# Chapter 1
# General Features of the Cardiovascular System

Paul A. Iaizzo

**Abstract** The purpose of this chapter is to provide a general overview of the cardiovascular system, to serve as a quick reference on the underlying physiological composition of this system. The rapid transport of molecules over long distances between internal cells, the body surface, and/or various specialized tissues and organs is the primary function of the cardiovascular system. This body-wide transport system is composed of several major components: blood, blood vessels, the heart, and the lymphatic system. When functioning normally, this system adequately provides for the wide-ranging activities that a human can accomplish. Failure in any of these components can lead to grave consequence. Subsequent chapters will cover, in greater detail, the anatomical, physiological, and/or pathophysiological features of the cardiovascular system.

**Keywords** Cardiovascular system · Blood · Blood vessels · Blood flow · Heart · Coronary circulation · Lymphatic system

## 1.1 Introduction

Currently, approximately 80 million individuals in the United States alone have some form of cardiovascular disease. More specifically, heart attacks continue to be an increasing problem in our society. Coronary bypass surgery, angioplasty, stenting, the implantation of pacemakers and/or defibrillators, and valve replacement are currently routine treatment procedures, with growing numbers of such procedures being performed each year. However, such treatments often provide only temporary relief of the progressive symptoms of cardiac disease. Optimizing therapies and/or the development of new treatments continues to dominate the cardiovascular biomedical industry (e.g., coated vascular or coronary stents, left ventricular assist devices, biventricular pacing, and transcatheter-delivered valves).

The purpose of this chapter is to provide a general overview of the cardiovascular system, to serve as a quick reference on the underlying physiological composition of this system. More details concerning the pathophysiology of the cardiovascular system and state-of-the-art treatments can be found in subsequent chapters. In addition, the reader should note that a list of source references is provided at the end of this chapter.

## 1.2 Components of the Cardiovascular System

The principle components considered to make up the cardiovascular system include blood, blood vessels, the heart, and the lymphatic system.

### *1.2.1 Blood*

Blood is composed of formed elements (cells and cell fragments) which are suspended in the liquid fraction known as plasma. Blood, considered as the only liquid connective tissue in the body, has three general functions: (1) transportation (e.g., $O_2$, $CO_2$, nutrients, waste, and hormones); (2) regulation (e.g., pH, temperature, and osmotic pressures); and (3) protection (e.g., against foreign molecules and diseases, as well as for clotting to prevent excessive loss of blood). Dissolved within the plasma are many proteins, nutrients, metabolic waste products, and various other molecules being transported between the various organ systems.

The formed elements in blood include red blood cells (erythrocytes), white blood cells (leukocytes), and the cell

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fragments known as platelets; all are formed in bone marrow from a common stem cell. In a healthy individual, the majority of bloods cells are red blood cells (~99%) which have a primary role in $O_2$ exchange. Hemoglobin, the iron-containing heme protein which binds oxygen, is concentrated within the red cells; hemoglobin allows blood to transport 40–50 times the amount of oxygen that plasma alone could carry. The white cells are required for the immune process to protect against infections and also cancers. The platelets play a primary role in blood clotting. In a healthy cardiovascular system, the constant movement of blood helps keep these cells well dispersed throughout the plasma of the larger diameter vessels.

The *hematocrit* is defined as the percentage of blood volume that is occupied by the red cells (erythrocytes). It can be easily measured by centrifuging (spinning at high speed) a sample of blood, which forces these cells to the bottom of the centrifuge tube. The leukocytes remain on the top and the platelets form a very thin layer between the cell fractions (other more sophisticated methods are also available for such analyses). Normal hematocrit is approximately 45% in men and 42% in women. The total volume of blood in an average-sized individual (70 kg) is approximately 5.5 l; hence the average red cell volume would be roughly 2.5 l. Since the fraction containing both leukocytes and platelets is normally relatively small or negligible, in such an individual, the plasma volume can be estimated to be 3.0 l. Approximately 90% of plasma is water which acts: (1) as a solvent; (2) to suspend the components of blood; (3) in the absorption of molecules and their transport; and (4) in the transport of thermal energy. Proteins make up 7% of the plasma (by weight) and exert a colloid osmotic pressure. Protein types include albumins, globulins (antibodies and immunoglobulins), and fibrinogen. To date, more than 100 distinct plasma proteins have been identified, and each presumably serves a specific function. The other main solutes in plasma include electrolytes, nutrients, gases (some $O_2$, large amounts of $CO_2$ and $N_2$), regulatory substances (enzymes and hormones), and waste products (urea, uric acid, creatine, creatinine, bilirubin, and ammonia).

### 1.2.2 Blood Vessels

Blood flows throughout the body tissues in blood vessels via bulk flow (i.e., all constituents together and in one direction). An extraordinary degree of blood vessel branching exists within the human body, which ensures that nearly every cell in the body lies within a short distance from at least one of the smallest branches of this system—a capillary. Nutrients and metabolic end products move between the capillary vessels and the surroundings of the cell through the interstitial fluid by diffusion. Subsequent movement of these molecules into a cell is accomplished by both diffusion and mediated transport. Nevertheless, blood flow through all organs can be considered as passive and occurs only because arterial pressure is kept higher than venous pressure via the pumping action of the heart.

