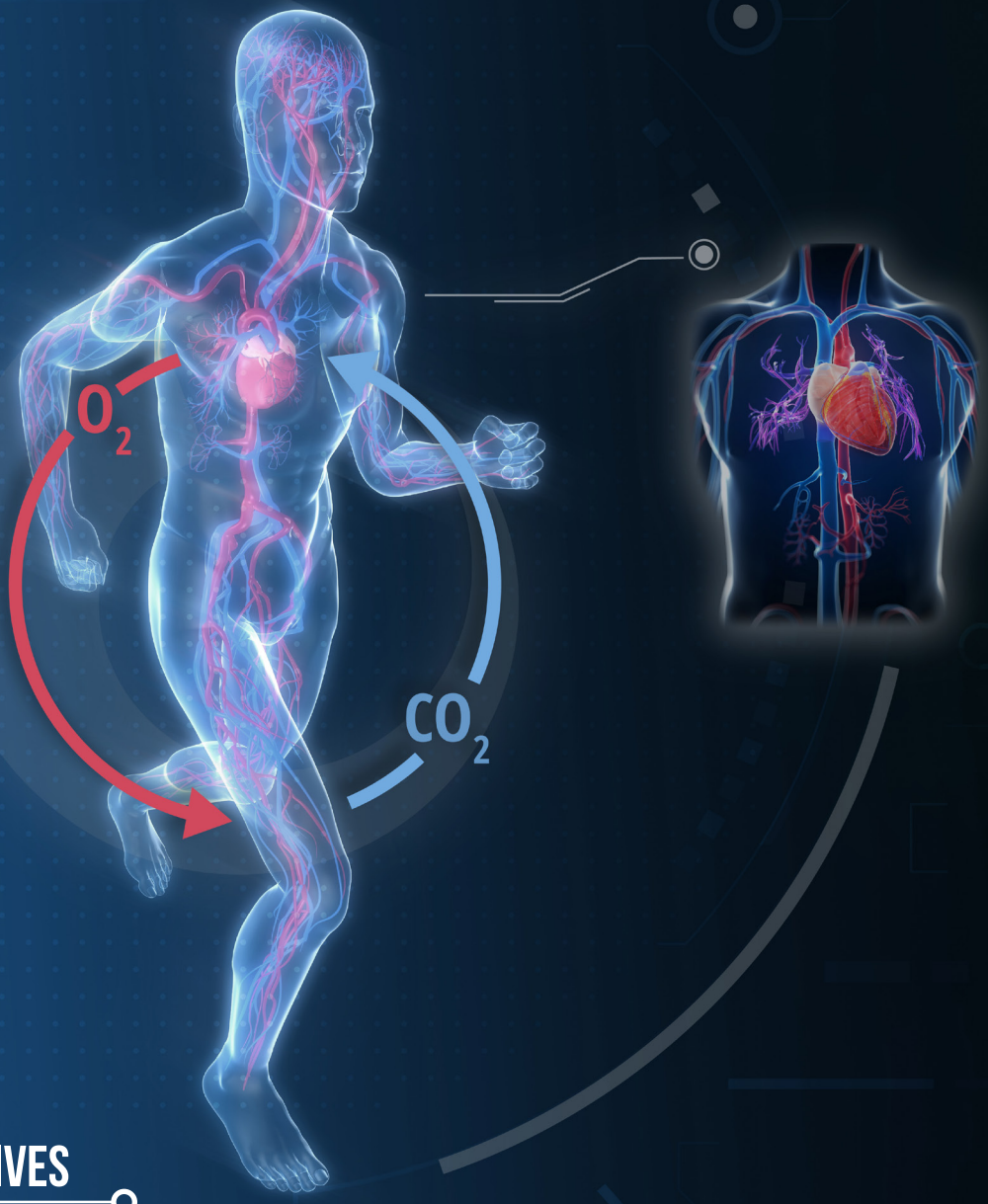
THE CIRCULATORY SYSTEM AND ITS RESPONSES TO EXERCISE



LEARNING OBJECTIVES

+ **DESCRIBE** the changes in blood flow distribution during exercise and the mechanisms for these changes.
+ **DISCUSS** the factors that influence blood pressure during exercise.
+ **IDENTIFY** key inputs to the cardiovascular control center.

THE CIRCULATORY SYSTEM AND ITS RESPONSES TO EXERCISE

In earlier times, it was believed that blood was produced by the liver and consumed by the organs. Galen, the influential Greek physician and philosopher (199–216 AD), proposed that blood did not recirculate through the body; rather, all blood arriving to the organs had been newly produced. This belief persisted for over 1,400 years until English physician William Harvey (1578–1657) discovered that blood comes out of the left side of the heart, passes through the tissues, and returns to the right side of the heart in a closed circulatory loop ***(Figure 1)***. In spite of Harvey's extensive experimental evidence, it took many years before his discovery of a closed circulatory system was fully accepted. Harvey's scientific revolutionary contributions have led others to call him the "Father of Modern Physiology."

The previous chapter discussed how alteration of the electrical activity of the heart increases cardiac output. This chapter explains how the heart and blood vessels increase delivery of blood and oxygen to contracting muscles in response to exercise.

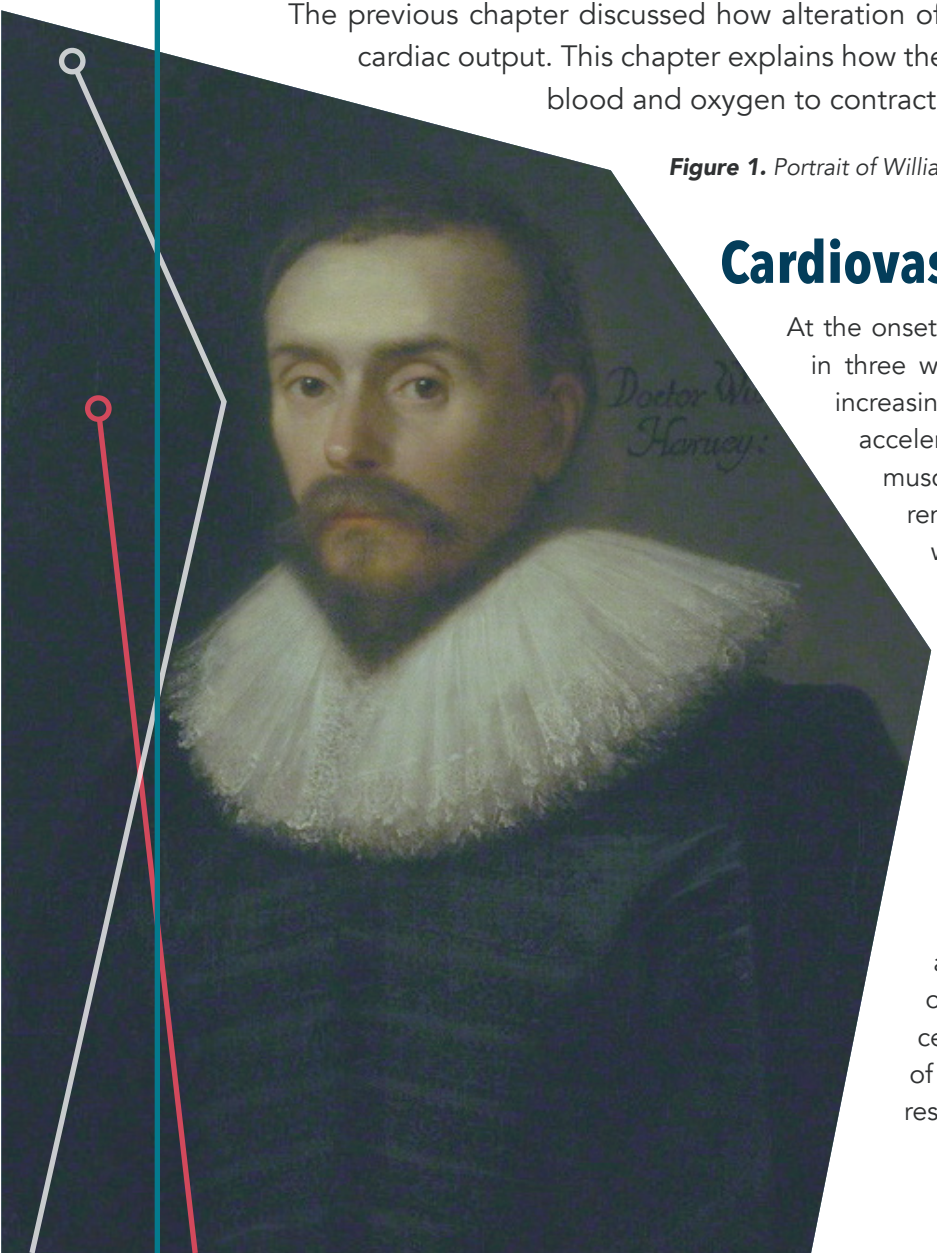


Figure 1. *Portrait of William Harvey by artist Daniël Mijtens. Source: Wikimedia*

Cardiovascular Control Center

At the onset of exercise, the cardiovascular system responds in three ways: the heart starts beating faster and harder, increasing cardiac output; blood pressure increases, accelerating blood flow; and blood flow to exercising muscles increases, delivering more oxygen and removing carbon dioxide to those tissues. So, when we start to exercise, how do the heart and circulatory system know how to respond? The short answer is the autonomic nervous system. The heart and circulatory system are innervated by sympathetic and parasympathetic nerves that control heart rate and contractility, and dilation and constriction of the blood vessels. The control originates in several areas of the medulla oblongata and pons in the brain, collectively referred to as the *cardiovascular control center* ***(Figure 2)***. Like other areas of the central nervous system that send out efferent signals, the cardiovascular control center receives and interprets a continuous stream of sensory input before determining appropriate responses of the heart and blood vessels.

