Section Three: Chapter 16: Blood Vessels: Resistance and Pressure

Blood Vessels of the Body

The blood that is pumped by the heart is transported to and from the body by blood vessels. There are five basic types of blood vessels in the body.

1. **Arteries**:
   Both large **elastic** and **muscular** arteries have 3 layers. Role is for **transporting** High Pressure Blood and maintaining Blood Pressure.
2. **Arterioles**:
   Have 2 layers, including **vascular smooth muscle** (VSM), can exhibit large changes in diameter = '**Resistance**' vessels.
3. **Capillaries**:
   Have only 1 layer, 1 cell thick, called endothelium, for **exchange** (3 types of beds).
4. **Venules**:
   Have 2 layers, for **collection** of blood from capillary beds.
5. **Veins**:
   Have 3 layers and **venous valves**. For return of Low Pressure blood to heart.

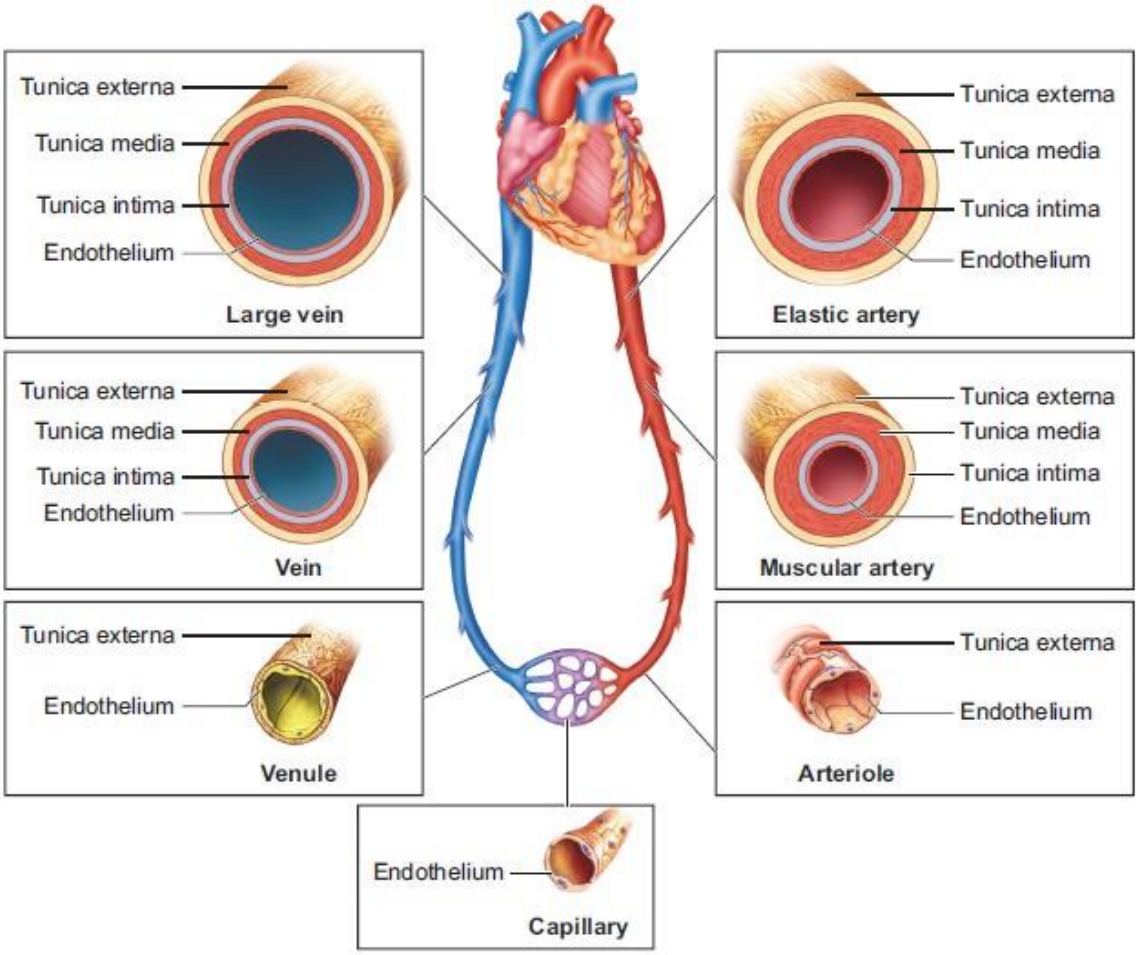


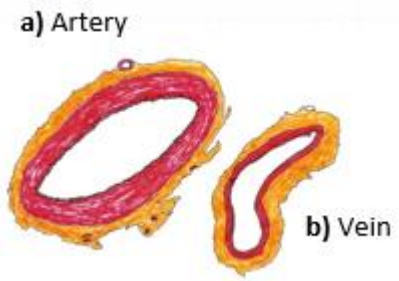
Figure 16.1 This shows a blood sample of **a)** whole (or mixed) blood, and **b)** separated blood after having been spun at high speeds in a centrifuge. In the spun blood we can see the 2 major components of blood, the plasma, which is the supernatant on top and the heavier formed cellular elements on the bottom.

The different types of blood vessels vary in their structures, but they share some similar general features. Each blood vessel has the same innermost layer called the **endothelium**, made of simple squamous epithelium. All vessels have a **lumen**, the central area through which blood flows. In general blood vessels transport blood in this vessel order: Arteries, arterioles, capillaries, venules and veins. This leads back to the heart. There are some important exceptions (e.g., portal systems) but most commonly it is in this sequence of vessels that blood is circulating.

Arteries and arterioles have thicker walls than veins and venules because by virtue of their close proximity to the heart, they are handling blood at a far greater pressures than the thinner walled venules and veins. By the time blood has traveled to the capillaries and entered venules, the pressure initially imparted on it by the ventricles of the heart contracting has significantly diminished. In comparison to arteries, veins encounter **much lower pressure** from the blood that flows through them. Their walls are considerably thinner and their lumens are correspondingly much **larger in diameter**, this allows more blood to flow with less vessel resistance. In addition, veins also contain **venous valves** that assist the unidirectional flow of blood back toward the heart. This is very important as the lower pressure of veins in the extremities makes it necessary to have additional strategies to promote adequate venous return.

The Blood Vessels in more Detail

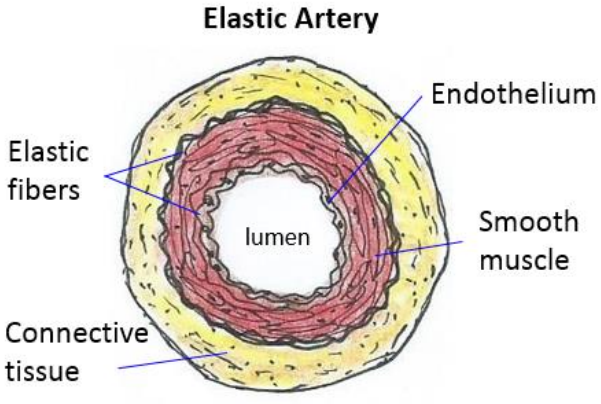
Arteries

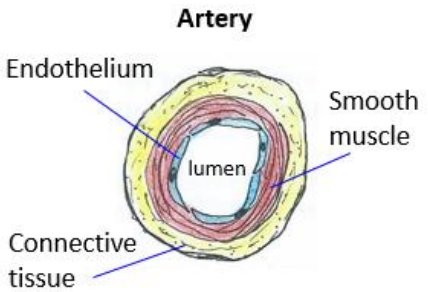


Arteries have very thick walls, but smaller lumens than veins, a characteristic that helps to maintain the pressure of blood moving through the system. Together, their thicker walls and smaller diameters give arterial lumens a more rounded appearance in cross section than the lumens of veins (see drawing at right).