In an individual at rest at a given moment, approximately only 5% of the total circulating blood is actually in capillaries. Yet, this volume of blood can be considered to perform the primary functions of the entire cardiovascular system, specifically the supply of nutrients and removal of metabolic end products. The cardiovascular system, as reported by the British physiologist William Harvey in 1628, is a closed loop system, such that blood is pumped out of the heart through one set of vessels (arteries) and then returns to the heart in another (veins).

More specifically, one can consider that there are two closed loop systems which both originate and return to the heart—the pulmonary and systemic circulations (Fig. 1.1). The pulmonary circulation is composed of the

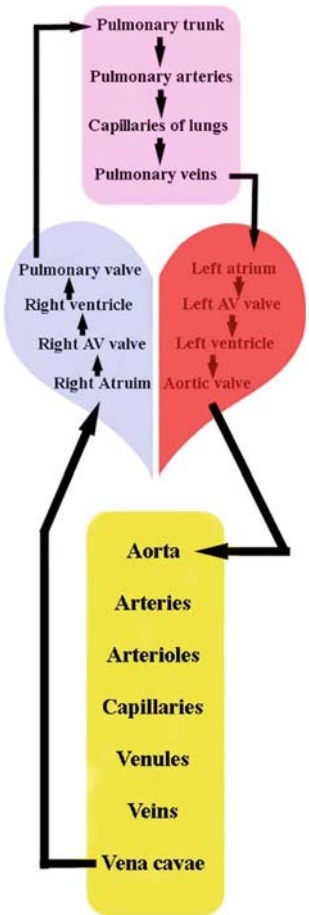


**Fig. 1.1** The major paths of blood flow through pulmonary and systemic circulatory systems. AV, atrioventricular

right heart pump and the lungs, whereas the systemic circulation includes the left heart pump which supplies blood to the systemic organs (i.e., all tissues and organs except the gas exchange portions of the lungs). Because the right and left heart pumps function in a series arrangement, both will circulate an identical volume of blood in a given minute (cardiac output, normally expressed in liters per minute).

In the systemic circuit, blood is ejected out of the left ventricle via a single large artery—the aorta. All arteries of the systemic circulation branch from the aorta (this is the largest artery of the body, with a diameter of 2–3 cm) and divide into progressively smaller vessels. The aorta's four principle divisions are the ascending aorta (begins at the aortic valve where, close by, the two coronary artery branches have their origin), arch of the aorta, thoracic aorta, and abdominal aorta.

The smallest of the arteries eventually branch into arterioles. They, in turn, branch into an extremely large number of the smallest diameter vessels—the capillaries (with an estimated 10 billion in the average human body). Next, blood exits the capillaries and begins its return to the heart via the venules. "Microcirculation" is a term coined to collectively describe the flow of blood through arterioles, capillaries, and the venules (Fig. 1.2).

Importantly, blood flow through an individual vascular bed is profoundly regulated by changes in activity of the sympathetic nerves innervating the arterioles. In addition, arteriolar smooth muscle is very responsive to changes in local chemical conditions within an organ (i.e., those changes associated with increases or decreases in the metabolic rates within a given organ).

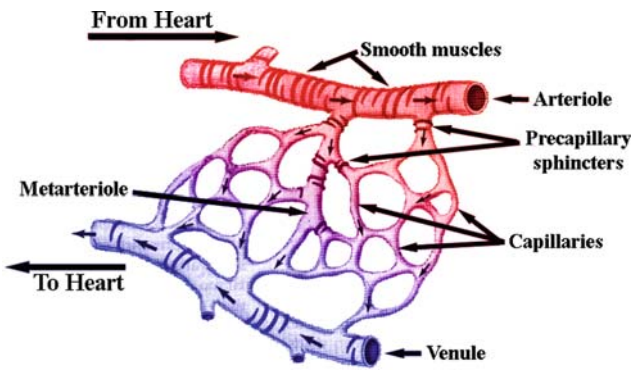


**Fig. 1.2** The microcirculation including arterioles, capillaries, and venules. The capillaries lie between, or connect, the arterioles and venules. They are found in almost every tissue layer of the body, but their distribution varies. Capillaries form extensive branching networks that dramatically increase the surface areas available for the rapid exchange of molecules. A metarteriole is a vessel that emerges from an arteriole and supplies a group of 10–100 capillaries. Both the arteriole and the proximal portion of the metarterioles are surrounded by smooth muscle fibers whose contractions and relaxations regulate blood flow through the capillary bed. Typically, blood flows intermittently through a capillary bed due to the periodic contractions of the smooth muscles (5–10 times per minute, vasomotion), which is regulated both locally (metabolically) and by sympathetic control. (Figure modified from Tortora and Grabowski, 2000)

Capillaries, which are the smallest and most numerous blood vessels in the human body (ranging from 5 to 10 μm in diameter) are also the thinnest walled vessels; an inner diameter of 5 μm is just wide enough for an erythrocyte (red blood cell) to squeeze through. Furthermore, it is estimated that there are 25,000 miles of capillaries in an adult, each with an individual length of about 1 mm.

Most capillaries are little more than a single cell layer thick, consisting of a layer of endothelial cells and a basement membrane. This minimal wall thickness facilitates the capillary's primary function, which is to permit the exchange of materials between cells in tissues and the blood. As mentioned above, small molecules (e.g., $O_2$, $CO_2$, sugars, amino acids, and water) are relatively free to enter and leave capillaries readily, promoting efficient material exchange. Nevertheless, the relative permeability of capillaries varies from region to region with regard to the physical properties of these formed walls.

