

DR Ismail AL karagully [2015]

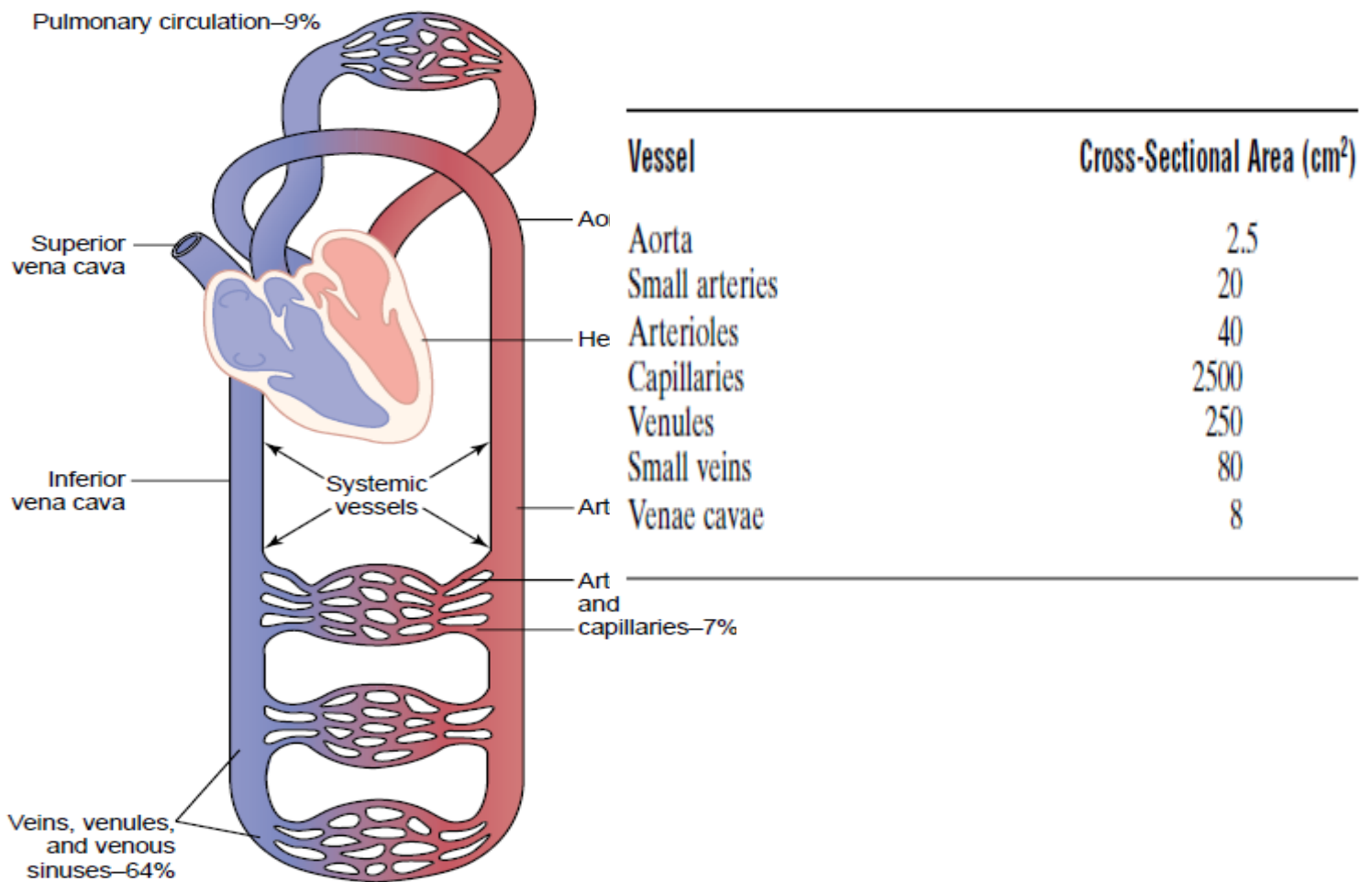
The circulatory system

The function of the circulation is to service the needs of the body tissues- to transport nutrients to the body tissues, to transport waste products away, in general , to maintain an appropriate environment in all the tissue fluids of the body for optimal survival and function of the cells.

