found before it ruptures.
- ***Atherosclerosis:*** A stage of arteriosclerosis involving fatty deposits (atheromas) inside the arterial walls, thus narrowing the arteries

2) Disorders of veins

- **Phlebitis**: inflammation of a vein. This condition is most common in the veins of the legs, because they are subjected to great pressure as the blood is returned to the heart against the force of gravity. Often no specific cause can be determined, but advancing age, obesity, and blood disorders may be predisposing factors. If a superficial vein is affected, the area may be tender or painful, but blood flow is usually maintained because there are so many anastomoses among these veins. Deep vein phlebitis is potentially more serious, with the possibility of clot formation (thrombophlebitis) and subsequent dislodging ofthe clot to form an embolism.
- **Varicose veins**: swollen and distended veins that occur most often in the superficial veins of the legs.This condition may develop in people who must sit or stand in one place for long periods of time. Without contraction of the leg muscles, blood tends to pool in the leg veins,

stretching their walls. If the veins become overly stretched, the valves within them no longer close properly. These incompetent valves no longer prevent backflow of blood, leading to further pooling and even further stretching of the walls of the veins. Varicose veins may cause discomfort and cramping in the legs, or become even more painful. Severe varicosities may be removed surgically.This condition may also develop during pregnancy when the enlarged uterus presses against the iliac veins and slows blood flow into the inferior vena cava. Varicose veins of the anal canal are called **hemorrhoids**, which may also be a result of pregnancy or of chronic constipation and straining to defecate. Hemorrhoids that cause discomfort or pain may also be removed surgically. Developments in laser surgery have made this a simpler procedure than it was in the past.

3) ***Pulse sites***

A pulse is the heartbeat that is felt at an arterial site. What is felt is not actually the force exerted by the blood, but the force of ventricular contraction transmitted through the walls of the arteries. This is why pulses are not felt in veins; they are too far from the heart for the force to be detectable.The most commonly used pulse sites are:

- ✓ ***Radial****:* the radial artery on the thumb side of the wrist.
- ✓ ***Carotid****:* the carotid artery lateral to the larynx in the neck.
- ✓ ***Temporal****:* the temporal artery just in front of the ear.
- ✓ ***Femoral****:* the femoral artery at the top of the thigh.
- ✓ ***Popliteal****:* the popliteal artery at the back of the knee.
- ✓ ***Dorsalis pedis****:* the dorsalis pedis artery on the top of the foot (commonly called the pedal pulse).

Pulse rate is, of course, the heart rate. However, if the heart is beating weakly, a radial pulse may be lower than an **apical pulse** (listening to the heart itself with a stethoscope).

This is called a **pulse deficit** and indicates heart disease of some kind. When taking a pulse, the careful observer also notes the rhythm and force of the pulse.

Abnormal rhythms may reflect cardiac arrhythmias, and the force of the pulse (strong or weak) is helpful in assessing the general condition of the heart and arteries.

4) Hypertension

Hypertension is high blood pressure, that is, a resting systemic pressure consistently above the normal range (90 to 120/60 to 80 mmHg). Clinicians now consider 125 to 139/85 to 89 mmHg to be prehypertension.A systolic reading of 140 to 159 mmHg or a diastolic reading of 90 to 99 mmHg may be called stage 1 hypertension, and a systolic reading above 160 mmHg or a diastolic reading above 100 mmHg may be called stage 2 hypertension.The term "essential hypertension" means that no specific cause can be determined; most cases are in this category.

For some people, however, an overproduction of renin by the kidneys is the cause of their hypertension. Excess renin increases the production of angiotensin II, which raises blood pressure. Although hypertension often produces no symptoms, the long-term consequences may be very serious. Chronic hypertension has its greatest effects on the arteries and on the heart. Although the walls of arteries are strong, hypertension weakens them and contributes to arteriosclerosis. Such weakened arteries may rupture or develop aneurysms, which may in turn lead to CVA or kidney damage.

Hypertension affects the heart because the left ventricle must now pump blood against the higher arterial pressure. The left ventricle works harder and, like any other muscle, enlarges as more work is demanded; this is called **left ventricular hypertrophy**. This abnormal growth of the myocardium, however, is not accompanied by a corresponding growth in coronary capillaries, and the blood supply of the left ventricle may not be adequate for all situations. Exercise, for example, puts further demands on the heart, and the person may experience angina due to a lack of oxygen or a myocardial infarction if there is a severe oxygen deficiency.

Although several different kinds of medications (diuretics, vasodilators) are used to treat hypertension, people with moderate hypertension may limit their dependence on medications by following certain guidelines:

1. Don't smoke, because nicotine stimulates vasoconstriction, which raises BP. Smoking also damages arteries, contributing to arteriosclerosis.

2. Lose weight if overweight. A weight loss of as little as 10 pounds can lower BP. A diet high in fruits and vegetables may, for some people, contribute to lower BP.

3. Cut salt intake in half. Although salt consumption may not be the *cause* of hypertension, reducing salt intake may help lower blood pressure by decreasing blood volume.

4. Exercise on a regular basis. A moderate amount of aerobic exercise (such as a half hour walk every day) is beneficial for the entire cardiovascular system and may also contribute to weight loss.

5) Circulatory shock

Circulatory shock is any condition in which cardiac output decreases to the extent that tissues are deprived of oxygen and waste products accumulate.

A. Causes of Shock

Cardiogenic shock: occurs most often after a severe myocardial infarction but may also be the result of ventricular fibrillation. In either case, the heart is no longer an efficient pump, and cardiac output decreases.