Based on such differences, capillaries are commonly grouped into two major classes: continuous and fenestrated capillaries. In the continuous capillaries, which are more common, the endothelial cells are joined together such that the spaces between them are relatively narrow (i.e., tight intercellular gaps). These capillaries are permeable to substances having small molecular sizes and/or high lipid solubilities (e.g., $O_2$, $CO_2$, and steroid hormones) and are somewhat less permeable to small water-soluble substances (e.g., $Na^+$, $K^+$, glucose, and amino acids). In fenestrated capillaries, the endothelial cells possess relatively large pores that are wide enough to allow proteins and other large molecules to pass through. In some such capillaries, the gaps between the endothelial cells are even wider than usual, enabling quite large proteins (or even small cells) to pass through. Fenestrated capillaries are primarily located in organs whose functions depend on the rapid movement of materials across capillary walls, e.g., kidneys, liver, intestines, and bone marrow.

If a molecule cannot pass between capillary endothelial cells, then it must be transported across the cell membrane. The mechanisms available for transport across a capillary wall differ for various substances depending on their molecular size and degree of lipid solubility. For example, certain proteins are selectively transported across endothelial cells by a slow, energy-requiring process known as *transcytosis*. In this process, the endothelial cells initially engulf the proteins in the plasma within

capillaries by *endocytosis*. The molecules are then ferried across the cells by vesicular transport and released by *exocytosis* into the interstitial fluid on the other side. Endothelial cells generally contain large numbers of endocytotic and exocytotic vesicles, and sometimes these fuse to form continuous vesicular channels across the cell.

The capillaries within the heart normally prevent excessive movement of fluids and molecules across their walls, but several clinical situations have been noted where they may become "leaky." For example, "capillary leak syndrome," which may be induced following cardiopulmonary bypass, may last from hours up to days. More specifically, in such cases, the inflammatory response in the vascular endothelium can disrupt the "gatekeeper" function of capillaries; their increased permeability will result in myocardial edema.

From capillaries, blood throughout the body then flows into the venous system. It first enters the venules which then coalesce to form larger vessels—the veins (Fig. 1.2). Then veins from the various systemic tissues and organs (minus the gas exchange portion of the lungs) unite to produce two major veins—the inferior vena cava (lower body) and superior vena cava (above the heart). By way of these two great vessels, blood is returned to the right heart pump, specifically into the right atrium.

Like capillaries, the walls of the smallest venules are very porous and are the sites where many phagocytic white blood cells emigrate from the blood into inflamed or infected tissues. Venules and veins are also richly innervated by sympathetic nerves and smooth muscles which constrict when these nerves are activated. Thus, increased sympathetic nerve activity is associated with a decreased venous volume, which results in increased cardiac filling and therefore an increased cardiac output (via Starling's Law of the Heart).

Many veins, especially those in the limbs, also feature abundant valves (which are notably also found in the cardiac venous system) which are thin folds of the intervessel lining that form flap-like cusps. The valves project into the vessel lumen and are directed toward the heart (promoting unidirectional flow of blood). Because blood pressure is normally low in veins, these valves are important in aiding in venous return by preventing the backflow of blood, which is especially true in the upright individual. In addition, contractions of skeletal muscles (e.g., in the legs) also play a role in decreasing the size of the venous reservoir and thus the return of blood volume to the heart (Fig. 1.3).

The pulmonary circulation is comprised of a similar circuit. Blood leaves the right ventricle in a single great vessel, the pulmonary artery (trunk) which, within a short distance (centimeters), divides into the two main pulmonary arteries, one supplying the right lung and another the left. Once within the lung proper, the arteries continue to branch down to arterioles and then ultimately form capillaries. From there, the blood flows into venules, eventually forming four main pulmonary veins which empty into the left atrium. As blood flows through the lung capillaries, it picks up oxygen supplied to the lungs by breathing air; hemoglobin within the red blood cells is loaded up with oxygen (oxygenated blood).

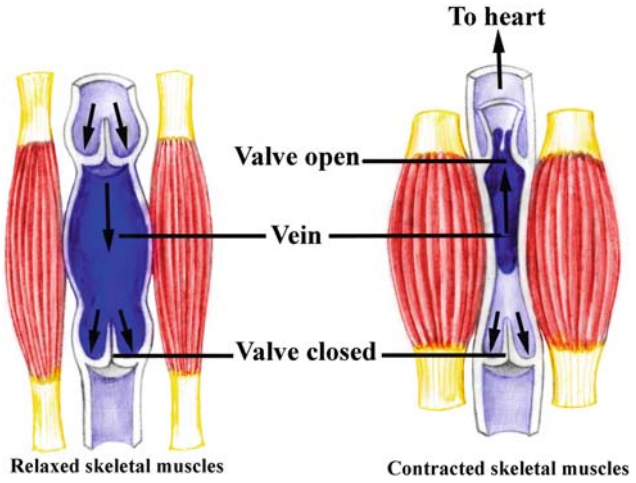


**Fig. 1.3** Contractions of the skeletal muscles aid in returning blood to the heart—skeletal muscle pump. While standing at rest, the relaxed vein acts as a reservoir for blood; contractions of limb muscles not only decrease this reservoir size (venous diameter), but also actively force the return of more blood to the heart. Note that the resulting increase in blood flow due to the contractions is only toward the heart due to the valves in the veins