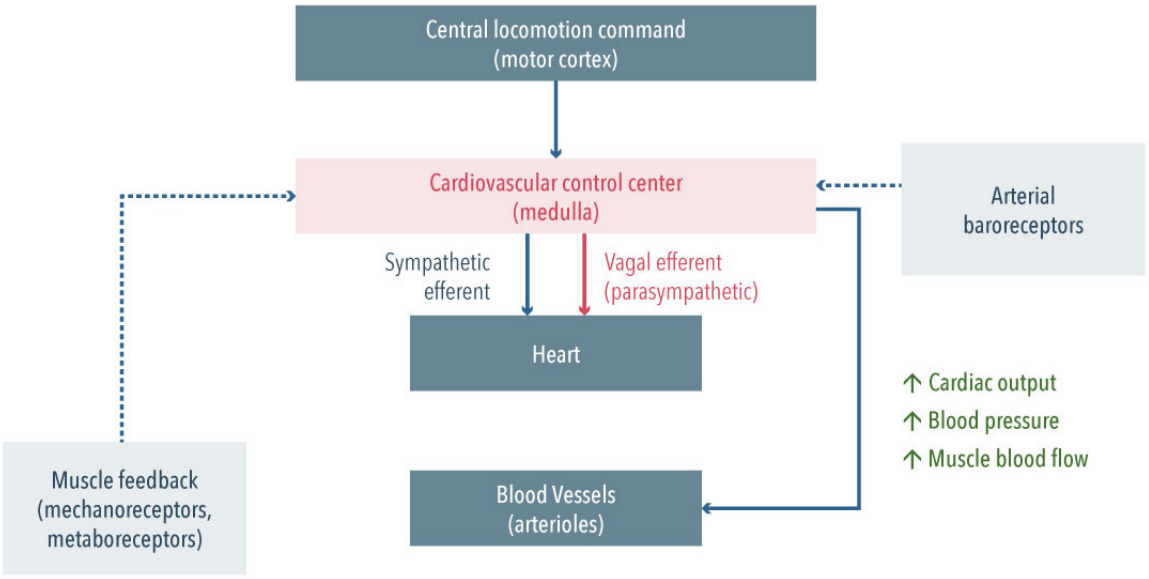


Figure 2. *The cardiovascular control center relies on input from various sources to help it determine the appropriate cardiovascular response.*

The cardiovascular control center receives input from three primary sources. One is the motor cortex. As the motor cortex signals skeletal muscles to contract, it also sends parallel signals to the cardiovascular control center to increase cardiac output. In this way, the motor cortex functions as a feed-forward control because when it initiates movement, it also anticipates how the cardiovascular system should respond. In addition, the motor cortex receives sensory feedback from skeletal muscles about perception of effort, which it uses to modify signals sent to the cardiovascular control center.[1]

The second source of sensory input to the cardiovascular control system is skeletal muscle. This includes *mechanoreceptors*—muscle spindles and Golgi tendon organs—and *metaboreceptors* which provide information about muscle metabolites, such as K^+ and H^+. This sensory input informs the cardiovascular control center that muscles are exercising and require additional blood and oxygen.

The third sensory input comes from the *baroreceptor reflex*. Located in the walls of the aortic arch and carotid arteries are stretch receptors which have primary short-term control of blood pressure. These baroreceptors increase or decrease their signaling rate to the cardiovascular control center depending upon how much they are stretched: the higher the blood pressure, the more the baroreceptors are stretched. The cardiovascular center responds by making appropriate adjustments to the autonomic signals it sends out to restore normal blood pressure by modifying cardiac output and total peripheral resistance, the two factors that determine blood pressure. The baroreceptor reflex is quickly responsive and reacts to a change in pressure within two heartbeats.

FAST FACTS

You have probably experienced your baroreceptors in action. If you have ever suddenly stood up and become slightly dizzy, it is because your blood pressure dropped suddenly, decreasing blood flow to your brain. Fortunately, your cardiovascular control center rapidly senses from your baroreceptors this decreased blood pressure and sends sympathetic signals to blood vessels to increase vasoconstriction, returning blood pressure to normal within a second or two.

Cardiac Output Response to Exercise

When beginning to exercise, contracting muscles increase synthesization of ATP, which requires an increased supply of oxygen. This is accomplished by a rise in cardiac output resulting from increased heart rate and stroke volume (remember, $\dot{Q} = HR \times SV$). Escalating heart rate, the result of increased sympathetic stimulation of the heart by the autonomic nerves, is linearly related to exercise intensity (***Figure 3***). *Norepinephrine*, the neurotransmitter of sympathetic neurons, speeds leakage of Na^+ into autorhythmic fibers, causing threshold to be reached sooner, which quickens depolarization and heart rate.

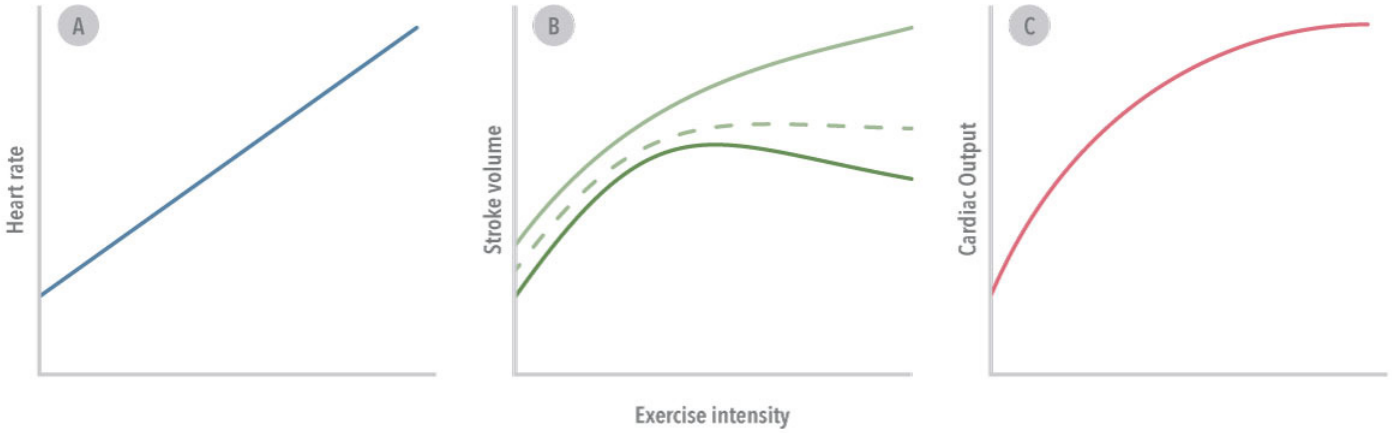


Figure 3. *In panel B, typical stroke volume responses to an elite endurance athlete (thin line), non-elite endurance-trained individual (dashed line), and average individual (thick line).*

Unlike heart rate, stroke volume does not increase linearly with exercise intensity. Moreover, the way that stroke volume changes with exercise intensity varies among individuals; the reason for this variability is another unanswered exercise physiology question.[2] Some studies report stroke volume reaching a peak at about 40% of maximal effort, and then it either plateaus or decreases as exercise intensity continues rising to maximal effort.[3, 4] These studies reason that stroke volume decreases at higher intensities because as heart rate increases, diastole is shortened, reducing the time available to fill the ventricles. Other studies have observed that stroke volume does not peak until an exercising individual reaches maximal effort.[5, 6] Yet others have reported that stroke volume peaks at a submaximal intensity in untrained individuals, but peaks at maximal intensity in endurance-trained subjects, which could explain, in part, why endurance-trained individuals have a higher exercise capacity.[7, 8] One explanation for the conflicting reports is difference in exercise protocols as well as variables in subject age, gender, fitness level and body position.

