

Blood vessels are the tubes through which the heart pumps blood. There are 3 major types of blood vessels: arteries, capillaries, and veins.

Arteries take blood away from the heart. As they move away from the heart, they branch repeatedly, forming smaller and smaller arteries and eventually the smallest arteries – the arterioles. Arteries typically carry oxygenated blood (exception – pulmonary arteries).

Capillaries are the smallest and most numerous vessel type. They are the sites of exchange between blood and tissue fluid. Exchange is facilitated by their thinness and vast number (≈ 10 billion – SURFACE AREA!). They “connect” arteries and veins.

Veins take blood toward the heart. As they move toward the heart, they converge and join, forming larger and larger vessels. The smallest veins are the venules, which receive blood from capillaries. Veins typically carry deoxygenated blood (exception – pulmonary veins).

Arteries and veins have 3 basic layers or tunics that surround a central blood-containing space, the lumen. They are: tunica interna, tunica media, and tunica externa. Capillaries contain only the tunica interna.

The tunica interna is a.k.a. the tunica intima. It lines the lumen and consists primarily of endothelium, a simple squamous epithelium underlain by loose connective tissue. This helps provide a smooth surface ideal for fluid flow.

The tunica media consists of circularly arranged smooth muscle cells and sheets of the protein elastin. The smooth muscle tone is regulated by vasomotor fibers of the sympathetic nervous system, hormones, and local chemicals. An increase in tone leads to vasoconstriction – a decrease in vessel diameter. A decrease in tone leads to vasodilation – an increase in vessel diameter. There is a tonic release of NE onto vascular smooth muscle by vasomotor neurons. Increasing NE release causes smooth muscle contraction (vasoconstriction). Decreasing NE release causes smooth muscle relaxation (vasodilation). The tunica media is the most prominent layer in arteries.

Tunica externa is a.k.a. tunica adventitia. It consists of mostly collagen fibers that protect, reinforce, and support the vessel. It is the most prominent layer in veins.

There are 3 basic types of arteries: elastic arteries, muscular arteries, and arterioles.

Elastic arteries are a.k.a. conducting arteries. They are the arteries closest to the heart, e.g., the aorta and its major branches (e.g., common iliacs, common carotids). They contain a great deal of elastic tissue in all 3 layers. This allows these vessels to absorb the surges of pressure associated with each ventricular contraction. This helps produce continuous blood flow even while the heart is in diastole.

Muscular arteries are a.k.a. distributing arteries. They are primarily involved in regional distribution of blood, i.e., delivery of blood to specific organs (e.g., splenic artery, renal artery). They contain a very thick tunica media.

Arterioles are the smallest vessels of the arterial tree. Large arterioles have all 3 tunics. Smaller ones may only have smooth muscle cells circling an endothelium. They are very important in regulation of blood pressure and flow. Of all the artery types, they are innervated to the greatest extent by sympathetic vasomotor fibers. Thus their level of muscle tone is the most adjustable and the most often adjusted.

Capillaries are the smallest vessels. They contain only a tunica interna. There are billions of capillaries in the human body. This presents a huge surface area for exchange. They're arranged in networks (beds) and are in rich supply in metabolically active tissues, e.g., lungs, liver, kidneys, skeletal muscle and cardiac muscle. They're absent in epithelia, cartilage, and the corneas and lenses of the eyes. Their thin walls facilitate exchange between blood and ISF.

There are 3 types of capillaries: continuous, fenestrated, and sinusoidal.

Continuous capillaries are the most common type and are abundant in skin and muscle. They are "continuous" in terms of each cell (i.e., no holes within the cell membrane). They do contain intercellular clefts (spaces btwn endothelial cells). Continuous capillaries are found in areas where exchange of large items is unnecessary.

Fenestrated capillaries are similar to continuous except the membranes of the endothelial cells are riddled with pores (fenestrations). They also contain intercellular clefts. They are much more permeable than continuous capillaries. They are found in sites of active absorption (e.g., intestines) or filtrate formation (e.g., glomeruli of the kidneys).

Sinusoidal capillaries are highly modified, very permeable capillaries found in liver, bone marrow, lymphoid tissues, and some endocrine organs. They're fenestrated and contain huge intercellular clefts. Large molecules and even blood cells can exit/enter. They're twisty, which slows down blood flow. Macrophages can form portions of the capillary lining in the liver so as to monitor the blood for bacteria and other undesirables.