### 1.2.3 Blood Flow

The task of maintaining an adequate interstitial homeostasis (the nutritional environment surrounding cells) requires that blood flows almost continuously through each of the millions of capillaries in the body. The following is a brief description of the parameters that govern flow through a given vessel. All blood vessels have certain lengths ($L$) and internal radii ($r$) through which blood flows when the pressure in the inlet and outlet is unequal ($P_i$ and $P_o$, respectively); in other words there is a pressure difference ($\Delta P$) between the vessel ends, which supplies the driving force for flow. Because friction develops between moving blood and the stationary vessels' walls, this fluid movement has a given resistance (vascular), which is the measure of how difficult it is to create blood flow through a vessel. One can then describe a relative relationship between vascular flow,

the pressure difference, and resistance (i.e., the basic flow equation):

$$\text{Flow} = \frac{\text{Pressure difference}}{\text{resistance}} \quad \text{or} \quad Q = \frac{\Delta P}{R}$$

where $Q$ is the flow rate (volume/time), $\Delta P$ the pressure difference (mmHg), and $R$ the resistance to flow (mmHg × time/volume).

This equation not only may be applied to a single vessel, but can also be used to describe flow through a network of vessels (i.e., the vascular bed of an organ or the entire systemic circulatory system). It is known that the resistance to flow through a cylindrical tube or vessel depends on several factors (described by Poiseuille) including: (1) radius; (2) length; (3) viscosity of the fluid (blood); and (4) inherent resistance to flow, as follows:

$$R = \frac{8L\eta}{\pi r^4}$$

where $r$ is the inside radius of the vessel, $L$ the vessel length, and $\eta$ the blood viscosity.

It is important to note that a small change in vessel radius will have a very large influence (fourth power) on its resistance to flow; e.g., decreasing vessel diameter by 50% will increase its resistance to flow by approximately 16-fold. If one combines the preceding two equations into one expression, which is commonly known as the Poiseuille equation, it can be used to better approximate the factors that influence flow though a cylindrical vessel:

$$Q = \frac{\Delta P \pi r^4}{8L\eta}$$

Nevertheless, flow will only occur when a pressure difference exists. Hence, it is not surprising that arterial blood pressure is perhaps the most regulated cardiovascular variable in the human body, and this is principally accomplished by regulating the radii of vessels (e.g., primarily within the arterioles and metarterioles) within a given tissue or organ system. Whereas vessel length and blood viscosity are factors that influence vascular resistance, they are not considered variables that can be easily regulated for the purpose of the moment-to-moment control of blood flow. Regardless, the primary function of the heart is to keep pressure within arteries higher than those in veins, hence a pressure gradient to induce flow. Normally, the average pressure in systemic arteries is approximately 100 mmHg, and this decreases to near 0 mmHg in the great caval veins.

The volume of blood that flows through any tissue in a given period of time (normally expressed as ml/min) is called the *local blood flow*. The velocity (speed) of blood flow (expressed as cm/s) can generally be considered to be inversely related to the vascular cross-sectional area, such that velocity is slowest where the total cross-sectional area is largest. Shown in Fig. 1.4 are the relative pressure drops one can detect through the vasculature; the pressure varies in a given vessel also relative to the active and relaxation phases of the heart function (see below).

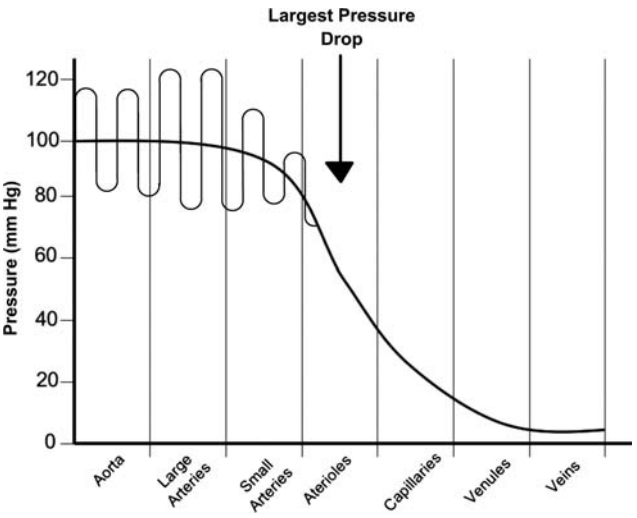


**Fig. 1.4** Shown here are the relative pressure changes one could record in the various branches of the human vascular system due to contractions and relaxation of the heart (pulsatile pressure changes). Note that pressure may be slightly higher in the large arteries than that leaving the heart into the aorta due to their relative compliance and diameter properties. The largest drops in pressures occur within the arterioles which are the active regulatory vessels. The pressures in the large veins that return blood to the heart are near zero

### 1.2.4 Heart

The heart lies in the center of the thoracic cavity and is suspended by its attachment to the great vessels within a fibrous sac known as the *pericardium*; note that humans have relatively thick-walled pericardiums compared to those of the commonly studied large mammalian cardiovascular models (i.e., canine, porcine, or ovine; see also Chapter 8). A small amount of fluid is present within the sac, *pericardial fluid*, which lubricates the surface of the heart and allows it to move freely during function (contraction and relaxation). The pericardial sac extends upward enclosing the proximal portions of the great vessels (see also Chapters 4 and 5).