The Physical Characteristics of the Circulation

The circulation is divided into the systemic circulation & pulmonary circulation .Because the systemic circulation supplies blood flow to all the tissues of the body except the lungs, it also called the greater or peripheral circulation.

The Functional Parts of the Circulation



[1] The arteries: The walls of the aorta and other arteries of large diameter contain *large amount of elastic tissue* which stretched during systole and recoil on the blood during diastole. This elastic nature of the arteries is important for two principal reasons;

[A] It prevents the pressure from rising extremely high during systolic contraction of the heart.

[B] The elastic recoil tendency of the arterial tree maintains a high arterial pressure between heartbeats so that blood can continue to flow through the tissues without interruption.

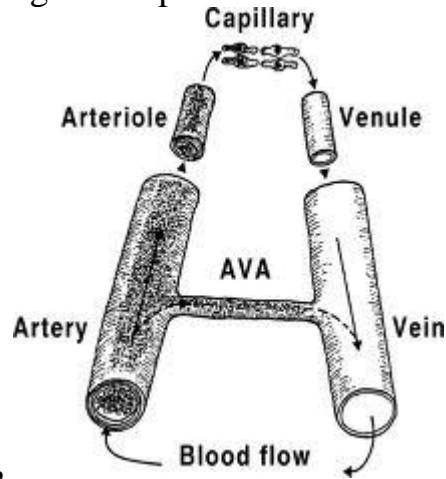
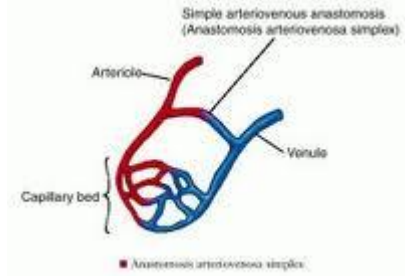
So the blood flow in arteries is pulsatile, strong in systole and weak in diastole [blood pressure in the artery is [120/ 80mmHg]

[2] The arterioles: Each arteriole supplies 10-100 capillaries. The wall of the arterioles contain less elastic tissue but much more smooth muscle which is innervated by noradrenergic vasoconstrictor sympathetic nerve fibers. Therefore, the arterioles are the major site of the resistance to blood flow, and small changes in their caliber cause large changes in the total peripheral resistance, they can remarkably alter blood flow to the tissues. the blood pressure droop in arterioles from 100 to 35-40 mmHg , so conversion of blood flow from pulsatile to continuous therefore wounds shows pulsatile bleeding in arteries & after arterioles shows continuous bleeding.

[3] Capillaries: With diameter of 5-10 μm . The openings of the arterial side of the capillaries are surrounded by minute smooth muscle called precapillary sphincters. When the sphincters are dilated, the diameter of the capillaries is just sufficient to permit RBCs to squeeze through the lumen. the degree of opening & closing is regulate **by concentration of oxygen in the tissues** in which when the consumption of oxygen increased by the tissues caused increase opening for long duration to supply oxygen to the tissues i.e. the blood usually does not flow continuously through the capillaries instead , it flows intermittently turning on and off every few seconds or minutes this is called vasomotion which is caused by intermittent contraction at the metarterioles and precapillary sphincters The total area of all capillaries walls in the body exceeds 6300 m^2 in the adults. The wall thickness of the capillary is about 1 μm which is made up of single layer of endothelial cells which join with themselves to permit passage of molecules only as large as 10 nm in diameter. . If all the capillaries in your body were placed end to end, their combined length would be more than 25,000 miles, enough to circle the planet. All chemical and gaseous exchange between blood and interstitial fluid takes place across capillary walls.[function of capillaries] blood pressure has dropped to approximately 35 mm Hg and by the end of the capillary beds is only around 17 mm Hg.

