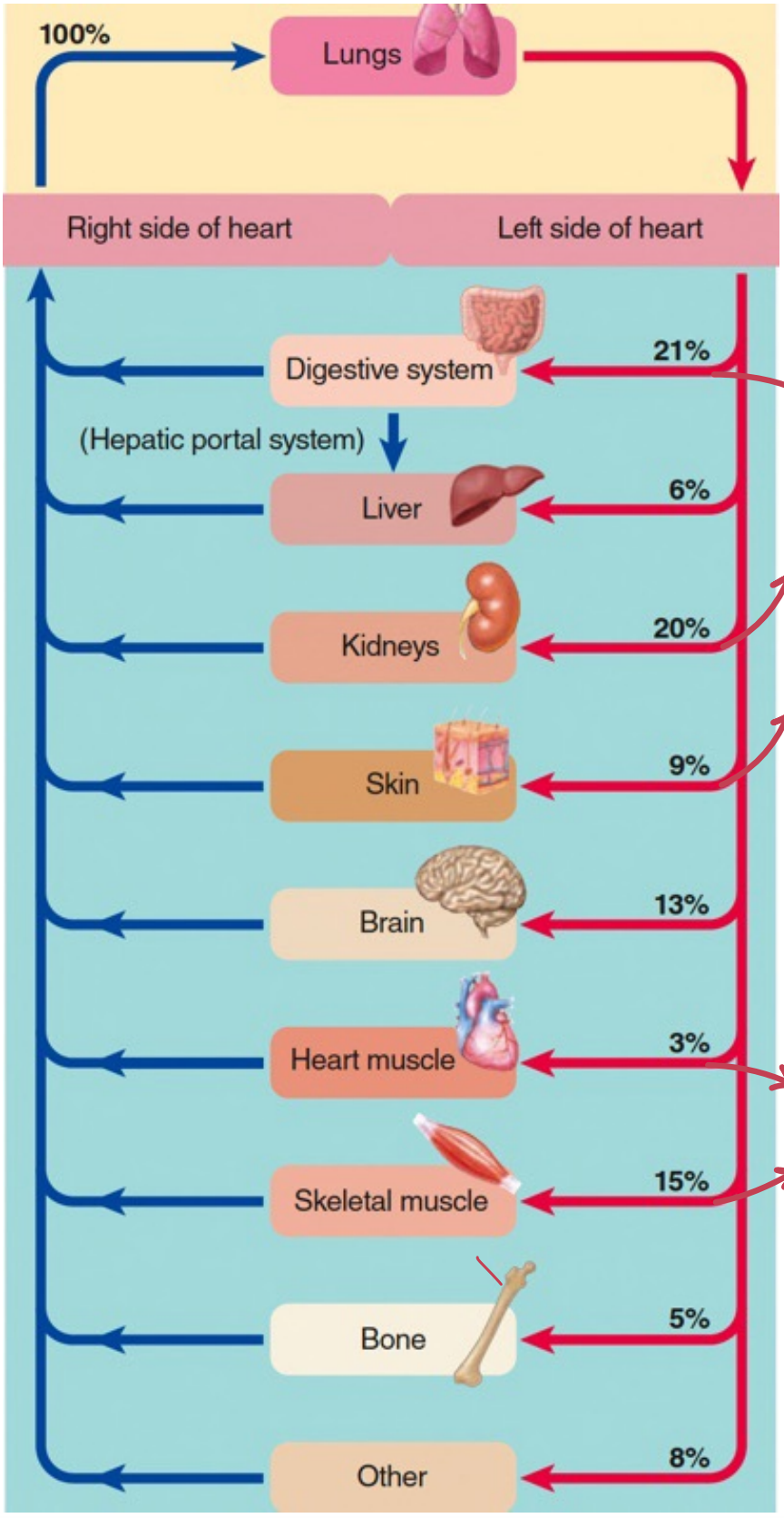
Vascular physiology

The function of the vascular system is to serve the needs of the body tissues by transporting nutrients to the cells, waste products away, transporting hormones from one part of the body to another, and to maintain appropriate environment in all the tissue fluids for survival and optimal function of the cells.



The blood pumped by the left ventricle into the systemic circulation is distributed in various proportions to the organs through a parallel arrangement of vessels that branch from the aorta.

The overall blood flow in the total circulation of an adult person at rest is about 5000 ml/min. This is called the cardiac output.

This is a Reconditioning organ, meaning it normally receives much more blood flow than is necessary to meet its basic metabolic needs,

-can adjust the extra blood to achieve homeostasis

-can withstand temporary reductions in blood flow much better.

The brain in particular suffers permanent damage when transiently deprived of blood supply.
Therefore, constant delivery of adequate blood to the brain is a high priority.

Blood flow to the heart or skeletal muscle matches their metabolic needs and can be adjusted according to their level of activity.

Parallel arrangement of vessels ensures that all organs receive blood of the same composition.

◉ True ✔ ○ False

Also because of this parallel arrangement, blood flow through each systemic organ can be independently adjusted as needed.

Hemodynamics

The principles that govern blood flow in the cardiovascular system.

BLOOD FLOW

Blood flow through a blood vessel is determined by two factors:

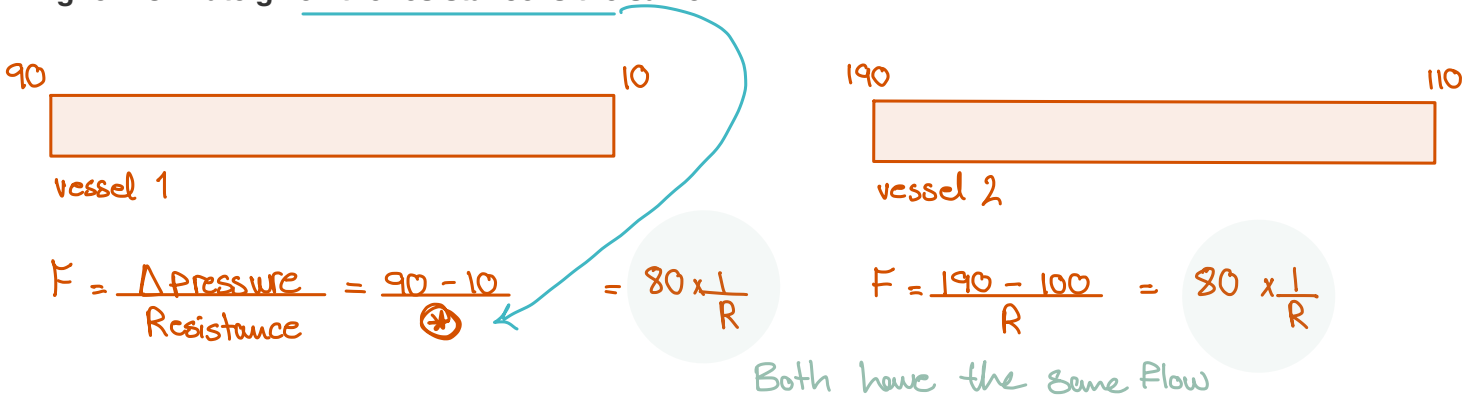
(1) pressure difference of the blood between the two ends of the vessel, also called the pressure gradient, which pushes the blood through the vessel.

(2) the impediment to blood flow through the vessel, which is called vascular resistance.

$$F = \frac{\Delta P}{R}$$

Note that it is the difference in pressure between the two ends of the vessel that determines flow rate, not the absolute pressure in the vessel.

⭐ **If P = 90 mm Hg at the beginning of vessel 1, and P = 10 mm Hg at the end of vessel 1, whereas P = 190 mm Hg at the beginning of vessel 2, and P = 110 mm Hg at the end of vessel 2. Which one has higher flow rate given the resistance is the same?**



Blood flows from an area of higher pressure to an area of lower pressure down a pressure gradient. Contraction of the heart imparts pressure to the blood, which is the main driving force for flow through a vessel.

Because of frictional losses (resistance), the pressure drops as blood flows throughout the vessel's length. establishing a pressure gradient for forward flow of blood through the vessel.
The greater the pressure gradient forcing blood through a vessel, the greater the flow rate through that vessel. —> positive / direct relationship

Resistance
As resistance to flow increases, it is more difficult for blood to pass through the vessel, so as long as the pressure gradient does not change, the flow rate will decrease.
In order to maintain a uniform flow rate, the pressure gradient will have to increase accordingly if resistance is increased. —> Inverse relationship

In a direct relationship or a positive correlation as one variable increases, the other variable also increases.
علاقة طردية

Inverse relationship refers to a situation where two variables change in opposite directions
علاقة عكسية

Resistance to blood flow is
(1) directly proportional to viscosity of the blood.
(2) directly proportional to vessel length.
(3) inversely proportional to vessel radius, which is by far the most important.

Resistance occurs as a result of friction between the flowing blood and the intravascular endothelium all along the inside of the vessel.

The factors that affect flow rate through a vessel are integrated in
Poiseuille's law

$$\text{Flow rate} = \frac{\pi \Delta P r^4}{8 \eta L}$$

ΔP is the pressure difference between the ends of the vessel.
r is the radius of the vessel.

Because the circulatory system is a closed system, the volume of blood flowing through any level of the system must equal the CO.

Therefore, the flow rate is the same at all levels of the circulatory system.

watch video

https://youtu.be/a8QVUWI5-jk

⭐ **One of the following statements is correct regarding laminar flow:**

Turbulent flow is always pathological ❌
All blood particles flow in the same speed within a vessel ❌
It has parabolic profile of velocity ✅

in steady, fully developed laminar flow through a circular pipe, the velocity profile is parabolic. The velocity is highest at the center of the pipe and decreases smoothly to zero at the pipe's walls. This parabolic profile is a result of the viscous forces within the fluid, and it is a characteristic feature of laminar flow in confined geometries.

Reynold's number is a dimensionless number that is used to predict whether blood flow will be laminar or turbulent.

When Reynolds' number rises above approximately 2000, turbulence will usually occur, even in a straight, smooth vessel.

Reynolds' number for flow in the vascular system normally rises to 200 to 400, even in large arteries.
As a result, there is almost always some flow turbulence at the branches of these vessels.
In the proximal portions of the aorta and pulmonary artery, Reynolds' number can rise to several thousand during the rapid phase of ejection by the ventricles.

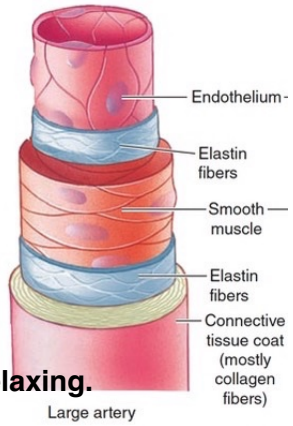
$$Re = \frac{v \cdot d \cdot \rho}{\eta}$$

ρ = Density of blood
d = Diameter of blood vessel
v = Velocity of blood flow
η = Viscosity of blood

Drag the words into the correct boxes

Reynolds number is increased ✔ in anemia due to decrease ✔ in blood viscosity, and increase ✔ in the velocity of blood flow.
Because of turbulent ✔ blood flow, functional murmurs can be heard in patients with anemia.

4/4



-What are the types of arteries?

1) Elastic arteries (2) Muscular arteries

-Functions of arteries :

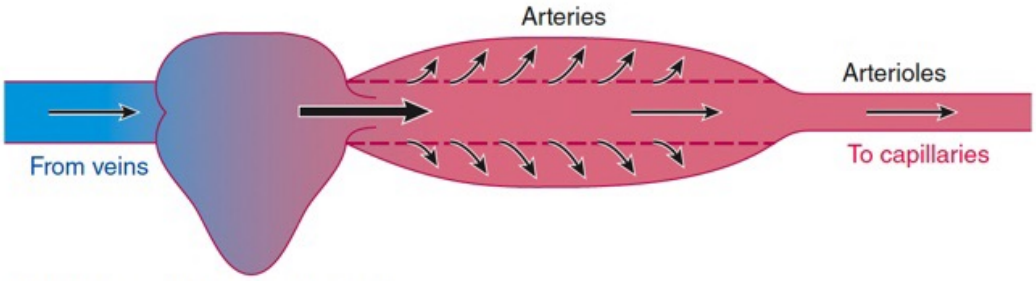
1. Serve as rapid-transit passageways for blood from the heart to the organs.

2. Act as a pressure reservoir to provide the driving force for blood when the heart is relaxing.

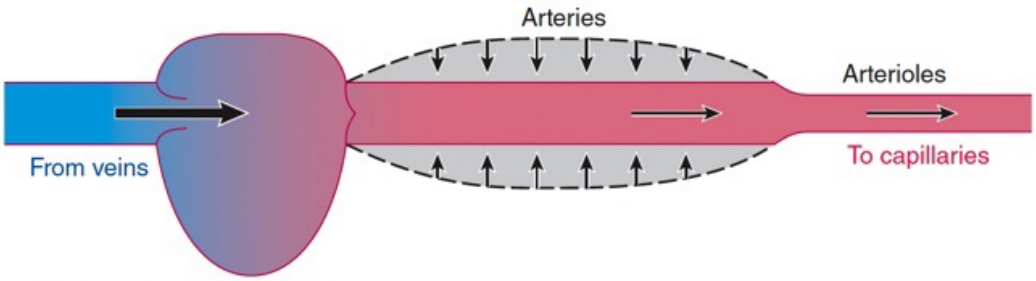
-Rapid-transit passageways for bloodfrom the heart to the organs : Because of their large radius, arteries offer little resistance to blood flow.

-Pressue reservoir when the heart is relaxing :

The heart alternately contracts to pump blood into the arteries and then relaxes to refill with blood from the veins. When the heart is relaxing and refilling, no blood is pumped out.
However, capillary flow does not fluctuate between cardiac systole and diastole—that is, blood flow is continuous through the capillaries supplying the organs.
The driving force for the continued flow of blood to the organs during cardiac relaxation is provided by elastic recoil of the walls of large arteries.