What is known is that stroke volume increases because of increased venous return (Frank-Starling law of the heart). Recall that stroke volume is the difference between end-diastolic volume (filled ventricular volume) and end-systolic volume (emptied ventricular volume) (***Figure 4***). Exercise has little effect on end-systolic volume, as the ventricles empty to a similar volume whether at rest or during exercise. Rather, stroke volume increases because of increased end-diastolic volume. This occurs because the exercise-induced higher venous return stretches the cardiac fibers, allowing the heart to work at a higher region of the ascending limb of the length-tension relationship, which increases force output. In addition, further stretching of cardiac fibers increases Ca^{2+} influx to the fiber, raising the Ca^{2+} signal, and increasing sensitivity of troponin to Ca^{2+} (less Ca^{2+} is needed to gain the same effect).

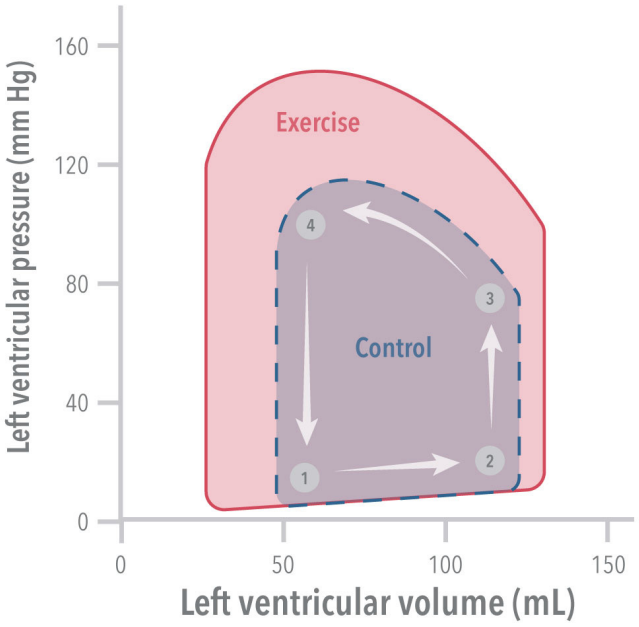


Figure 4. *The pressure-volume loop shows how pressure in the left ventricle is affected by ventricular volume at rest and during exercise. Data Source: Cardiovascular Physiology Concepts*

Increase in Venous Return

What, then, influences venous return? There are three major factors: venous constriction, muscle pump and venous one-way valves, and respiratory pump (the act of breathing).

The first factor is increased *venoconstriction* (constriction of the veins). During rest, the body has more blood than it needs, and because the veins are so *compliant* (easily stretched), they expand and "store" extra blood in the venous system. When the body needs to increase cardiac output, the veins constrict, forcing the stored blood toward the heart thereby increasing venous return.

The second factor that determines venous return is the dual action of the muscle pump and one-way valves in veins (***Figure 5***). Contracting skeletal muscle compresses the small veins that pass through it, which temporarily *occludes* (stops) blood flow until the muscle relaxes. Also during muscle contraction, blood is squeezed out of the muscle, but it is prevented from flowing backward by one-way valves located in the veins. These valves function like doors that open only in the direction toward the heart. Blood that tries to flow in the opposite direction forces shut the one-way valves, keeping flow always moving toward the heart. This alternating contraction-relaxation action coupled with the one-way valves acts like a pump that forces blood toward the heart. This muscle pump can generate sufficient upward force to overcome the downward force of gravity, preventing blood from pooling in the lower extremities; this is why your feet swell if you stand too long without contracting your leg muscles.

The third factor affecting venous return is the respiratory pump that occurs from the action of breathing. During expiration, thoracic pressure increases. The higher thoracic pressure squeezes against and constricts the vena cavae, located within the thoracic cavity, thereby decreasing blood flow into the atria. However, during inspiration thoracic pressure decreases, which reduces pressure on the vena cavae allowing them to expand and increasing venous return.

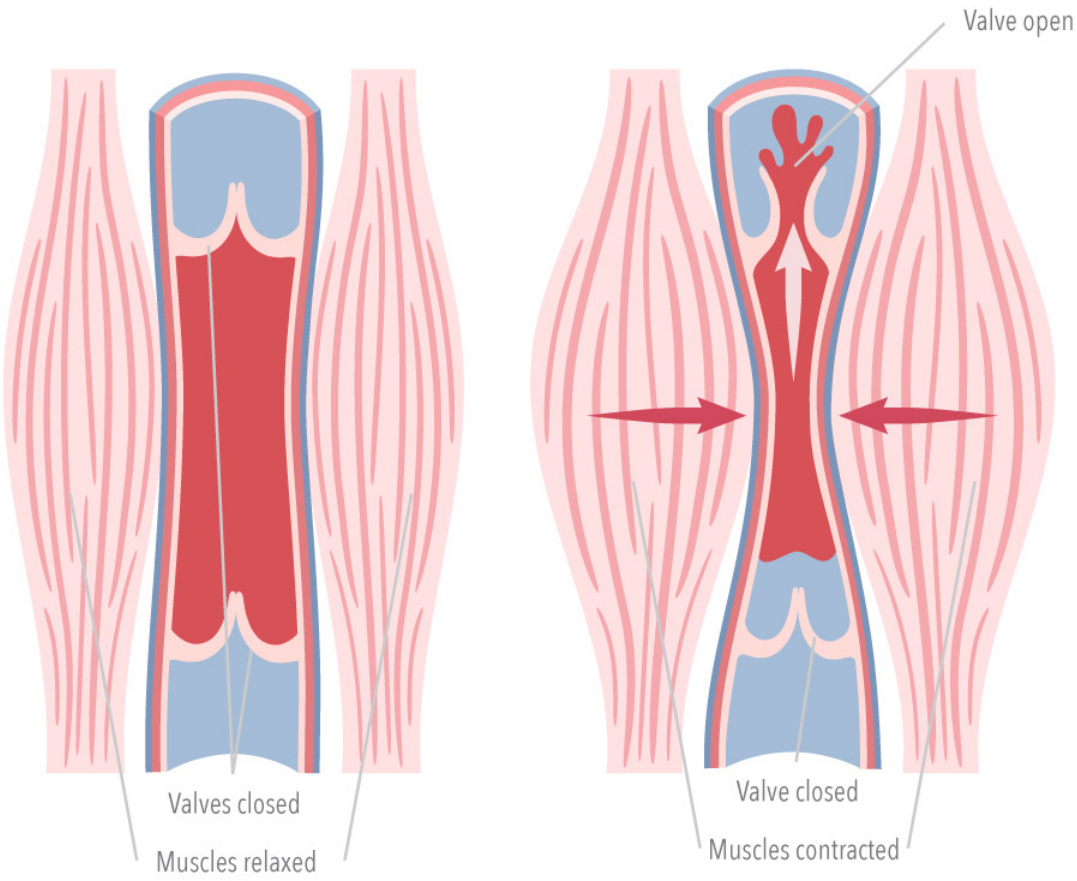


Figure 5. *Contraction of muscle and one-way valves prevent blood from flowing backward and act as a pump moving blood toward the heart.*

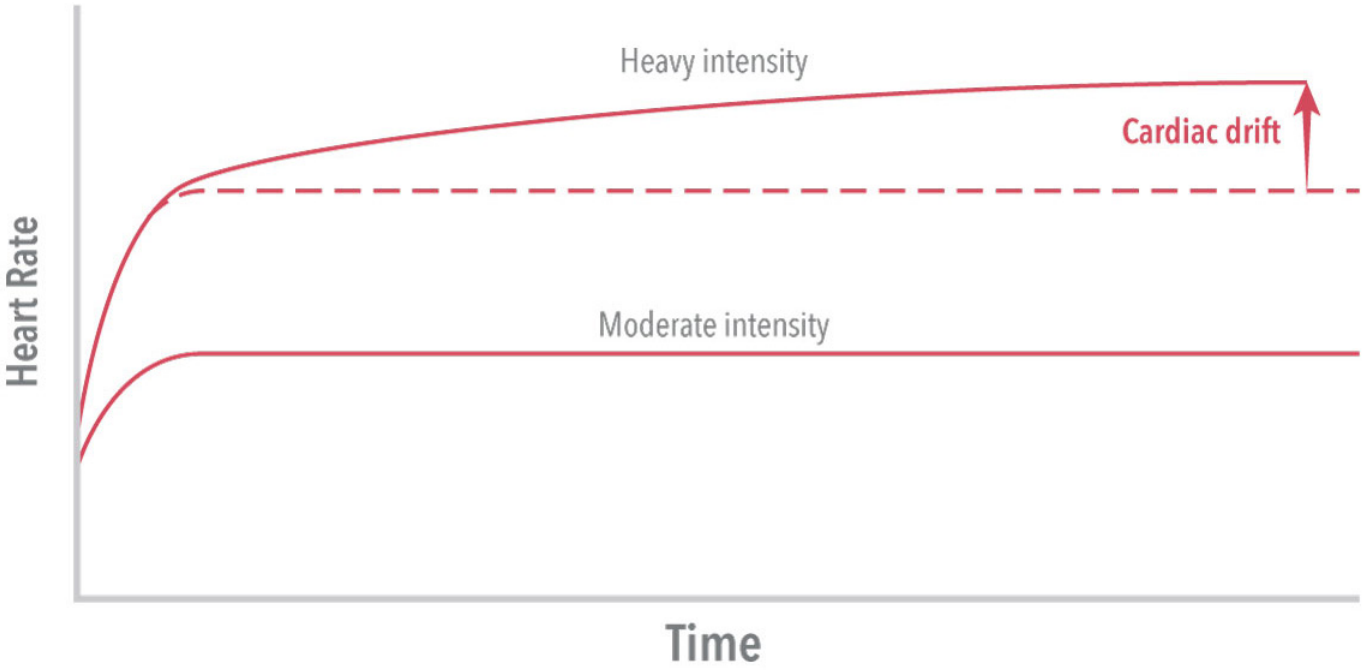


Figure 6. *Heart rate drifts upward over time during prolonged periods of moderate intensity steady-state exercise, but it does not increase during exercise of below moderate intensity.*