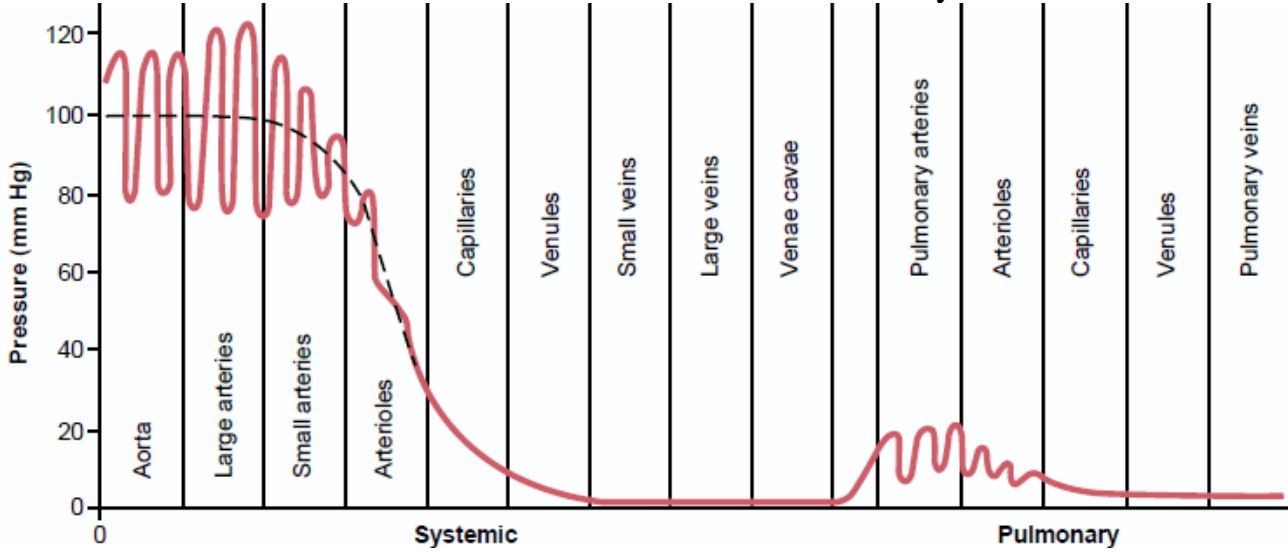
[4] The venules and veins: The venules collect blood from the capillaries; they gradually coalesce into larger veins. The veins function as conduits for transport of blood from the tissue back to the heart [venous return] and they serve as a major reservoir of blood. Since the pressure in the venous system is very *low* in which *pressure gradient in the veins, from venules to the termini of the venae cavae, is only about 15 mm Hg (but from the aorta to the ends of the arterioles is about 60 mm Hg).*, the venous walls *are thin*. The veins contain the highest proportion of the blood in the CVS and this blood volume is called unstressed volume.i.e 64% of blood store in vein and can call when need as in bleeding

[5] Arteriovenous anastomoses: In the fingers, palms, and ear lobes of humans, there are short channels that connect arterioles to venules bypassing the capillaries. These **arteriovenous (A-V)**

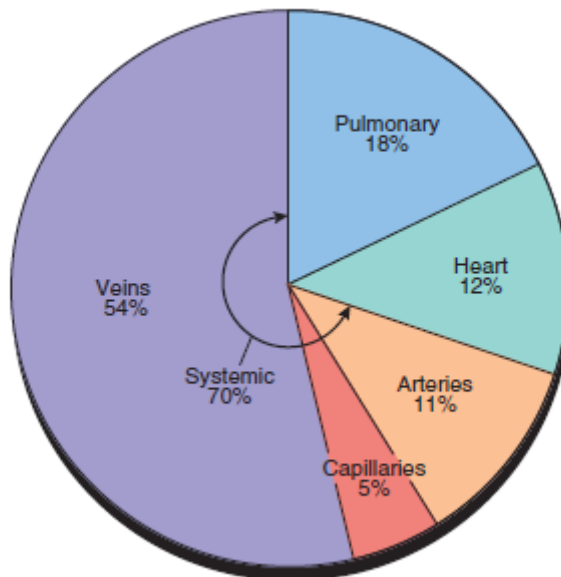


anastomoses, or shunts,

have thick muscular walls and are innervated by vasoconstrictor nerve fibers.



Distribution of blood



[A] Blood flow:[cardiac output]= 5-6L/ minute. Or 100ml /second.

Can be expressed by the following equation: $Q = \Delta P/R$. Where Q = Flow or cardiac output (mL/min), ΔP = Pressure gradient (mm Hg), R = resistance or total peripheral resistance (mm Hg/mL/min).

[B] Velocity of blood flow:

Can be expressed by the following equation: $V = Q/A$. Where V = Velocity cm/sec), Q = Blood flow (mL/min), A = Cross-sectional area (cm²).