(a) Heart contracting and emptying



(b) Heart relaxing and filling

Self reading : you are required to read about arterial stiffness ⬇️ (from chatGPT)

Arterial stiffness refers to the reduced ability of arteries to expand and contract in response to changes in pressure and blood flow. It is a crucial aspect of cardiovascular health and is influenced by the structural and mechanical properties of the arterial walls. The main components contributing to arterial stiffness are elastin, collagen, smooth muscle cells, and endothelial function.

1. Elastin and Collagen:
-Elastin: Arteries contain elastic fibers, particularly in the walls of large arteries. Elastin allows arteries to stretch during systole (heart's contraction) and recoil during diastole (heart's relaxation), helping to maintain continuous blood flow.
- Collagen: Over time, may increase in arterial walls, leading to decreased arterial compliance.

2. Smooth Muscle Cells:
play a role in regulating arterial tone. Increased smooth muscle tone can lead to increased stiffness.

3. Endothelial Function:
- The endothelium produces substances like nitric oxide that help regulate vascular tone. Healthy endothelial function promotes vasodilation, contributing to arterial compliance.

4. Calcification:
- from the deposition of calcium in the arterial walls. More common in conditions like atherosclerosis and aging.

5. Pulse Wave Velocity (PWV):
- Arterial stiffness is often assessed by measuring pulse wave velocity—the speed at which the pressure wave travels through the arteries. Increased PWV is associated with stiffer arteries and is an independent predictor of cardiovascular risk.

6. Clinical Implications:
- Arterial stiffness is considered a marker of vascular aging and is associated with various cardiovascular conditions, including hypertension, atherosclerosis, and heart failure.
- Stiffer arteries contribute to increased systolic blood pressure, leading to higher workload on the heart.

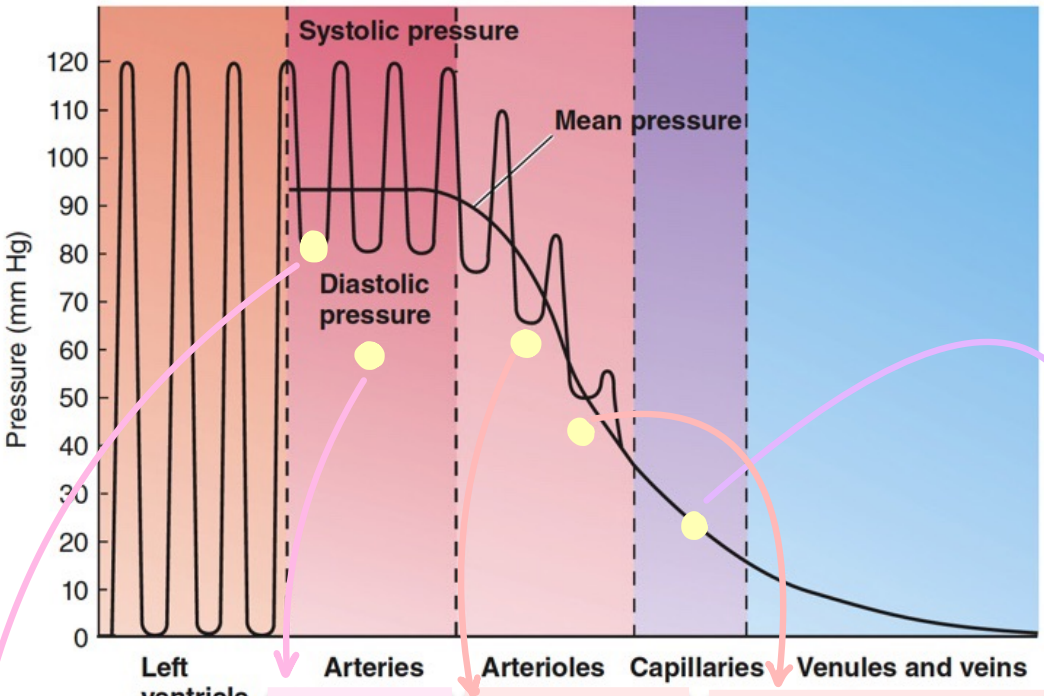
Blood pressure (BP) depends on the volume of blood contained within the vessel and the compliance, or distensibility, of the vessel walls.
During ventricular systole, a stroke volume of blood enters the arteries from the ventricle, while only about one third as much blood leaves the arteries to enter the arterioles. During diastole, no blood enters the arteries, while blood continues to leave, driven by elastic recoil.

Systolic pressure (SBP) is the highest arterial pressure measured during a cardiac cycle. It is the pressure in the arteries after blood has been ejected from the left ventricle during systole.

Diastolic pressure (DBP) is the lowest arterial pressure measured during a cardiac cycle and is the pressure in the arteries during ventricular relaxation when no blood is being ejected from the left ventricle.

Pulse pressure (PP) is the difference between systolic and diastolic blood pressures, Two major factors affect the pulse pressure are (1) the stroke volume of the heart; and (2) the compliance (total distensibility) of the arterial tree.

The **mean arterial pressure (MAP)** is the average of the arterial pressures over a period of time. It is not half way between the systolic and diastolic pressures because at normal heart rates, a greater fraction of the cardiac cycle is spent in diastole than in systole. Thus, the arterial pressure remains closer to diastolic pressure than to systolic pressure during the greater part of the cardiac cycle. The mean arterial pressure is therefore determined about 60% by the diastolic pressure and 40% by the systolic pressure. However, at very high heart rates, diastole comprises a smaller fraction of the cardiac cycle, and the mean arterial pressure is more closely approximated as the average of systolic and diastolic pressures.



Although ventricular pressure falls to 0 mm Hg during diastole, arterial pressure does **not** fall to 0 mm Hg because the next cardiac contraction refills the arteries before all the blood drains off.

Pressure is of the same magnitude throughout the arteries.

Because of the arterioles' high resistance, the pressure drops significantly and the systolic-todiastolic swings in pressure are converted to a nonpulsatile pressure when blood flows through the arterioles.

This progressive diminution of the pulsations in the periphery is called damping of the pressure pulses. The cause of this damping is two fold:
(1) resistance to blood movement in the vessels;

(2) compliance of the vessels.

The pressure continues to decline but at a slower rate as blood flows through the capillaries and venous system.

The pulse pressure in old age sometimes rises to twice normal because the arteries have stiffened with arteriosclerosis and therefore are relatively noncompliant.

In persons with aortic valve stenosis, the diameter of the aortic valve opening is reduced significantly, and the aortic pressure pulse is decreased significantly because of diminished blood flow outward through the stenotic valve.

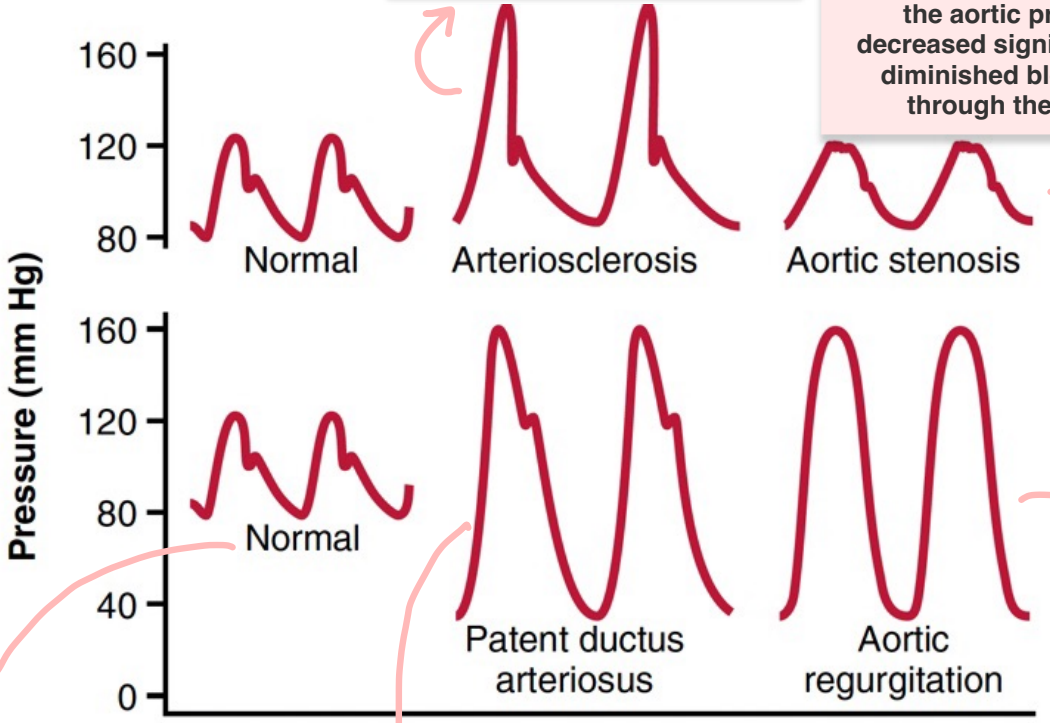
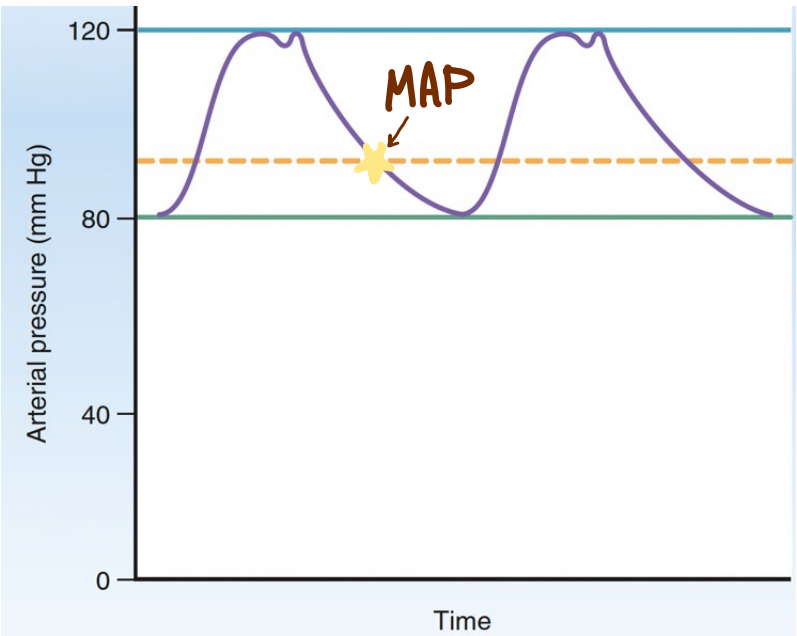


Figure 15-4. Aortic pressure pulse contours in arteriosclerosis, aortic stenosis, patent ductus arteriosus, and aortic regurgitation.

dicrotic notch (or incisura), is produced when the aortic valve closes. Aortic valve closure produces a brief period of retrograde flow from the aorta back toward the valve, briefly decreasing the aortic pressure below the systolic value.

In persons with patent ductus arteriosus, 50% or more of the blood pumped into the aorta by the left ventricle flows immediately backward through the wide open ductus into the pulmonary artery and lung blood vessels, thus allowing the diastolic pressure to fall very low before the next heartbeat and increasing the pulse pressure

In persons with aortic regurgitation, the aortic valve is absent or does not close completely. Therefore, after each heartbeat, the blood that has just been pumped into the aorta flows immediately backward into the left ventricle. As a result, the aortic pressure can fall all the way to zero between heartbeats. Also, there is no incisura in the aortic pulse contour because there is no aortic valve to close



-Autoregulation is local arteriolar myogenic and chemical mechanisms that keep tissue blood flow fairly constant despite rather wide deviations in mean arterial driving pressure.

-Blood pressure is the force exerted by the blood against any unit area of the vessel wall.

-Compliance or capacitance of a blood vessel is the volume of blood the vessel can hold at a given pressure.

-Conductance is a measure of the blood flow through a vessel for a given pressure difference.

Diastolic blood pressure is the minimum pressure within the arteries when blood is draining off into the rest of the vessels during diastole.

-Distensibility of the vessel walls is how easily they can be stretched.

-Flow rate of blood is the quantity of blood that passes a given point in the circulation in a given period of time.

-Hemodynamics is the principles that govern blood flow in the cardiovascular system.

-Mean arterial pressure is the average pressure driving blood forward into the tissues throughout the cardiac cycle.

-Pressure gradient is the difference in pressure between the beginning and the end of a vessel.

-Pulse Pressure is the difference between systolic blood pressure and diastolic blood pressure.

-Resistance is a measure of the hindrance or opposition to blood flow through the vessel, caused by friction between the moving fluid and the stationary vascular walls.

-Reynolds number is a dimensionless number that is used to predict whether blood flow will be laminar or turbulent.

-Shear stress is longitudinal force applied on the endothelial cells in the direction of the flow.

***-Systolic blood pressure* is the maximum pressure exerted in the arteries when blood is ejected into them during systole.**

-Velocity of blood flow is the rate of displacement of blood per unit time.

-Viscosity is the friction developed between the molecules of a fluid as they slide over each other during flow of the fluid.

Vascular physiology 2

ARTERIOLES

When an artery reaches the organ it is supplying, it branches into numerous arterioles within the organ.

Arterioles are the main resistance vessels in the vascular tree because their radius is small enough to offer considerable resistance to flow.

In contrast to the low resistance of the arteries, the high degree of arteriolar resistance causes a marked drop in mean pressure as blood flows through these small vessels.

This helps establish the pressure gradient that encourages the flow of blood from the heart to the organs downstream.

Arteriolar resistance also converts the pulsatile systolic-to-diastolic pressure swings in the arteries into the nonfluctuating pressure present in the capillaries.

VASCULAR TONE

The extent of contraction of arteriolar smooth muscle depends on the cytosolic Ca++ concentration.
Arteriolar smooth muscle normally displays a state of partial constriction known as vascular tone, which establishes a baseline of arteriolar resistance.

Two factors are responsible for vascular tone.