The pathway of blood flow through the chambers of the heart is indicated in Fig. 1.5. Recall that venous blood returns from the systemic organs to the right atrium via the superior and inferior venae cavae. It next passes through the tricuspid valve into the right ventricles and from there is pumped through the pulmonary valve into the pulmonary artery. After passing through the

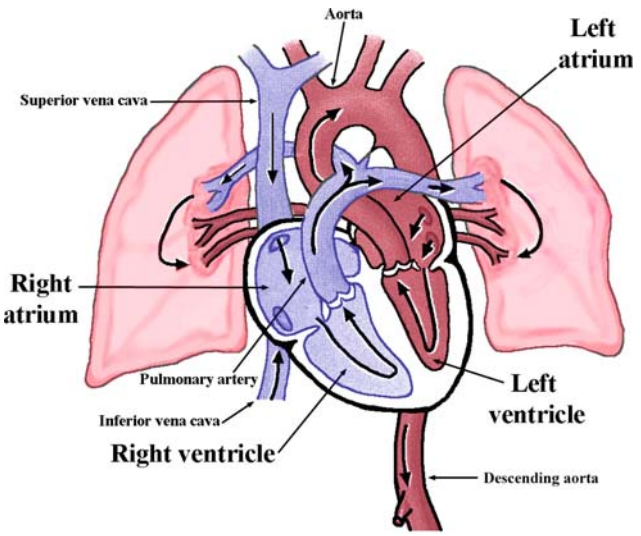


**Fig. 1.5** Pathway of blood flow through the heart and lungs. Note that the pulmonary artery (trunk) branches into left and right pulmonary arteries. There are commonly four main pulmonary veins that return blood from the lungs to the left atrium. (Modified from Tortora and Grabowski, 2000)

pulmonary capillary beds, the oxygenated pulmonary venous blood returns to the left atrium through the pulmonary veins. The flow of blood then passes through the mitral valve into the left ventricle and is pumped through the aortic valve into the aorta.

In general, the gross anatomy of the right heart pump is considerably different from that of the left heart pump, yet the pumping principles of each are primarily the same. The ventricles are closed chambers surrounded by muscular walls, and the valves are structurally designed to allow flow in only one direction. The cardiac valves passively open and close in response to the direction of the pressure gradient across them.

The myocytes of the ventricles are organized primarily in a circumferential orientation; hence when they contract, the tension generated within the ventricular walls causes the pressure within the chamber to increase. As soon as the ventricular pressure exceeds the pressure in the pulmonary artery (right) and/or aorta (left), blood is forced out of the given ventricular chamber. This active contractile phase of the cardiac cycle is known as *systole*. The pressures are higher in the ventricles than the atria during systole; hence the tricuspid and mitral (atrioventricular) valves are closed. When the ventricular myocytes relax, the pressure in the ventricles falls below that in the atria, and the atrioventricular valves open; the ventricles refill and this phase is known as *diastole*. The aortic and pulmonary (semilunar or outlet) valves are closed during diastole because the arterial pressures (in the aorta and pulmonary artery) are greater than the intraventricular pressures. Shown in Fig. 1.6 are the average pressures within the various chambers and great vessels of the heart. For more details on the cardiac cycle, see Chapter 18.

The effective pumping action of the heart requires that there be a precise coordination of the myocardial contractions (millions of cells), and this is accomplished via the conduction system of the heart. Contractions of each cell are normally initiated when electrical excitatory impulses (action potentials) propagate along their surface membranes. The myocardium can be viewed as a functional syncytium; action potentials from one cell conduct to the next cell via the gap junctions. In the healthy heart, the normal site for initiation of a heartbeat is within the sinoatrial node, located in the right atrium. For more details on this internal electrical system, refer to Chapter 11.

The heart normally functions in a very efficient fashion and the following properties are needed to maintain this effectiveness: (1) the contractions of the individual myocytes must occur at regular intervals and be synchronized (not arrhythmic); (2) the valves must fully open (not stenotic); (3) the valves must not leak (not insufficient or regurgitant); (4) the ventricular contractions must be forceful (not failing or lost due to an ischemic event); and (5) the ventricles must fill adequately during diastole (no arrhythmias or delayed relaxation).

### 1.2.5 Regulation of Cardiovascular Function

Cardiac output in a normal individual at rest ranges between 4 and 6 l/min, but during severe exercise the heart may be required to pump three to four times this amount. There are two primary modes by which the blood volume pumped by the heart, at any given moment, is regulated: (1) intrinsic cardiac regulation, in response to changes in the volume of blood flowing into the heart; and (2) control of heart rate and cardiac contractility by the autonomic nervous system. The intrinsic ability of the heart to adapt to changing volumes of inflowing blood is known as the *Frank–Starling* mechanism (law) of the heart, named after two great physiologists of a century ago.

In general, the Frank–Starling response can simply be described—the more the heart is stretched (an increased blood volume), the greater will be the subsequent force of ventricular contraction and, thus, the amount of blood ejected through the aortic valve. In other words, within its physiological limits, the heart will pump out nearly all the blood that enters it without allowing excessive damming of blood in veins. The underlying basis for this phenomenon is related to the optimization of the lengths of "sarcomeres," the functional subunits of striate muscle; there is optimization in the potential for the contractile