Velocity is directly proportional to blood flow, and inversely proportional to cross-sectional area so any level of cardiovascular the cross-sectional area in the aorta **is less** than in the sum of all of the capillaries (large cross-sectional area) , so lower velocity of blood flow in the capillaries optimizes conditions for exchange of substances across the capillary wall.

[C] Resistance to blood flow.

Resistant to blood flow in a vessel. It is measured in our body indirectly from measurement of blood flow & pressure difference in a vessel.

$$R = \frac{P}{Q}$$



Total Peripheral Resistance = (Mean Arterial Pressure - Mean Venous Pressure) / Cardiac Output

The units are (PRU) = peripheral resistance units

$$= \frac{P = 100 \text{ mmHg}}{Q = 100 \text{ ml/sec}} = 1 [\text{PRU}]$$

The resistance to blood flow is generated by friction between the flowing blood & the vascular wall.

Total peripheral resistance .

The rate of blood in normal person at rest is about 100 ml/sec & the pressure difference from the systemic arteries to the systemic veins is around 100 mmHg; therefore, the resistance in the entire systemic circulation is about 100/100 or 1.PRU (total peripheral resistance). In some conditions where the blood vessels of the body are constricted, the total peripheral resistance may increase to 4 PRU & when the vessels become greatly dilated it can decrease to only zero

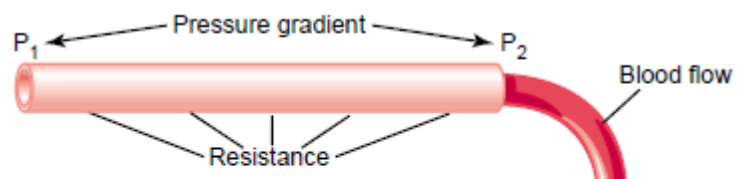


Figure 14-3

Interrelationships among pressure, resistance, and blood flow.

Total pulmonary resistance .

In the pulmonary system, the pressure in pulmonary arteries is about 16 mmHg & in left atrium 2 mmHg & since the flow is the same as in systemic circulation, then the total pulmonary resistance is about 0.14 PRU.

There are many methods for measuring blood flow such as:

[1] Electromagnetic flowmeter: Which depends on principle that a voltage is generated in a conductor (here is the blood) moving through a magnetic field and that the magnitude of voltage (is measured by placing electrode on the surface of the vessel) is proportionate to the speed of movement.

[2] The ultrasonic Doppler flowmeter: Which depends on sending ultrasonic waves into a vessel diagonally from one-crystal, and the waves reflected from the red and white blood cells are picked up by a second, down-stream crystal. The frequency of the reflected waves is higher by an amount that is proportionate to the rate of flow toward the second crystal because of the Doppler effect.

[3] Plethysmograph: in which the forearm is sealed in a watertight chamber (plethysmograph), changes in the volume of the forearm, reflecting changes in the amount of blood and interstitial fluid it contains, displace the water, and this displacement is measured with a volume recorder. When the venous drainage of the forearm is occluded, the rate of increase in the volume of the forearm is a function of the arterial blood flow (venous occlusion plethysmography).

[4] Fick principle: Which is used to measure flow in an organ such as the use of para-aminohippuric acid renal clearance to measure the renal blood flow.

Factors affecting resistance

Poiseuille`s equation gives factors that change the resistance of blood vessels. $R = 8 \eta L / \pi r^4$. Where R = Resistance, r = Radius of a the vessel, η = The viscosity of blood, L = The length of the vessel.

Resistance is directly proportional to the viscosity of the blood. For example, increasing viscosity by increasing Hct [hematocrit] will increase resistance and decrease blood flow.

Resistance is directly proportional to the length of vessel.

Resistance is inversely proportional to the **fourth power of the vessel radius**.

1- The diameter of the blood vessel:

Slight changes in the diameter of a blood vessel causes tremendous changes in its ability to conduct blood when the blood flow is laminar (streamline) conductance increase in proportion to the fourth power of the diameter(fourth power law)

Conductance \propto diameter⁴

R=resistance

$R \propto 1/r^4$ r=radius.

$Q \propto r^4$ → the blood flow is directly proportional to the fourth power of the radius of the vessels

Q= flow.