Capillaries form interconnected networks known as capillary beds. Capillary beds are bounded by an arteriole and venule. A typical capillary bed consists of a vascular shunt (a channel that directly connects the arteriole to the venule) and the true capillaries (the actual exchange vessels). A cuff of smooth muscle surrounds the entry to each true capillary. This muscular cuff is the precapillary sphincter. If the precapillary sphincters are open, blood will flow through the true capillaries. If the precapillary sphincters are closed, blood will flow through the vascular shunt from the arteriole to the venule. Whether the sphincters are open or closed is determined primarily by the metabolic needs of the tissue. Precapillary sphincters relax in response to low O₂, high CO₂, as well as the accumulation of the byproducts of metabolism.

Venules are formed when capillaries unite. They coalesce to form small veins.

Veins contain all 3 tunics, but in different proportions than arteries. The most prominent layer is the tunica externa. The walls of veins are thin and their lumens are large. They have very low resistance and are extremely compliant. B/c of this compliance they typically contain 65% of the body's blood volume and are known as capacitance vessels or blood reservoirs. Venous muscle tone (the contraction of the tunica media as controlled by the SNS) prevents the veins from being distended too much. Venous blood pressure is quite low b/c they are so far from the

pumping action of the heart. The low BP necessitates venous valves (extensions of endothelium reminiscent of the cardiac semilunar valves) to prevent backflow. There are far more valves in the lower extremities than compared to the upper extremities.

Venous sinuses (e.g. coronary sinus, dural sinuses) are flattened veins whose walls are composed only of endothelium.

Blood flow is the volume of blood flowing through a vessel, an organ, or the entire circulation in a given period (e.g., ml/min). Under resting conditions, blood flow thru the entire vascular system is equal to cardiac output and is relatively constant. Blood flow to individual organs varies greatly.

Blood pressure is the force per unit area exerted on the vessel wall by the contained blood. It's expressed in millimeters of mercury (mmHg). All vessels have an associated pressure; however the term "blood pressure" typically refers to arterial pressure. Similar to what we saw w/i the heart, it is differences in blood pressure (i.e., pressure gradients) that drive blood flow.

The vessel with the highest BP is the aorta (b/c of its proximity to the heart) while the vessels with the lowest BP are the venae cavae. BP drops to 0 within the right atrium. The most significant drop in BP occurs in the arterioles – b/c this is where resistance is the highest.

Resistance is opposition to flow and a measure of the friction blood encounters as it passes thru blood vessels. B/c most friction is encountered in the peripheral blood vessels, resistance is often termed peripheral resistance. Altering vessel resistance is one way to direct blood flow. The 3 main sources of resistance are: blood viscosity, total blood vessel length, and blood vessel radius.

Blood viscosity refers to the thickness or stickiness of the blood. It's directly proportional to resistance. Viscosity is relatively constant in a normal, healthy individual. An increase in RBC count (due to a rise in EPO levels for example) would increase viscosity.

Total blood vessel length is also directly proportional to resistance. The longer the vessel, the more friction blood will encounter. Total vessel length is also relatively constant in a normal, healthy individual. Growth of adipose tissue results in new blood vessel formation and thus an ↑ in total vessel length.

Blood vessel radius is the most important of the 3 factors for two reasons. First, in a normal individual, viscosity and vessel length are relatively constant whereas radius is quite variable. Second, resistance is directly proportional to viscosity and length but is inversely proportional to *radius to the 4th power*. Thus small changes in vessel radius will result in large changes in the friction btwn the blood and the vessel walls and hence large changes in resistance. As vessel radius increases (vasodilation), resistance decreases. As vessel radius decreases (vasoconstriction), resistance increases. If a blood vessel doubled in length or doubled in viscosity of contained blood, the resistance would simply double. If blood vessel radius doubles, the resistance decreases by a factor of 16!

Blood flow btwn 2 points is directly proportional to the pressure gradient btwn those 2 points and inversely proportional to the resistance of the vessel connecting those 2 points. $F \propto \Delta P/R$

Arterial blood pressure is what people refer to when they speak of blood pressure. The arterial system can be thought of as analogous to a series of branching elastic tubes. Fluid is pumped into this system through a 1-way valve and the outlet of each branch can be either wide or narrow.

The more fluid that is pumped into the system, the higher the pressure in the system will be. The amount of fluid pumped into the system per minute is the cardiac output. Thus BP is directly proportional to CO. Review the impact of venous return, stroke volume, and heart rate on cardiac output if necessary.