Heart Rate Response to Exercise

Heart rate during prolonged steady state exercise performed at low-to-moderate intensities remains at a plateau throughout the bout. However, if exercise is performed at above moderate intensity, heart rate rises slowly over time, which is referred to as *cardiovascular drift* (*Figure 6*).

Exercise intensity is not the only factor influencing cardiac drift. One early explanation for cardiovascular drift focused on decreased venous return over the course of exercise. As body temperature rises during prolonged exercise, the body responds with increased sweating and sending more blood to the skin to dissipate the extra heat produced by the muscles. This theory contends that the fluid for the increased sweat rate came mostly from the plasma in blood, thereby reducing blood volume venous return and stroke volume. Thus, to maintain cardiac output, heart rate must increase.

However, more recent work suggests that cardiovascular drift is caused by increased stress and sympathetic nervous stimulation.[9, 10] Exercise at low-to-moderate intensity does not stress the body much, but it does at higher intensities. Body temperature increases more during prolonged, intense exercise, adding to the stress. The body reacts to physiological stress with a general sympathetic response that stimulates the release of epinephrine into the blood from the adrenal medulla. Epinephrine speeds the leakiness of Na^+ into the autorhythmic cells, which increases heart rate. The greater the stress, the more epinephrine released, and the greater the cardiac drift.

Increased Work of the Myocardium

As exercise begins, the myocardium must work harder to increase cardiac output. How much work the heart does is determined by venous return, heart rate, and arterial blood pressure. The volume of blood returning to the heart after diastole, known as the *preload*, reflects venous return and governs the extent of stretch of the ventricles. Preload mirrors the volume of blood that the heart must eject—in other words, stroke volume.

Ventricles must generate sufficient force and pressure to open the aortic and pulmonary valves, which are forced shut by the higher blood pressure in the aorta and pulmonary artery; this is the *afterload*. The valves open only when the ventricular pressure becomes greater than the afterload. Thus, the greater the arterial pressure, the greater the force the heart must generate and the harder the heart must work to force open the aortic and pulmonary valves. To visualize this, let your classroom represent the left ventricle and the classroom door the aortic valve. At the end of class, you move toward the door, like blood moving toward the aortic valve when

the left ventricle contracts. You push on the door to go into the hallway; however, students outside the door are pushing inward on the door preventing it from opening. Consequently, it requires you and several classmates pushing outward to overcome the inward force on the door. In this example, the amount of inward force exerted by students outside the classroom represents afterload.

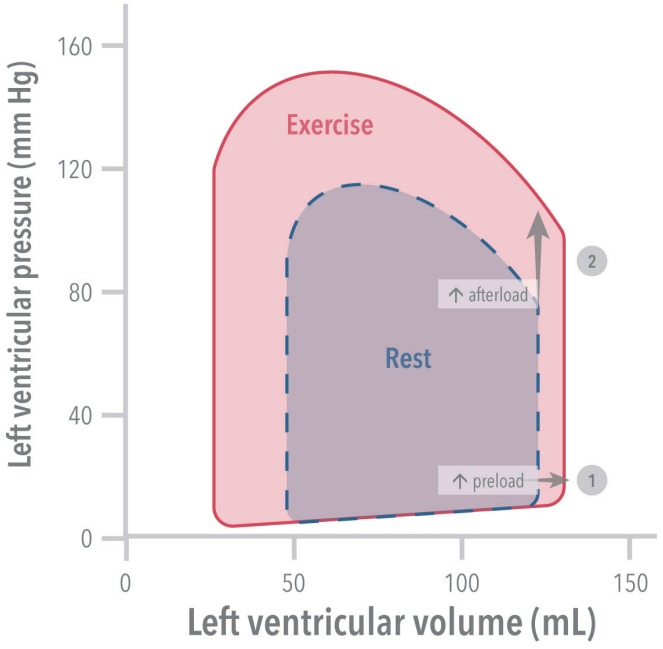


Figure 7. *Exercise increases work by the myocardium because of increased heart rate, preload, and afterload. During exercise, heart rate increases, preload increases because of increased venous return (1) and afterload increases because arterial blood pressure increases (2).*
Data Source: Cardiovascular Physiology Concepts

Exercise causes the heart to work harder due to an increase of preload, afterload, and heart rate *(Figure 7)*. A common laboratory method for estimating how much work the heart is doing is the *double product* or rate-pressure product, which is the product of heart rate and systolic blood pressure:

Double product =
Heart rate × Systolic blood pressure

A typical double product at rest is 8,000 (68 bpm × 118 mm Hg). At maximal exercise intensities of rhythmic exercises such as running or cycling, the double product rises to 42,000 or higher (200 bpm × 210 mm Hg), a more than five-fold increase *(Table 1)*.

Table 1. Double-Rate Product

Heart rate (bpm)	Systolic Pressure (mm Hg)	Double Product
50	110	5,500
100	125	12,500
150	140	21,000
200	155	31,000

Like skeletal muscle, when the heart works harder, it requires oxygen in amounts proportional to how hard it is working *(Figure 8)*. However, while skeletal muscle increases oxygen delivery from a combination of increased muscle blood flow and greater oxygen extraction from the blood, the heart must increase oxygen delivery primarily from increased coronary blood flow. At rest, skeletal muscle extracts approximately 25% of the oxygen from blood as it passes through the muscle, while the heart extracts approximately 75% of the oxygen passing through coronary circulation.[11] Thus, myocardial oxygen uptake is increased primarily from elevated coronary blood flow caused by increased sympathetic stimulation of the coronary blood vessels. However, sympathetic stimulation has the opposite effect on coronary blood vessels than it does on blood vessels in systemic circulation: rather than causing vasoconstriction, as it does in the systemic circulation, sympathetic stimulation causes vasodilation of the coronary vessels. This is because the norepinephrine receptors in coronary arteries differ from those in the systemic circulation, resulting in the reverse effect. At maximal intensity exercise, the heightened sympathetic stimulation typically increases coronary blood flow four- to six-fold.

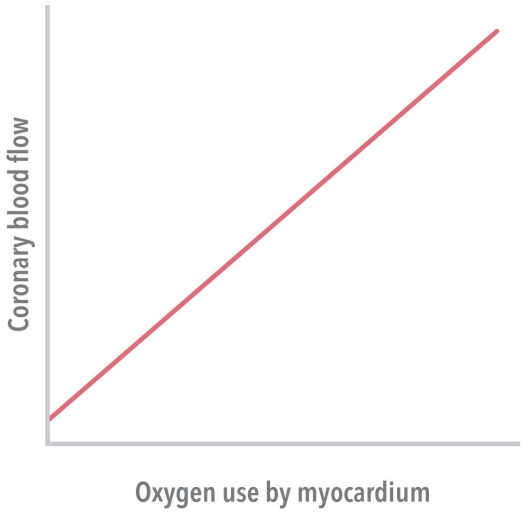


Figure 8. *Coronary blood flow increases proportionally to increases of myocardial oxygen use, reflecting the amount of work being done by the heart.*

The Circulatory System: Transporting Blood And Oxygen

Blood and blood vessels have many vital roles in the body. Blood functions to deliver oxygen and nutrients to tissues throughout the body as well as remove carbon dioxide and other metabolic end products such as the lactate and H^+ produced during vigorous exercise. In addition, blood transports many hormones, including the catecholamines. During prolonged intense exercise, blood transports the additional heat produced by the muscles to the skin, where it radiates off and cools the body.