This factor is the most important factor that controls the blood flow through changes in the diameter of the blood vessel to change the resistance.

The arterioles (which have thick muscular wall) control the flow in such way:-

During constriction → ↑resistance → ↓flow

During dilation → ↓resistance → ↑flow

In the systemic circulation 2/3 of the PR is in the small arterioles that can have a diameter ranging from 4-25 micrometers.

2-The length of blood vessels:

The more the length, the higher the resistance due to more friction & thus the lower the flow.

(this point is limited in our body because there is no change in the vessel length

$$R \propto L$$

3-Blood viscosity:-

Increased blood viscosity leads to increased resistance due to increased friction (not only between blood & the walls but also between the parts of the blood itself)

∴ Increased hematocrit (the percentage of blood that is cells) or increased plasma proteins lead to increase blood viscosity → increase resistance → decrease flow

dehydration (decreased body water) also increase blood viscosity.

The effect of pressure on vascular resistance

Increase in arterial pressure cause a proportional increase in blood flow through various parts of the body

$$Q = \frac{P}{R} \rightarrow Q \propto P$$

The **increase in arterial pressure** not only **increase** the force that tend to push blood through the vessel but also **distends** the vessel at the sometime thus, **decreasing** its, resistance. So increased pressure have 2 effects that increase the blood flow.

The effect of pressure on flow is limited in our body because blood press. Is **usually kept constant** by multiple mechanism

[D] Laminar flow versus turbulent flow:

laminar flow is streamlined (in a straight line); **turbulent flow** is not.

Reynold`s number (Re) ;predicts whether blood flow will be laminar or turbulent.

When Re is increased, there is a greater tendency for turbulence, which causes audible vibrations called **bruits**. Re (and therefore turbulence) is **increased** by the following factors:

1-Decreased blood viscosity (example decrease Hct[hematocrit], anemia).

2-Increased blood velocity (example narrowing of a vessel& valves as in aortic and mitral stenosis]

[E] Vascular compliance.

Compliance is the ability of a hollow organ (vessel) to distend and increase volume with increasing transmural pressure or the tendency of a hollow organ to resist recoil toward its original dimensions on application of a distending or compressing force. It is the reciprocal of "elastance", hence elastance is a measure of the tendency of a hollow organ to recoil toward its original dimensions upon removal of a distending or compressing force

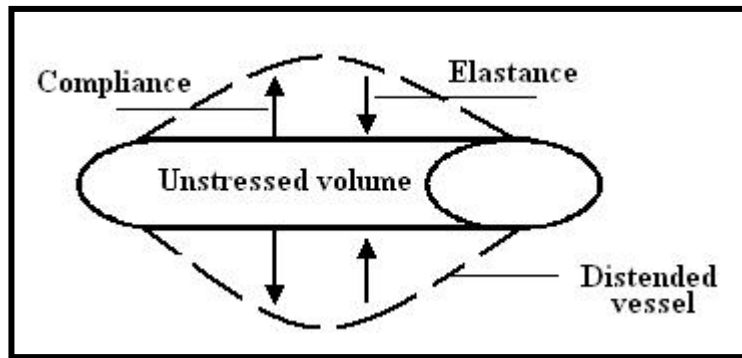
Venous compliance is approximately 30 times larger than arterial compliance. Compliance is calculated using the following equation, where ΔV is the change in volume, and ΔP is the change in pressure:

$$C = \frac{\Delta V}{\Delta P}$$

Compliance of veins are much more than that of arteries.

As a result, more blood volume is contained in the veins (**unstressed volume**) than in the arteries (**stressed volume**).

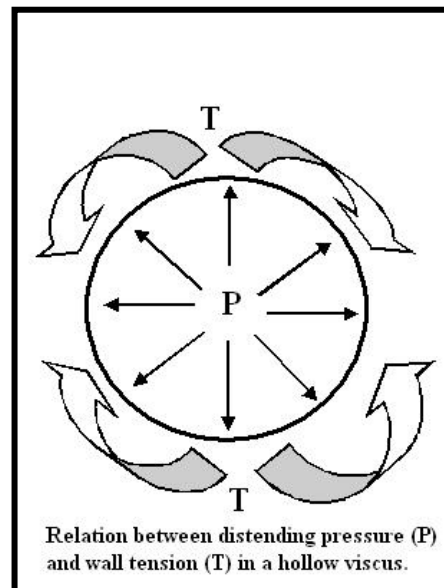
The veins are called **capacitance vessels** and the small arteries and arterioles are referred to as **resistance vessels** (because they are the principle site of the peripheral resistance).