An **artery** is a blood vessel that conducts blood away from the heart. All arteries in the systemic circuit have thick walls in order to withstand the high pressure of blood ejected from the heart, it is the arteries closest to the heart that have the thickest walls, with 2 layers elastic fibers on either side of the tunica media (smooth muscle). These are called **elastic arteries**.

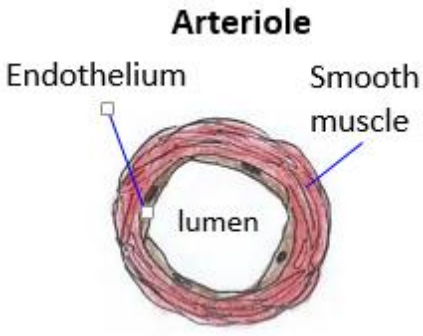
An elastic artery is also known as a conducting or transport artery, because the large diameter (over 10 mm) enables it to accept a large volume of blood from the heart and conduct it to smaller branches. The elastic fibers allow the vessels to expand in response to the infusion of blood pumped from the ventricles. Once the blood passes, the vessels then recoil due to elasticity. This is important for 2 reasons: **1)** flexible vessels expansion reduces resistance to blood flow, thus the heart does not have to work harder as it would if vessels were stiff and inflexible (as in atherosclerosis); **2)** the recoiling of the vessel after the heart pumps acts to maintain blood the pressure gradient that drives the blood in the arterial system.





Arterioles

After arteries, blood flows into **arterioles**, like the name implies, they are 'tiny' arteries that then deliver blood to a capillaries. These vessels essentially have 2 layers, the inner endothelium and a layer of **vascular smooth muscle** (VSM). These vessels have diameters (or lumens) that can dramatically change by either contraction of the VSM, which causes vasoconstriction, or relaxation of the VSM, which causes vasodilation. Vasoconstriction causes a decrease in blood flow and an increase blood pressure. Vasodilation causes an increase in blood flow and a decrease blood pressure. Because of this, arterioles are referred to as the **Resistance** vessels.



All blood vessels exhibit vascular tone due to the partial contraction of smooth muscle. The importance of the arterioles is that they are the primary site of both resistance and regulation of blood pressure. The diameter of arterioles can be controlled by neural and chemical controls. Vasoconstriction and vasodilation in the arterioles are the primary mechanisms for distribution of blood flow and are a big influencer on peripheral resistance.

Capillaries

A **capillary** is the **smallest**, **thinnest** blood vessel in the body. Its primary function is as an **exchange** vessel in the tissues throughout the entire body. It exchanges gases, nutrients and waste between the blood and the surrounding cells and interstitial fluid, in a process called **perfusion**. The diameter of a capillary ranges from 5–10 µm. This is snuggly for the passage of RBCs that range from 7-9 µm. The term **microcirculation** describes blood flow through capillaries.

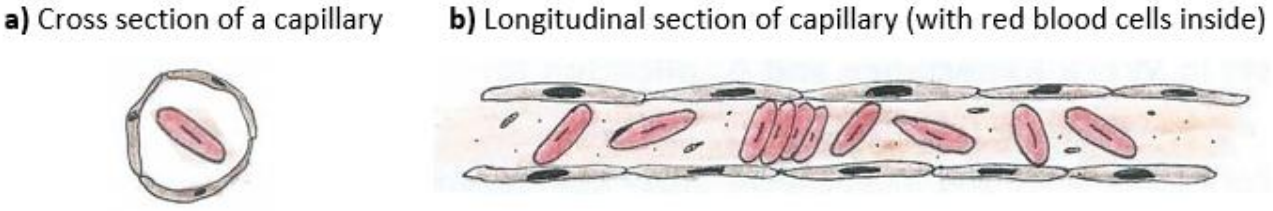


Figure 16.2 Shows **a)** the cross section of a capillary, composed only of a single endothelial cell layer with red blood cells contained inside it. The endothelial cells represent to walls for exchange with the surrounding tissues. Shown in **b)** is a longitudinal (length-wise view) of capillary with red blood cells flowing through it.

Capillaries are composed of a single layer of endothelial cells surrounded by a basement membrane. For capillaries to function, their walls must be 'leaky', meaning they need to allow substances to pass through them. There are 3 major types of capillary beds, which differ in their degree of "leakiness".
The 3 types of capillaries are: **1)** continuous, **2)** fenestrated, and **3)** sinusoidal capillaries.

1) **Continuous Capillaries –** These are the most common type of capillary in the body, found in almost all vascularized tissues. They are characterized by **tight junctions** between endothelial cells. Metabolic substance, such as water, glucose, and small lipophilic molecules like gases and hormones, as well as leukocytes can pass between cells. Both capillaries and venules are the primary sites of **diapedesis**, this refers to the passage of white blood cells through intact endothelial cell linings of vessel walls into the interstitial spaces and tissues. Capillaries associated

with the brain are part of the blood-brain barrier and have a thicker basement membrane (from astrocyte extensions) to restrict the movement of many substances.

2) **Fenestrated Capillaries –** These are capillaries that are characterized by having **pores** (or fenestrations, a Latin word meaning 'window') in their walls. These pores make this capillary bed more permeable or 'leakier' to larger molecules. The location of fenestrated capillaries is found where this additional leakiness is needed and include the kidneys, which filter the blood, synovial joints, some regions of the small intestine, as well as the hypophyseal portal system (connection between hypothalamus and anterior pituitary gland).

3) **Sinusoidal Capillaries –** These are the least common type of capillary bed and the most leaky! They are characterized by an incomplete basement membrane and large, extensive intercellular gaps between adjacent endothelial cells. This, combined with intercellular clefts and fenestrations makes these vessels leakiest of all capillaries and allow large molecules, including plasma proteins and even cells to pass in and out. These vessels are also very convoluted, meaning they twist and turn. This promotes even slower blood flow through sinusoidal vessels, allowing for greater time for exchange of gases, nutrients and wastes. Sinusoids are found most predominately in the **liver** and the **spleen**, in addition to **red bone marrow**. This capillary bed allows for the passage of blood cells that can only move through the large openings. The liver also requires extensive specialized sinusoid capillaries in order to process the materials brought to it by the ***hepatic portal vein*** from both the digestive tract and spleen, and to release ***large plasma proteins*** into circulation.

Shown below is a comparison of the 3 types of capillary beds.

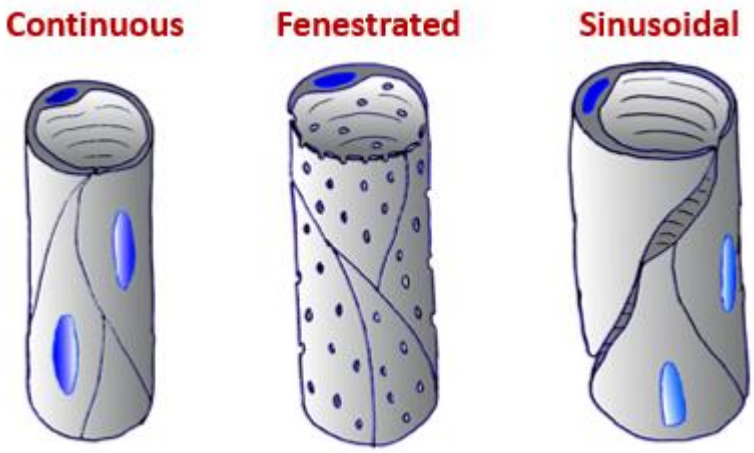
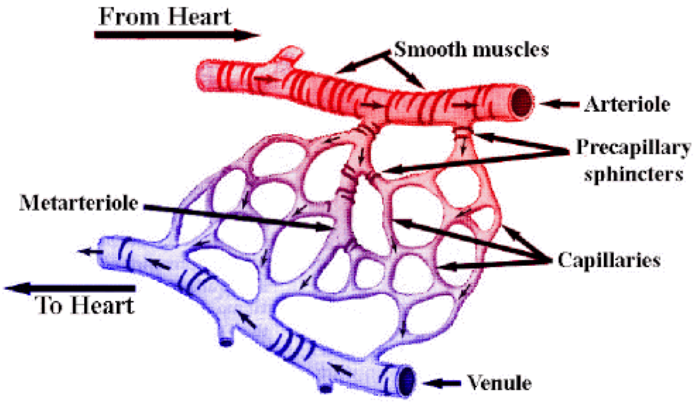


Figure 16.3 A comparison of the three main types of capillary beds is shown above. The continuous capillary beds are the most common in the body and the least permeable. Fenestrated capillary beds have pores and are more permeable. Sinusoidal capillary beds are the least common, have large gaps and are the most permeable.