About 7% of our body weight is composed of blood, so a 70-kg person would have about 5 L of blood in their circulation. Blood is comprised of two main components—*plasma* and formed elements. Plasma, which is a light golden color, is the fluid portion of blood and is about 92% water. Plasma transports a small amount of oxygen and carbon dioxide dissolved in the plasma, and also a number of essential ions including Na^+, K^+, Ca^{2+}, and HCO_3^-, as well as glucose, fatty acids, amino acids, and vitamins.

The formed elements are white blood cells (leukocytes), platelets, and *red blood cells (erythrocytes)* (ĕ-rith'rŏ-sīts). White blood cells play an important role in our immune system by fighting potential infections and clearing cellular debris. A key function of platelets is to help blood clot after a wound. The primary function of red blood cells, the most numerous cells of the formed elements, is to transport oxygen and some carbon dioxide. Red blood cells are produced in the bone marrow and have an average life of about 120 days. Within each red blood cell is hemoglobin, a pigmented molecule that carries oxygen and gives blood its red color. Hemoglobin has four iron-containing heme groups that can reversibly bind with oxygen molecules as well as with some carbon dioxide.

In 5 L of blood, about 3 L is plasma and the remaining 2 L is the formed cells. The percentage of formed elements in blood is the *hematocrit*. Men typically have a hematocrit of 42–48%, while women have a hematocrit of 37–42%. The difference is primarily because men have more red blood cells than women. This allows men to carry more oxygen, which may give them an advantage in endurance events that require a high rate of oxygen delivery to exercising muscles.

FAST FACTS

Gases like carbon monoxide, a gas produced from incomplete combustion such as from gas home heating systems or automobiles, also bind to hemoglobin and displace oxygen, which reduces oxygen delivery to the body. When carbon monoxide is inhaled in sufficient quantities, the result is carbon monoxide poisoning. The medical treatment for patients with carbon monoxide poisoning is to breathe 100% oxygen, which speeds displacement of carbon monoxide from hemoglobin, allowing oxygen to replace it. Carbon monoxide poisoning is not an uncommon occurrence—over 150 people in the U.S. alone die every year from unintentional carbon monoxide poisoning.

Blood Vessels

Arterial blood vessels transport blood away from the heart; venous vessels return blood to the heart. The major arterial blood vessels leaving the heart, the aorta and pulmonary artery, branch into smaller arteries that branch into still smaller arteries ***(Figure 9)***. The smallest arterial vessels are the *arterioles*, which carry blood to the tissues and organs of the body. From there, arterioles branch into very narrow and thin-walled vessels called *capillaries*.

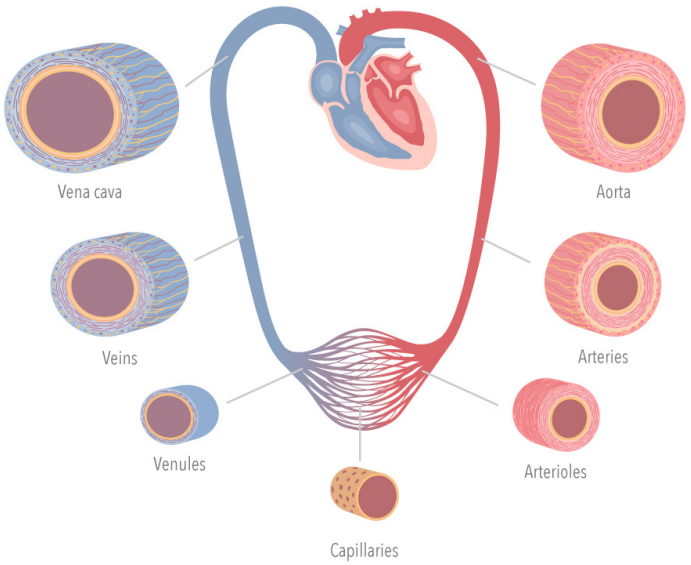


Figure 9. *Various levels of branches in the circulatory system*

Capillaries, the smallest blood vessels, have cell walls that are only one cell thick and require a microscope to be seen. Interestingly, the diameter of a red blood cell is about 25% larger than the diameter of a capillary; thus, red blood cells must flatten out as they pass through a

capillary. The exchange of gases, nutrients, and end-products between the blood and tissues occurs in the capillaries. Hence, thinness of the capillary wall is vital to ensuring a rapid exchange between the blood and tissues.

As blood leaves the tissues to return to the heart, the capillaries converge into venules. The venules unite into small veins that, in turn, join to form progressively larger veins, eventually leading to the superior and inferior vena cavae.

The walls of arteries and veins contain elastic and fibrous connective tissue as well as layers of *vascular smooth muscle* innervated by sympathetic nerves (***Figure 10***). When sympathetic nerves stimulate vascular smooth muscle in systemic circulation, the smooth muscle contracts, which constricts the blood vessel. This makes the vessel smaller in diameter, referred to as *vasoconstriction*, and creates more resistance to blood flow. Conversely, *vasodilation* is an increase in vessel diameter when the vascular smooth muscle relaxes.

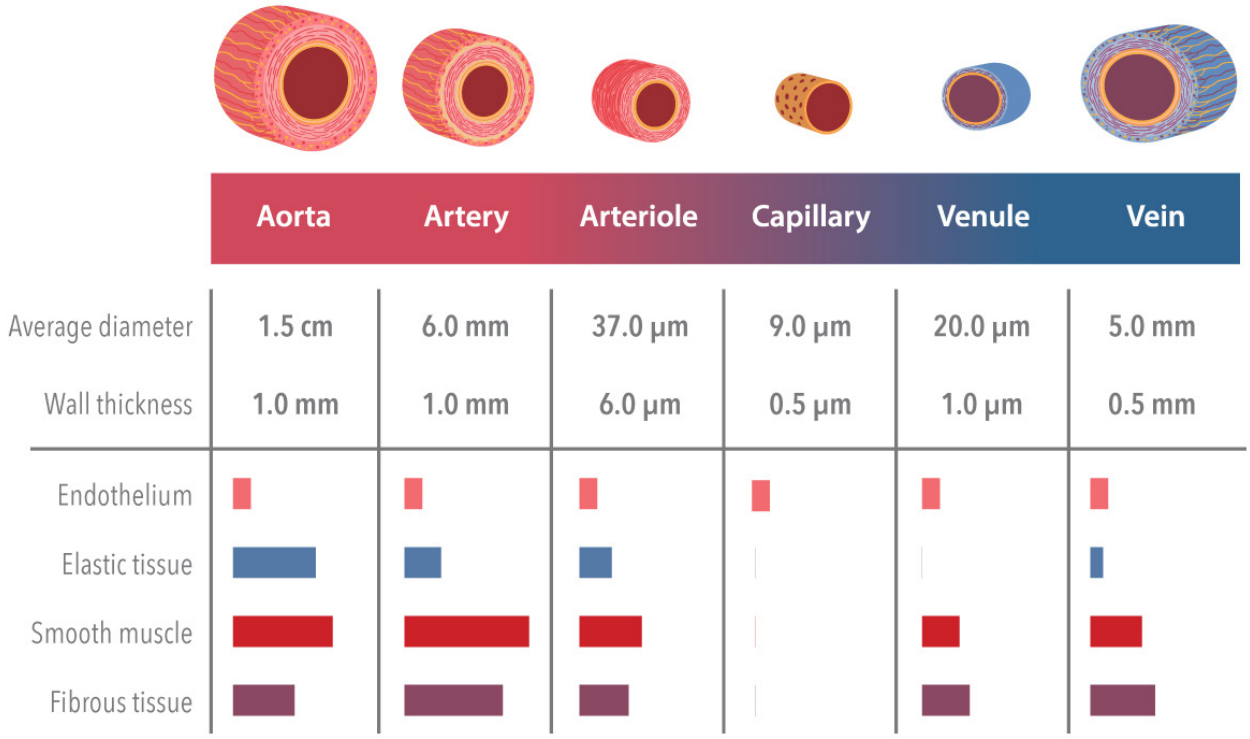


Figure 10. *Comparison of vascular smooth muscle in different blood vessels*

FAST FACTS

During coronary bypass surgery, it is common for the surgeon to harvest the great saphenous vein from the lower leg and use the grafts to bypass the blocked coronary arteries. Because there are numerous veins that drain the lower leg and return blood to the heart, removal of a single vein usually does not have any serious consequences on circulation.

Arterioles contain less elastic and fibrous connective tissue, but more vascular smooth muscle than the larger arteries. Thus, arterioles constrict more than any other blood vessel, which allows them considerable control of blood flow to an organ or tissue. For example, when oxygen requirements of a tissue are low, such as during rest, the tissue has little need of blood, so arterioles leading to that tissue constrict, which *shunts* (directs away) blood to another tissue. However, when the tissue becomes metabolically active, such as when skeletal muscles are contracting during exercise, arterioles to those muscles dilate to increase blood flow to the exercising muscles.