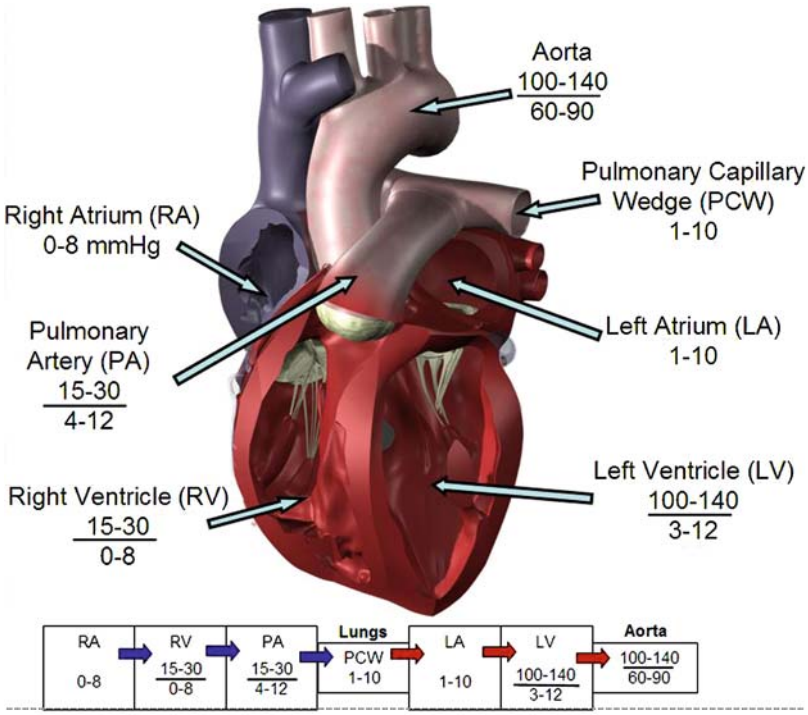


**Fig. 1.6** Average relative pressures within the various chambers and great vessels of the heart. During filling of the ventricles the pressures are much lower and, upon the active contraction, they will increase dramatically. Relative pressure ranges that are normally elicited during systole (active contraction; ranges noted above lines) and during diastole (relaxation; ranges noted below lines) are shown for the right and left ventricles, right and left atria, the pulmonary artery and pulmonary capillary wedge, and aorta. Shown at the *bottom* of this figure are the relative pressure changes one can detect in a normal healthy heart as one moves from the right heart through the left heart and into the aorta; this flow pattern is the series arrangement of the two-pump system

proteins (actin and myosin) to form "crossbridges". It should also be noted that "stretch" of the right atrial wall (e.g., because of an increased venous return) can directly increase the rate of the sinoatrial node by 10–20%; this also aids in the amount of blood that will ultimately be pumped per minute by the heart. For more details on the contractile function of heart, refer to Chapter 10.

The pumping effectiveness of the heart is also effectively controlled by the sympathetic and parasympathetic components of the autonomic nervous system. There is extensive innervation of the myocardium by such nerves (for more details on innervation see Chapter 12). To get a feel for how effective the modulation of the heart by this innervation is, investigators have reported that cardiac output often can be increased by more than 100% by sympathetic stimulation and, by contrast, output can be nearly terminated by strong parasympathetic (vagal) stimulation.

Cardiovascular function is also modulated through reflex mechanisms that involve baroreceptors, the chemical composition of the blood, and via the release of various hormones. More specifically, "baroreceptors," which are located in the walls of some arteries and veins, exist to monitor the relative blood pressure. Those specifically located in the carotid sinus help to reflexively maintain normal blood pressure in the brain, whereas those located in the area of the ascending arch of the aorta help to govern general systemic blood pressure (for more details, see Chapters 12, 13, and 19).

Chemoreceptors that monitor the chemical composition of blood are located close to the baroreceptors of the carotid sinus and arch of the aorta, in small structures known as the carotid and aortic bodies. The chemoreceptors within these bodies detect changes in blood levels of $O_2$, $CO_2$, and $H^+$. Hypoxia (a low availability of $O_2$), acidosis (increased blood concentrations of $H^+$), and/or hypercapnia (high concentrations of $CO_2$) stimulate the chemoreceptors to increase their action potential firing frequencies to the brain's cardiovascular control centers. In response to this increased signaling, the central nervous system control centers (hypothalamus), in turn, cause an increased sympathetic stimulation to arterioles and veins, producing vasoconstriction and a subsequent increase in blood pressure. In addition, the chemoreceptors simultaneously send neural input to the respiratory control centers in the brain, to induce the appropriate control of respiratory function (e.g., increase $O_2$ supply and reduce $CO_2$ levels). Features of this hormonal regulatory system

include: (1) the renin–angiotensin–aldosterone system; (2) the release of epinephrine and norepinephrine; (3) antidiuretic hormones; and (4) atrial natriuretic peptides (released from the atrial heart cells). For details on this complex regulation, refer to Chapter 13.

The overall functional arrangement of the blood circulatory system is shown in Fig. 1.7. The role of the heart needs to be considered in three different ways: as the right pump, as the left pump, and as the heart muscle tissue which has its own metabolic and flow requirements. As described above, the pulmonary (right heart) and system (left heart) circulations are arranged in a series (see also Fig. 1.6). Thus, cardiac output increases in each at the same rate; hence an increased systemic need for a greater cardiac output will automatically lead to a greater flow of blood through the lungs (simultaneously producing a greater potential for $O_2$ delivery).

In contrast, the systemic organs are functionally arranged in a parallel arrangement; hence, (1) nearly all systemic organs receive blood with an identical composition (arterial blood) and (2) the flow through each organ can be and is controlled independently. For example, during exercise, the circulatory response is an increase in blood flow through some organs (e.g., heart, skeletal muscle, brain) but not others (e.g., kidney and gastrointestinal system). The brain, heart, and skeletal muscles typify organs in which blood flows solely to supply the metabolic needs of the tissue; they do not recondition the blood.