Metarterioles and Capillary Beds

The term 'meta' means beyond, so this vessel is beyond an arteriole but not quite a capillary. A **metarteriole** is a short micro-vessel that links arterioles and capillaries by way of a **precapillary sphincter** that forms a ring around and encircles the entrance to capillary beds. Each metarteriole arises from a terminal arteriole and branches to supply blood to a capillary bed that may consist of 10–100 capillaries.

The **precapillary sphincters** (which are made of circular smooth muscle cells where the metarteriole connects with the capillary) act to closely regulate blood flow from a metarteriole to the capillaries it supplies. The capillaries are widespread and abundant, this is why precapillary sphincters are very important, because if all of the capillary beds were open at the same time, they would soon hold all of the blood in the body! If that were the case, then would be no blood in arteries, arterioles, venules, veins, or the heart itself. The default is that precapillary sphincters are closed. When local tissues need O_2 or nutrients, or have excess waste products, the precapillary sphincters open, allowing blood to flow and exchange to occur before closing again. If all of the precapillary sphincters in a capillary bed are closed, blood will flow from the metarteriole directly into a **thoroughfare channel** and then into the venous circulation, bypassing the capillary bed entirely. This creates what is known as a **vascular shunt** (like an anastomoses). In addition, an **arteriovenous anastomosis** may bypass the capillary bed and lead directly to the venous system.



The flow of blood in capillaries is not smooth and continuous, but rather more irregular and pulsating. This is called **vasomotion** and is regulated by signals molecules that are triggered in response to changes in internal conditions, such as O_2, CO_2, H^+, and lactic acid levels. If metabolic demand (e.g., during exercise or digestion) is increased, the capillary beds open. This is compared to periods of rest or sleep, where vessels are largely more closed.

Figure 16.4 Shown above is the arrangement of precapillary sphincters emerging from an arteriole at the entry point into the capillary beds. These connect to metarterioles that then merge into capillaries and exit into venules.

Venules

A **venule** is basically a small vein (from 8–100 µm) that collects blood from multiple capillaries exiting a capillary bed. As they continue to travel back to the heart, venules join to form veins. The walls of venules consist of endothelium, plus an outer layer of connective tissue. Recall that venules and capillaries are the primary sites of **diapedesis**, such that there is still some degree of exchange that occurs in venules with the local tissues.

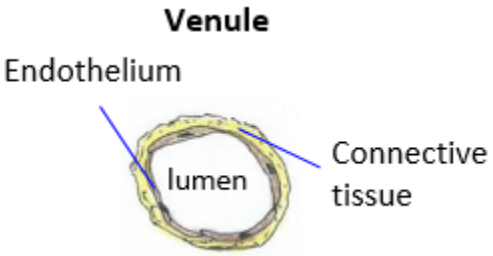
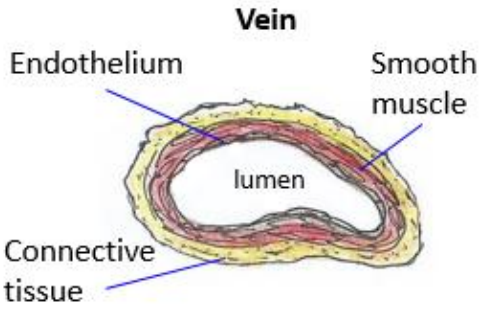


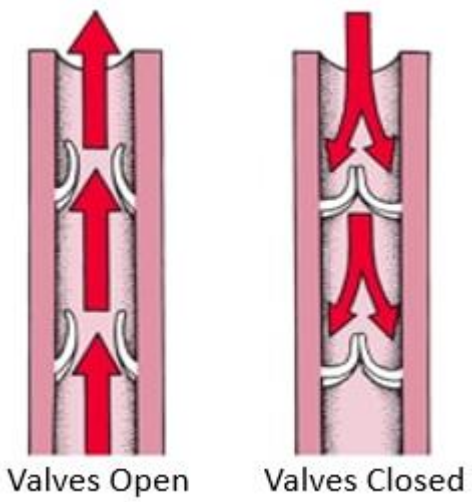
Figure 16.5 Shows the cross section of a venule.

Veins



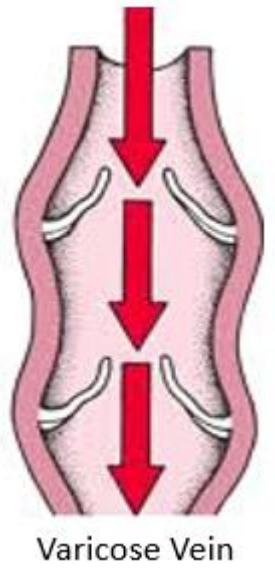
The largest blood vessels in the body, in terms of diameter, are veins **Figure 16.7**. A **vein** by definition is a blood vessel that carries blood back toward the heart. Veins, like arteries, are composed of 3 layers, however veins have much **thinner walls** compared to arteries but have **larger lumens**. Often the lumen of veins are described as 'irregular', but this is typically because when sectioned vessels are viewed it is when the vessels are empty, and the thinner walled veins tend to collapse when they are empty.

Figure 16.7 The cross section of a large vein is seen with the three layers, endothelium, smooth muscle and connective tissue from innermost to outermost respectively.



Veins are low-pressure vessels, and for this reason they typically have **venous valves** that assist in returning blood to the heart, preventing backflow inherent in low blood pressure vessels (see **Figure 16.8** to left). The regular arrangement of valves along a vein also act to segment the vessel. This ensures that even when there is a drop in pressures and the blood falls back (see diagram below), it can only drop back as far as the last valve, closing the valve in the process. When the pulsatile pressure of the blood increases again it pushes the valve open once more allowing flow in one direction only. In addition, the blood cannot fall back from that segment once it has advanced.

Figure 16.8 An important component of vein are their valves. When blood pressure is high enough, the venous valve open along blood flow (above left). As venous blood pressure drops (above right), the valves are closed by the weight of the blood and prevent backflow of blood in veins.



Varicose Veins are enlarged, swollen, and convoluted (twisting) veins (see **Figure 16.9** left), often appearing blue or dark purple on the surface of the skin. Most often varicose veins are caused by insufficient venous valves that cannot completely close and therefore allow back flow of blood to occur. This increase in blood volume in that segment of the vein causes blood to pool and exert more strain on the subsequent valve, which can then become **insufficient**, causing the typical contorted formation of the vein.

Varicose veins are generally benign, but cause aching pain and discomfort or may signal an underlying circulatory problem. Treatment involves compression stockings, exercise, or procedures to close or remove the veins.

Figure 16.9 The condition of varicose veins (left) can be seen when venous valves lose their ability to remain closed during periods of lower blood pressure and allow backflow or retrograde flow of blood to occur in veins.