Hypovolemic shock: is the result of decreased blood volume, often due to severe hemorrhage. Other possible causes are extreme sweating (heat stroke) or extreme loss of water through the kidneys (diuresis) or intestines (diarrhea). In these situations, the heart simply does not have enough blood to pump, and cardiac output decreases. ***Anaphylactic shock,*** also in this category, is a massive allergic reaction in which great amounts of histamine increase capillary permeability and vasodilation throughout the body. Much plasma is then lost to tissue spaces, which decreases blood volume, blood pressure, and cardiac output.

Septic shock is the result of septicemia, the presence of bacteria in the blood. The bacteria and damaged tissues release inflammatory chemicals that cause vasodilation and extensive loss of plasma into tissue spaces.

B. Stages of Shock

Compensated shock: the responses by the body maintain cardiac output. Following a small hemorrhage, for example, the heart rate increases, the blood vessels constrict, and the kidneys decrease urinary output to conserve water. These responses help preserve blood volume and maintain blood pressure, cardiac output, and blood flow to tissues.

Progressive shock: the state of shock leads to more shock. Following a severe hemorrhage, cardiac output decreases and the myocardium itself is deprived of blood. The heart weakens, which further decreases cardiac output. Arteries that are deprived of their blood supply cannot remain constricted.

As the arteries dilate, venous return decreases, which in turn decreases cardiac output. Progressive shock is a series of such vicious cycles, and medical intervention is required to restore cardiac output to normal.

Irreversible shock: no amount of medical assistance can restore cardiac output to normal. The usual cause of death is that the heart has been damaged too much to recover. A severe myocardial infarction, massive hemorrhage, or septicemia may all be fatal despite medical treatment.

8.2 THE LYMPHATIC SYSTEM AND IMMUNITY

A child falls and scrapes her knee. Is this likely to be a life-threatening injury? Probably not, even though the breaks in the skin have permitted the entry of thousands or even millions of bacteria. Those bacteria, however, will be quickly destroyed by the cells and organs of the lymphatic system.

Although the lymphatic system may be considered part of the circulatory system, we will consider it separately because its functions are so different from those of the heart and blood vessels. Keep in mind, however, that all of these functions are interdependent.
The lymphatic system is responsible for returning tissue fluid to the blood and for protecting the body against foreign material. The parts of the lymphatic system are the lymph, the system of lymph vessels, and lymphatic tissue, which includes lymph nodes and nodules, the spleen, and the thymus gland.

Functions of the Lymphatic System

The lymphatic system has three primary functions:

- ✓ First of all, it returns excess interstitial fluid to the blood. Of the fluid that leaves the capillary, about 90 percent is returned. The 10 percent that does not return becomes part of the interstitial fluid that surrounds the tissue cells. Small protein molecules may "leak" through the capillary wall and increase the osmotic pressure of the interstitial fluid. This further inhibits the return of fluid into the capillaries, and fluid tends to accumulate in the tissue spaces.
  If this continues, blood volume and blood pressure decrease significantly and the volume of tissue fluid increases, which results in edema (swelling). Lymph capillaries pick up the excess interstitial fluid and proteins and return them to the venous blood. After the fluid enters the lymph capillaries, it is called lymph.

- ✓ The second function of the lymphatic system is the absorption of fats and fat-soluble vitamins from the digestive system and the subsequent transport of these substances to the venous circulation. The mucosa that lines the small intestine is covered with fingerlike projections called villi. There are blood capillaries and special lymph capillaries, called lacteals, in the center of each villus. The blood capillaries absorb most nutrients, but the fats and fat-soluble vitamins are absorbed by the lacteals. The lymph in the lacteals has a milky appearance due to its high fat content and is called chyle.

- ✓ The third and probably most well known function of the lymphatic system is defense against invading microorganisms and disease. Lymph nodes and other lymphatic organs filter the lymph to remove microorganisms and other foreign particles. Lymphatic organs contain lymphocytes that destroy invading organisms.

LYMPH

Lymph is the name for tissue fluid that enters lymph capillaries. As you may recall, filtration in capillaries creates tissue fluid from blood plasma, most of which returns almost immediately to the blood in the capillaries by osmosis. Some tissue fluid, however, remains in interstitial spaces and must be returned to the blood by way of the lymphatic vessels. Without this return, blood volume and blood pressure would very soon decrease.