The elasticity of the arteries **decreases with age**; as a person ages, the arteries become stiffer and less distensible, [atherosclerosis].

Therefore, **veins** can be called capacitance vessels because they are *distensible* and blood reservoir because *more than half of the circulating blood is located within them*. -Specific blood reservoir:

The spleen stores about -- 100 ml of blood.
 The liver --- Several hundred ml
 Large abdominal veins --- 300 ml.
 Skin venous plexuses ...Several hundreds .
 Heart) not part of the circulation 50-100 ml
 Lung) not part of the circulation 100-200 ml.
 These can contribute to supply blood to circulation when needed [as in bleeding]



[K] : Venous Blood Pressure .The pressure in any vessel below heart level **is increased** (approaching about 90 mm Hg more at the feet) and that in any vessel above heart level **is decreased** (approaching about [-10] mm Hg less at the sagittal sinus of the skull) by the effect of **gravity**. Accordingly, the neck veins collapse almost completely all way to the skull due to atmospheric pressure on the outside of the neck. This collapse causes the pressure in these veins to remain zero along their entire extent

In fact, **under normal dynamic conditions**, the pressure inside the veins of the lower limb is about 25 mm Hg rather than 90 mm Hg. venous pressure is normally too low to promote adequate venous return. For this reason, **three functional adaptations are critically important to venous return:**

1-the **venous pump** or **muscle pump** the lower limb veins are supplied with *valves* which allow the direction of blood flow only toward the heart. This is assisted by the *contraction of the lower leg muscles* which compress the veins that pass through them and the adjacent veins, and this squeezes the blood out of the veins. Consequently, every time a person moves the legs or even tenses the muscles, a certain amount of blood is propelled toward the heart, and the pressure in the dependent veins of the body is lowered. This pumping system is known as the **venous pump** or **muscle pump**. If the human being stands perfectly still, the venous pump does not work, and the venous pressures in the lower part of the leg can rise to the full hydrostatic value of 90 mm Hg in about 30 sec. Under such circumstances the pressures within capillaries also increase greatly, and fluid leaks from the circulatory system into the tissue spaces resulting edema. As a result, the legs swell, and the blood volume diminishes. In addition, if the venous valves become incompetent, as occurs in overstretching the veins by a prolonged excess venous pressure which occurs for example in pregnancy or in jobs that require standing position for prolonged period of time, in these cases the valves will no longer close completely. Therefore, backflow of blood is expected and causing an enlarged veins with failure of venous pump. This condition is known as **varicose veins**, in which the lower limbs veins are enlarged and the legs are edematous.

2-The respiratory pump: The respiratory pump moves blood up toward the heart as pressure changes in the ventral body cavity during breathing. As we inhale, abdominal pressure increases, squeezing local veins and forcing blood toward the heart. At the same time, the pressure in the chest decreases, allowing thoracic veins to expand and speeding blood entry into the right atrium.

3- Sympathetic venoconstriction: Sympathetic venoconstriction reduces the volume of blood in the veins—the capacitance vessels. As the layer of smooth muscle around the veins constricts under sympathetic control, venous volume is reduced and blood is pushed toward the heart.