Veins act as a Large Blood Reservoir

In terms of where the blood in the cardiovascular system resides while a person is at rest, the answer is, at rest the vast majority of blood is in the venous system. In this way, veins are considered to the 'blood reservoir' of the body. In the systemic circuit, the veins have about **65%** of the total blood volume at any given time. Large veins have the capacity to expand (distend) and store large volumes of blood, even at a low pressure. The large diameters and relatively thin walls of veins make them much more distensible than arteries. This is why veins are said to be **capacitance** vessels, as they have the ability to hold high volumes of blood. When veins constrict, they have the potential to deliver a great volume back to the heart. That is important.

Constriction of Large Veins

Vasoconstriction of large veins can produce a large amount of blood returning to the heart, which is called **venous return**. As we have already seen in discussions of cardiac output, increases in venous return cause an increase in end diastolic volume (**EDV**), which increases in **preload**. These increases cause the cardiac muscle to stretch and the ventricles to contract more forcefully, increasing **stroke volume**. This enables the mobilization of blood from the low pressure venous system, back into the central pump and quickly into the high pressure arterial system for subsequent redistribution to other parts of the circulation.

Again, since veins hold this '**venous reserve'**, vasoconstriction of veins can very quickly redistribute the great volume of blood from the low pressure venous system to the high pressure arterial system. This change in the distribution of blood makes it ready to deliver to tissues in need. The integration center for this redistributed is the **vasomotor center** located in the **medulla oblongata** (MO). Recall this center is one of the three 'vital centers' in the MO and is for the control of blood vessel diameter. The vasomotor center sends out **sympathetic stimulation** to the vascular smooth muscle (VSM) of veins, causing venous constriction which sets the redistribution of blood in motion.

Arterio-Venous Anastomoses

In the body, there are many vascular arrangements that vary from the typical one that has been described, that being: Artery -> arteriole-> capillary -> venuole -> vein arrangement.

As seen below (in **Figure 16.5**), there are several important interconnected vascular arrangements that exists in the body called **arterio-venous anastomoses** (AVAs). The term **anastomosis** is used to describe the union or inter-communication of vessels from one system with those of another. From Greek the etymology for anastomosis is: ana meaning "again, anew" and stoma meaning "mouth". Together meaning an outlet, or opening,"

The AVAs are direct connections between small arteries and small veins. These AVAs are short vessel segments with a large inner diameter and a very thick muscular wall which are richly innervated with **adrenergic** axons. When they are open, they provide a low-resistance connection between arteries and veins, which acts to shunt blood directly into the venous plexuses of the limbs. For example, they are numerous in the hairless (glabrous) skin of the palms of the hands and the soles of the feet.

Thermoregulation of Arterio-Venous Anastomoses

The arterio-venous anastomoses, or AVAs, also play an important role in **thermoregulation** of the body, and regulating body temperature (T_b) to maintain its **thermo-neutra**l zone, which is about 79°F to 97°F (26°C to 36°C) for a naked human at rest, and lower if a person is active and clothed.

Regulation from the body temperature control center in the **preoptic nucleus** of the hypothalamus cause surges of nerve impulses to be sent to all AVAs simultaneously. As a consequence, the AVAs are closed near the lower end, and opened near the upper end of the thermo-neutral zone. The small veins in the skin of the arms and legs are contracted near the lower end of the thermo-neutral zone and dilate to a wider cross section as the ambient temperature rises. At the cooler end of the thermo-neutral range, the blood returns to the heart through the deep set of veins and exchanges heat with the arterial blood through a countercurrent mechanism. As the ambient temperature rises, more blood is returned through the superficial set of veins, allowing the heating of the skin's surface on all of the limbs. It is this skin surface that is responsible for a significant loss of body heat toward the upper end of the thermo-neutral zone.

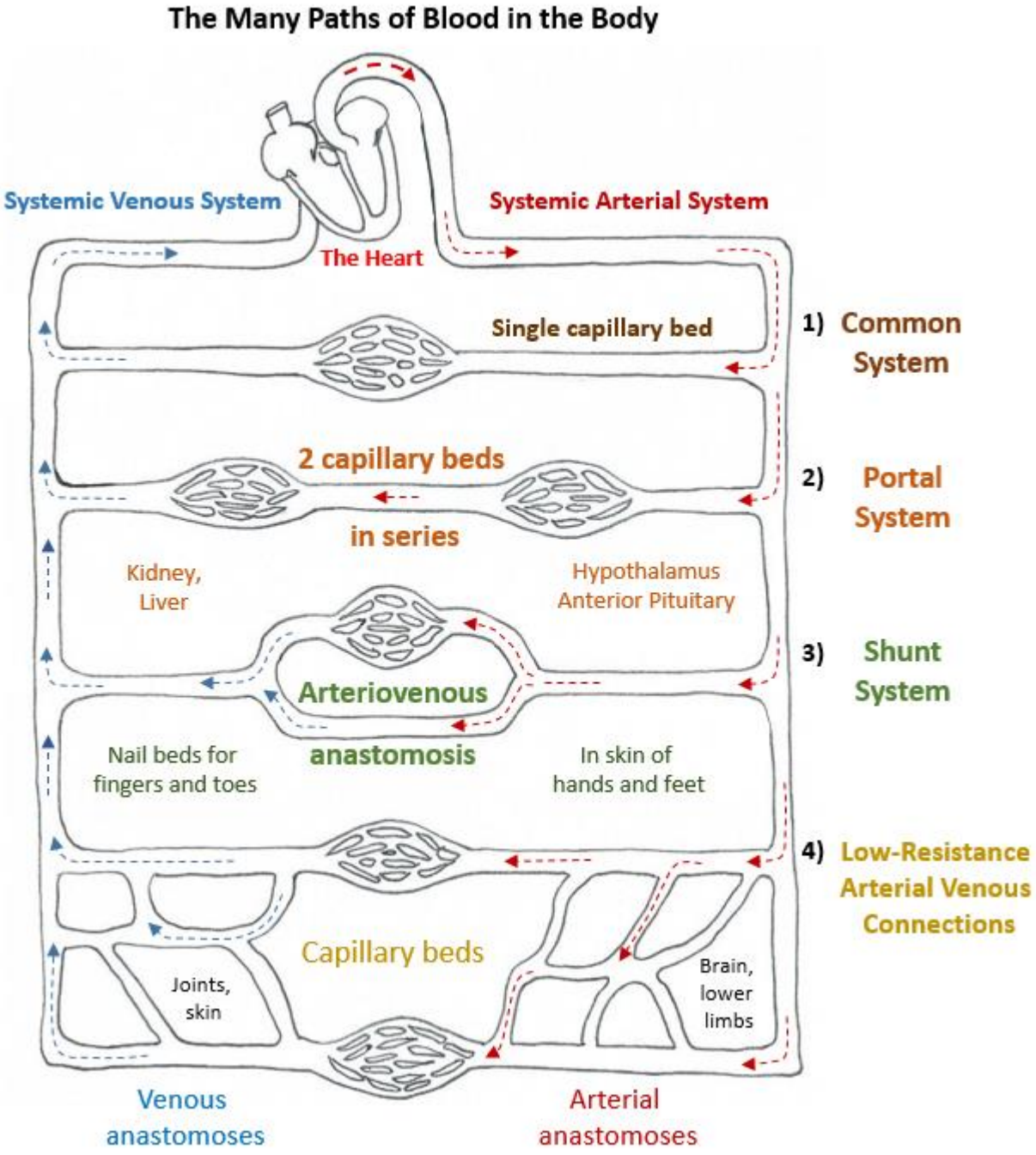


Figure 16.10 From and back to the heart, there are several main categories of blood vessel arrangements in the body. Show above are: **1)** the common single capillary bed in between the arterial and venous systems; **2)** the portal system with two capillary beds arranged in series; **3)** the shunt which can bypasses a capillary bed; and **4)** the low resistance venous connections that have a highly variable and wondering path of return to the heart.