1. Arteriolar smooth muscle is tonic smooth muscle that has sufficient surface-membrane voltage-gated Ca++ channels open to trigger partial contraction.
This myogenic activity is independent of any neural or hormonal influences, leading to self-induced contractile activity.

2. The sympathetic fibers supplying most arterioles continually release norepinephrine, which further enhances vascular tone.

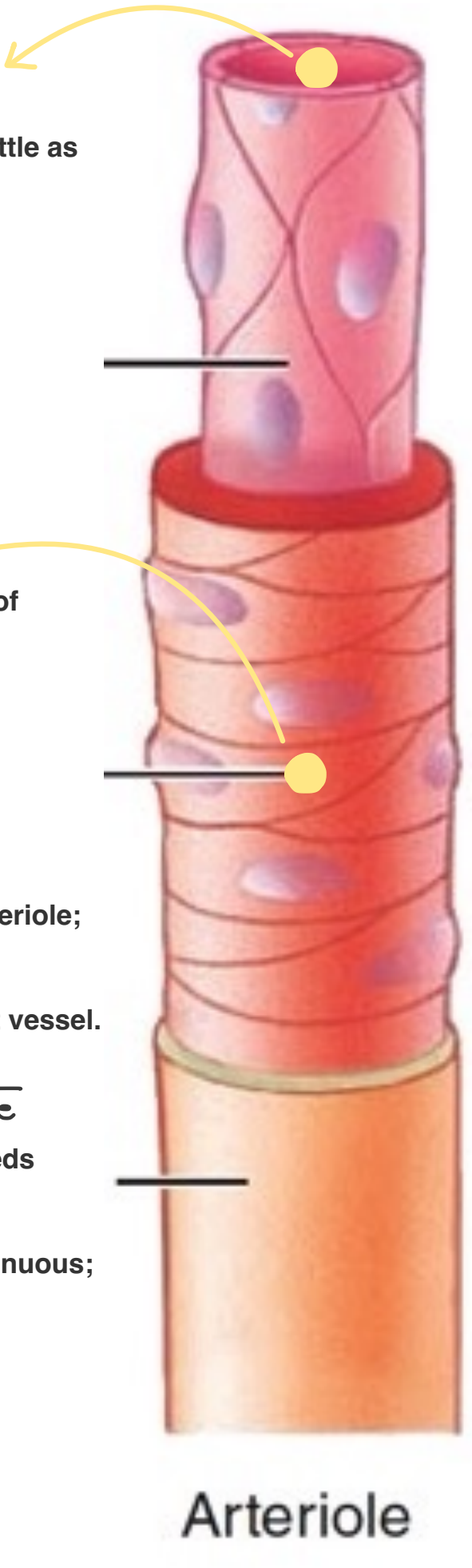
This ongoing tone makes it possible to either increase or decrease contractile activity to accomplish vasoconstriction or vasodilation, respectively.

Vascular smooth muscle can undergo graded changes in force in response to chemical, physical, and neural factors without undergoing action potentials.
These agents largely act via second-messenger pathways.

Arterioles are arteries with a diameter <0.1 mm.

The internal diameters of the arterioles range from as little as 4 micrometers to as much as 25 micrometers.

However, their strong vascular walls allow the internal diameters to change tremendously, often as much as fourfold.



The TUNICA MEDIA of arterioles consists of 1-3 layers of smooth muscle cells.

Smooth muscles are richly innervated by sympathetic nerve fibers, and sensitive to :
-many local chemical changes,
-to a few circulating hormones
-to mechanical factors such as stretch.

The smooth muscle layer runs circularly around the arteriole; so when the smooth muscle layer contracts, the vessel's circumference becomes smaller, increasing resistance and decreasing flow through that vessel.

$$\text{Flow} \propto \text{vessel circumference} \propto \frac{1}{\text{resistance}}$$

The terminal arterioles that supply blood to capillary beds are called metarterioles.

The smooth muscle layer of meta-arterioles is not continuous; rather, individual muscle cells are spaced apart, and each encircles the endothelium of a capillary arising from the meta-arteriole, allowing them to act as a sphincter upon contraction, controlling blood flow into the capillary bed.

VASCULAR RESISTANCE

-In the systemic circulation, about two thirds of the total systemic resistance to blood flow is resistance in the arterioles.
-Blood pumped by the heart flows from the high-pressure part of the systemic circulation to the low-pressure side through blood vessels arranged in series and in parallel.
-The arteries, arterioles, capillaries, venules, and veins are collectively arranged in series.

When blood vessels are arranged in series, flow through each blood vessel is the same, and the total resistance to blood flow is equal to the sum of the resistances of each vessel:

$$R(total) = R1 + R2 + R3$$

-The total peripheral vascular resistance is therefore equal to the sum of resistances of the arteries, arterioles, capillaries, venules, and veins.
-Blood vessels branch extensively to form parallel circuits that supply blood to the many organs and tissues of the body.
-This parallel arrangement permits each tissue to regulate its own blood flow, to a great extent, independently of flow to other tissues.

For blood vessels arranged in parallel, the total resistance to blood flow is expressed as follows:

$$\frac{1\ (total)}{R} = \frac{1}{R1} + \frac{1}{R2} + \frac{1}{R3}$$

It is obvious that for a given pressure gradient, far greater amounts of blood will flow through this parallel system than through any of the individual blood vessels.
Therefore, the total resistance is far less than the resistance of any single blood vessel.

Flow through each of the parallel vessels is determined by the pressure gradient and its own resistance, not the resistance of the other parallel blood vessels.

However, increasing the resistance of any of the blood vessels increases the total vascular resistance.

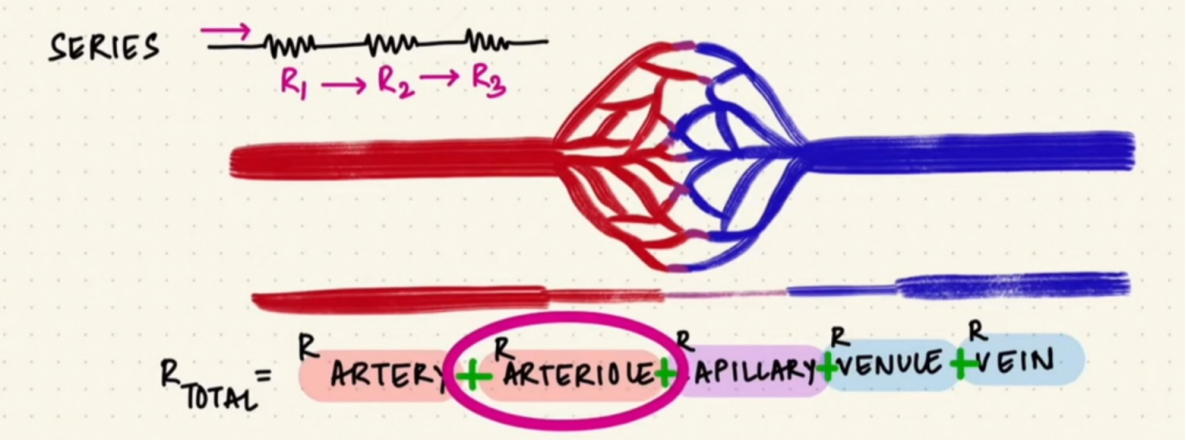
It may seem paradoxical that adding more blood vessels to a circuit reduces the total vascular resistance.
Many parallel blood vessels, however, make it easier for blood to flow through the circuit because each parallel vessel provides another pathway, or conductance, for blood flow.

The total conductance (the reciprocal of resistance) for blood flow is the sum of the conductance of each parallel pathway: For example, brain, kidney, muscle, gastrointestinal, skin, and coronary circulations are arranged in parallel, and each tissue contributes to the overall conductance of the systemic circulation.

Blood flow through each tissue is a fraction of the total blood flow (cardiac output) and is determined by the resistance for blood flow in the tissue, as well as the pressure gradient.

Therefore, amputation of a limb or surgical removal of a kidney also removes a parallel circuit and reduces the total vascular conductance and total blood flow while increasing the total peripheral vascular resistance.

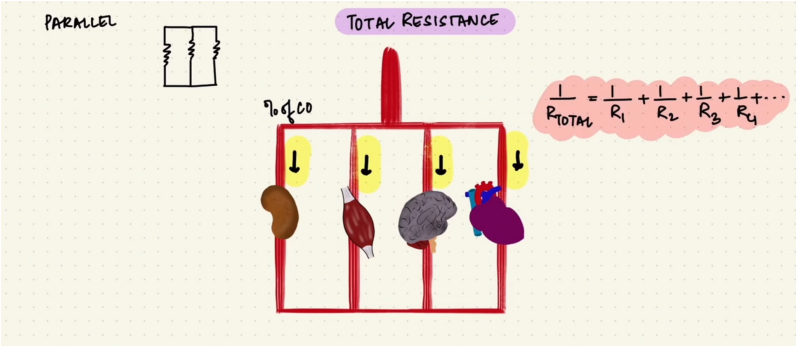
Video content : starting from 4:29

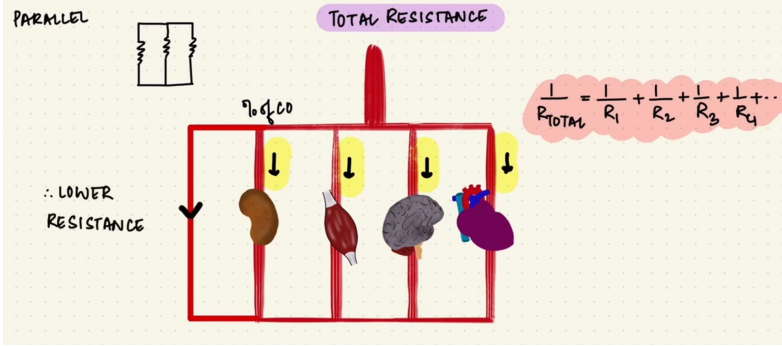


The resistance through vessels is like resistance in a circuit, so vessels can be arranged in **series** or in **parallel**.
A series arrangement would mean that all the blood flows through each of the vessel systems in the circuit, one after the other.

To understand this, consider all the arteries as one unit, all the arterials as one, and so on.
overall, the blood that goes through the arteries has no choice but to go through the arterioles then the capillaries, the venules and the veins.

basically all the blood has to go through one vessel after another : we can get the total resistance by adding them up.
And remember that the highest resistance is offered by the arterioles.





parallel circuit means that blood is flowing through different paths at once, so not all the blood goes through each path.

This is like how the arteries supply the organ systems.
They each get a fraction of the cardiac output at the same time.

The total resistance of the unit will be lower than any one of them and that's because blood has lots of paths to travel through, lowering the overall resistance.

So this is calculated as one over the total resistance is equal to one over r, one plus one over r two, and so on depending on how many paths there are.

Now, if there is an additional path, the resistance will reduce further because there's an extra path for blood to flow.
If there's one lesser path, there's more resistance.

If you removed a kidney for a patient, what will be the effect on total resistance?

- Total resistance will not change
- Total resistance will decrease
- Total resistance will increase ✓

Local control of blood flow

It is not possible simply to increase blood flow everywhere in the body when a particular tissue demands increased flow.
Instead, the microvessels of each tissue, especially the arterioles, continuously monitor tissue needs. Then dilate or constrict to control local blood flow at the level required for the tissue activity.

Also, nervous control of the circulation from the central nervous system and hormones provides additional help in controlling tissue blood flow.

Arterioles change blood flow based on 2 control systems:
1. Intrinsic (local) control.
2. Extrinsic control.

LOCAL

Local controls are changes within an organ that adjust blood flow through the organ by affecting the smooth muscle of the organ's arterioles to alter their caliber and resistance.

Local influences may be either chemical or physical.

Local chemical influences on arteriolar radius include:
(1) local metabolic changes.
(2) histamine release.

Local physical influences include:
(1) how much the vessel is stretched.
(2) the extent of shear stress.
(3) local application of heat or cold.

These local chemical changes act on arteriolar endothelial cells.
Arteriolar endothelial cells release vasoactive substances which act on the underlying smooth muscle to alter its state of contraction, thus locally regulating arteriolar caliber.

NO is an important vasodilator, whereas endothelin is a potent vasoconstrictor

Histamine is another local chemical mediator that influences arteriolar smooth muscle, but it is not released in response to local metabolic changes and is not derived from endothelial cells.

When organs are injured or during allergic reactions, histamine is released and acts as a paracrine in the damaged region. By promoting relaxation of arteriolar smooth muscle, histamine is the major cause of vasodilation in an injured area.
The resultant increase in blood flow into the area produces the redness and contributes to the swelling seen with inflammatory responses.

Local blood flow control can be divided into two phases: acute & long-term

Acute control

Is achieved by rapid changes in local vasodilation or vasoconstriction of the arterioles, metarterioles, and precapillary sphincters that occur within seconds to minutes to provide rapid maintenance of appropriate local tissue blood flow.

Long-term control (page 12)

Slow, controlled changes in flow over a period of days to months. In general, these long-term changes provide better control of the flow in proportion to the needs of the tissues. These changes come about as a result of an increase or decrease in the physical sizes and numbers of blood vessels supplying the tissues.

According to the vasodilator theory:

The greater the rate of metabolism or the less the availability of oxygen or some other nutrients to a tissue, the greater the rate of formation of vasodilator substances in the tissue cells.
The vasodilator substances are then believed to diffuse through the tissues to the precapillary sphincters, metarterioles, and arterioles to cause dilation.

Some of the different vasodilator substances are:

adenosine, carbon dioxide, adenosine phosphate compounds, histamine, potassium ions, and hydrogen ions.