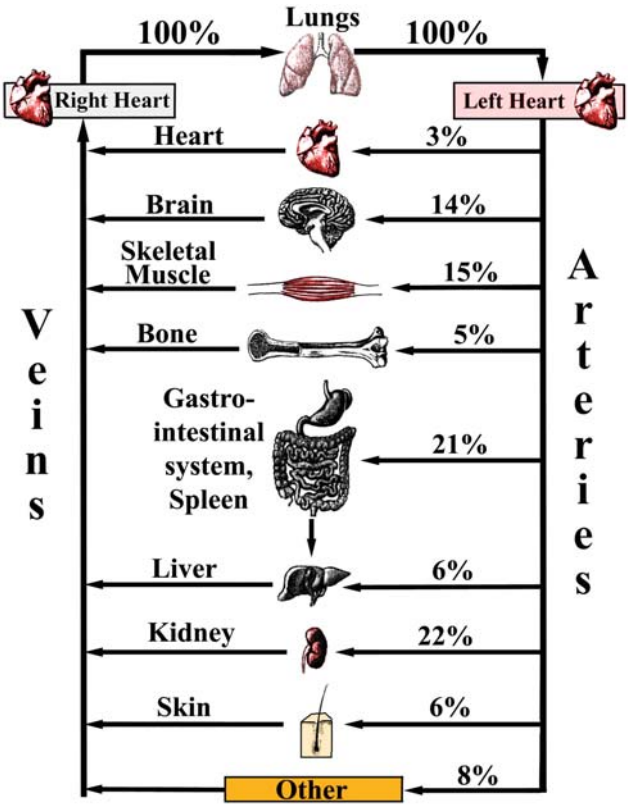


**Fig. 1.7** A functional representation of the blood circulatory system. The percentages indicate the approximate relative percentage of the cardiac output that is delivered, at a given moment in time, to the major organ systems within the body

The blood flow to the heart and brain is normally only slightly greater than that required for their metabolism; hence small interruptions in flow are not well tolerated. For example, if coronary flow to the heart is interrupted, electrical and/or functional (pumping ability) activities will noticeably be altered within a few beats. Likewise, stoppage of flow to the brain will lead to unconsciousness within a few seconds and permanent brain damage can occur in as little as 4 min without flow. The flow to skeletal muscles can dramatically change (flow can increase from 20 to 70% of total cardiac output) depending on use, and thus their metabolic demand.

Many organs in the body perform the task of continually reconditioning the circulating blood. Primary organs performing such tasks include: (1) the lungs ($O_2$ and $CO_2$ exchange); (2) the kidneys (blood volume and electrolyte composition, $Na^+$, $K^+$, $Ca^{2+}$, $Cl^-$, and phosphate ions); and (3) the skin (temperature). Blood-conditioning organs can often withstand, for short periods of time, significant reductions of blood flow without subsequent compromise.

### 1.2.6 The Coronary Circulation

In order to sustain viability, it is not possible for nutrients to diffuse from the chambers of the heart through all the layers of cells that make up the heart tissue. Thus, the coronary circulation is responsible for delivering blood to the heart tissue itself (the myocardium). The normal heart functions almost exclusively as an aerobic organ with little capacity for anaerobic metabolism to produce energy. Even during resting conditions, 70–80% of the oxygen available within the blood circulating through the coronary vessels is extracted by the myocardium.

It then follows that because of the limited ability of the heart to increase oxygen availability by further increasing oxygen extraction, increases in myocardial demand for oxygen (e.g., during exercise or stress) must be met by equivalent increases in coronary blood flow. Myocardial ischemia results when the arterial blood supply fails to meet the needs of the heart muscle for oxygen and/or metabolic substrates. Even mild cardiac ischemia can result in anginal pain, electrical changes (detected on an electrocardiogram), and the cessation of regional cardiac contractile function. Sustained ischemia within a given myocardial region will most likely result in an infarction.

As noted above, as in any microcirculatory bed, the greatest resistance to coronary blood flow occurs in the arterioles. Blood flow through such vessels varies approximately with the fourth power of these vessels' radii; hence, the key regulated variable for the control of coronary blood flow is the degree of constriction or dilatation of coronary arteriolar vascular smooth muscle. As with all systemic vascular beds, the degree of coronary arteriolar smooth muscle tone is normally controlled by multiple independent negative feedback loops. These mechanisms include various neural, hormonal, local non-metabolic, and local metabolic regulators.

It should be noted that the local metabolic regulators of arteriolar tone are usually the most important for coronary flow regulation; these feedback systems involve oxygen demands of the local cardiac myocytes. In general, at any point in time, coronary blood flow is determined by integrating all the different controlling feedback loops into a single response (i.e., inducing either arteriolar smooth muscle constriction or dilation). It is also common to consider that some of these feedback loops are in opposition to one another. Interestingly, coronary arteriolar vasodilation from a resting state to one of intense exercise can result in an increase of mean coronary blood flow from approximately 0.5–4.0 ml/min/g. For more details on metabolic control of flow, see Chapters 13 and 19.