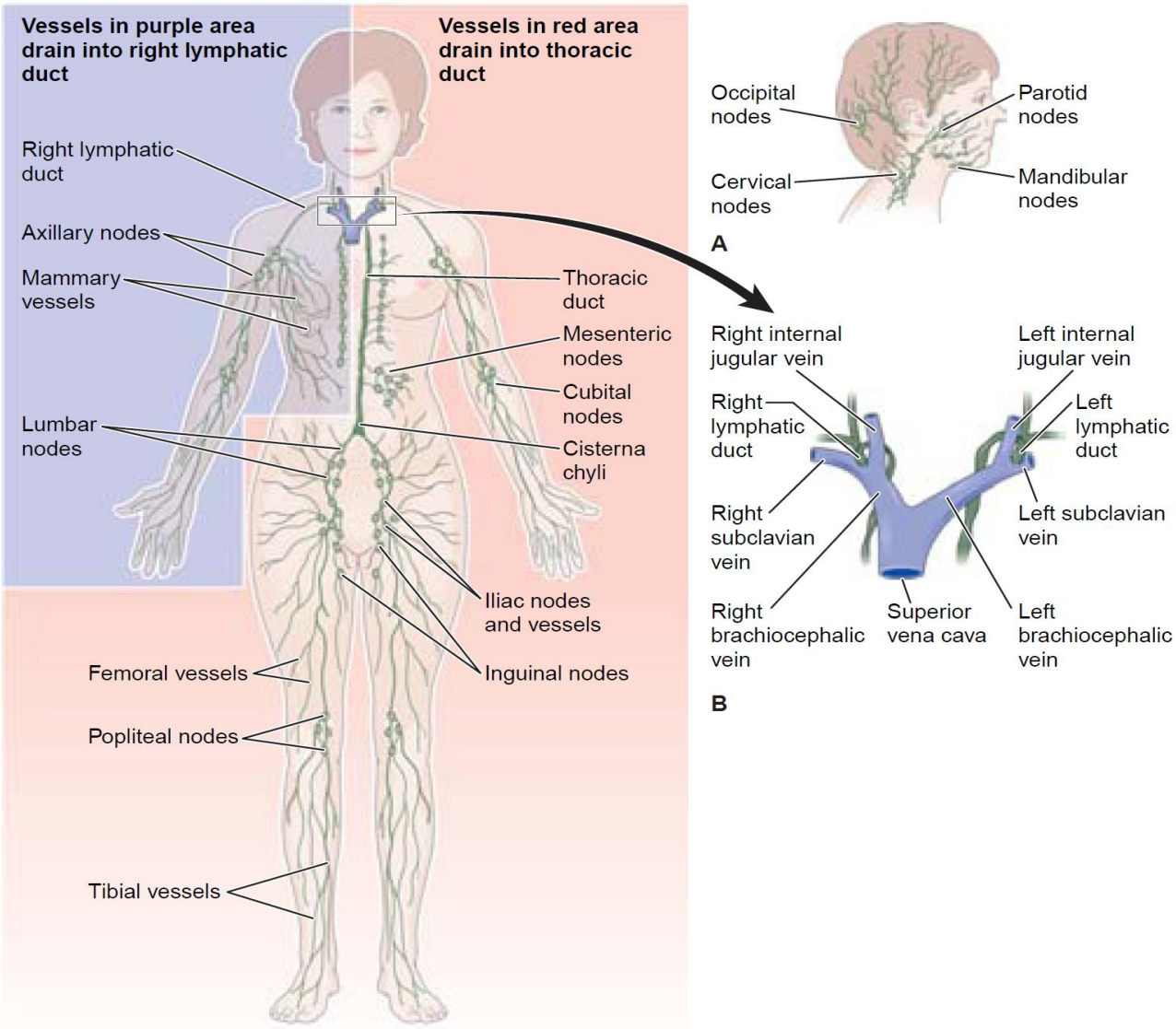


Figure: Vessels and nodes of the lymphatic system. **(A)** Lymph nodes and vessels of the head. **(B)** Drainage of right lymphatic duct and thoracic duct into subclavian veins.

Lymph vessels

The system of lymph vessels begins as dead-end **lymph capillaries** found in most tissue spaces. Lymph capillaries are very permeable and collect tissue fluid and proteins. **Lacteals** are specialized lymph capillaries in the villi of the small intestine; they absorb the fat-soluble end products of digestion, such as fatty acids and vitamins A, D, E, and K. Lymph capillaries unite to form larger lymph vessels, whose structure is very much like that of veins.

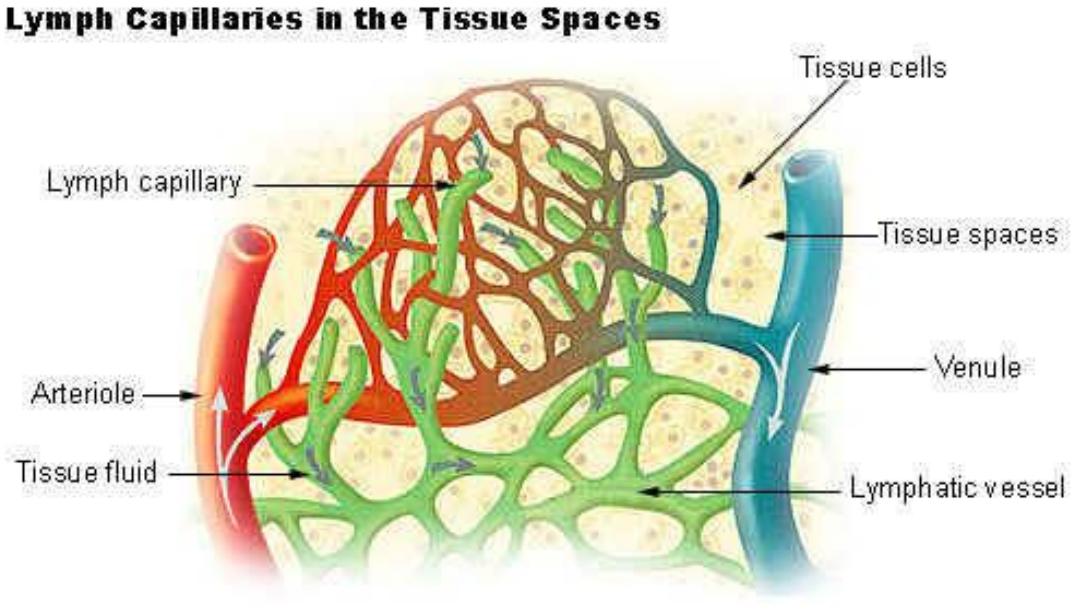
There is no pump for lymph (as the heart is the pump for blood), but the lymph is kept moving within lymph vessels by the same mechanisms that promote venous return.