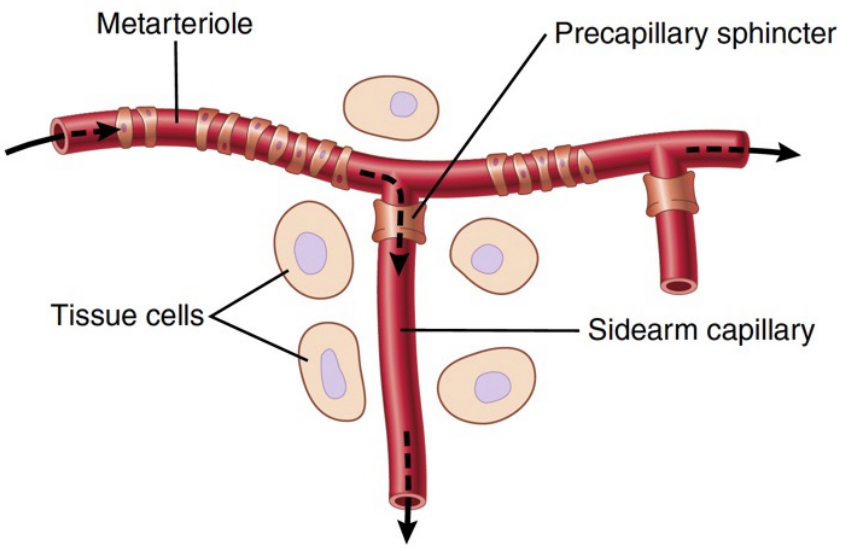
High Oxygen level is also a vasodilator.

○ True ◉ False ✔

The number of precapillary sphincters that are open at any given time is roughly proportional to the requirements of the tissue for nutrition.

The precapillary sphincters and metarterioles open and close cyclically several times per minute, with the duration of the open phases being proportional to the metabolic needs of the tissues for oxygen.

The cyclical opening and closing is called vasomotion.



Another theory is called the oxygen demand theory or the nutrient demand theory.

Oxygen is one of the metabolic nutrients required to cause vascular muscle contraction, with other nutrients required as well.
Therefore, in the absence of adequate oxygen, it is reasonable to believe that the blood vessels would relax and therefore dilate.

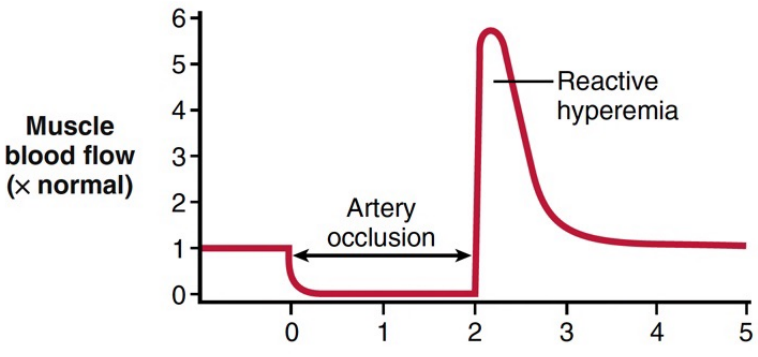
Also, *increased* utilization of oxygen in the tissues as a result of *increased* metabolism theoretically could *decrease* the availability of oxygen to the smooth muscle fibers in the local blood vessels, causing local vasodilation.

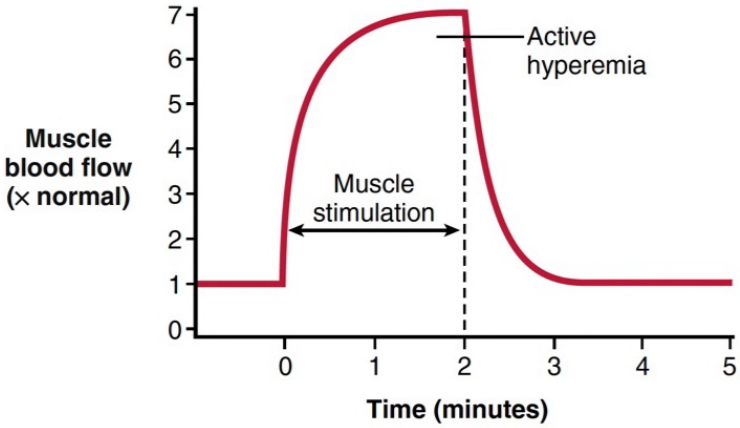
When the blood supply to a tissue is blocked for a few seconds to as long as 1 hour or more and then is unblocked, blood flow through the tissue usually increases immediately to four to seven times normal.
This increased flow will continue for a few seconds if the block has lasted only a few seconds but sometimes continues for as long as many hours if the blood flow has been stopped for an hour or more.

This phenomenon is called REACTIVE HYPEREMIA

The increase in local metabolism causes the cells to consume tissue fluid nutrients rapidly and release large quantities of vasodilator substances.
The result is dilation of local blood vessels and increased local blood flow.
In this way, the active tissue receives the additional nutrients required to sustain its new level of function.

Active hyperemia in skeletal muscle can increase local muscle blood flow as much as 20-fold during intense exercise.





VIDEO

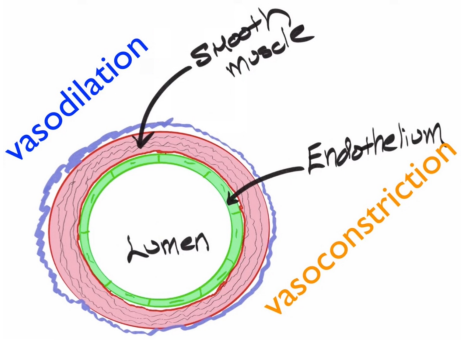
In this video, I want to talk about how tissues and their related blood vessels going specifically to those tissues. Can self regulate blood flow going to them and this is what's known as myogenic autoregulation.
If we take a look at a blood vessel right here. Just the anatomy of it. The innermost lining that we see in green right here is endothelium composed of simple squamous epithelial cells.
The outermost layer that we see in blue right here is connective tissue
between the endothelium and the connective tissue is the bulk of the layer of blood vessels known as the tunica media that's composed of smooth muscle. And the space within the blood vessel that the blood actually flows through is the lumen.
If that lumen gets smaller, it's known as vasoconstriction. If it gets larger, it's known as vasodilation.

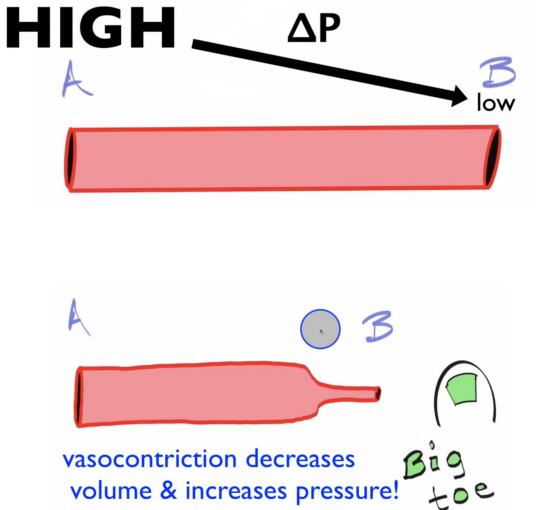
Here we see just the blood vessels. So in black on each end we can see the lumen. That's the space once again that the blood would flow through.
And blood is going to travel from point A to point B, down pressure gradients from an area of high pressure to an area of lower pressure. Now. I'm not showing it here, but the high pressures created by the left ventricle that would be upstream of all of this.

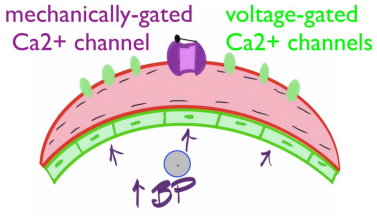
Here we can see elevated blood pressure within the lumen. So this space right here, this is only a partial snapshot of the blood vessel that we just saw in cross-section earlier in green is the endothelium.
This is one smooth muscle cell. Lininh the sarcolemma of this smooth muscle cell is a mechanically gated calcium channel or a stretch sensitive calcium channel, and these in green are voltage sensitive calcium channels.

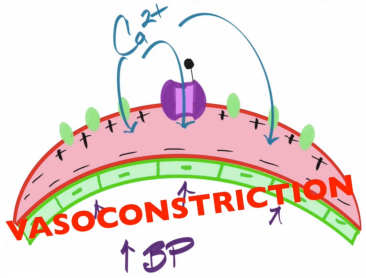
So if there is elevated blood pressure that's going to cause this smooth muscle cell to stretch, activating this mechanically gated calcium channel opens up that channel we get an influx of calcium which is going to depolarize the smooth muscle cell, activate these voltage sensitive calcium channels, and allow even more calcium to come into the smooth muscle cell and cause vasoconstriction. It's going to cause contraction of the smooth muscle cells, which will result in vasoconstriction, decreasing the diameter of the blood vessel lumen.

Right here, we can see that the blood vessel that I'm talking about. And let's just pretend this blood vessel is going to the big toe. I could have any tissue or organ in the body represented over here on the right. But if for whatever reason, this blood vessel is exhibiting elevated blood pressure, it will minimize that blood pressure by myogenic autoregulation, which is just what we describe, that elevated pressure is going to cause this region of the blood vessel to vasoconstrict.
Now, while we may have high blood pressure still at point A. We now have higher blood pressure down in this area (B), and since blood flow does not move from high to higher, this is going to cut off blood flow or if nothing else, minimize blood flow to specific area.
That is how Myogenic autoregulation works. It comes into practice when blood vessels are detecting elevated blood pressure, specifically the arterioles. And it protects those fragile capillaries downstream.









Autoregulation

The effect of arterial pressure on blood flow in many tissues is usually far less than one might expect. This is because an increase in arterial pressure not only increases the force that pushes blood through the vessels, but also initiates compensatory increases in vascular resistance within a few seconds through activation of the local control mechanism.

Conversely, with reductions in arterial pressure, vascular resistance is promptly reduced in most tissues, and blood flow is maintained at a relatively constant rate.

The ability of each tissue to adjust its vascular resistance and to maintain normal blood flow during changes in arterial pressure between approximately 70 and 175 mm Hg is called blood flow autoregulation.

Blood flow changes rarely last for more than a few hours in most tissues, even when increases in arterial pressure or increased levels of vasoconstrictors are sustained.
The reason for the relative constancy of blood flow is that each tissue's local autoregulatory mechanisms eventually override most of the effects of vasoconstrictors to provide a blood flow that is appropriate for the needs of the tissue.

When the arterial pressure becomes too great, the excess flow provides too much oxygen and too many other nutrients to the tissues and washes out the vasodilators released by the tissues.

These nutrients (especially oxygen) and decreased tissue levels of vasodilators then cause the blood vessels to constrict and return flow to nearly normal, despite the increased pressure.

The myogenic theory, however, suggests that another mechanism not related to tissue metabolism explains the phenomenon of autoregulation.
This theory is based on the observation that a sudden stretch of small blood vessels causes the smooth muscle of the vessel wall to contract.

Therefore, it has been proposed that when high arterial pressure stretches the vessel, reactive vascular constriction results, which reduces blood flow nearly back to normal.
Conversely, at low pressures, the degree of stretch of the vessel is less, so the smooth muscle relaxes, reducing vascular resistance and helping to return flow toward normal.

The myogenic response is inherent to vascular smooth muscle and can occur in the absence of neural or hormonal influences. It is most pronounced in arterioles but can also be observed in arteries, venules, veins, and even lymphatic vessels.

Myogenic contraction is initiated by stretch-induced vascular depolarization, which then rapidly increases calcium ion entry from the extracellular fluid into the cells, causing them to contract.
Changes in vascular pressure may also open or close other ion channels that influence vascular contraction.
The myogenic mechanism appears to be important in preventing excessive stretching of blood vessels when blood pressure is increased.

Norepinephrine & Epinephrine

Norepinephrine is an especially powerful vasoconstrictor hormone; epinephrine is less powerful as a vasoconstrictor and, in some tissues, even causes mild vasodilation.

When the sympathetic nervous system is stimulated in most parts of the body during stress or exercise, the sympathetic nerve endings in the individual tissues release norepinephrine, which excites the heart and constricts the veins and arterioles.

In addition, the sympathetic nerves to the adrenal medullae cause these glands to secrete norepinephrine and epinephrine into the blood.

Angiotensin II

The effect of angiotensin II is to constrict the small arterioles powerfully.

The real importance of angiotensin II is that it normally acts on many arterioles of the body at the same time to increase the total peripheral resistance and decrease sodium and water excretion by the kidneys, thereby increasing the arterial pressure.

Thus, this hormone plays an integral role in the regulation of arterial pressure,

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Vasopressin

Vasopressin, also called antidiuretic hormone, is even more powerful than angiotensin II as a vasoconstrictor, thus making it one of the body's most potent vascular constrictor substances.

It is formed in nerve cells in the hypothalamus of the brain but is then transported downward by nerve axons to the posterior pituitary gland, where it is finally secreted into the blood.

It is clear that vasopressin could have enormous effects on circulatory function. Yet, because only minute amounts of vasopressin are secreted in most physiological conditions, most physiologists have thought that vasopressin plays little role in vascular control.
However, experiments have shown that the concentration of circulating blood vasopressin after severe hemorrhage can increase enough to attenuate reductions in arterial pressure markedly. In some cases, this action can, by itself, bring the arterial pressure almost back up to normal.

Vasopressin has the major function of greatly increasing water reabsorption from the renal tubules back into the blood and therefore helps control body fluid volume.

Ca++

An increase in intracellular calcium ion concentration causes vasoconstriction because of the general effect of calcium to stimulate smooth muscle contraction.

H+

An increase in hydrogen ion concentration (decrease in pH) causes dilation of the arterioles.
Conversely, a slight decrease in hydrogen ion concentration causes arteriolar constriction.

Bradykinin

Several substances called kinins cause powerful vasodilation when formed in the blood and tissue fluids of some organs.

Bradykinin causes both powerful arteriolar dilation and increased capillary permeability.

Kinins appear to play special roles in regulating blood flow and capillary leakage of fluids in inflamed tissues. It is also believed that bradykinin plays a normal role to help regulate blood flow in the skin, as well as in the salivary and gastrointestinal glands.

Histamin

Histamine is released in almost every tissue of the body if the tissue becomes damaged or inflamed or is the subject of an allergic reaction.