Circulatory System – Brief Comments on Lymphatic Vessels

The movement of water and solutes back and forth across a capillary wall is constantly occurring. Recall there is a small residual amount of this 'tissue fluid' which remains in the interstitium, and this is ultimately returned to the cardiovascular system by **lymphatic vessels** of the **lymphatic system**. In terms of tissues fluid regulation, it is the extensive lymphatic vessels of the body that provide the **one way drainage of tissue fluid back to the heart**. In this way, the cardiovascular and lymphatic are linked together as the **circulatory system**. Normally of the fluid that is pushed out of a capillary at the arterial end, about **90%** of it is reabsorbed at the venous (lower pressure) end. Therefore, about **10%** of that fluid remains in the interstitium (tissues spaces) and is called **interstitial fluid** (or tissue fluid). It is continuously drained by the one way lymphatic vessel in the tissues. These are called **initial lymphatics** vessels (or lymphatics capillaries). Once the interstitial fluid enters the initial lymphatics, the fluid becomes lymph. The word lymph is Latin for 'clear water' or 'colorless fluid', because it is clear and colorless, although it can also appear as opaque. Generally it has very no proteins in it and very few cells, except when circulating leukocytes (namely T cells and B cells) are present.

With relation to blood pressure within the cardiovascular system, an increased blood volume in a vein can increase the pressure within it, which has a domino effect and reflects back to smaller veins, venules, and even the capillaries. This elevated pressure not only promotes greater flow of fluids out of the capillaries and into the interstitial fluid, but also hampers the reabsorption of fluid back into the capillaries. This can cause an excessive increase in tissue fluid around cells, a condition called **edema**. Edema is deleterious because it expands the distance for exchange to cells, and this hampers vital gas and nutrient exchange in the tissues. Significant edema has many potential causes, including hypertension and heart failure, severe protein deficiency, renal failure, and many others. Later we will examine the changes in transcapillary fluid dynamics that cause edema.

Blood Flow through the Cardiovascular System

Pressure, Volume, Flow and Resistance

Liquids and gases flow from areas of higher pressure to areas of lower pressure - that is to say, they flow *down their pressure gradients*. The high pressure generated when the ventricles contract forces blood to flow into vessels that exist at lower pressure. The pressure of the fluid (blood pressure) continues to fall as blood moves away from the heart. The vessels with the highest pressure are the aorta and other large systemic arteries. Veins are the vessels with lowest pressures, with the inferior vena cava being the lowest. Blood flow in the body is expressed in volume of blood per unit of time. The matter of resistance to flow will be expanded upon in the section below outlining the issue 'Resistance Opposes Flow'.

Compressing a Fluid Raises its Pressure

Blood pressure is the **Hydrostatic Pressure** (HP) of blood, and it falls off over distance as energy is lost to friction. Ventricular contraction compresses the volume of the ventricle and increases the pressure. This is the driving pressure created within the ventricles to drive blood through the vessels. As the heart chambers relax, pressure falls and allows blood to flow in (thus volume increases). Just like chambers, blood vessel volume can also change. In the body, when vessel vasodilation occurs (an increase in blood vessel diameter) this results in increased blood volume in that vessel and decreased pressure. When vasoconstriction occurs (a decrease in blood vessel diameter), this results in decreased blood volume in that vessel and increased pressure.

Blood Pressure

As a reminder, the term **systole** means **contraction** and also implies ejection of blood. The term **diastole** means **relaxation** and indicates filling. Systemic arterial blood pressure is measured in mmHg and recorded as **systolic pressure** (the high #) over **diastolic pressure** (the low #). For example, normal blood pressure is presented as 120/80 mmHg. This measure is giving information about how hard the heart is working when it's contracting (in systole) and when relaxing (in diastole).

Mean Arterial Blood Pressure

The average blood pressure is reported as **mean arterial pressure (MAP)** in arteries. This is a calculated mean, which is not a strict average but the formula takes into account that the heart at rest spends more time in diastole than in systole. The MAP formula is:

$$\text{MAP} = \text{Diastolic Pressure} + 1/3\,(\text{Systolic-Diastolic Pressure})$$

Sample calculation: If we use standard values of systolic pressure = 120 mmHg and diastolic pressure 80 mmHg. The MAP would be = 80 + 1/3 x (120 − 80) = 93 mmHg.

Typically, normal MAP falls in the range of 70–110 mmHg. If MAP falls under 60 mmHg for an extended time, blood pressure will not be high enough to ensure circulation to and throughout the tissues, which results in **ischemia**, a restriction in blood supply to tissues. A condition called **hypoxia** (inadequate oxygenation of tissues) is associated with ischemia. Hypoxemia is low O_2 levels in systemic arterial blood, which can of course lead to hypoxia. Note: Neurons are very sensitive to hypoxia.

Blood Flows Down its Pressure Gradient

Blood moves down its pressure gradient, the highest pressure being generated from the ventricles of the heart, going to the various tissues and then back to the heart. Blood flows from an area of higher pressure to one of lower pressure. The difference in pressure between 2 ends of a tube creates a pressure gradient (ΔP). For example, from below $\Delta P = P_1 - P_2$

Fluid flow depends on the change in pressure from one region to the next. The greater the pressure gradient, the greater the driving force for fluid flow. We can derive from this that the **Pressure Gradient is the driving force for blood flow.**

Resistance Opposes Flow

Blood flowing through blood vessels encounters *friction* from the vessel walls and the components of blood colliding with each other. The term **Resistance** (R) refers to the tendency of the cardiovascular system to oppose blood flow. Increased resistance leads to decreased flow. Thus, **Flow $\propto 1/R$** ($\propto$ = proportional to). In other words, this equation can read as: Flow is indirectly proportional to Resistance, the flow is less when the resistance is greater (if the pressure gradient is kept constant).

There are three parameters that contribute to resistance to flow of fluid through tube:

1. **Tube Length (L)** - as the tube lengthens, resistance increases. In the body, length is determined by the anatomy of the vascular system and this remains fairly constant.

2. **Fluid Viscosity (η)** - describes the 'thickness' of a fluid. The viscosity of blood is about 5-6 times greater than water (due to blood cells and plasma proteins). The more viscous the fluid the greater the resistance to flow. The viscosity of blood in the body is normally maintained to remain constant.

3. **Tube Radius (r)** - the radius can be simplified to mean the diameter of the tube. As the radius of the tube decreases, the resistance to flow increases; conversely, as the radius of the tube increases, the resistance to flow decreases. This parameter does not remain constant in the body - the diameter of blood vessels change continuously - thus, the radius of blood vessels is the main determinant of resistance to blood flow in the body.

The relationship between these parameters and flow of a fluid through a tube can be expresses by:

Poiseuille's Equation: $R = 8 L\eta/\pi r^4$

Where the numbers 8 and π (pi) are constants. The number pi represents the ratio of a circle's circumference to its diameter. The variables for vessel length (L), viscosity (η) and radius (r) are also shown. This formula however, can be simplified in humans to this: $R \propto 1/r^4$. This is because the other factors are fairly constant in the human body, such that blood vessel radius becomes the main determinant of peripheral resistance (R). **Vasoconstriction** leads to increased resistance and decreased flow. **Vasodilation** leads to decreased resistance and increased flow. Therefore, blood flow is described by this formula:

$$\text{Flow} \propto \frac{\Delta P}{R} \quad \textbf{OR} \quad \frac{\Delta P}{1/r^4}$$

If the driving force remains constant, flow varies **inversely** with resistance (determined by radius, **r**).