Veins are more numerous than arteries, and although they also carry blood, they have a somewhat different purpose. Veins have less vascular smooth muscle and connective tissue, making them more elastic and *compliant* (able to expand and hold large volumes of blood), like a balloon can stretch and hold a large volume of water. During rest, the body has more blood than it needs. To set aside this unneeded blood, the veins dilate, storing about two-thirds of all the blood in the body.

Unlike arteries and veins, capillaries have no vascular smooth muscle, so they cannot constrict. However, *precapillary sphincters*, small bands of smooth muscle, surround the openings of capillaries *(Figure 11)*. When a precapillary sphincter constricts, blood is shunted from the part of the tissue served by its capillary. While arterioles control blood flow to capillaries in tissue, blood flow is fine-tuned by precapillary sphincters.

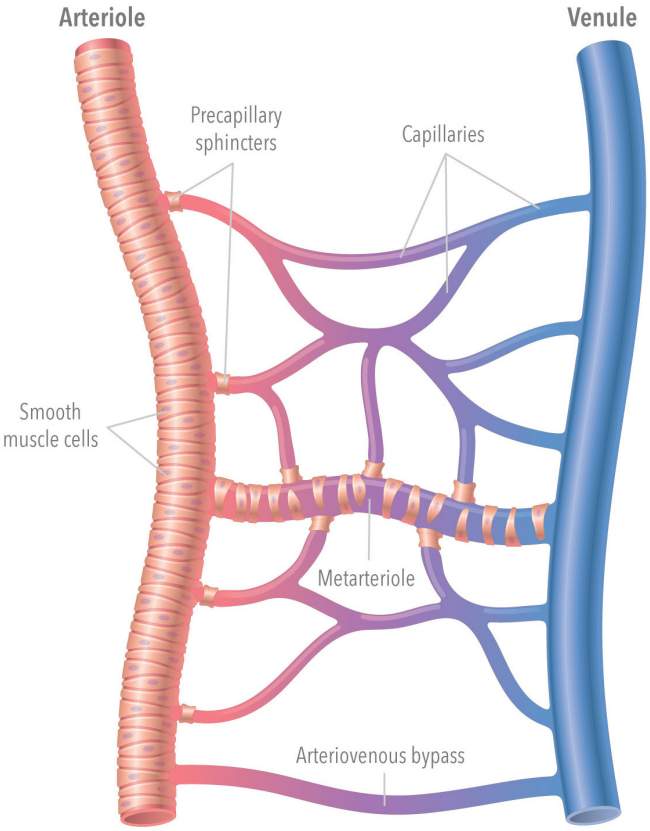


Figure 11. *Arterioles control blood flow to the tissues while precapillary sphincters fine-tune blood flow within the tissues.*

Control of Blood Flow During Exercise

At the onset of exercise, there is an overall sympathetic response that includes stimulating the vascular smooth muscle of arterial and venous vessels, causing a general vasoconstriction. This has a significant impact on circulation. While the body at rest has more blood than it needs, the body at exercise has less blood than it needs. To make the best use of the available blood, the vasoconstriction squeezes blood out and to the heart, increasing venous return. This increases stroke volume (the Frank-Starling principle) and cardiac output, making more blood available to the exercising skeletal muscles. Importantly, because arterial vessels (particularly the arterioles) have more vascular smooth muscle, they are heavily innervated and easily constrict.

There are two notable exceptions to the vasoconstriction response to sympathetic stimulation of blood vessels. During exercise, as already discussed, vascular smooth muscle around the coronary arteries dilates. Similarly, cerebral arterioles also dilate (although by a different mechanism) during exercise, facilitating blood flow.[12] Thus, during exercise when blood flow is reduced, blood flow to the brain and heart is never compromised.

Local Factors that Control Blood Flow

If arterioles vasoconstrict in response to sympathetic stimulation, how do contracting muscles receive more blood and oxygen during exercise? The short answer is that there are local (immediate area around the fibers) metabolic factors released by the contracting fibers that override the sympathetic stimulation to result in local vasodilation.

As muscles become active, numerous metabolic changes occur within the fibers. When fibers contract, they use oxygen, produce carbon dioxide and H^+, generate heat, and leak K^+. In addition, some ADP from ATP breakdown is further broken down to AMP and then to adenosine. The combined effect of these factors is strong enough to override local sympathetic stimulation, and instead cause relaxation of local arterioles allowing blood to be directed to the exercising fibers *(Table 2)*.

Table 2. Local Metabolic Changes in Exercising Muscle

Change	Caused by
↑ CO_2	produced in mitochondria from aerobic ATP production
↑ H^+	produced during anaerobic ATP production
↑ K^+	leaked out of muscle cell
↑ temperature	produced during ATP production
↑ adenosine	end-product of ATP breakdown
↑ nitric oxide (NO)	produced in endothelial cells from shear stress of blood flow

Another important factor that increases local blood flow is *nitric oxide*, a powerful vasodilator. As blood flow through the vessels gains in velocity, it increases what is called *shear stress* on the inside of the vessel walls. Sheer stress causes *endothelial cells*, cells lining the inside wall of blood vessels, to release several signaling molecules. The most important of these signaling molecules is nitric oxide, which causes local vascular smooth muscle to relax and dilate the blood vessel, facilitating blood flow. As such, when increased cardiac output increases blood flow, the resulting shear stress contributes to a rise of local blood flow.

Arterioles feeding contracting fibers are fully dilated within 5 to 10 s of starting exercise.[13] The more active a muscle becomes, the greater extent of vasodilation. In addition, even though precapillary sphincters are not under sympathetic control, the aforementioned local metabolic changes cause the local precapillary sphincters to relax and direct blood flow only to contracting skeletal fibers. Muscles use oxygen at a rate proportional to exercise intensity, so blood must be delivered at a rate proportional to the oxygen use. Consequently, the amount of muscle activity directly determines the amount of vasodilation, and thus blood delivery to match oxygen requirements of the muscles.

When muscles stop contracting, oxygen levels in the local area return to resting levels, as do carbon dioxide, K^+, adenosine, temperature, and nitric oxide. Since the local area is no longer metabolically active, arterioles and precapillary sphincters revert to their resting levels, returning blood flow to its resting level.

Redistribution of Blood

When skeletal muscles are inactive at rest, they need little blood. At rest, only 10 to 15% of cardiac output (approximately 0.75 L·min-1) flows through skeletal muscles, while about half of cardiac output goes to the kidneys and gastrointestinal tract *(**Figure 12**)*. However, exercising muscles require greater blood flow to meet their increased demand for oxygen. At maximal exercise, cardiac output might increase to 25 $L \cdot min^{-1}$ or higher, of which 80 to 85% flows through the exercising muscles. Accordingly, skeletal muscle blood flow goes from less than 1 $L \cdot min^{-1}$ at rest to 20 $L \cdot min^{-1}$ or more during maximal exercise.

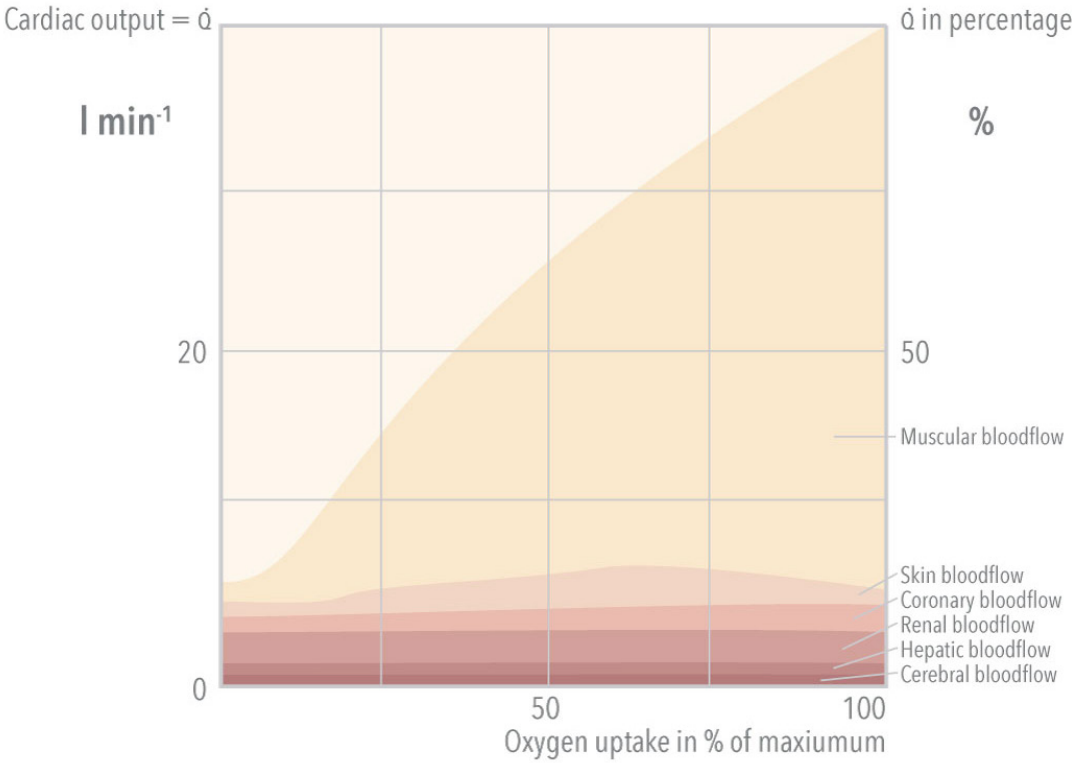


Figure 12. *Distribution of cardiac output (Q̇) based on the percentage of maximal aerobic capacity. Absolute cardiac output is shown on the left axis and relative cardiac output is shown on the right axis. Data Source: New Human Physiology*