Most of the histamine is derived from mast cells in the damaged tissues and from basophils in the blood. Histamine has a powerful vasodilator effect on the arterioles and, like bradykinin, has the ability to increase capillary porosity greatly, allowing leakage of fluid and plasma protein into the tissues.

In many pathological conditions, the intense arteriolar dilation and increased capillary porosity produced by histamine cause large quantities of fluid to leak out of the circulation into the tissues, inducing edema.

K+

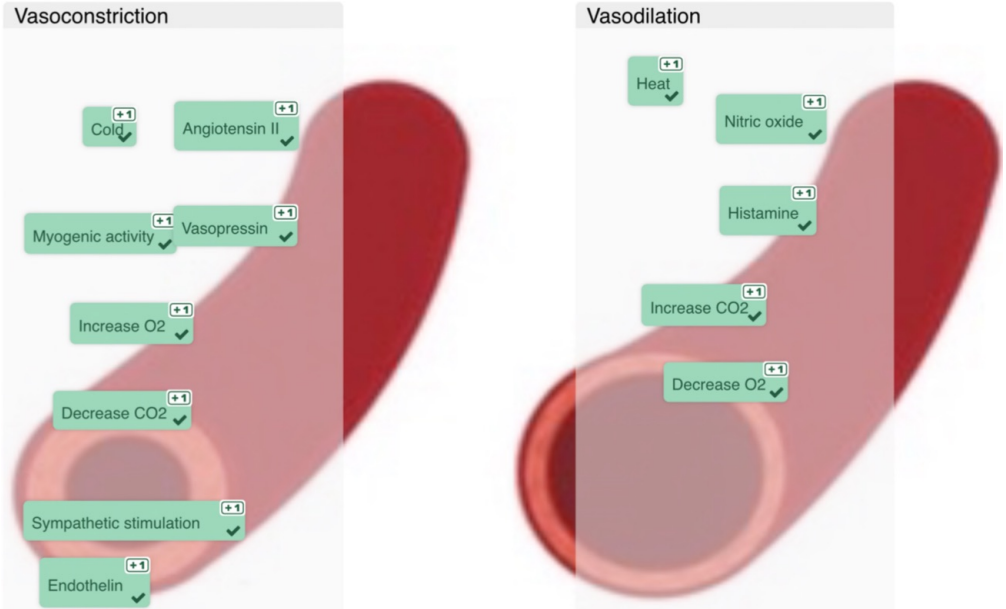
An increase in potassium ion concentration, within the physiological range, causes vasodilation. This effect results from the ability of potassium ions to inhibit smooth muscle contraction.

Mg++

An increase in magnesium ion concentration causes powerful vasodilation because magnesium ions inhibit smooth muscle contraction.

CO2

An increase in carbon dioxide concentration causes moderate vasodilation in most tissues but marked vasodilation in the brain.
Also, carbon dioxide in the blood, acting on the brain vasomotor center, has an extremely powerful indirect effect, transmitted through the sympathetic nervous vasoconstrictor system, that causes widespread vasoconstriction throughout the body.



Long-term control of blood flow

Long-term regulation of blood flow is especially important when the metabolic demands of a tissue change. Thus, if a tissue becomes chronically overactive and requires increased quantities of oxygen and other nutrients, the arterioles and capillary vessels usually increase both in number and size within a few weeks to match the needs of the tissue, unless the circulatory system has become pathological or too old to respond.

A key mechanism for long-term local blood flow regulation is to change the amount of vascularity of the tissues. For example, if the metabolism in a tissue is increased for a prolonged period, vascularity increases, a process generally called angiogenesis; if the metabolism is decreased, vascularity decreases.
Thus, actual physical reconstruction of the tissue vasculature occurs to meet the needs of the tissues. This reconstruction occurs rapidly in young subjects. It also occurs rapidly in new growth tissue, such as in cancerous tissue, but occurs much more slowly in old, well-established tissues.

Therefore, the time required for long-term regulation to take place may be only a few days in the neonate or as long as months in older adults. Furthermore, the final degree of response is much better in younger than in older tissues; thus, in the neonate, the vascularity will adjust to match almost exactly the needs of the tissue for blood flow, whereas in older tissues, vascularity frequently lags far behind the needs of the tissues.

Oxygen is important not only for acute control of local blood flow but also for long-term control. Some of the factors involved are Vascular endothelial growth factor (VEGF), fibroblast growth factor, platelet-derived growth factor (PDGF), angiogenin, hypoxia inducible factors (HIFs).

Angiogenesis begins with new vessels sprouting from other small vessels. The first step is dissolution of the basement membrane of the endothelial cells at the point of sprouting. This step is followed by rapid reproduction of new endothelial cells, which stream outward through the vessel wall in extended cords directed toward the source of the angiogenic factor. The cells in each cord continue to divide and rapidly fold over into a tube. Next, the tube connects with another tube budding from another donor vessel (another arteriole or venule) and forms a capillary loop through which blood begins to flow.

If the flow is great enough, smooth muscle cells eventually invade the wall, so some of the new vessels eventually grow to be new arterioles or venules or perhaps even larger vessels. Thus, angiogenesis explains how metabolic factors in local tissues can cause growth of new vessels. Certain other substances, such as some steroid hormones, have the opposite effect on small blood vessels, occasionally even causing dissolution of vascular cells and disappearance of vessels. Therefore, blood vessels can also be made to disappear when they are not needed. Peptides produced in the tissues can also block the growth of new blood vessels. Such as angiostatin and Endostatin.

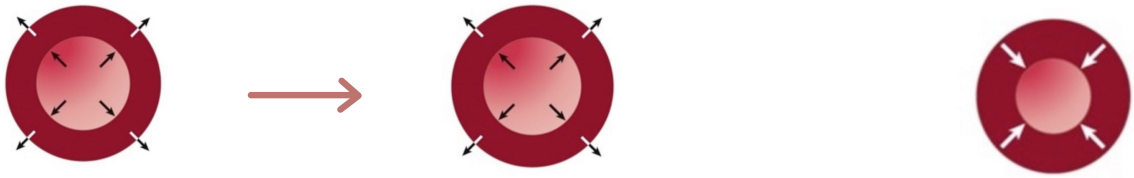
An especially valuable characteristic of long-term vascular control is that vascularity is determined mainly by the maximum level of blood flow required by the tissue rather than by average need. However, after extra vascularity does develop, the extra blood vessels normally remain mainly vasoconstricted, opening to allow extra flow only when appropriate local stimuli such as a lack of oxygen, nerve vasodilatory stimuli, or other stimuli call forth the required extra flow.

Collateral Circulation

In most tissues of the body, when an artery or a vein is blocked, a new vascular channel usually develops around the blockage and allows at least partial resupply of blood to the affected tissue. The first stage in this process is dilation of small vascular loops that already connect the vessel above the blockage to the vessel below. This dilation occurs within the first minute or two, indicating that the dilation is likely mediated by metabolic factors.

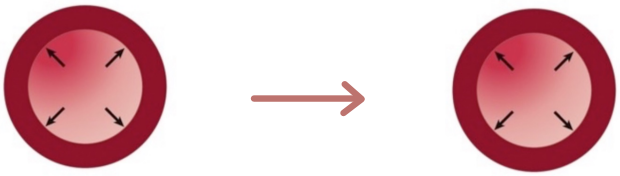
After this initial opening of collateral vessels, the blood flow often is still less than 25% of that required to supply all the tissue needs. However, further opening occurs within the ensuing hours, so that within 1 day as much as half the tissue needs may be met and, within a few days, the blood flow is usually sufficient to meet the tissue needs.
The collateral vessels continue to grow for many months thereafter, usually forming multiple small collateral channels rather than one single large vessel.

Under resting conditions, the blood flow may return to nearly normal, but the new channels seldom become large enough to supply the blood flow needed during strenuous tissue activity.
Thus, development of collateral vessels follows the usual principles of acute and long-term local blood flow control; the acute control is rapid metabolic dilation, followed chronically by growth and enlargement of new vessels over a period of weeks and months.



Vascular remodeling in the venous side of arteriovenous (A-V) fistula in patients on renal dialysis.

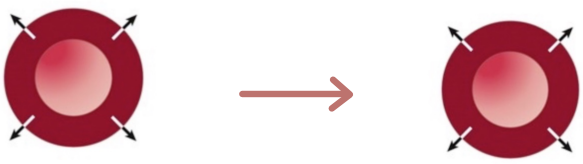
Outward hypertrophic remodeling



Vascular remodeling in the arterial side of arteriovenous (A-V) fistula in patients on renal dialysis.

Outward remodeling

Vascular remodeling in the arterioles in patient with chronic hypertension.



Vascular remodeling in the Saphenous vein in patient for coronary artery bypass graft procedure.

Hypertrophic remodeling

Inward eutrophic remodeling

Remodeling in Hypertension

In Hypertension:

in small blood vessels that constrict in response to increased blood pressure, the vascular smooth muscle cells and endothelial cells gradually rearrange themselves around the smaller lumen diameter, a process called inward eutrophic remodeling, with no change in the total cross-sectional area of the vascular wall.

In larger arteries that do not constrict in response to the increased pressure, the vessel wall is exposed to increased wall tension that stimulates a hypertrophic remodeling response and an increase in the cross-sectional area of the vascular wall.

The hypertrophic response increases the size of vascular smooth muscle cells and stimulates formation of additional extracellular matrix proteins, such as collagen and fibronectin, that reinforce the strength of the vascular wall to withstand the higher blood pressures. However, this hypertrophic response also makes the large blood vessels stiffer, which is a hallmark of chronic hypertension.

Remodeling in CABG

CABG procedure:

When a large vein (often the saphenous vein) is implanted in a patient for a coronary artery bypass graft procedure. Veins are normally exposed to much lower pressures than arteries and have much thinner walls, but when a vein is sewn onto the aorta and connected to a coronary artery, it is exposed to increases in intraluminal pressure and wall tension. The increased wall tension initiates hypertrophy of vascular smooth muscle cells and increased extracellular matrix formation, which thicken and strengthen the wall of the vein; as a result, several months after implantation into the arterial system, the vein will typically have a wall thickness similar to that of an artery.

Remodeling in A-V fistula

A-V fistula in Renal failure patients

The creation of a fistula connecting a large artery and large vein, thereby completely bypassing high-resistance small vessels and capillaries, provides an especially interesting example of remodeling in the affected artery and vein. In patients with renal failure who undergo dialysis, anarteriovenous (A-V) fistula directly from the radial artery to the antecubital vein of the forearm is created to permit vascular access for dialysis. The blood flow rate in the radial artery increases. As a result of the high flow rate and high shear stress on the vessel wall, the luminal diameter of the radial artery increases progressively (outward remodeling), whereas the thickness of the vessel wall may remain unchanged, resulting in an increase in cross-sectional area of the vascular wall. In contrast, wall thickness, lumen diameter, and cross-sectional area of the vascular wall on the venous side of the fistula increase in response to increases in pressure and blood flow (outward hypertrophic remodeling).

SUMMARY

This pattern of remodeling is consistent with the idea that long-term increases in vascular wall tension cause hypertrophy and increased wall thickness in large blood vessels, whereas increased blood flow rate and shear stress cause outward remodeling and increased luminal diameter to accommodate the increased blood flow.

Chronic reductions in blood pressure and blood flow have effects opposite to those previously described. When blood flow is greatly reduced, the diameter of the vascular lumen is also reduced and, when blood pressure is reduced, the thickness of the vascular wall usually decreases.

Thus, vascular remodeling is an important adaptive response of the blood vessels to tissue growth and development, as well as to physiological and pathological changes in blood pressure and blood flow to the tissues.

VASCULAR PHYSIOLOGY 3

Extrinsic control of arteriolar radius includes both neural and hormonal influences, the effects of the sympathetic nervous system being the most important.

Increased sympathetic activity produces generalized arteriolar vaso*constriction*, whereas decreased sympathetic activity leads to generalized arteriolar vasodilation.

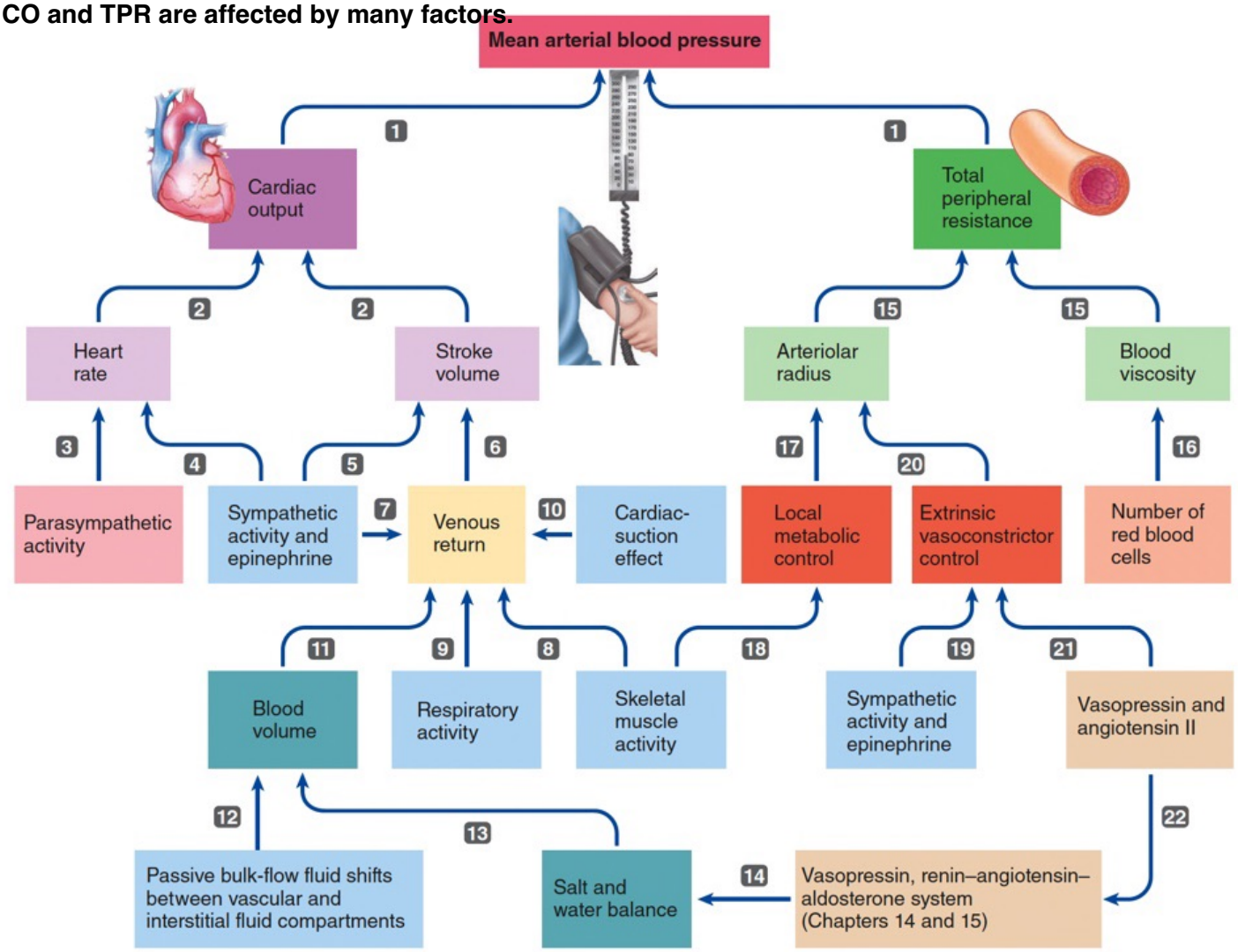
These widespread changes in arteriolar resistance bring about changes in mean arterial pressure because of their influence on total peripheral resistance.