Vessel Diameter, Cross Sectional Area, Velocity Flow of and Blood Pressure

It is critical to understand blood flow and pressure in relation to the specific type of blood vessel. It is particularly important to know what is occurring at the capillaries. If we examine the graphs below (in **Figure 16.11**), it is useful to focus on what is occurring at the capillaries to best understand the role of these vessels in the control of blood flow and in the dynamics of exchange at the tissue level.

The anatomy of the capillary beds is such that they have the smallest diameters **(a)** but because there are so many of them, they have the greatest cross-sectional area **(b)**. The actual area they cover is the greatest of any vessel in the body. This makes sense since their function is exchange at the tissues, so the greater the area the better the coverage. As the vessels move closer to the heart, the pressure continues to drop, this ensures that blood is always flowing back to the heart **(c)**. The speed (velocity) of blood is seen in **(d)** shows that it decreases dramatically as the blood moves from arteries to capillaries. This is perfect for the role of capillaries, the very low flow rate allows greater time for exchange to occur, and picks up again as blood exits the capillaries to return to the heart.

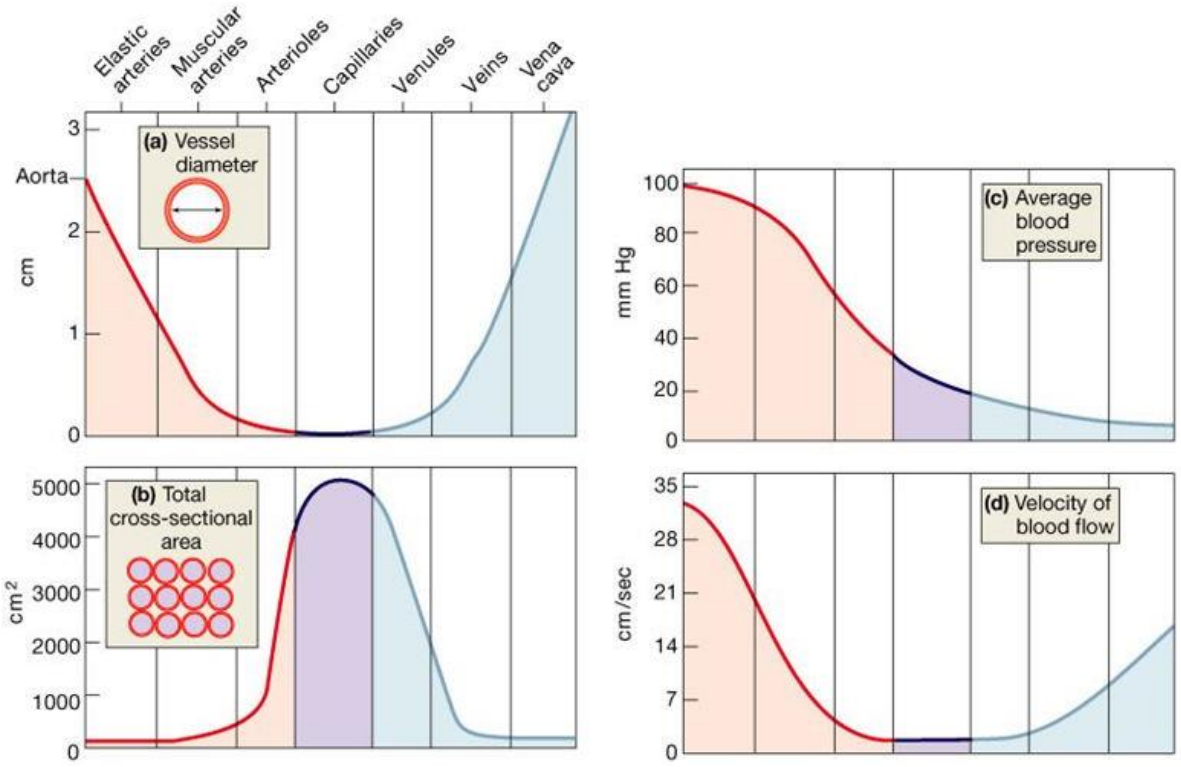


Figure 16.11 See here are a summary of blood vessel attributes, such as **(a)** vessel diameters, **(b)** the total cross-sectional area of vessels (greatest in capillaries), **(c)** the average blood pressure in the different vessels, and **(d)** the speed (velocity) of blood flow, (slowest in capillaries).

Note: The arterioles are the **resistance vessels**, because they can change the size of their lumen greatly, and this can dramatically change the flow of blood from arteries, which also impacts pressure, as the greater the resistance to flow, the greater the driving force of the pressure must be to overcome it! This explains why vasodilation and vasoconstriction of arterioles play more significant roles in regulating blood pressure than do the vasodilation and vasoconstriction of other vessels.

The 4 main Factors that Affect Mean Arterial Pressure (MAP)

1. Cardiac Output (HR and SV, which relates to EDV and preload)
2. Peripheral Resistance (blood vessel length, blood viscosity, and diameter of blood vessels)
3. Total Blood Volume
4. Distribution of Blood in the Body

1. Cardiac Output

As we have already seen, CO is the measure of blood pumped from one ventricle of the heart and is measured in liters per minute (L/min). It is directly controlled by **Heart Rate** and **Stroke Volume**. If either (or both) of these parameters go up, CO is increased and this will increase MAP! Any factor that decreases HR or SV (or both), will decrease CO and therefore decrease MAP.

Factors that will increase Cardiac Output are:

a) Sympathetic Innervation.
b) Hormones (epinephrine and norepinephrine, thyroid hormones).
c) Increased venous return (increase preload) increases Ca^{2+} levels, and increase force (SV).

Factors that will decreases Cardiac Output are:

a) Parasympathetic innervation.
b) Hormones (ANP, BNP).
c) Decreased Ca^{2+} levels (decreased SV).

Therefore, factors that causes CO to increase, will usually elevate MAP (if blood vessel diameter and peripheral resistance are constant), and factors that cause CO to decrease will usually depress MAP (again, if blood vessel diameter and peripheral resistance are constant). A significant role in the ANS and the antagonistic effects of the Sympathetic and Parasympathetic divisions of the ANS.

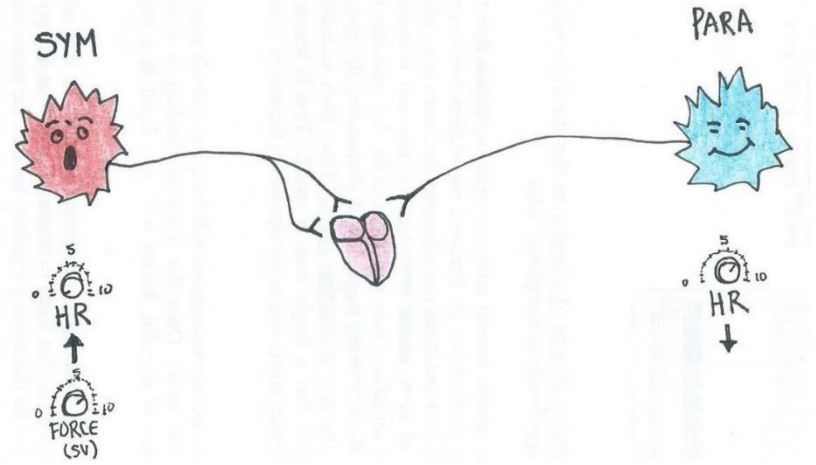


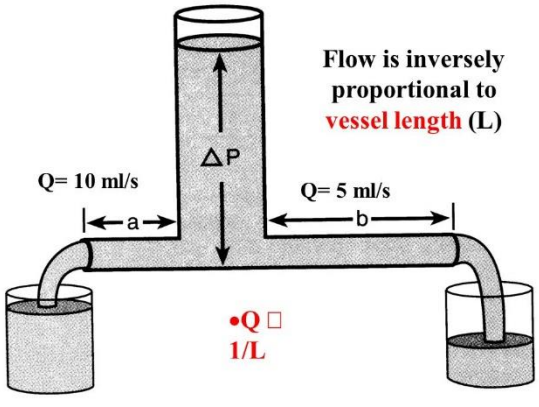
Figure 16.12 The sympathetic (SYM) and parasympathetic (PARA) both impact cardiac output.