The smooth muscle layer of the larger lymph vessels constricts, and the one-way valves (just like those of veins) prevent backflow of lymph. Lymph vessels in the extremities, especially the legs, are compressed by the skeletal muscles that surround them; this is the **skeletal muscle pump**.

The **respiratory pump** alternately expands and compresses the lymph vessels in the chest cavity and keeps the lymph moving. Where is the lymph going?

Back to the blood to become plasma again. The lymph vessels from the lower body unite in front of the lumbar vertebrae to form a vessel called the **cisterna chyli**, which continues upward in front of the backbone as the **thoracic duct**. Lymph vessels from the upper left quadrant of the body join the thoracic duct, which empties lymph into the left subclavian vein.

Lymph vessels from the upper right quadrant of the body unite to form the right lymphatic duct, which empties lymph into the right subclavian vein. Flaps in both subclavian veins permit the entry of lymph but prevent blood from flowing into the lymph vessels.



Lymphatic tissue

Lymphatic tissue consists mainly of lymphocytes in a mesh-like framework of connective tissue. Recall that most lymphocytes are produced from stem cells in the red bone marrow, and then migrate to the lymph nodes and nodules, to the spleen, and to the thymus.

In these structures, lymphocytes become activated and proliferate in response to infection (this is a function of all lymphatic tissue). The thymus has stem cells that produce a significant portion of the T lymphocytes.

Lymph nodes and nodules

Lymph nodes and **nodules** are masses of lymphatic tissue. Nodes and nodules differ with respect to size and location. Nodes are usually larger, 10 to 20 mm in length, and are encapsulated; nodules range from a fraction of a millimeter to several millimeters in length and do not have capsules. **Lymph nodes** are found in groups along the pathways of lymph vessels, and lymph flows through these nodes on its way to the subclavian veins. Lymph enters a node through several afferent lymph vessels and leaves through one or two efferent vessels. As lymph passes through a lymph node, bacteria and other foreign materials are phagocytized by fixed (stationary) **macrophages**. **Plasma cells** develop from lymphocytes exposed to pathogens in the lymph and produce antibodies. These antibodies will eventually reach the blood and circulate throughout the body. There are many groups of lymph nodes along all the lymph vessels throughout the body, but three paired groups deserve mention because of their strategic locations. These are the **cervical**, **axillary**, and **inguinal** lymph nodes.

Notice that these are at the junctions of the head and extremities with the trunk of the body. Breaks in the skin, with entry of pathogens, are much more likely to occur in the arms or legs or head rather than in the trunk. If these pathogens get to the lymph, they will be destroyed by the lymph nodes before they get to the trunk, before the lymph is returned to the blood in the subclavian veins.You may be familiar with the expression "swollen glands," as when a child has a strep throat (an inflammation of the pharynx caused by *Streptococcus* bacteria). These "glands" are the cervical lymph nodes that have enlarged as their macrophages attempt to destroy the bacteria in the lymph from the pharynx. **Lymph nodules** are small masses of lymphatic tissue found just beneath the epithelium of all **mucous membranes**.

The body systems lined with mucous membranes are those that have openings to the environment: the respiratory, digestive, urinary, and reproductive tracts. You can probably see that these are also strategic locations for lymph nodules, because any natural body opening is a possible portal of entry for pathogens.

For example, if bacteria in inhaled air get through the epithelium of the trachea, lymph nodules with their macrophages are in position to destroy these bacteria before they get to the blood. Some of the lymph nodules have specific names. Those of the small intestine are called **Peyer's patches**, and those of the pharynx are called **tonsils**.

The palatine tonsils are on the lateral walls of the pharynx, the adenoid (pharyngeal tonsil) is on the posterior wall, and the lingual tonsils are on the base of the tongue. The tonsils, therefore, form a ring of lymphatic tissue around the pharynx, which is a common pathway for food and air and for the pathogens they contain. A **tonsillectomy** is the surgical removal of the palatine tonsils and the adenoid and may be performed if the tonsils are chronically inflamed and swollen, as may happen in children. As mentioned earlier, the body has redundant structures to help ensure survival if one structure is lost or seriously impaired. Thus, there are many other lymph nodules in the pharynx to take over the function of the surgically removed tonsils.

8.2.1 SPLEEN

The **spleen** is located in the upper left quadrant of the abdominal cavity, just below the diaphragm, behind the stomach. The lower rib cage protects the spleen from physical trauma. In the fetus, the spleen produces red blood cells, a function assumed by the red bone marrow after birth. After birth the spleen is very much like a large lymph node, except that its functions affect the blood that flows through it rather than lymph. The functions of the spleen after birth are:

1. Contains plasma cells that produce antibodies to foreign antigens.
2. Contains fixed macrophages (RE cells) that phagocytize pathogens or other foreign material in the blood. The macrophages of the spleen also phagocytize old red blood cells and form bilirubin. By way of portal circulation, the bilirubin is sent to the liver for excretion in bile.
3. Stores platelets and destroys them when they are no longer useful. The spleen is not considered a vital organ, because other organs compensate for its functions if the spleen must be removed. The liver and red bone marrow will remove old red blood cells and platelets from circulation. The many lymph nodes and nodules will phagocytize pathogens (as will the liver) and have lymphocytes to be activated and plasma cells to produce antibodies.

Despite this redundancy, a person without a spleen is somewhat more susceptible to certain bacterial infections such as pneumonia and meningitis.