At rest, about two-thirds of blood is in the veins. With the onset of exercise, there is a sympathetic response that, among other things, causes the veins to constrict, increasing venous return and cardiac output. As muscles begin to contract, they require more blood, oxygen, and nutrients as well as removal of carbon dioxide and other metabolic end products. Thus, blood must be distributed to exercising muscles in proportion to their oxygen needs. The redistribution of blood, which is called the *two-effector model of blood flow redistribution*, is accomplished in two ways: arterioles leading to less active tissue vasoconstrict, which decreases blood flow to those tissues, and arterioles feeding exercising muscles dilate to increase blood delivery. Thus, the redistribution of blood flow is accomplished by shunting blood away from tissues that have less metabolic activity and toward more metabolically active tissues with greater need of oxygen.

Blood Pressure and Blood Flow

According to Newton's First Law of Motion, an object at rest will not move until a force acts on it. For blood to circulate, it must be acted on by a force, which is the pressure generated by contracting ventricles. The force of ventricular contraction creates a pressure gradient within the circulatory system, causing blood to move from an area of higher pressure to an area of lower pressure. Like water flows downstream because of the force of gravity, blood flows down the circulatory system because of the higher pressure in the aorta and pulmonary artery. Blood is pushed out of the ventricles, increasing blood volume and pressure in the aorta and pulmonary artery; to equalize this pressure, blood flows down the circulatory system where the pressure progressively drops.

Total Peripheral Resistance

Two factors control the pressure gradient and determine blood pressure in the circulatory system. First is the force generated by blood being ejected from the heart; this force is determined by cardiac output. The second factor is the resistance that blood encounters as it passes through the circulation. This resistance is partially dependent on the diameter of arterial blood vessels. If the diameter of blood vessels becomes larger, resistance to blood flow decreases, and vice versa. The sum of resistance to blood flow by all the vessels in the body is termed the *total peripheral resistance (TPR)*. Therefore, the average arterial blood pressure is calculated by the product of the cardiac output and the total peripheral resistance:

Mean arterial pressure (MAP) =
Cardiac output ($\dot{Q}$) × Total peripheral resistance (TPR)

Blood flow is related to the pressure gradient and resistance to blood flow, and can be mathematically expressed as follows:

Blood flow =
Pressure gradient ÷ Total peripheral resistance

These equations can be illustrated by a garden hose connected to a water spigot. If you want to get a drink from the hose but the water is only trickling out, you turn the valve on the spigot to further open it. This action increases water flow in the hose as well as water pressure. However, if the water is spouting too forcefully from the hose to get a drink, you could partially bend the hose to reduce flow. Downstream from the bend, water pressure and water flow are reduced, but upstream from the bend, water pressure increases because of the increased resistance to water flow encountered at the bend. In this example, the rate of flow from the spigot represents cardiac output and the bend in the hose represents total peripheral resistance. Changing either cardiac output or total peripheral resistance affects the pressure gradient and changes blood pressure.

So, where in the circulatory system is the "kink" in the hose, the point that offers the greatest resistance to blood flow? Look at ***Figure 13*** which shows how blood pressure changes as it flows through the different levels of the systemic circulation. What level of the circulatory system has the largest drop in blood pressure, the kink in the hose? It is the arterioles. Blood entering the arterioles has an average pressure of about 75 mm Hg, and before blood reaches the capillaries, the pressure has been reduced to about 20 mm Hg. It is essential that pressure is reduced before blood enters the one-cell thick capillaries, which cannot tolerate high pressures.

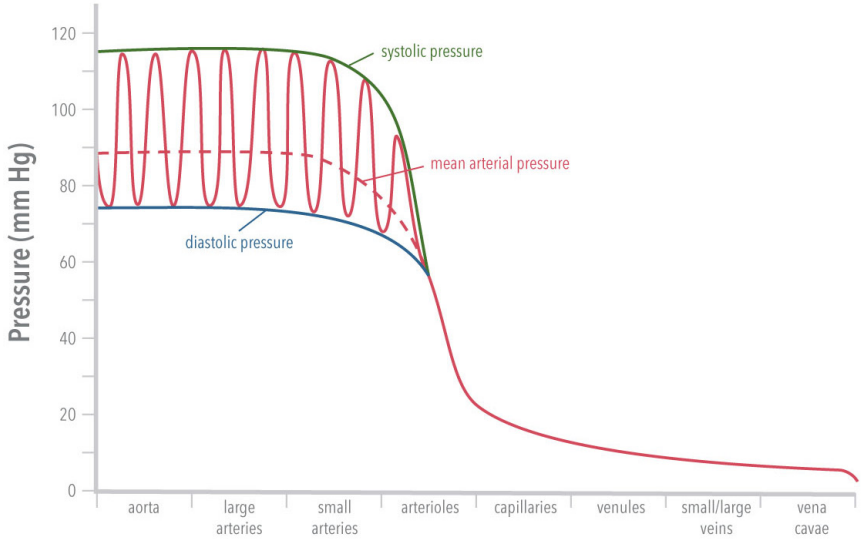


Figure 13. *Blood pressure at various levels within systemic circulation*

Systolic and Diastolic Pressures

In the cardiovascular system, arterial blood pressure is never constant as it rises and falls with each cardiac cycle. During systole, while blood is ejected from the ventricles, pressure against the arterial walls exerted by the rising volume of blood increases arterial blood pressure. The pressure peaks at the end of systole—the *systolic pressure*—which is typically below 120 mm Hg. During diastole, when the ventricles relax, blood in the arteries has been flowing down the circulatory system causing arterial pressure to drop. At the end of diastole, the pressure reaches its *nadir* (lowest point), the *diastolic pressure*, which is typically less than 80 mm Hg. At the start of systole, blood pressure begins another up-and-down cycle, a cycle that begins with your first heartbeat while in the womb and continues until death.

Because pressure is constantly changing, the *mean arterial pressure (MAP)*, which is the average pressure in the arterial system, is sometimes used to report blood pressure. It is estimated as follows:

MAP = Diastolic pressure +
⅓ (Systolic pressure – Diastolic pressure)

Notice in the equation that greater weight is given to diastolic pressure because at rest, systole is about only one-third as long as diastole.

Clinical Application

Measurement of Arterial Blood Pressure

Blood pressure is commonly measured with a *sphygmomanometer* (sfig'mō-mă-nom'ĕ-tĕr) ***(Figure 14)***. An inflatable cuff with a pressure gauge is placed around an arm, usually the right, just below the cuff over the brachial artery and inflated to a pressure that exceeds the systolic pressure. This stops blood flow into and out of the arm. As pressure in the cuff is slowly released, a series of sounds, called *Korotkoff sounds*, begin to be heard through a stethoscope. These sounds are created by the *turbulent* (agitated, not smooth) arterial blood flow as it spurts past the *occlusion* (blockage of a blood vessel) of the pressure cuff.

The first sound is heard when the cuff pressure drops below the systolic pressure and blood flow through the artery resumes. The initial sound is faint, but as the cuff pressure continues to decrease, the sound becomes louder and then softer before finally disappearing. The cuff pressure at which the sound is first heard is the systolic pressure and the cuff pressure when the sounds disappear is the diastolic pressure. Arterial blood pressure is expressed as two numbers: the systolic pressure over diastolic pressure—for example, 110/72 mm Hg. The unit used to report blood pressure, millimeters of mercury (mm Hg), reflects the force required to raise a column of mercury, measured in millimeters.

Figure 14. *Arterial blood pressure can be measured manually using a sphygmomanometer.*

Elevation of arterial blood pressure forces the heart to work harder. For example, if diastolic pressure increases from 80 mm Hg to 95 mm Hg, the ventricles must generate even greater force to overcome the additional resistance (afterload) in order to eject blood. If arterial blood pressure remains elevated over time, the extra strain on the heart leads to a type of heart failure due to *cardiac myopathy* (enlarged heart). *Chronically* (long term) elevated blood pressure, a condition known as hypertension, is a systolic pressure above 140 mm Hg and a diastolic pressure greater than 90 mm Hg. Prehypertension is a systolic pressure between 120 and 140 mm Hg and/or a diastolic pressure between 80 and 90 mm Hg.