Mean arterial pressure MAP is the main driving force for propelling blood to the tissues.

This pressure must be closely regulated for two reasons.
1. it must be high enough to ensure sufficient driving pressure; without this pressure, the brain and other organs do not receive adequate flow, no matter what local adjustments are made in the resistance of the arterioles supplying them.

the pressure must not be so high that it creates extra work for the heart and increases the risk of vascular damage and possible rupture of small blood vessels.

The two determinants of MAP are CO and TPR.
CO and TPR are not independent variables. Changes in TPR can alter CO and changes in CO can indirectly alter TPR. Therefore it cannot be stated that if TPR doubles, MAP also doubles.
CO and TPR are affected by many factors.



AUTONOMIC NERVOUS SYSTEM

The nervous system controls the circulation almost entirely through the autonomic nervous system.

Sympathetic innervation:
In most tissues, all the vessels except the capillaries are innervated by sympathetic neurons.
The sympathetic nerves carry large numbers of vasoconstrictor nerve fibers and only a few vasodilator fibers.
The vasoconstrictor fibers are distributed to essentially all segments of the circulation, but more to some tissues than to others.
This sympathetic vasoconstrictor effect is especially powerful in the kidneys, intestines, spleen, and skin but is much less potent in skeletal muscle, heart.

Parasympathetic innervation:
Arterioles have no significant parasympathetic innervation, with the exception of the abundant parasympathetic vasodilator supply to the arterioles of the penis and clitoris.
The rapid, profuse vasodilation induced by parasympathetic stimulation in these organs (by means of promoting release of NO) is largely responsible for accomplishing erection.
Vasodilation elsewhere is produced primarily by decreasing sympathetic vasoconstrictor activity below its normal tone level.
When MAP rises above normal, reflex reduction in sympathetic vasoconstrictor activity accomplishes generalized arteriolar vasodilation to help bring the driving pressure down toward normal.
Also, the hormone epinephrine causes vasodilation in arteriolar smooth muscle specifically in the skeletal muscles and heart.

CARDIOVASCULAR CONTROL CENTER IN THE BRAIN

The main region of the brain that adjusts sympathetic output to the arterioles is the cardiovascular control center in the medulla of the brain stem.
This is the integrating center for blood pressure regulation.

Several other brain regions also influence blood distribution, the most notable being the hypothalamus, which, as part of its temperature-regulating function, controls blood flow to the skin to adjust heat loss to the environment.

BARORECETOR REFLEX

Any change in MAP triggers an autonomically mediated baroreceptor reflex that influences the heart and blood vessels to adjust CO and TPR in an attempt to restore blood pressure toward normal.

Although the baroreceptors are sensitive to the absolute level of pressure, they are even more sensitive to changes in pressure and the rate of change of pressure. The strongest stimulus for the baroreceptors is a rapid change in arterial pressure.

Because the baroreceptor system opposes increases or decreases in arterial pressure, it is called a pressure buffer system, and the nerves from the baroreceptors are called buffer nerves.
A primary purpose of the arterial baroreceptor system is therefore to reduce the minute by minute variation in arterial pressure to about one-third that which would occur if the baroreceptor system were not present.

CHEMORECEPTOR REFLEX

Peripheral chemoreceptors for O2 are located in the carotid bodies near the bifurcation of the common carotid arteries and in the aortic bodies along the aortic arch.

Their chemoreceptors are primarily sensitive to decreases in (PO2). The chemoreceptors also are sensitive to increases in (PCO2) and decreases in pH, particularly when PO2 is simultaneously decreased.
The response of the peripheral chemoreceptors to decreased arterial PO2 is greater when the PCO2 is increased or the pH is decreased.

When arterial PO2 decreases, there is an increased firing rate of afferent nerves from the carotid and aortic bodies that activates sympathetic vasoconstrictor centers. As a result, there is arteriolar vasoconstriction in skeletal muscle, renal, and splanchnic vascular beds.
The chemoreceptors excite nerve fibers that along with the baroreceptor fibers, pass through Hering's nerves and the vagus nerves into the vasomotor center of the brain stem.

It is at the lower pressures that this reflex becomes important to help prevent further decreases in arterial pressure.
It is related to respiratory control.

CENTRAL CHEMORECPTORS

The brain is intolerant of decreases in blood flow, and therefore it is not surprising that chemoreceptors are located in the medulla itself.

These chemoreceptors are most sensitive to CO2 and pH and less sensitive to O2.
Changes in PCO2 or pH stimulate the medullary chemoreceptors, which then direct changes in outflow of the medullary cardiovascular centers.

If the brain becomes ischemic (i.e., there is decreased cerebral blood flow), cerebral PCO2 immediately increases and pH decreases.

The medullary chemoreceptors detect these changes and direct an increase in sympathetic outflow that causes intense arteriolar vasoconstriction in many vascular beds and an increase in TPR.
Blood flow is thereby redirected to the brain to maintain its perfusion. As a result of this vasoconstriction, BP increases dramatically, even to life-threatening levels.

The Cushing reaction:
When intracranial pressure increases (e.g., tumors, head injury), there is compression of cerebral arteries, which results in decreased perfusion of the brain.
There is an immediate increase in PCO2 and a decrease in PH.
The medullary chemoreceptors respond to these changes in PCO2 and pH by directing an increase in sympathetic outflow to the blood vessels to increase TPR and dramatically increase BP.

ATRIAL AND PULMONARY ARTREY REFLEX

The atria and pulmonary arteries have stretch receptors in their walls called low-pressure receptors.

Low-pressure receptors are similar to the baroreceptor stretch receptors of the large systemic arteries.

These low-pressure receptors play an important role, especially in minimizing arterial pressure changes in response to changes in blood volume.

Even though the low-pressure receptors in the pulmonary artery and in the atria cannot detect the systemic arterial pressure, they do detect simultaneous increases in pressure in the low-pressure areas of the circulation caused by increase in volume.

Stretch of the atria and activation of low-pressure atrial receptors also causes reflex reductions in renal sympathetic nerve activity, decreased tubular reabsorption, and dilation of afferent arterioles in the kidneys. Signals are also transmitted simultaneously from the atria to the hypothalamus to decrease secretion of antidiuretic hormone (ADH).

All these mechanisms that tend to return blood volume back toward normal after a volume overload act indirectly as pressure controllers, as well as blood volume controllers, because excess volume drives the heart to greater cardiac output and higher arterial pressure.

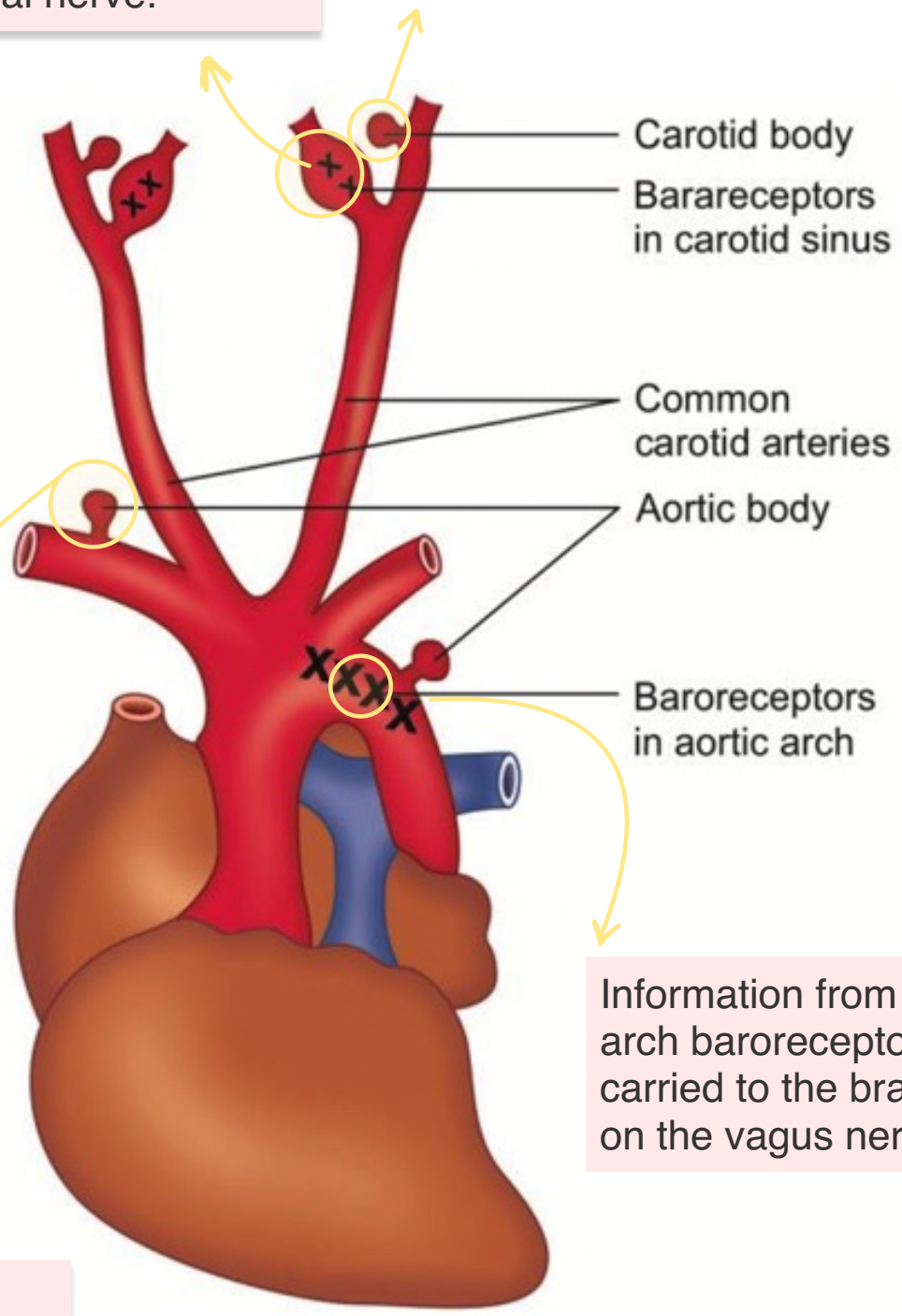
Information from the low pressure atrial receptors travels in the vagus nerve to the nucleus tractus solitarius (as does information from the high-pressure arterial receptors involved in the baroreceptor reflex).

The difference lies in the response of the medullary cardiovascular centers to the low- and high-pressure receptors. Whereas an increase in pressure at the arterial high-pressure receptors produces a decrease in heart rate (trying to lower arterial pressure back to normal), an increase in pressure at the venous low-pressure receptors produces an increase in heart rate (Bainbridge reflex).

The low-pressure atrial receptors, sensing that blood volume is too high, direct an increase in heart rate and thus an increase in cardiac output; the increase in cardiac output leads to increased renal perfusion and increased Na+ and water excretion.