As with all systemic circulatory vascular beds, the aortic and/or arterial pressures (perfusion pressures) are vital for driving blood through the coronaries, and thus need to be considered as additional important determinants of coronary flow. More specifically, coronary blood flow varies directly with the pressure across the coronary microcirculation, which can be essentially considered as the immediate aortic pressure, since coronary venous pressure is near zero. However, since the coronary circulation perfuses the heart, some very unique determinants for flow through these capillary beds may also occur; during systole, myocardial extravascular compression causes coronary flow to be near zero, yet it is relatively high during diastole (note that this is the opposite of all other vascular beds in the body). For more details on the coronary vasculature and its function, refer to Chapter 7.

### 1.2.7 Lymphatic System

The lymphatic system represents an accessory pathway by which large molecules (proteins, long-chain fatty acids, etc.) can reenter the general circulation and thus not accumulate in the interstitial space. If such particles accumulate in the interstitial space, then filtration forces exceed reabsorptive forces and edema occurs. Almost all tissues in the body have lymph channels that drain excessive fluids from the interstitial space (exceptions include portions of skin, the central nervous system, the endomysium of muscles, and bones which have pre-lymphatic channels).

The lymphatic system begins in various tissues with blind-end-specialized lymphatic capillaries that are roughly the size of regular circulatory capillaries, but they are less numerous (Fig. 1.8). However, the lymphatic capillaries are very porous and, thus, can easily collect the large particles within the interstitial fluid known as lymph. This fluid moves through the converging lymphatic vessels and is filtered through lymph nodes where bacteria and other particulate matter are removed. Foreign particles that are trapped in the lymph nodes can then be destroyed (phagocytized) by tissue macrophages which line a meshwork of sinuses that lie within. Lymph nodes also contain T and B lymphocytes which can destroy foreign substances by a variety of immune responses. There are approximately 600 lymph nodes located along the lymphatic vessels; they are 1–25 mm long (bean shaped) and covered by a capsule of dense connective tissue. Lymph flow is typically unidirectional through the nodes (Fig. 1.8).

The lymphatic system is also one of the major routes for absorption of nutrients from the gastrointestinal tract (particularly for the absorption of fat- and lipid-soluble vitamins A, D, E, and K). For example, after a fatty meal, lymph in the thoracic duct may contain as much as 1–2% fat.

The majority of lymph then reenters the circulatory system in the thoracic duct which empties into the venous

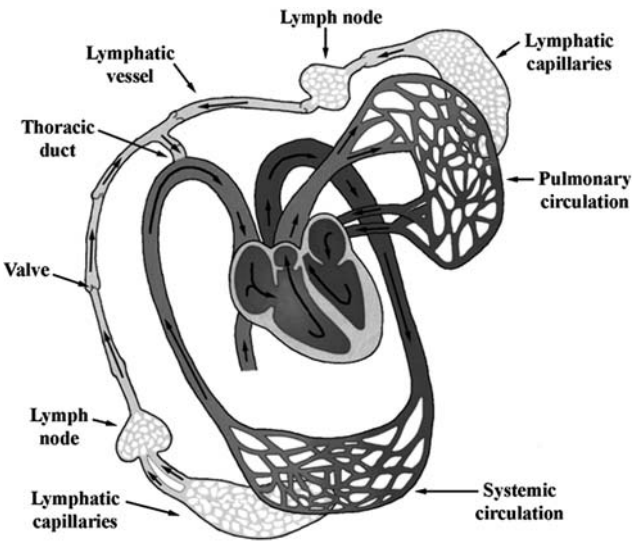


**Fig. 1.8** Schematic diagram showing the relationship between the lymphatic system and the cardiopulmonary system. The lymphatic system is unidirectional, with fluid flowing from interstitial space back to the general circulatory system. The sequence of flow is from blood capillaries (systemic and pulmonary) to the interstitial space, to the lymphatic capillaries (lymph), to the lymphatic vessels, to the thoracic duct, into the subclavian veins (back to the right atrium). (Modified from Tortora and Grabowski, 2000)

system at the juncture of the left internal jugular and subclavian veins (which then enters into the right atrium; see Chapters 4 and 5). The flow of lymph from tissues toward the entry point into the circulatory system is induced by two main factors: (1) higher tissue interstitial pressure and (2) the activity of the lymphatic pump (contractions within the lymphatic vessels themselves, contractions of surrounding muscles, movement of parts of the body, and/or pulsations of adjacent arteries). In the largest lymphatic vessels (e.g., thoracic duct), the pumping action can generate pressures as high as 50–100 mmHg. Valves located in the lymphatic vessel, like in veins, aid in the prevention of the backflow of lymph.

Approximately 2.5 l of lymphatic fluid enters the general blood circulation (cardiopulmonary system) each day. In the steady state, this indicates a total body net transcapillary fluid filtration rate of 2.5 l/day. When compared with the total amount of blood that circulates each day (approximately 7,000 l/day), this seems almost insignificant; however, blockage of such flow will quickly cause serious edema. Therefore, the lymphatic circulation plays a critical role in keeping the interstitial protein concentration low and also in removing excess capillary filtrate from tissues throughout the body.

### *1.2.8 Summary*

The rapid transport of molecules over long distances between internal cells, the body surface, and/or various specialized tissues and organs is the primary function of the cardiovascular system. This body-wide transport system is composed of several major components: blood, blood vessels, the heart, and the lymphatic system. When functioning normally, this system adequately provides for the wide-ranging activities that a human can accomplish. Failure in any of these components can lead to grave consequence. Many of the subsequent chapters in this book will cover, in greater detail, the anatomical, physiological, and pathophysiological features of the cardiovascular system. Furthermore, the normal and abnormal performance of the heart and various clinical treatments to enhance function will be discussed.

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