8.2.2 THYMUS

The **thymus** is located inferior to the thyroid gland.In the fetus and infant; the thymus is large and extends under the sternum. With increasing age, the thymus shrinks, and relatively little thymus tissue is found in adults, though it is still active. The stem cells of the thymus produce T lymphocytes or **T cells**; their functions are discussed in the next section. Thymic hormones are necessary for what may be called "immunological competence." To be competent means to be able to do something well. The thymic hormones enable the T cells to participate in the recognition of foreign antigens and to provide immunity. This capability of T cells is established early in life and then is perpetuated by the lymphocytes themselves.

The newborn's immune system is not yet fully mature, and infants are more susceptible to certain infections than are older children and adults. Usually by the age of 2 years, the immune system matures and becomes fully functional. This is why some vaccines, such as the measles vaccine, are not recommended for infants younger than 15 to 18 months of age. Their immune systems are not mature enough to respond strongly to the vaccine, and the protection provided by the vaccine may be incomplete.

8.2.3 IMMUNITY

Immunity may be defined as the ability to destroy pathogens or other foreign material and to prevent further cases of certain infectious diseases. This ability is of vital importance because the body is exposed to pathogens from the moment of birth.

Antigens are chemical markers that identify cells. Human cells have their own antigens that identify all the cells in an individual as "self". When antigens are foreign, or "non-self," they may be recognized as such and destroyed. Bacteria, viruses, fungi, and protozoa are all foreign antigens that activate immune responses, as are cell products such as bacterial toxins.

Malignant cells, which may be formed within the body as a result of mutations of normal cells, are also recognized as foreign and are usually destroyed before they can establish themselves and cause cancer. Unfortunately, organ transplants are also foreign tissue, and the immune system may reject (destroy) a transplanted kidney or heart. Sometimes the immune system mistakenly reacts to part of the body itself and causes an autoimmune disease.

Most often, however, the immune mechanisms function to protect the body from the microorganisms around us and within us. Immunity has two main components: innate immunity and adaptive immunity. Before we describe each component, a brief general comparison may be helpful. Innate immunity may be called nonspecific, does not create memory, and its responses are always the same regardless of the target.

Adaptive immunity is very specific as to its target, may involve antibodies, does create memory, and may become more efficient. Both kinds of immunity work together to prevent damage and disease.

Innate immunity

Innate immunity has several aspects: anatomic and physiological barriers, phagocytic and other defensive cells, and chemical secretions and reactions, including inflammation. These are not separate and distinct; rather there is a great deal of overlap among them, as you will see. The innate immune responses are always the same, and their degree of efficiency does not increase with repeated exposure.

- **Barriers**

The stratum corneum of the epidermis of the skin is non-living, and when unbroken is an excellent barrier to pathogens of all kinds. The fatty acids in sebum help limit the growth of bacteria on the skin. The living cells of the epidermis produce defensins, which are antimicrobial chemicals. The mucous membranes of the respiratory, digestive, urinary, and reproductive tracts are living tissue, yet still a good barrier. The ciliated epithelium of the upper respiratory tract is an especially effective barrier. Dust and pathogens are trapped on the mucus, the cilia sweep the mucus to the pharynx, and it is swallowed. The hydrochloric acid of the gastric juice destroys most pathogens that enter the stomach, either in mucus or with food and drink.

Lysozyme, an enzyme found in saliva and tears, inhibits the growth of bacteria in the oral cavity and on the warm, wet surface of the eye. The subcutaneous tissue contains many white blood cells (WBCs), as does the areolar connective tissue below the epithelium of mucous membranes.

- **Defensive Cells**

Remember that many of our defensive cells are white blood cells. Macrophages, both fixed and wandering, have receptors for the pathogens humans are likely to encounter (this probably reflects millions of years of coexistence) and are very efficient phagocytes. Other cells capable of phagocytosis of pathogens or other foreign antigens are the neutrophils and, to a lesser extent, the eosinophils. Phagocytic cells use intracellular enzymes and chemicals such as hydrogen peroxide (H2O2) to destroy ingested pathogens. The Langerhans cells of the skin, and other dendritic cells throughout the body, also phagocytize foreign material, not merely to destroy it, but to take it to a lymph node where the lymphocytes of adaptive immune mechanisms are then activated. The macrophages are also involved in activating these lymphocytes. This is a very important link between the two components of immunity.

Natural killer cells (NK cells) circulate in the blood but are also found in the red bone marrow, spleen, and lymph nodes. They are a small portion (about 10%) of the total lymphocytes, but are able to destroy many kinds of pathogens and tumor cells. NK cells make direct contact with foreign cells, and kill them by rupturing their cell membranes (with chemicals called perforins) or by inflicting some other kind of chemical damage. Basophils and mast cells (a type of connective tissue cell) are also defensive cells that are found throughout areolar connective tissue. They produce histamine and leukotrienes. Histamine causes vasodilation and makes capillaries more permeable; these are aspects of inflammation. Leukotrienes also increase capillary permeability and attract phagocytic cells to the area.

- **Chemical Defenses**

Chemicals that help the body resist infection include the interferons, complement, and the chemicals involved in inflammation. The **interferons** (alpha-, beta-, and gamma-interferons) are proteins produced by cells infected with viruses and by T cells. Viruses must be inside a living

cell to reproduce, and although interferon cannot prevent the entry of viruses into cells, it does block their reproduction. When viral reproduction is blocked, the viruses cannot infect new cells and cause disease. Interferon is probably a factor in the self-limiting nature of many viral diseases (and is used in the treatment of some diseases, such as hepatitis C). **Complement** is a group of more than 20 plasma proteins that circulate in the blood until activated. They are involved in the lysis of cellular antigens and the labeling of noncellular antigens. Some stimulate the release of histamine in inflammation; others attract WBCs to the site.