If the outlets of our model (i.e., the arterioles) are widened, it will be easier for fluid to leave the system and pressure will drop. If the outlets are narrowed, it will be harder for fluid to leave and thus pressure will rise. Since narrowing the outlets corresponds to increasing the resistance in the arterioles, we can say that BP is directly proportional to the peripheral resistance.

So far we have 2 factors affecting arterial BP: cardiac output and total peripheral resistance. Additional factors include blood volume and arterial compliance.

An increase in the total volume of fluid in our model will cause the elastic tubes to stretch to accommodate the extra fluid. This will increase the tension in the walls of the tubes and thus increase pressure in the system. Thus BP is directly proportional to blood volume. The kidneys control blood volume via regulation of urine output.

The stiffer the tubes are (i.e., the less elastic or compliant they are) the greater the resistance to stretch will be and the higher the pressure will be. Thus a lack of arterial compliance (the colloquial “hardening of the arteries”) will cause an increase in BP.

The same model that we use for BP can also describe blood distribution. Suppose 2 of the outlets are wide and the rest are narrow: as fluid enters the system more fluid will come out of those wide 2 outlets than all the others.

There is one additional point to remember. When an outlet is narrowed the pressure behind it (i.e., closer to the pump) will rise, while the pressure in front will be reduced.

During ventricular systole, BP rises b/c the quantity of blood entering the arterial system exceeds the run off to the periphery. At the peak pressure (the systolic blood pressure, e.g., 120mmHg) the inflow and run off are equal. Pressure then declines as the heart relaxes b/c run off to the periphery exceeds the inflow from the heart. The lowest pressure (the diastolic blood pressure, e.g., 80mmHg) in the arterial system occurs just prior to the next ventricular contraction. The recoil of the elastic arteries helps propel blood onward through the system as the heart relaxes. In other words, the elastic arteries act as auxiliary pumps.

As blood flows farther and farther from the heart, the difference btwn the systolic and diastolic pressure decreases – b/c the vessels contain less and less elastic tissue. By the capillaries, the pressure is relatively constant.

The pulse you feel at any artery is actually the difference btwn the expanded, stretched artery and the recoiling artery. Each pulse is caused by a single ventricular contraction. Thus pulse rate is equivalent to heart rate.

Mathematically, the difference btwn the systolic BP and diastolic BP is known as the pulse pressure. $PP = SBP - DBP$. Pulse pressure varies directly with stroke volume and indirectly with arterial compliance.

B/c of the fluctuating nature of arterial BP, it's helpful to have a value that represents the average pressure driving blood flow. This mean arterial pressure is a weighted average of the systolic and diastolic BP's. Mathematically it can be expressed as

$MAP = \frac{2}{3}DBP + \frac{1}{3}SBP$. This eqtn can be rearranged to $MAP = DBP + \frac{1}{3}PP$. The MAP depends more on diastolic BP b/c of the greater amt of time spent in diastole.

By the time blood reaches the capillaries the pressure no longer fluctuates and is quite lower than it was in the arteries. Low capillary BP is advantageous b/c: capillaries are fragile and high BP could cause them to burst; and capillaries are quite permeable and high BP could cause excess fluid loss.

Venous BP is also steady and lower than that of the arteries and capillaries. The low pressure allows veins to be in superficial locations, whereas arteries are usually deeper. There is a gradient of about 20mmHg btwn venules and the venae cavae. This is not enough by itself to drive blood flow back to the heart. Several other factors enhance venous return to the right atrium. Gravity helps return blood from the head and neck when upright but opposes return from the legs. Ventricular contraction pulls the atrioventricular ring downward creating a suction effect that pulls blood from the venae cavae. The skeletal muscle pump is the term given to the squeezing of veins by leg muscles that forces blood upwards. The respiratory pump refers to the effect on venous blood flow created by the diaphragm and other inspiratory muscles. During inspiration, the downward motion of the diaphragm coupled with the outward motion of the ribs and sternum lowers the intra-thoracic pressure. This helps draw blood upwards from the lower limbs. Sympathetic activation can cause an increase in venomotor tone, i.e., an increase in smooth muscle tone of medium and large veins. This causes an increase in venous return – as would be helpful during the sympathetic response. B/c of the intermittent nature of all these subsidiary venous pumps, valves are quite necessary to prevent backflow.