Hydrostatic Pressure

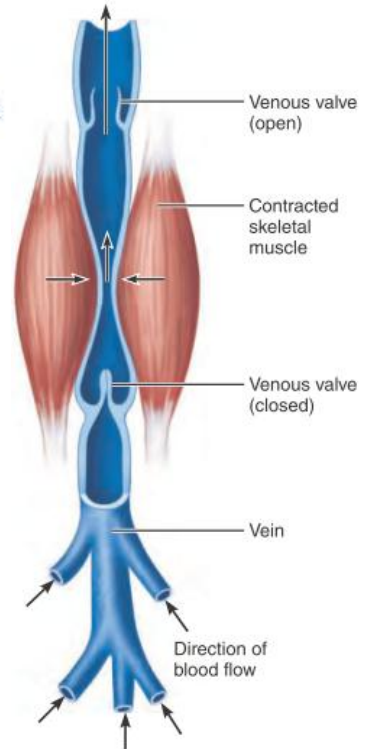
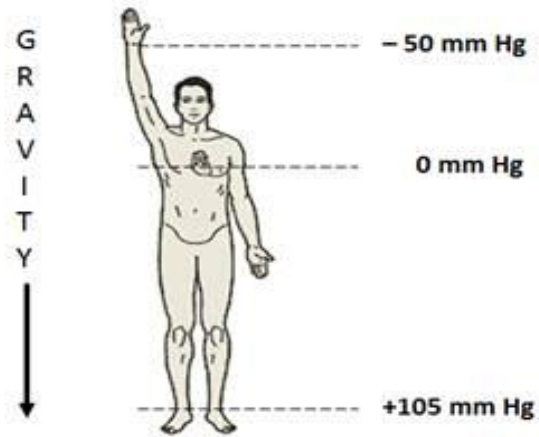
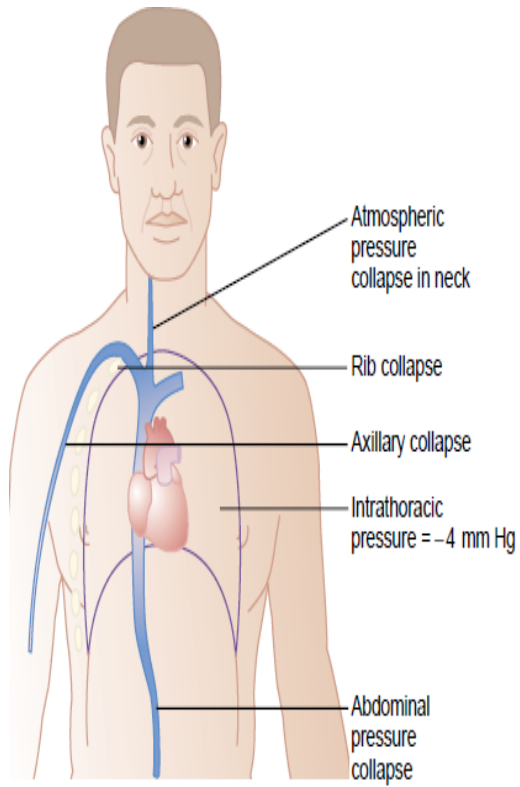


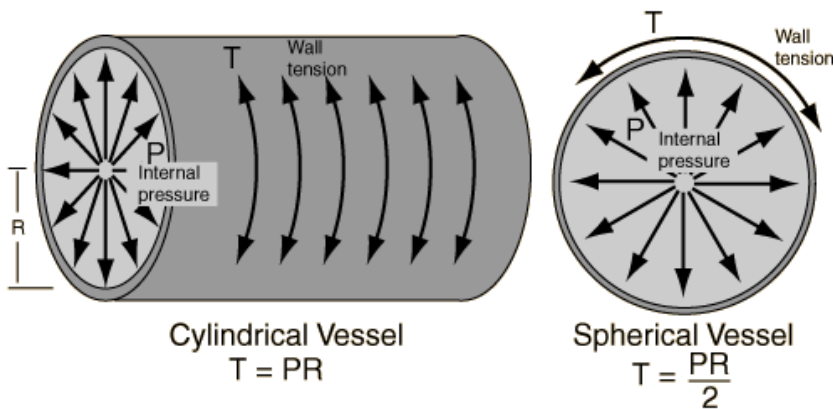
Figure 7.36: Muscular pump of the venous blood.



[F] Law of Laplace: The distending pressure (P) in a distensible spherical hollow object is equal at equilibrium to the tension in the wall (T) multiply by the wall thickness (h), divided by the radius (r) of the curvature of the object. Wall tension is the force that squeezes down on the contained volume.

$P = 2 \times T \times h/r$ OR $T = [P \times r] / h$, so the higher pressure difference, the more tension will be ,or thicker wall the less tension and also larger radius – more tension.

P (dynes/cm²) is actually the trans mural pressure, the pressure on one side of the wall minus that on the other side. T is expressed in dynes/cm, r in cm and h in cm. Consequently, the smaller the radius of a blood vessel, the lower the tension in the wall necessary to balance the distending pressure. The larger the vessel radius, the larger the wall tension required to withstand a given internal fluid pressure.