Inflammation is a general response to damage of any kind: microbial, chemical, or physical. Basophils and mast cells release histamine and leukotrienes, which affect blood vessels as previously described.Vasodilation increases blood flow to the damaged area, and capillaries become more permeable; tissue fluid and WBCs collect at the site. The purpose of inflammation is to try to contain the damage, keep it from spreading, eliminate the cause, and permit repair of the tissue to begin. From even this brief description you can see why the four signs of inflammation are redness, heat, swelling, and pain: redness from greater blood flow, heat from the blood and greater metabolic activity, swelling from the accumulation of tissue fluid, and pain from the damage itself and perhaps the swelling. Inflammation is a positive feedback mechanism that may become a vicious cycle of damage and more damage. The hormone cortisol is one brake that prevents this, and at least one of the complement proteins has this function as well. There are probably other chemical signals (in general called **cytokines** and **chemokines**) that help limit inflammation to an extent that is useful. In summary, innate immunity is nonspecific, is always the same, does not create memory, and does not become more efficient upon repeated exposures. Some cells of innate immune mechanisms also activate the adaptive immune mechanisms.

Adaptive immunity

To adapt means to become suitable, and adaptive immunity can become "suitable" for and respond to almost any foreign antigen. Adaptive immunity is specific and is carried out by lymphocytes and macrophages. The majority of lymphocytes are the T lymphocytes and B lymphocytes, or, more simply, **T cells** and **B cells**. In the embryo, T cells are produced in the bone marrow and thymus. They must pass through the thymus, where the thymic hormones bring about

their maturation. The T cells then migrate to the spleen, lymph nodes, and lymph nodules, where they are found after birth. Produced in the embryonic bone marrow, B cells migrate directly to the spleen and lymph nodes and nodules.

When activated during an immune response, some B cells will divide many times and become plasma cells that produce antibodies to a specific foreign antigen. The mechanisms of immunity that involve T cells and B cells are specific, meaning that one foreign antigen is the target each time a mechanism is activated. A macrophage has receptor sites for foreign chemicals such as those of bacterial cell walls or flagella, and may phagocytize just about any foreign material it comes across (as will the Langerhans or dendritic cells). T cells and B cells, however, are very specific.

The first step in the destruction of a pathogen or foreign cell is the recognition of its antigens as foreign. Both T cells and B cells are capable of this, but the immune mechanisms are activated especially well when this recognition is accomplished by macrophages and a specialized group of T lymphocytes called **helper T cells** (also called CD4 T cells). The foreign antigen is first phagocytized by a macrophage, and parts of it are "presented" on the macrophage's cell membrane. Also on the macrophage membrane are "self" antigens that are representative of the antigens found on all of the cells of the individual.

Therefore, the helper T cell that encounters this macrophage is presented not only with the foreign antigen but also with "self" antigens for comparison. The helper T cell becomes sensitized to and specific for the foreign antigen, the one that does not belong in the body.The recognition of an antigen as foreign initiates one or both of the mechanisms of adaptive immunity. These are **cell-mediated immunity** (sometimes called simply cellular immunity), in which T cells and macrophages participate, and **antibody-mediated immunity** (or **humoral immunity**), which involves T cells, B cells, and macrophages.

a) Cell-Mediated Immunity

This mechanism of immunity does not result in the production of antibodies, but it is effective against intracellular pathogens such as viruses, fungi, malignant cells, and grafts of foreign tissue. As mentioned earlier, the first step is the recognition of the foreign antigen by macrophages and helper T cells, which become activated and are specific.

These activated T cells, which are antigen specific, divide many times to form **memory T cells** and **cytotoxic** (**killer**) **T cells** (also called CD8 T cells). The memory T cells will remember the specific foreign antigen and become active if it enters the body again. Cytotoxic T cells are able to chemically destroy foreign antigens by disrupting cell membranes. This is how cytotoxic T cells destroy cells infected with viruses and prevent the viruses from reproducing. These T cells also produce cytokines, which are chemicals that attract macrophages to the area and activate them to phagocytize the foreign antigen and cellular debris.

It was once believed that another subset of T cells served to stop the immune response, but this may not be so. It seems probable that the CD_4 and CD_8 T cells also produce feedback chemicals to limit the immune response once the foreign antigen has been destroyed. The memory T cells, however, will quickly initiate the cell-mediated immune response should there be a future exposure to the antigen.

b) Antibody-Mediated Immunity

The first step is the recognition of the foreign antigen, this time by B cells as well as by macrophages and helper T cells. The sensitized helper T cell presents the foreign antigen to B cells, which provides a strong stimulus for the activation of B cells specific for this antigen. The activated B cells begin to divide many times, and two types of cells are formed. Some of the new B cells produced are **memory B cells**, which will remember the specific antigen and initiate a rapid response upon a second exposure. Other B cells become **plasma cells** that produce antibodies specific for this one foreign antigen.**Antibodies**, also called **immune globulins** (**Ig**) or **gamma globulins**, are proteins shaped somewhat like the letter Y.

Antibodies do not themselves destroy foreign antigens, but rather become attached to such antigens to "label" them for destruction. Each antibody produced is specific for only one antigen. Because there are so many different pathogens, you might think that the immune system would have to be capable of producing many different antibodies, and in fact this is so.

It is estimated that millions of different antigen- specific antibodies can be produced, should there be a need for them. The antibodies produced will bond to the antigen, forming an antigen–antibody complex. This complex results in **opsonization**, which means that the antigen is now "labeled" for phagocytosis by macrophages or neutrophils.