Controlling mean arterial blood pressure is quite necessary. It must be high enough to adequately drive blood flow but not so high that it causes damage to fragile organs. Short-term MAP control is performed primarily by altering cardiac output and peripheral resistance. This is accomplished both neurally and hormonally. Long-term control is achieved primarily by altering blood volume. The kidneys accomplish this.

Altering peripheral resistance counteracts most moment-to-moment fluctuations of MAP. In addition to its cardioacceleratory and cardioinhibitory centers, the cardiovascular center in the medulla oblongata also contains a cluster of neurons known as the vasomotor center. The vasomotor center works toward short-term MAP control as well as altering blood distribution during special situations (e.g., exercise). Increased activity of the vasomotor center leads to increased sympathetic NE release on arterioles and an increase in vasomotor tone and thus

peripheral resistance. Likewise, a decrease in vasomotor activity would yield a decrease in peripheral resistance. The activity of the vasomotor center is affected by baroreceptors, chemoreceptors, and higher brain centers.

Most short-term alterations in MAP are countered via the baroreceptor reflex. There are specialized neurons that can measure arterial BP. These baroreceptors are found primarily in the aortic arch and carotid sinuses (dilations in the internal carotid arteries), but also in most large arteries of the neck and thorax. Baroreceptors continually send impulses to the medulla via branches of the glossopharyngeal and vagus nerves (cranial nerves IX and X). The frequency of these impulses varies directly with the BP. Increased BP yields increased baroreceptor activity, which in turn affects the cardiovascular centers. The response causes an increase in the activity of the parasympathetic cardioinhibitory center and thus, an increase in vagal tone (i.e., an increase in acetylcholine release on the SA and AV nodes by the vagus nerve). This results in a decrease in HR and thus CO and thus BP. The response also includes a decrease in the activity of the sympathetic cardioacceleratory center and thus, a decrease in the activity of the sympathetic cardiac nerves (i.e., a decrease in NE release on the SA and AV nodes and the ventricular myocardium). This results in a decrease in HR, contractility, and SV and thus CO and thus BP. The final portion of the response is a decrease in activity of the vasomotor center and a decrease in vasomotor tone - a decrease in NE release onto arteriolar smooth muscle. This results in an increase in arterial diameter and thus a decrease in TPR and thus a decrease in BP. There is also an increase in venous diameter which allows blood to pool in the veins, thus decreasing venous return and therefore decreasing CO and BP.

Unfortunately baroreceptors are ineffective at dealing with sustained changes in BP – as occurs in hypertensive individuals.

Another reflex that affects the MAP in the short term is the chemoreceptor reflex. It is an emergency response to changes in the levels of plasma gases and pH. Located near the major baroreceptors are chemoreceptors, which monitor plasma levels of O_2 , CO_2 , and H^+ (i.e., plasma pH). Chemoreceptors are activated by:

1. An increase in plasma CO_2 .
2. An increase in plasma H^+ . (Decrease in plasma pH.)
3. A decrease in plasma O_2 .

Activated chemoreceptors project to the respiratory centers in the medulla and pons and increase respiration rate and depth. They also project to the cardiovascular centers and act to increase cardioacceleratory activity and decrease cardioinhibitory activity. These cause an increased cardiac output and increased MAP, which helps move oxygen from the lungs to the tissues and carbon dioxide from the tissues to the lungs.

The adrenal medullary mechanism is also important. The adrenal glands sit atop the kidneys and their medullae secrete epinephrine (and a small amt of NE) in response to large decreases in BP, sudden/substantial increases in physical activity, or stressful conditions. The epinephrine increases HR, SV, and TPR. Thus it causes BP to increase.

The cerebral cortex and hypothalamus can exert effects on MAP during emotional situations, stress, and sexual activity. This usually occurs via increases in the activity of the sympathetic medullary centers (i.e., vasomotor and cardioacceleratory).

The kidneys achieve long-term MAP regulation by altering blood volume. There are both direct and indirect mechanisms.

The direct mechanism occurs when a major increase in MAP causes an increase in urine formation. This reduces MAP by decreasing blood volume. Likewise, a major decrease in MAP causes a decrease in urine output and resists further decreases in BV and MAP.