2. Peripheral Resistance

As we have already discussed, peripheral resistance encompasses the various ways that resistance to flow can arise. It includes blood vessel **length**, blood **viscosity**, and **diameter** of blood vessels. All of these contribute to afterload.

Vessel Length and Diameter

The length of a blood vessel is directly proportional to its resistance: The shorter the vessel, the lower the resistance and the greater the flow (if all else held constant). Conversely, the longer the vessel, the greater the resistance, and the lower the flow (if all else held constant), as seen in image at right.



As blood flows along a vessel surface, the greater the surface area of the vessel (the longer it is), the more it will impede the flow of blood. And the shorter the vessel, the lower the resistance and the greater the flow. As adults the length of our blood vessels is relatively constant under normal physiological conditions. A person of 150 lbs. has about 60,000 miles of vessels in their body! Taller and larger people ultimately have longer vessels, which tends to increase peripheral resistance. Again, these blood vessel lengths are fairly constant in most adults.

Blood Viscosity

This relates to the 'thickness' of blood, the more viscous, the greater its resistance and the more resistant it is to flow. **Centipoise** is the unit of dynamic **viscosity**, described as the amount of force necessary to move a layer of liquid in relation to another liquid. Water has a viscosity of **1 centipoise** (cps) at 20°C.

The viscosity of blood is directly proportional to resistance and inversely proportional to flow – this means that any factor that increases blood viscosity will increase its resistance to flow (thus flow will decrease if all else is constant). And, any factor decreasing viscosity of blood will decrease its resistance to flow (thus flow will increase if all else is constant). As the chart to the left shows, blood is thicker than water, and honey is about 200 to 300 times thicker than blood!

Normally the viscosity of blood is fairly constant. The more hydrated (watery) the blood is, the less viscous it is. Normally the two primary factors determining blood viscosity are the cells and the plasma proteins in blood. Since 99% of the cells in blood are RBC (erythrocytes), conditions that affect erythropoiesis (RBC production) can alter blood viscosity, e.g., polycythemia or anemia. Since most plasma proteins are made by the liver, conditions that affect liver function can also change the blood viscosity and alter blood flow. Liver abnormalities like hepatitis, cirrhosis, and drug toxicities can alter blood content and viscosity. While leukocytes and platelets are normally a small component of the formed elements, some conditions with severe overproduction can impact viscosity as well.

Blood Vessel Diameter (radius)

Of the three (3) factors that affect resistance to fluid flow through a tube (length, viscosity and diameter of the tube), it is blood vessel diameter that is the most significant in its impact on resistance.

All vessels with **vascular smooth muscle** (VSM) exhibit **vascular tone**, which is the baseline contractile state of a vessel and determines diameter (thus resistance to flow). The diameter of many vessels may change quite frequently in the course of a day. It may occur in response to a number of signals (neural, hormonal, and local) that will trigger vasodilation or vasoconstriction.

The effect of vessel diameter (often equated with radius for convenience) on resistance is very significant and is indirectly proportional (or inverse): When blood vessel diameter is increased, less blood is flowing across and contacting the vessel wall, this lower friction and results in lower resistance, subsequently increasing blood flow. When blood vessel is decreased, there is more blood contact with the vessel wall, this increases friction, which increases resistance, therefore decreasing blood flow.

Even slight changes in vessel diameter (radius) will causes huge changes in resistance to flow. This is because if we go back to our simplified version of Poiseuille's Law (with little r being the most influential factor), $\mathbf{R} = 1/r^4$. This means if an arteriole dilates to two times its size, the resistance (R) to flow is now $1/16^{th}$ its original value and this means flow is now increased 16 times. Do the math! If we just double the vessel's radius (diameter) this is then raised to the power of four in the formula, so small changes in

diameter can have an enormous impact on resistance and thus flow. If a vessel constricts to ½ of its original radius, the resistance to flow will increase 16 times!

This is why vasodilators and vasoconstrictors are so important in the body.

Table 16.1 Important Endogenous **Vasoconstrictors** and **Vasodilators** in the Human Body.

Vasoconstrictor	**Norepinephrine and Epinephrine**	**Endothelin**	**Vasopressin (Antidiuretic Hormone)**	**Angiotensin II**
Source (Receptors)	ANS (Sym) Adrenal Medulla Via **α** receptors *NE higher affinity for α receptors*	Endothelium of blood vessels	Posterior Pituitary gland	Made in the Liver Activated by Renin
Vasodilator	**Norepinephrine and Epinephrine**	**Nitric Oxide**	**Acetylcholine (ACh)**	**Histamine**
Source (Receptors)	ANS (Sym) Adrenal Medulla Via **β** receptors *E has higher affinity for β receptors*	Endothelium of blood vessels	Prostaglandins (via NO) (*muscarinic*)	Basophils and Mast cells

Note: Activation of **β adrenergic receptors** leads to relaxation of smooth muscle in the lung, and **dilation** and opening of the airways. The **β adrenergic receptors** are coupled to a stimulatory G protein of adenylyl cyclase. This enzyme produces the second messenger cyclic adenosine monophosphate (cAMP).

3. Total Blood Volume

Hopefully the relationship between total blood volume and Mean Arterial Pressure (MAP) will be self-evident. If we take a very simple analogy of a water balloon it can become very clear. If the water in the water balloon represents the total blood volume in a body, then the more water we add to the closed water balloon, the greater the pressure will become inside it. The balloon, like the circulatory system, is closed so any additional volume will increase the pressure within it. In the body, as the total blood volume increases, this will result in an increase in MAP.

If we take a pin and prick the full water balloon and water starts to leak out, this decrease in the total volume of water in the balloon will result in a decrease in the pressure of the balloon. Thus, decreases in total blood volume in the body will result in a decrease in MAP.

Typically the total blood volume for a 150 lbs man is about 5.0 L. Out blood volume is very closely regulated homeostatically and for this reason typically does not exhibit large changes, although depending on our state of hydration we can small variations in total blood volume.

Hypovolemia means lower than normal blood volume. This can be caused by dehydration, by hemorrhage (bleeding, internally or externally), vomiting, from having severe third degree burns, or as a consequence of various medications to treat hypertension. For whatever reason hypovolemia occurs, it will have the effect of lowering MAP (if all other factors are held constant).

An individual may be down 10–20 % of their blood volume and still be asymptomatic since the body is very effective at regulating and maintaining blood pressure. The treatment for hypovolemia is the replacement of the fluid that has been lost, including doing so with intravenous solutions.

Hypervolemia, is higher than normal (or excessive) fluid volume in the body. This may be caused by retention of water and minerals which may occur in some forms of renal (kidney) disease. It can also occur in those with congestive heart failure, liver cirrhosis, hyperaldosteronism (too much of the hormone **aldosterone**), or glucocorticoid steroid treatments. Reestablishing volumetric homeostasis in these instances will depend on addressing the primary condition that triggered the hypervolemia. For whatever reason hypervolemia occurs, it will have the effect of inreasing MAP, (if all other factors are held constant).

Note: It is important to recognize that fluid intake (or lack of it) can have an impact on total blood volume and therefore on MAP.