The antigen–antibody complex also stimulates the process of complement fixation. Some of the circulating complement proteins are activated, or fixed, by an antigen–antibody complex.

Complement fixation may be complete or partial. If the foreign antigen is cellular, the complement proteins bond to the antigen–antibody complex, then to one another, forming an enzymatic ring that punches a hole in the cell to bring about the death of the cell. This is complete (or entire) complement fixation and is what happens to bacterial cells (it is also the cause of hemolysis in a transfusion reaction). If the foreign antigen is not a cell—let's say it's a virus for example—partial complement fixation takes place, in which some of the complement proteins bond to the antigen–antibody complex. This is a chemotactic factor.

Chemotaxis means "chemical movement" and is actually another label that attracts macrophages to engulf and destroy the foreign antigen. In summary, adaptive immunity is very specific, does create memory, and because it does, often becomes more efficient with repeated exposures.

Antibody Responses

The first exposure to a foreign antigen does stimulate antibody production, but antibodies are produced slowly and in small amounts. Let us take as a specific example the measles virus. On a person's first exposure to this virus, antibody production is usually too slow to prevent the disease itself, and the person will have clinical measles. Most people who get measles recover, and upon recovery have antibodies and memory cells that are specific for the measlesvirus.

On a second exposure to this virus, the memory cells initiate rapid production of large amounts of antibodies, enough to prevent a second case of measles. This is the reason why we develop immunity to certain diseases, and this is also the basis for the protection given by **vaccines.**

As mentioned previously, antibodies label pathogens or other foreign antigens for phagocytosis or complement fixation. More specifically, antibodies cause agglutination or neutralization of pathogens before their eventual destruction. **Agglutination** means "clumping" and this is what happens when antibodies bind to bacterial cells. The bacteria that are clumped together by attached antibodies are more easily phagocytized by macrophages.

The activity of viruses may be neutralized by antibodies. A virus must get inside a living cell in order to reproduce itself. However, a virus with antibodies attached to it is unable to enter a cell, cannot reproduce, and will soon be phagocytized.

Bacterial toxins may also be neutralized by attached antibodies. The antibodies change the shape of the toxin, prevent it from exerting its harmful effects, and promote its phagocytosis by macrophages. **Allergies** are also the result of antibody activity

Types of immunity

If we consider the source of immunity, that is, where it comes from, we can begin with two major categories: genetic immunity and acquired immunity. Genetic immunity is conferred by our DNA, and acquired immunity is developed or acquired by natural or artificial means. **Genetic immunity** does not involve antibodies or the immune system; it is the result of our genetic makeup. What this means is that some pathogens cause disease in certain host species but not in others. Dogs and cats, for example, have genetic immunity to the measles virus, which is a pathogen only for people. Mouse leukemia viruses affect only mice, not people; we have genetic immunity to them. This is not because we have antibodies against these mouse viruses, but rather that we have genes that are the codes for proteins that make it impossible for such pathogens to reproduce in our cells and tissues. Monkeys have similar protective genes and proteins for the human AIDS virus; HIV does not cause disease in these monkeys. Because this is a genetic characteristic programmed in DNA, genetic immunity always lasts a lifetime.

Acquired immunity does involve antibodies. **Passive immunity** means that the antibodies are from another source, whereas **active immunity** means that the individual produces his or her own antibodies. One type of naturally acquired passive immunity is the placental transmission of antibodies (IgG) from maternal blood to fetal circulation. The baby will then be born temporarily immune to the diseases the mother is immune to. Such passive immunity may be prolonged by breast-feeding, because breast milk also contains maternal antibodies (IgA).

Artificially acquired passive immunity is obtained by the injection of immune globulins (gamma globulins or preformed antibodies) after presumed exposure to a particular pathogen. Such immune globulins are available for German measles, hepatitis A and B, tetanus and botulism (anti-toxins), and rabies. These are *not* vaccines; they do not stimulate immune mechanisms, but rather provide immediate antibody protection.

Passive immunity is always temporary, lasting a few weeks to a few months, because antibodies from another source eventually break down.

Active immunity is the production of one's own antibodies and may be stimulated by natural or artificial means. Naturally acquired active immunity means that a person has recovered from a disease and now has antibodies and memory cells specific for that pathogen. Artificially acquired active immunity is the result of a vaccine that has stimulated production of antibodies and memory cells.

No general statement can be made about the duration of active immunity. Recovering from plague, for example, confers lifelong immunity, but the plague vaccine does not. Duration of active immunity, therefore, varies with the particular disease or vaccine.

AGING AND THE LYMPHATIC SYSTEM

The aging of the lymphatic system is apparent in the decreased efficiency of immune responses. Elderly people are more likely than younger ones to develop shingles, when an aging immune system cannot keep the chickenpox virus dormant. They are also more susceptible to infections such as influenza and to what are called secondary infections, such as pneumonia following a case of the flu. Vaccines for both of these are available, and elderly people should be encouraged to get them.

Elderly people should also be sure to get a tetanus-diphtheria booster every 10 years. Autoimmune disorders are also more common among older people; the immune system mistakenly perceives a body tissue as foreign and initiates its destruction. Rheumatoid arthritis and myasthenia gravis are examples of autoimmune diseases. The incidence of cancer is also higher. Malignant cells that once might have been quickly destroyed remain alive and proliferate.