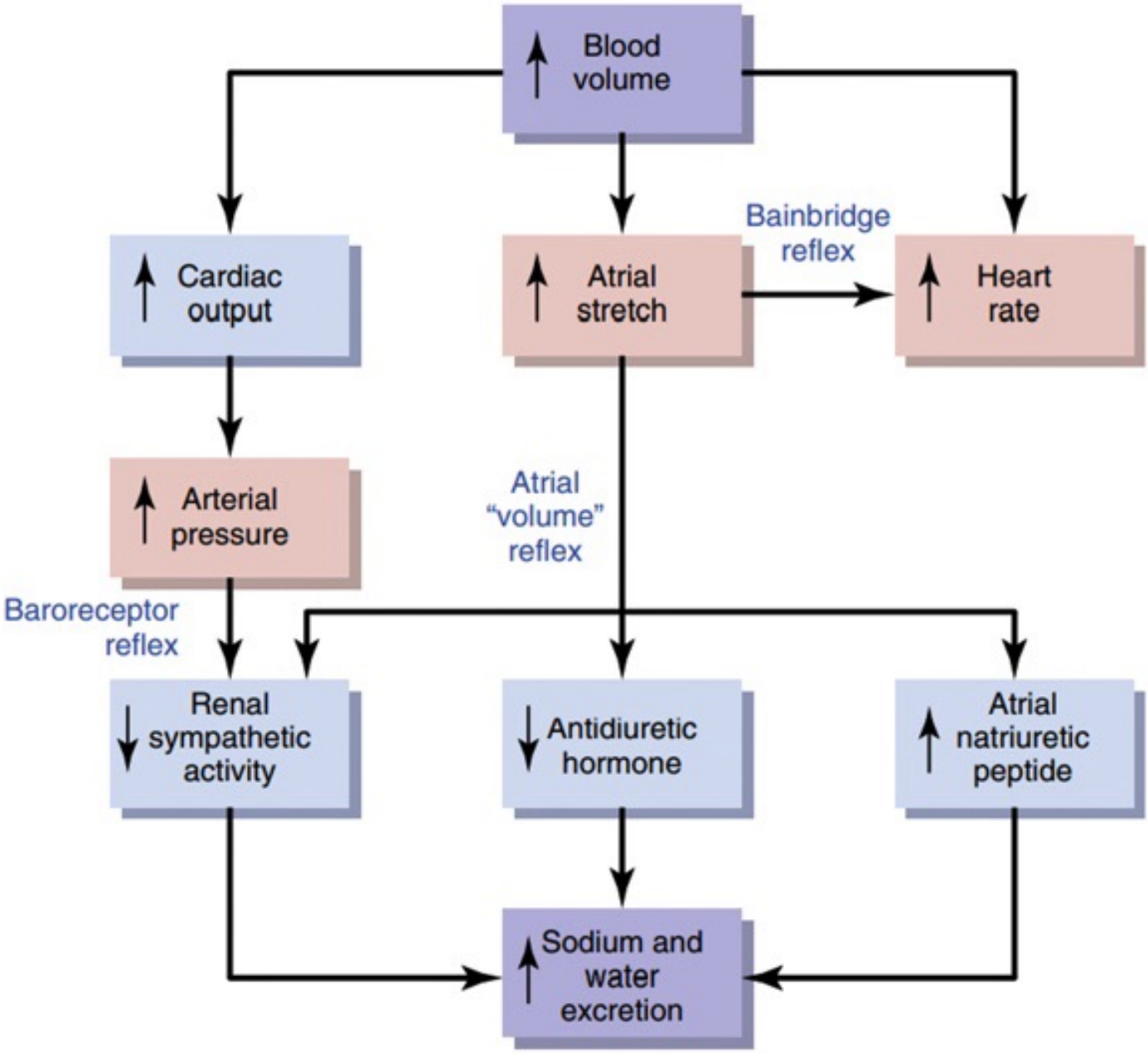
Information from the carotid sinus baroreceptors is carried to the brain stem on the carotid sinus nerve, which joins the glossopharyngeal nerve.

Peripheral chemoreceptors for O2 are located in the carotid bodies near the bifurcation of the common carotid arteries.



Information from the aortic arch baroreceptors is carried to the brain stem on the vagus nerve.

Peripheral chemoreceptors for O2 are located in the aortic bodies along the aortic arch.



Baroreceptor reflex does NOT work at all in patients with hypertension.

○ True ⊙ False ✔

correct!

1/1

The baroreceptors do not respond to bring blood pressure back to normal during hypertension because they adapt, or are "reset," to operate at a higher level. In the presence of chronically elevated blood pressure, the baroreceptors still function to regulate blood pressure, but they maintain it at a higher mean pressure.

Peripheral and central chemoreceptors are most sensitive to O2.

○ True ⊙ False ✔

You got 1 of 1 points

1/1

central chemoreceptors are most sensitive to CO2 and pH and less sensitive to O2.

ADRENAL EPINEPHRIN AND NOREEPINEPHRIN

Sympathetic stimulation of the adrenal medulla causes this endocrine gland to release epinephrine and norepinephrine.
Adrenal medullary norepinephrine combines with the same a1 receptors as sympathetically released norepinephrine to produce generalized vasoconstriction.

However, epinephrine, the more abundant of the adrenal medullary hormones, combines with both b2 and a1 receptors but has a much greater affinity for the b2 receptors. Activation of b2 receptors produces vasodilation, but not all tissues have b2 receptors; they are most abundant in the arterioles of the skeletal muscles and heart.

During sympathetic discharge, the released epinephrine combines with the b2 receptors in the skeletal muscles and heart to reinforce local vasodilatory mechanisms in these tissues.

Arterioles in digestive organs and kidneys, in contrast, are equipped only with a1 receptors. Therefore, the arterioles of these organs undergo more profound vasoconstriction during generalized sympathetic discharge than those in the skeletal muscles and heart do.

VASOPRESSIN

Vasopressin (antidiuretic hormone ADH) is primarily involved in maintaining water balance by regulating the amount of water the kidneys retain for the body during urine formation.

RENIN-ANGIOTENSIN-ALDESTERONE SYSTEM (RAAS)

The renin–angiotensin II–aldosterone system (RAAS) regulates P primarily by regulating blood volume.

This system is much slower than the baroreceptor reflex because it is hormonally mediated.

The renin–angiotensin II–aldosterone system is activated in response to a decrease in the P.

Activation of this system, in turn, produces a series of responses that attempt to restore arterial pressure to normal.

Required self reading:
https://www.ncbi.nlm.nih.gov/books/NBK470410/

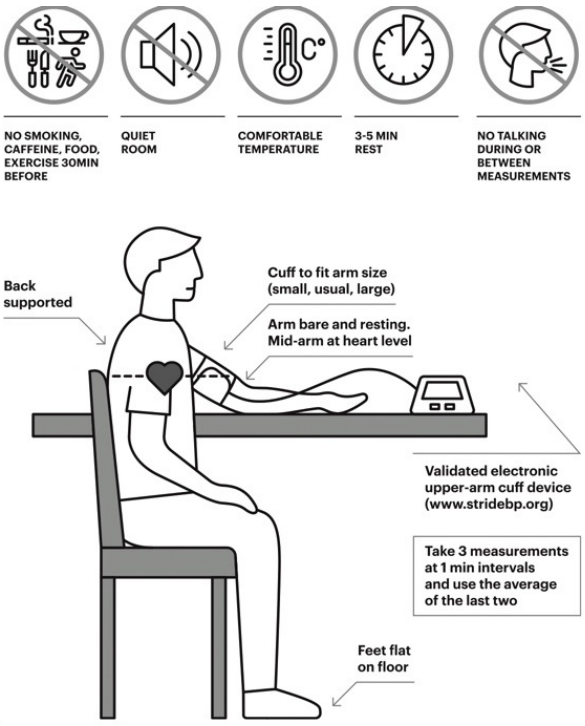


FIGURE 2 Poster of OBP measurement methodology.

Learn what is considered normal, as recommended by the American Heart Association.

BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)	and/or	DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

Whatever the underlying defect, once initiated, hypertension appears to be self-perpetuating.

Constant exposure to elevated blood pressure damages vessel walls and predisposes them to development of atherosclerosis.

The resultant narrowing of vessel lumens by atherosclerotic plaques increases TPR, which further elevates blood pressure.

Thus a detrimental positive-feedback cycle ensues where hypertension and atherosclerosis each promote development of the other.

Hypertension imposes stresses on both the heart and the blood vessels.

The heart has an increased workload because it is pumping blood out against an increased TPR, and the high internal pressure may damage blood vessels, particularly when the vessel wall is weakened by the degenerative process of atherosclerosis.

Complications of Hypertension:

(1) left ventricular hypertrophy maybe followed by systolic heart failure.

(2) stroke.

(3) heart attack.

(4) renal failure.

(5) retinal damage.

#4

Capllaries

Exchange of substances across the capillary wall

Not all capillaries are perfused with blood at all times. Rather, there is selective perfusion of capillary beds, depending on the metabolic needs of the tissues.

This selective perfusion is determined by the degree of dilation or constriction of the arterioles and precapillary sphincters (smooth muscle bands before the capillaries).

The exchange of solutes and gases across the capillary wall occurs by simple diffusion.

Gases such as O2 and CO2 are highly lipid soluble.

These gases readily cross the capillary wall by diffusing through the endothelial cells; diffusion is driven by the partial pressure gradient for the individual gas.

the rate of diffusion depends on the driving force (the partial pressure difference for the gas) and the surface area available for diffusion. Thus, the greater the number of open capillaries, the greater the surface area for diffusion.

Water-soluble substances such as water itself, ions, glucose, and amino acids are not lipid soluble; thus they cannot cross the endothelial cell membranes.

The diffusion of water-soluble substances is limited to the aqueous clefts between endothelial cells; hence, the surface area for their diffusion is much less than that for the lipid-soluble gases.

Factors enhancing diffusion across capillaries

Diffusion across the capillaries is fast due to the short distance of travel between blood and cells.

That's because of the thin capillary wall and small capillary diameter, coupled with the proximity of every cell to a capillary.
Exchange across capillaries
Vesicular transport also plays a limited role in passage of materials across the capillary wall.

Large molecules that are not lipid-soluble, such as protein hormones that must be exchanged between blood and surrounding tissues, in a process called transcytosis.

Velocity of blood flow

The velocity of blood flow is the rate of displacement of blood per unit time.
The velocity with which blood flows through the different segments of the vascular tree varies because velocity of flow is inversely proportional to the total cross-sectional area of all vessels at any given level.

V=Q/A

V= velocity of blood flow (cm/s)

A= cross-sectional area

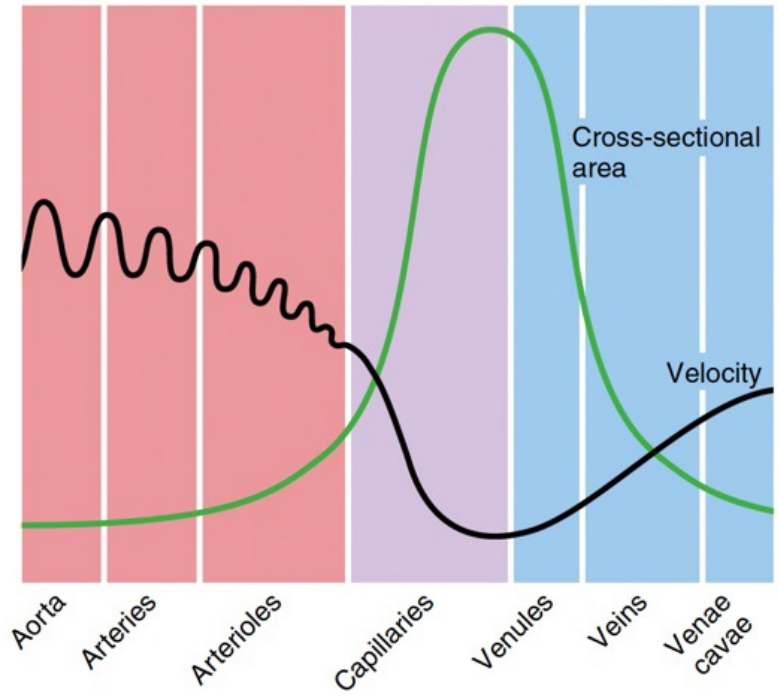
Velocity of blood flow through capillaries

Even though the cross-sectional area of each capillary is extremely small compared to that of the large aorta, the total cross-sectional area of all capillaries added together is about 750 times greater than the cross-sectional area of the aorta because there are so many capillaries.
Accordingly, blood slows considerably as it passes through the capillaries.

This slow velocity allows adequate time for exchange of nutrients and metabolic end products between blood and tissue cells.

As capillaries rejoin to form veins, the total cross-sectional area is again reduced, and the velocity of blood flow

Velocity of blood flow is slowest in the capillaries because they have the largest total cross-sectional area.



Capillaries role in resistance

Also, because of the capillaries' tremendous total cross-sectional area, the resistance offered by all capillaries is lower than that offered by all arterioles,
even though each capillary has a smaller radius than each arteriole.
Furthermore, capillary diameter can not be adjusted like in the arterioles.

Pressure in capillaries

In the capillaries, pressure decreases further for two reasons:
1. frictional resistance to flow.
2. filtration of fluid out of the capillaries.

When blood reaches the venules and veins, pressure has decreased even further, because capacitance of the veins is high, the veins can hold large volumes of blood at low pressure.

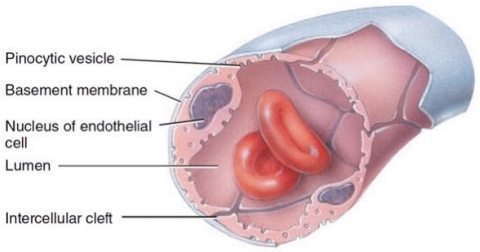
Capillary wall permeability

Diffusion across capillary walls depends on the walls' permeability to the materials being exchanged.

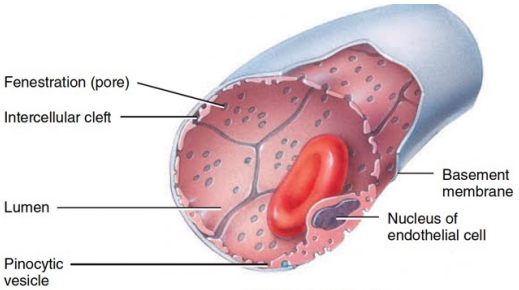
Most capillaries, endothelial cells are continuous, with only narrow clefts, or pores.

The size of capillary pores varies from organ to organ depending on the organ needs.

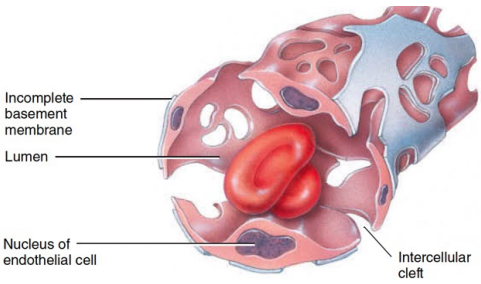
Endothelial cells can actively change to regulate capillary permeability in response to appropriate signals, Thus, the degree of leakiness does not necessarily remain constant for a given capillary bed.