Circulatory Responses to Exercise

To satisfy the demand of contracting muscles for more blood and oxygen, cardiac output must increase, which means both arterial blood pressure and blood flow must increase. However, in doing so, blood pressure must not be allowed to become too high or too low. Balancing the changing oxygen needs of the body requires the circulatory system to adapt to an appropriate, though higher, arterial blood pressure. Recall that blood pressure is the product of cardiac output and total peripheral resistance. The effect of exercise on cardiac output has been discussed; we now turn to the effects of exercise on total peripheral resistance and blood pressure.

Total Peripheral Resistance Response to Exercise

During exercise, vasoconstriction of most arterial blood vessels increases peripheral resistance and blood flow in those vessels. However, the increase in resistance is more than offset by the large vasodilation that occurs in arterioles of exercising muscles. Because the amount of vasodilation is greater than vasoconstriction, there is an overall decrease of total peripheral resistance *(Figure 15)*.

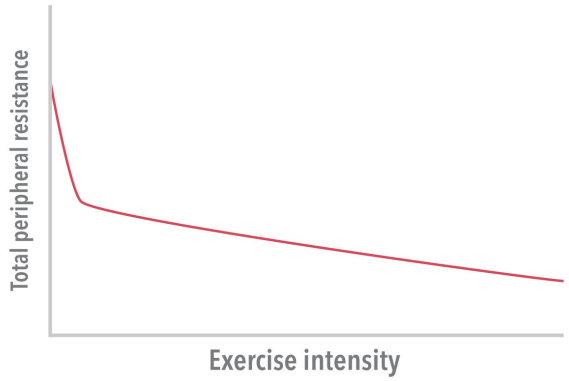


Figure 15. *During rhythmic exercise, total peripheral resistance decreases with exercise intensity.*

Blood Pressure Response to Exercise

Exercise increases mean arterial pressure, but systolic and diastolic pressure respond differently depending upon the type of exercise. Rhythmic exercise, such as running or cycling, increases cardiac output up to six-fold, although cardiac output rises little during resistance exercise. Blood easily flows through the circulatory system during rhythmic exercise, but is more restricted during the prolonged muscle contractions of resistance exercise. Even a muscle contracting at just 60% of maximal force completely occludes blood flow.[14]

In general, systolic pressure is affected more by cardiac output, while diastolic pressure is affected more by total peripheral resistance. During rhythmic exercise, systolic pressure rises proportionally to exercise intensity, but there is little change in diastolic pressure *(Figure 16)*. At maximal effort, systolic pressure might rise to 180 mm Hg while diastolic pressure could rise to only 84 mm Hg. However, because there is far greater resistance to blood flow during the prolonged muscle contractions in resistance exercise, and despite the small increase in cardiac output, both systolic and diastolic pressures rise higher during resistance exercise than during rhythmic exercise. When a muscle contracts, blood vessels passing through it are compressed and resist blood flow, so the longer the contraction, the greater that blood pressure rises. While lifting heavy weights, arterial blood pressure can rise to 400/250 mm Hg or higher. In contrast, during rhythmic exercise, each brief contraction is followed by relaxation, which allows blood flow to quickly resume, thereby having little impact on resistance to flow.

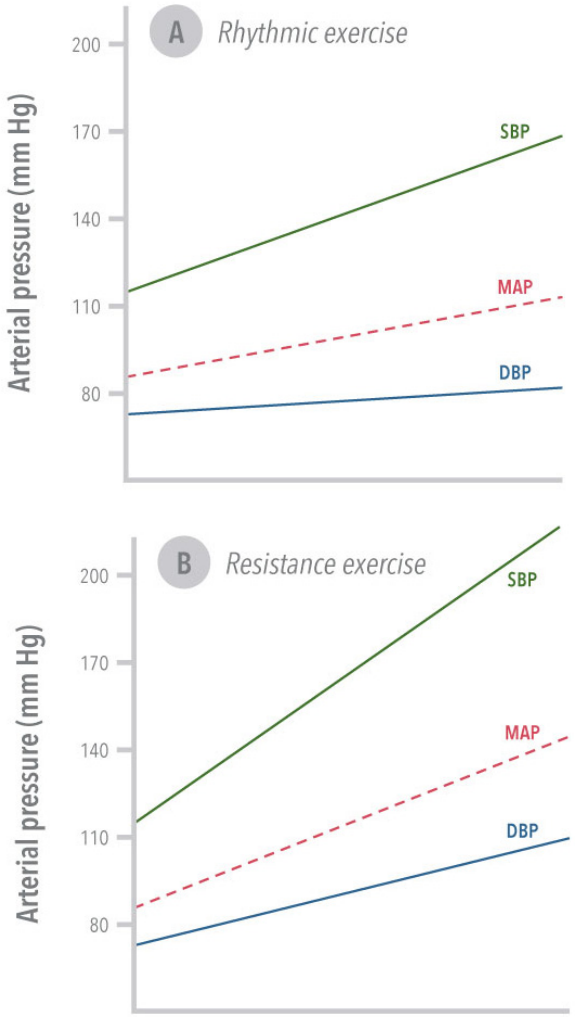


Figure 16. *Systolic, diastolic, and mean arterial blood pressure response during (A) cycling exercise and (B) heavy resistance exercise*

Increased blood pressure during exercise is necessary to deliver more blood and oxygen to contracting muscles. Recall that baroreceptors, located in the aortic arch and carotid bodies, are an important mechanism for short-term control of blood pressure. As arterial blood pressure rises above the baroreceptor set-point, the baroreceptors respond by increased signaling to the cardiovascular control center, which takes steps to decrease pressure. With the start of exercise, the cardiovascular control center receives input from the motor cortex and from the contracting muscles to increase cardiac output and blood pressure. To temporarily allow for higher pressures during exercise, the cardiovascular control center raises the baroreceptor set-point, thereby increasing the pressure at which the cardiovascular control center initiates steps to lower the pressure.

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GLOSSARY DEFINITIONS

cardiovascular control center: the collective areas of the brain that control the heart and vascular tone of the blood vessels; located in the medulla oblongata and pons

baroreceptor reflex: a neural reflex that operates on a negative feedback loop to maintain blood pressure homeostasis; pressure sensors are located in the aortic arch and carotid arteries

cardiovascular drift: the slow rise in heart rate that occurs during prolonged exercise that occurs at intensities above moderate; occurs because of increasing stress and sympathetic stimulation

preload: the amount of ventricular stretch at the end of diastolic filling; represented by end-diastolic ventricular volume

afterload: the pressure in the aorta that the ventricles must overcome during systole to eject blood; a high afterload puts excessive strain on the heart

double product: a method to estimate how much work the heart is doing; calculated as the product of heart rate and systolic blood pressure

plasma: the amber-colored component of blood that has been separated from the red and white blood cells and platelets; is 95% water and makes up 55–60% of the total blood volume

red blood cells (erythrocytes): cells in the blood that hold hemoglobin, the iron-containing molecules that reversibly bind with oxygen and carbon dioxide; constitute 40–50% of total blood volume

hematocrit: the volume percentage of the red blood cells in blood; 36–44% in females and slightly higher in males because of more red blood cells

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arterioles: small-diameter blood vessels surrounded by vascular smooth muscle that connect to capillaries; the greatest drop in blood pressure and velocity occurs in the arterioles

capillaries: blood vessels in tissues that have walls only a single cell thick; site of gas and nutrient exchange with the tissues

vascular smooth muscle: a type of smooth muscle surrounding blood vessels that controls diameter of the vessel, thus controlling blood pressure and velocity

vasoconstriction: contraction of the vascular smooth muscle in a blood vessel; reduces the vessel diameter which increases blood pressure and reduces blood flow

vasodilation: relaxation of the vascular smooth muscle in a blood vessel; increases the vessel diameter which decreases blood pressure and increases blood flow

precapillary sphincter: a band of smooth muscle surrounding the area where arterioles branch into capillaries; control blood flow to the tissue by constricting or relaxing, which is controlled by local factors

nitric oxide: a common signalling molecule in the body; production stimulated by stress from rapid blood flow

total peripheral resistance (TPR): the sum of resistance to blood flow throughout the body; calculated as the mean arterial pressure divided by cardiac output

systolic pressure: the highest arterial blood pressure; the pressure exerted against the arterial walls during a heart beat

diastolic pressure: the lowest arterial blood pressure; the pressure in the arteries between heart beats

mean arterial pressure (MAP): the average arterial blood pressure; calculated as the sum of diastolic blood pressure and one-third of the difference between the systolic and diastolic pressures

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