- **Applications to the nursing care**

1. Hodgkin's disease

Hodgkin's disease is a malignant disorder of the lymph nodes; the cause is not known. The first symptom is usually a swollen but painless lymph node, often in the cervical region. The individual is prompted to seek medical attention because of other symptoms: chronic fever, fatigue, and weight loss. The diagnosis involves biopsy of the lymph node and the finding of character-

istic cells. Treatment of Hodgkin's disease requires chemotherapy, radiation, or both. With early diagnosis and proper treatment, this malignancy is very often curable.

2. AIDS

Humanimmunodeficiency virus (HIV) is a retrovirus that infects helper T cells, macrophages, and other human cells. Once infected, the human cells contain HIV genes for the rest of their lives. Without sufficient helper T cells, the immune system is seriously impaired. Foreign antigens are not recognized, B cells are not activated, and killer T cells are not stimulated to proliferate.

The person with AIDS is susceptible to opportunistic infections, that is, those infections caused by fungi and protozoa that would not affect average healthy adults. Some of these infections may be treated with medications and even temporarily cured, but the immune system cannot prevent the next infection, or the next. As of this writing, AIDS is considered an incurable disease, although with proper medical treatment, some people with AIDS may live for many years. An infected person may unknowingly spread HIV to others before any symptoms appear.

It should be emphasized that AIDS, although communicable, is not a contagious disease. It is not spread by casual contact as is measles or the common cold. Transmission of AIDS occurs through sexual contact, by contact with infected blood, or by placental transmission of the virus from mother to fetus. At present we have no medications that will eradicate HIV, although certain combinations of drugs effectively suppress the virus in some people.For these people, AIDS may become a chronic but not fatal disease. Unfortunately, the medications do not work for everyone, and they are very expensive, beyond the means of most of the world's AIDS patients. Development of an AIDS vaccine has not yet been successful, although dozens of vaccines are undergoing clinical trials.

A vaccine stimulates antibody production to a specific pathogen, but everyone who has died of AIDS had antibodies to HIV. Those antibodies were not protective because HIV is a mutating virus; it constantly changes itself, making previously produced antibodies ineffective. An AIDS vaccine may not be entirely effective, may not have the 80% to 90% protection rate we have come to expect from vaccines. If we cannot cure AIDS and we cannot yet prevent it by vaccination, what recourse is left? Education.

Everyone should know how AIDS is spread. The obvious reason is to be able to avoid the high-risk behaviors that make acquiring HIV more likely. Yet another reason, however, is that everyone should know that they need not fear casual contact with people with AIDS. Healthcare personnel have a special responsibility, not only to educate themselves, but to provide education about AIDS for their patients and the families of their patients.

3. Vaccines

The purpose of vaccines is to prevent disease. A vaccine contains an antigen that the immune system will respond to, just as it would to the actual pathogen. The types of vaccine antigens are a killed or weakened (**attenuated**) pathogen, part of a pathogen such as a bacterial capsule, or an inactivated bacterial toxin called a **toxoid**. Because the vaccine itself does not cause disease (with very rare exceptions), the fact that antibody production to it is slow is not detrimental to the person. The vaccine takes the place of the first exposure to the pathogen and stimulates production of antibodies and memory cells.

On exposure to the pathogen itself, the memory cells initiate rapid production of large amounts of antibody, enough to prevent disease. We now have vaccines for many diseases. The tetanus and diphtheria vaccines contain toxoids, the inactivated toxins of these bacteria. Vaccines for pneumococcal pneumonia and meningitis contain bacterial capsules.

These vaccines cannot cause disease because the capsules are non-toxic and nonliving; there is nothing that can reproduce. Influenza and rabies vaccines contain killed viruses. Measles and the oral polio vaccines contain attenuated (weakened) viruses. Although attenuated pathogens are usually strongly antigenic and stimulate a protective immune response, there is a very small chance that the pathogen may regain its virulence and cause the disease. The live-virus oral polio vaccine (still being used in the quest to eliminate polio throughout the world) has a risk of 1 in 500,000 of causing polio. The killed-virus injectable polio vaccine has no such risk.

4. Allergies

An **allergy** is a hypersensitivity to a particular foreign antigen, called an **allergen**. Allergens include plant pollens, foods, chemicals in cosmetics, antibiotics such as penicillin, dust, and mold spores. Such allergens are not themselves harmful.

Most people, for example, can inhale pollen, eat peanuts, or take penicillin with no ill effects. Hypersensitivity means that the immune system overresponds to the allergen, and produces tissue damage by doing so.

Allergic responses are characterized by the production of IgE antibodies, which bond to mast cells. Mast cells are specialized connective tissue cells and are numerous in the connective tissue of the skin and mucous membranes. Chemicals in mast cells include histamine and leukotrienes, which are released by the bonding of IgE antibodies or when tissue damage occurs. These chemicals contribute to the process of inflammation by increasing the permeability of capillaries and venules. Tissue fluid collects and more WBCs are brought to the damaged area.

In an allergic reaction, the effects of inflammatory chemicals create symptoms such as watery eyes and runny nose (hay fever) or the more serious wheezing and difficult breathing that characterize asthma. Several medications are available to counteract these effects. Anaphylactic shock is an extreme allergic response that may be elicited by exposure to penicillin or insect venoms. On the first exposure, the person becomes highly sensitized to the foreign antigen.

On the second exposure, histamine is released from mast cells throughout the body and causes a drastic decrease in blood volume. The resulting drop in blood pressure may be fatal in only a few minutes. People who know they are allergic to bee stings, for example, may obtain a self-contained syringe of epinephrine to carry with them. Epinephrine can delay the progression of anaphylactic shock long enough for the person to seek medical attention.