- If there is an increase in fluid intake, this can lead to an increase in MAP.
- If there is a decrease in fluid intake, this can lead to a decrease in MAP.

The kidneys can conserve water to reduce the loss of vascular volume, but it cannot make more water! Thus, when the body needs to prevent a decrease in MAP, it conserves water by reducing the filtration (or work) done by the kidney until vascular volume is in the normal range.

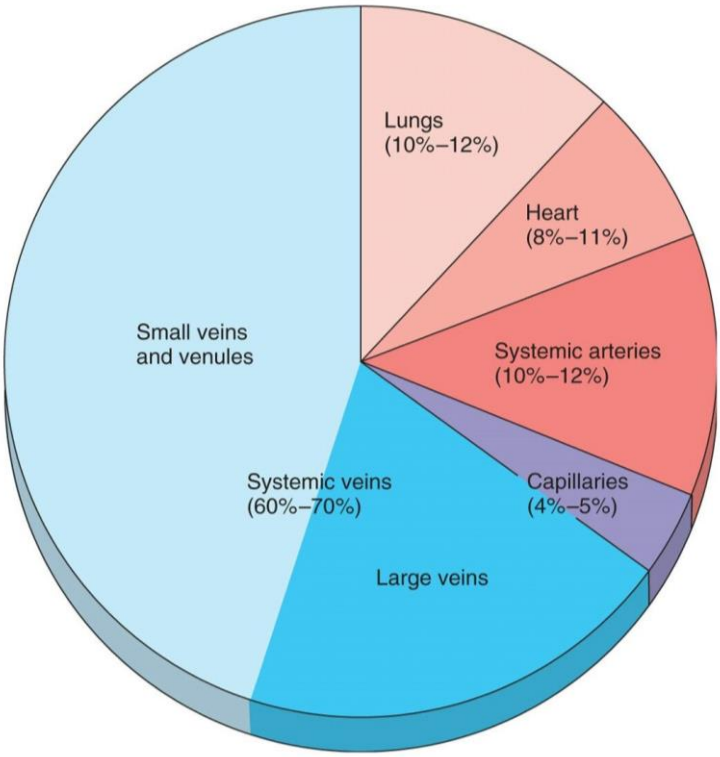
4. Distribution of Blood in the Body

The pumping action of the heart propels the blood into the arteries, from an area of higher pressure toward an area of lower pressure. If blood is to flow from the veins back into the heart, the pressure in the veins must be greater than the pressure in the atria of the heart. Two factors help maintain this pressure gradient between the veins and the heart. First, the pressure in the atria during diastole is very low, often approaching zero when the atria are relaxed (atrial diastole). Second, two physiologic "pumps" increase pressure in the venous system. The skeletal muscle pump and the respiratory pump that have already been mentioned in the first section of cardiac physiology notes.

The Blood in the Systemic Venous System

At rest, approximately **65 to 67%** of the total blood volume resides in **systemic veins**. Therefore, any action that increases the flow of blood through the veins will increase **venous return** to the heart. As mentioned previously, all vessels have some tone so that they do not completely distend with the addition of blood to them. Even large veins maintain vascular tone to prevent them from merely distending and absorbing

that force, which would dampen the flow of blood. Keeping that in mind, we will see that vasoconstriction in the systemic venous system actually enhances blood flow retuning to the heart.



As seen in **Figure 16.13** to the left, the vast majority of blood in the body when at rest is residing in the **systemic veins**, seen in shades of blue. In this particular image it shows that 60 to 70% of the blood at rest resides there. This vale can vary but it would be fair and usually accurate to report that on average, about **65%** is in the systemic veins. This represents almost 2/3 of the total blood volume.

Figure 16.13 This shows a blood sample of **a)** whole (or mixed) blood, and **b)** separated blood after having been spun at high speeds in a centrifuge. In the spun blood we can see the 2 major components of blood, the plasma, which is the supernatant on top and the heavier formed cellular elements on the bottom.

Venous Vasoconstriction: As previously discussed, vasoconstriction of an artery or arteriole decreases the radius, increasing resistance and pressure, but decreasing flow. This is different for venous vasoconstriction. Vasoconstriction increases pressure within a vein as it does in an artery, but in veins, the increased pressure increases flow! One reason is that the **one way valves** do not allow that increase in pressure to move the blood in any direction but back to the heart. Also, the thin and irregular walls of veins create a more rounded lumen when constricted, providing less surface area for friction, thus less resistance to flow.

Remember that the pressure in the atria (where this venous blood is flowing), is very low, approaching zero for part of the relaxation phase of the cardiac cycle. Thus, **venous vasoconstriction increases the return of blood to the heart**. It follows that venous vasoconstriction increases the **preload** (or EDV) and this stretches cardiac muscle. Not only does the sarcomere become optimal length, but more Ca^{2+} comes into the cells. This increases the force contraction, leading to a great stroke volume (SV). In summary, at rest, most blood is in venous system = **Venous Reservoir**. If there is a decrease in MAP, the mobilization of blood from the venous to the arterial system will increase MAP. The fastest most effective way to redistribute blood is by vasoconstriction of the systemic veins by the Sympathetic division of the ANS.

Review Questions for Chapter 16: Blood Vessels

1. The thinnest-walled blood vessels in the body that function as exchange vessels are
- **a)** metarterioles
- **b)** arterioles
- **c)** veins
- **d)** capillaries
- **e)** venules

2. Which are true of sinusoidal capillaries? Select all that apply.
1. They are the least common type of capillary bed.
2. These have fenestrations.
3. They are found in the kidneys.
4. They are found in the liver.
5. These are the most 'leaky' of the capillary beds.

3. Cardiogenic shock could be caused by which of the following
- **a)** cardiac tamponade
- **b)** myocardial infarction
- **c)** congestive heart failure
- **d)** vessel radius dramatically decreases
- **e)** systemic vasoconstriction occurs

4. Distinguishing characteristics of veins include which of the following?
- **a)** All veins carry deoxygenated blood.
- **b)** All veins carry blood toward the heart.
- **c)** All veins have thick, elastic walls.
- **d)** a and b.
- **e)** b and c.

5. Which of the following is the major force generating blood flow?
- **a)** blood vessel diameter
- **b)** total blood vessel length
- **c)** peripheral resistance
- **d)** blood viscosity
- **e)** contraction of the heart

6. If a person were experiencing **anaphylactic shock**, which of these statements would be most accurate?
- **a)** blood pressure would drop due to vasoconstrictors released from bacteria
- **b)** blood volume would significantly decrease
- **c)** an exaggerated inappropriate immune response causes systemic vasodilation
- **d)** cardiac output decreases and blood pressure would drop
- **e)** bacteria which release blockers to the endogenous vasoconstrictors in our body, and blood pressure would drop

7. According to Poiseuilles's law, blood flow decreases if
- **a)** venous return increases
- **b)** resistance decreases
- **c)** viscosity decreases
- **d)** the pressure gradient increases
- **e)** vessel radius decreases

8. Which of the following would make **Mean Arterial Pressure** (MAP) increase? Select all that apply.
- **1.** If the total blood volume increased
- **2.** if the blood shifted into the venous system
- **3.** if the peripheral resistance increased
- **4.** if cardiac output increased
- **5.** if the peripheral resistance decreased

9. Fenestrated capillaries:
- **a)** are found in the spleen and kidneys
- **b)** have pores in their walls
- **c)** are located in most tissue
- **d)** permit only one-way exchange of materials
- **e)** a and b

10. A metarteriole is a vessel that _____.
- **a)** connect arterioles and capillaries by way of a precapillary sphincter
- **b)** drains large capillary beds only
- **c)** is intermediate between the arteriole and the venules
- **d)** is intermediate between a capillary and a venule
- **e)** acts as an auxiliary channel

Answers in Appendix B