(a) Continuous capillary formed by endothelial cells



(b) Fenestrated capillary



(c) Sinusoid

Exchange across the capillaries

Exchanges between blood and surrounding tissues across capillary walls are accomplished in two ways:
(1) passive diffusion down concentration gradients, the primary mechanism for exchanging individual solutes.
(2) bulk flow, a process that determines the distribution of the ECF volume between the vascular and the interstitial fluid compartments.

Exchanges between blood and tissue cells are not made directly.
Interstitial fluid is the true internal environment in immediate contact with the cells.
Cells exchange materials directly with interstitial fluid, with the type and extent of exchange being governed by the properties of cellular plasma membranes.

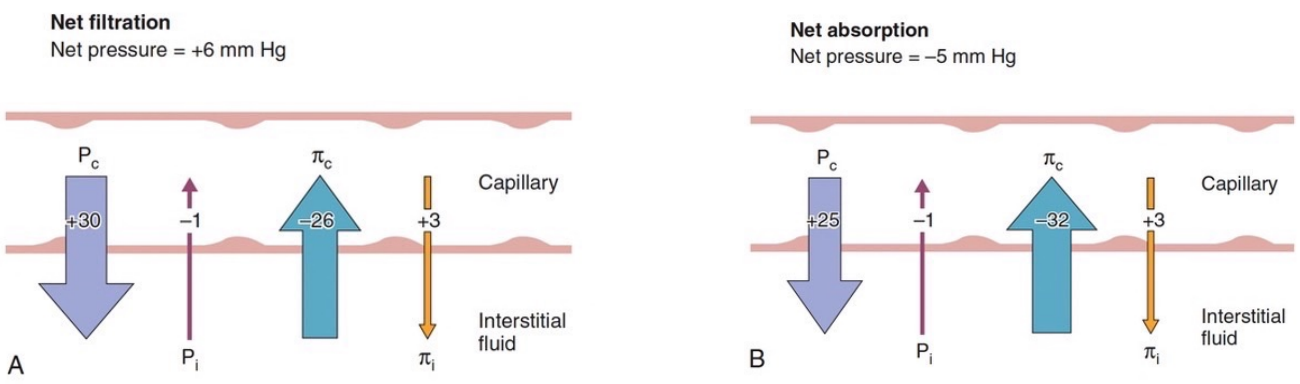
Bulk flow across capillaries

Bulk flow occurs because of differences in hydrostatic and colloid osmotic pressures between plasma and interstitial fluid.
Four forces influence fluid movement across the capillary wall

$$J_v = K_f[(P_c - P_i) - (\pi_c - \pi_i)]$$

J_v = Fluid movement (mL/min)
K_f = Hydraulic conductance (mL/min per mm Hg)
P_c = Capillary hydrostatic pressure (mm Hg)
P_i = Interstitial hydrostatic pressure (mm Hg)
π_c = Capillary oncotic pressure (mm Hg)
π_i = Interstitial oncotic pressure (mm Hg)

Starling equation



Bulk flow

Ultrafiltration and reabsorption, collectively known as bulk flow, are thus the result of a shift in the balance between the passive physical forces acting across the capillary wall.

No active forces or local energy expenditures are involved in bulk exchange of fluid between plasma and surrounding interstitial fluid.

Ultrafiltration occurs at the beginning of the capillary because capillary blood pressure exceeds plasma-colloid osmotic pressure, whereas by the end of the capillary, reabsorption (the slides are cutoff so idk the rest)

Significance of bulk flow

The composition of the fluid filtered out of the capillary is essentially the same as the composition of the fluid that is reabsorbed. Thus, ultrafiltration and reabsorption are not important in exchange of nutrients and wastes.

Bulk flow is extremely important in regulating the distribution of ECF between plasma and interstitial fluid.

Maintenance of proper arterial blood pressure depends in part on an appropriate volume of circulating blood.

Lymphatic system

Even under normal circumstances, slightly more fluid is filtered out of the capillaries into the interstitial fluid than is reabsorbed from the interstitial fluid back into the plasma.

Because of this pressure differential, on average more fluid is filtered out of the first half of the capillary than is reabsorbed in its last half.

The extra fluid filtered out as a result of this filtration– reabsorption imbalance is picked up by the lymphatic system.

This extensive network of one-way vessels provides an accessory route by which fluid can be returned from the interstitial fluid to the blood.

Functions of the lymphatics

1. Return of excess filtered fluid.
2. Defense against disease.
3. Transport of absorbed fat.
4. Return of filtered protein.

Edema

Excessive interstitial fluid does accumulate when one of the physical forces acting across the capillary walls becomes abnormal for some reason.
Whatever the cause of edema, an important consequence is reduced exchange of materials between blood and cells.

TABLE 4.6 Causes and Examples of Edema Formation

Cause	Examples
↑ P_c (capillary hydrostatic pressure)	Arteriolar dilation Venous constriction Increased venous pressure Heart failure Extracellular fluid volume expansion
↓ π_c (capillary oncotic pressure)	Decreased plasma protein concentration Severe liver failure (failure to synthesize protein) Protein malnutrition Nephrotic syndrome (loss of protein in urine)
↑ K_f (hydraulic conductance)	Burn Inflammation (release of histamine; cytokines)
Impaired lymphatic drainage	Standing (lack of skeletal muscle compression of lymphatics) Removal or irradiation of lymph nodes Parasitic infection of lymph nodes

Veins

Veins have a large radius, so they offer little resistance to flow.
Furthermore, because the total cross-sectional area of the venous system gradually decreases as smaller veins converge into progressively fewer but larger vessels, blood flow speeds up as blood approaches the heart.
In addition to serving as low-resistance passageways to return blood from the tissues to the heart, systemic veins also serve as a blood reservoir. Because of their storage capacity, veins are often called capacitance vessels.

Compliance in veins vs arteries

Compliance of the veins is high; in other words, the veins hold large volumes of blood at low pressure.

Compliance of the arteries is much lower than that of the veins; the arteries hold much less blood than the veins, and they do so at high pressure.

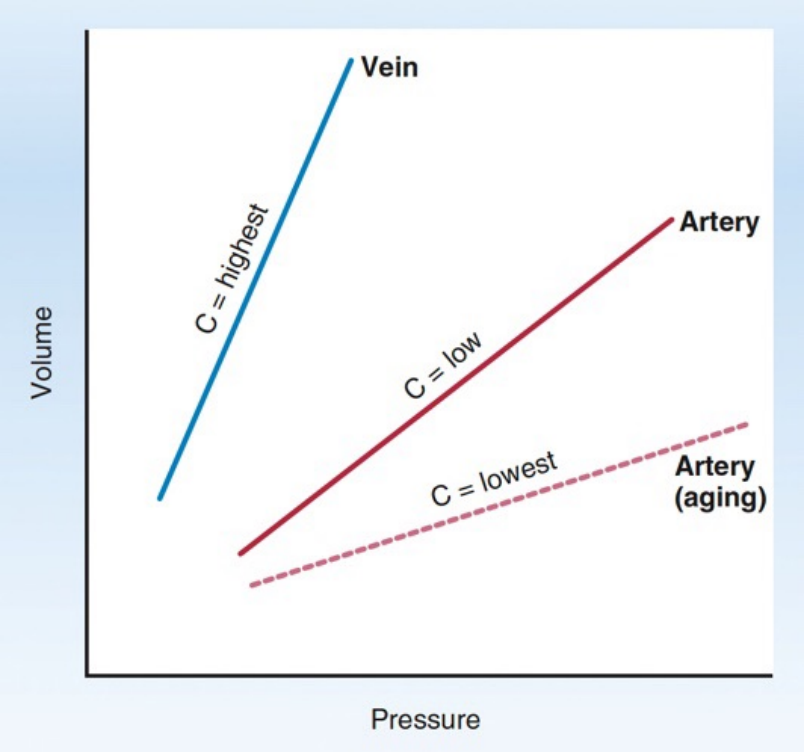
The veins are most compliant and contain the unstressed volume (large volume under low pressure).

Veins : Because of their storage capacity, veins are often called capacitance vessels.

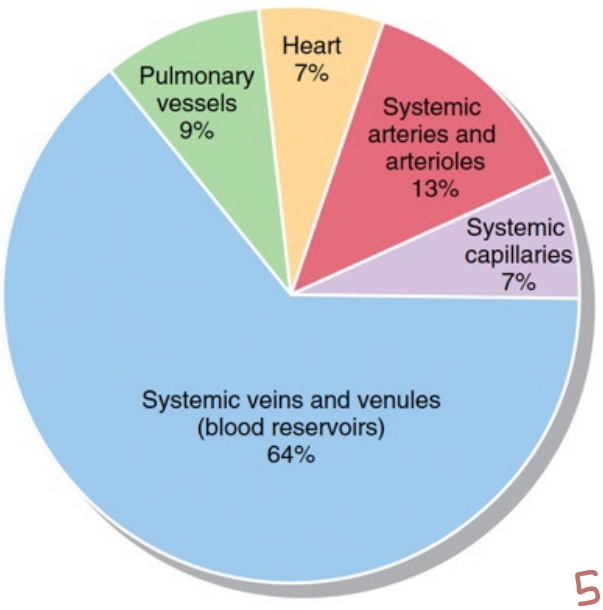
They easily distend to accommodate additional volumes of blood with only a small increase in venous pressure.

veins serve as a blood reservoir— that is, when demands for blood are low, the veins can store extra blood in reserve because of their passive distensibility.

Under resting conditions, the veins contain more than 60% of the total blood volume



Blood volume distribution in the circulation at rest



Venous capacity

Venous capacity (the volume of blood that the veins can accommodate) depends on the distensibility of the vein walls (how much they can stretch to hold blood) and the influence of any externally applied pressure squeezing inwardly on the veins.
At a constant blood volume, as venous capacity increases, more blood remains in the veins instead of being returned to the heart.

Such venous storage decreases the effective circulating blood volume, the volume of blood being returned to and pumped out of the heart.

Changes in venous capacity directly influence the magnitude of venous return, which in turn is one of the important determinants of effective circulating blood volume.

The effective circulating blood volume is also influenced short term by passive shifts in bulk flow between plasma and interstitial fluid and long term by factors that control total ECF volume, such as salt and water balance.

Venous return

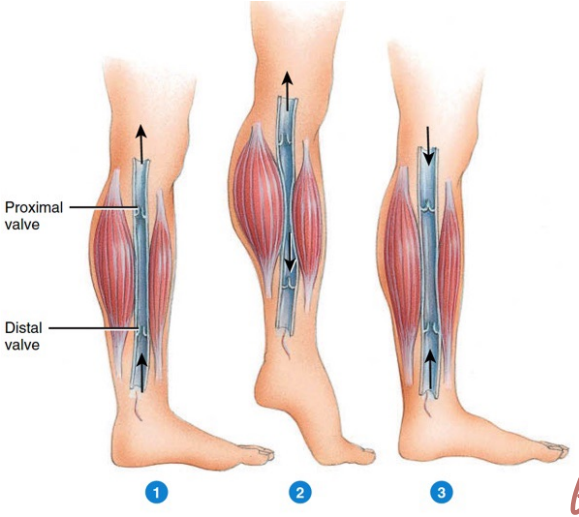
venous return refers to the volume of blood per minute entering each atrium from the veins.
In addition to the driving pressure imparted by cardiac contraction, five other factors enhance venous return: sympathetically induced venous vasoconstriction, skeletal muscle pump, venous valves, respiratory pump, and cardiac suction.
Most of these secondary factors affect venous return by increasing the pressure gradient between the veins and the heart.

Sympathetic stimulation

Sympathetic stimulation produces venous vasoconstriction, which modestly elevates venous pressure; this, in turn, increases the pressure gradient to drive more of the stored blood from the veins into the right atrium, thus enhancing venous return.

Skeletal muscle pump

This external venous compression decreases venous capacity and increases venous pressure, in effect squeezing blood in the veins forward toward the heart
The skeletal muscle pump also counters the effect of gravity on the venous system.



Venous valves

These venous valves also play a role in counteracting the gravitational effects of upright posture by helping minimize the backflow of blood that tends to occur when a person stands up and by temporarily supporting portions of the column of blood when the skeletal muscles are relaxed.

Varicose veins occur when the venous valves become incompetent and can no longer support the column of blood above them.

Respiratory pump

As the venous system returns blood to the heart from the lower regions of the body, it travels through the chest cavity, where it is exposed to this sub-atmospheric pressure.

This pressure difference pushes blood from the lower veins to the chest veins, promoting increased venous return.

Cardiac suction

During ventricular contraction, the AV valves are drawn downward, enlarging the atrial cavities. As a result, atrial pressure transiently drops below 0 mm Hg, thus increasing the vein-to-atria pressure gradient so that venous return is enhanced.

In addition, rapid expansion of the ventricular chambers during ventricular relaxation creates a transient negative pressure in the ventricles so that blood is "sucked in" from the atria and veins—that is, the negative ventricular pressure increases the vein-to-atria-to-ventricle pressure gradient, further enhancing venous return.

Special circulations

Circulation	Local Metabolic Control	Vasoactive Metabolites	Sympathetic Control	Mechanical Effects
Coronary	Most important mechanism	Hypoxia Adenosine	Least important mechanism	Mechanical compression during systole
Cerebral	Most important mechanism	CO_2 H^+	Least important mechanism	Increases in intracranial pressure decrease cerebral blood flow
Skeletal Muscle	Most important mechanism during exercise	Lactate CO_2 K^+ Adenosine	Most important mechanism at rest (α_1 receptors, vasoconstriction; β_2 receptors, vasodilation)	Muscular activity compresses blood vessels
Skin	Least important mechanism	—	Most important mechanism for temperature regulation (α_1 receptors, vasoconstriction)	—
Pulmonary	Most important mechanism	Hypoxia vasoconstricts	Least important mechanism	Lung inflation
Renal	Most important mechanism (myogenic; tubuloglomerular feedback)	—	Least important mechanism	—