The indirect mechanism is a bit more complicated. The kidneys exhibit a tonic release of the enzyme renin, which has important effects on MAP. In response to a drop in MAP, the kidney increases its release of renin. This begins a cascade of events that ultimately result in the increased production of a chemical called angiotensin II. Angiotensin II is a potent vasoconstrictor and therefore causes increased TPR and thus increased MAP. AgII also prompts antidiuretic hormone (ADH) release by the posterior pituitary. ADH causes vasoconstriction and a decrease in urine output. This further increases MAP by increasing TPR and blood volume. AgII also causes the adrenal cortex to release aldosterone, a hormone that promotes water retention. The resulting increased BV increases MAP. Lastly, AgII activates the body's thirst center. This increases BV and MAP. In response to a rise in MAP, the kidney's release of renin declines and as a result AgII, ADH, aldosterone, thirstiness, and MAP all decline. This pathway by which the kidney regulates MAP by regulating its release of renin is known as the renin-angiotensin-aldosterone system.

Adequate blood flow (tissue perfusion) is necessary to provide tissue cells with O₂ and nutrients and rid them of wastes. It is also necessary for proper gas exchange in the lungs, nutrient absorption in the small intestine, and urine formation in the kidneys.

The rate of blood flow varies in different parts of the vascular system. It's rapid in large vessels and slow in small vessels. Blood flow velocity varies inversely with the total cross-sectional area of a particular class of vessel. The total cross-sectional area can be determined by multiplying the cross-sectional area of a single vessel by the total # of those vessels. As you go from the aorta to the arteries to the capillaries, total cross-sectional area increases dramatically. (This is b/c of the incredibly large # of capillaries.) Thus the velocity of flow will decrease. The low velocity w/i capillaries allows for easy exchange btwn blood and interstitial fluid. As you go from capillaries to veins to the venae cavae, cross-sectional area decreases. As a result, blood flow increases in the venous system; although it does not achieve the speeds found in the arterial tree b/c of the lack of a pump.

Ventricular contraction is the source of the pressure that drives blood thru the arterial tree. The volume of blood delivered to specific organs depends on the needs of those organs. Such local allotment of blood flow is known as autoregulation. It depends on the automatic adjustment of blood flow to each tissue in proportion to the tissue's requirements at any instant. Blood flow is adjusted by altering the diameters of the local arterioles feeding the capillaries. Factors associated with increased tissue metabolism (such as ↓O₂ levels and ↑CO₂, K⁺, H⁺, and lactate) cause local arterioles to vasodilate. This reduces the local resistance and increases blood flow to the tissue that needs it. Most metabolites directly cause the relaxation of vascular smooth muscle while some prompt endothelial cells to release nitric oxide, which is a powerful vasodilator.

Capillaries are the sites of exchange between blood and tissue fluid. Nutrients, wastes, signaling molecules, and gases are exchanged primarily by diffusion (movement of solutes from areas of high concentration to areas of low concentration). Fluid is also exchanged at the level of the capillaries. (Recall that tissue fluid is derived from plasma itself.) 4 forces can affect the movement of water either into or out of the capillary: capillary hydrostatic pressure, capillary osmotic pressure, interstitial fluid hydrostatic pressure, and interstitial fluid osmotic pressure.

Capillary hydrostatic pressure refers to capillary BP. CHP tends to force fluid out of the capillary and into the interstitial space. This bulk flow of fluid is known as capillary filtration. The CHP declines by 50% from the arterial end of the capillary to the venous end of the capillary – b/c of the increased distance from the heart.

Capillary osmotic pressure opposes capillary hydrostatic pressure. It promotes fluid movement into the capillary from the interstitial space. This bulk flow of fluid is known as capillary reabsorption. The COP is primarily due to the abundant albumin w/i the plasma.

Interstitial fluid hydrostatic pressure, if substantial enough, would promote fluid movement into the capillary from interstitial space (reabsorption). However, it's normally inconsequential.

Interstitial fluid osmotic pressure, if substantial enough, would promote fluid movement into the interstitial space from the capillary (filtration). However, it's normally inconsequential due to the low protein content of interstitial fluid.

The balance of these 4 forces yields the net filtration pressure. It determines how much interstitial fluid is created as blood passes through a capillary. Typically a net filtration pressure of 10mmHg causes capillary filtration. This results in the formation of 1.5mL of ISF per minute. A system of lymphatic vessels functions to remove the majority of this fluid (as well as any "accidentally" leaked proteins) and send it back to the vascular system. Excess ISF due to excess formation or failure of the lymphatic drainage system is known as edema.