For a given vessel radius and internal pressure, a spherical vessel will have half the wall tension of a cylindrical vessel.

[Why does the wall tension increase with radius?](#)

[H] Arterial blood pressure: is the force that exerted by the circulating blood on the lateral wall of the blood vessels.

Is pulsatile.

Is not constant during cardiac cycle.

Systolic pressure: [normally 100- 140 mmHg]

Is the highest arterial pressure during a cardiac cycle.

Is measured after the heart contract (systole) and blood is ejected into the arterial system.

Diastolic pressure: [60- 90mmHg].

Is the lowest arterial pressure during a cardiac cycle.

It measured when the heart is relaxed (diastole) and blood is returning to the heart via the veins.

Pulse pressure [30-40 mmHg]

Pulse pressure is the pressure that is felt when feeling the pulse. Measured in millimeters of mercury (mmHg), the pressure difference between the systolic and diastolic pressures is the pressure

change to create the pulse, which is the pulse pressure. If resting blood pressure is (systolic- diastolic) $120 - 80 = 40$ millimeters of mercury (mmHg) is the pulse pressure .

The [aorta](#) has the highest compliance in the arterial system due in part to a relatively greater proportion of elastin fibers versus smooth muscle and collagen. This serves the important function of dampening the pulsatile output of the left ventricle, thereby reducing the pulse pressure. If the aorta becomes rigid in conditions such as [arteriosclerosis](#) or [atherosclerosis](#), the pulse pressure would be very high.

- Systemic pulse pressure = $P_{\text{systolic}} - P_{\text{diastolic}} = 120\text{mmHg} - 80\text{mmHg} = 40\text{mmHg}$
- Pulmonary pulse pressure = $P_{\text{systolic}} - P_{\text{diastolic}} = 25\text{mmHg} - 10\text{mmHg} = 15\text{mmHg}$

Low (Narrow) Pulse Pressure. The most common cause of a low (narrow) pulse pressure is a drop in left ventricular stroke volume. In trauma a low or narrow pulse pressure suggests significant blood loss (insufficient preload leading to reduced cardiac output). If the pulse pressure is extremely low, i.e. 25 mmHg or less, the cause may be low stroke volume, as in [Congestive Heart Failure](#) and/or [shock](#). A narrow pulse pressure is also caused by [aortic valve stenosis](#) and [cardiac tamponade](#).

Mean arterial pressure:[MAP].

It is defined as the average arterial pressure during a single [cardiac cycle](#).

Can be calculated approximately as **diastolic pressure + 1/3 of pulse pressure**

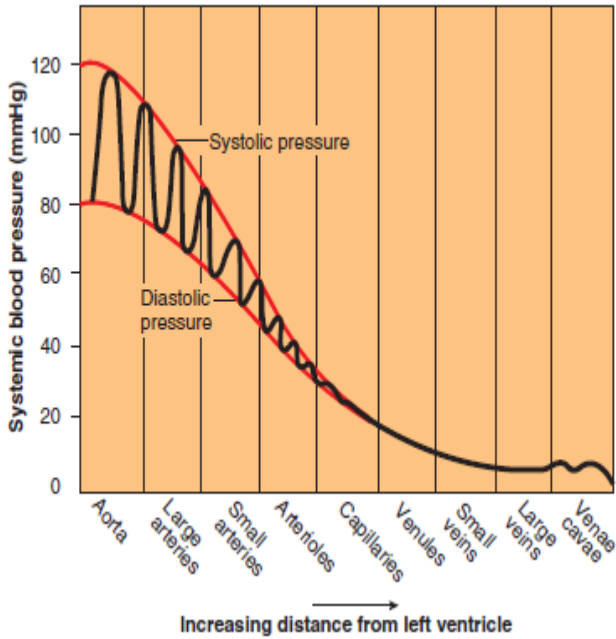
Clinical significance

MAP is considered to be the [perfusion pressure](#) seen by [organs](#) in the body.

It is believed that a *MAP* that is greater than 60 [mmHg](#) is enough to sustain the organs of the average person. *MAP* is normally between 70 to 110 [mmHg](#)^[6]

If the *MAP* falls significantly below this number for an appreciable time, the end organ will not get enough blood flow, and will become [ischemic](#).

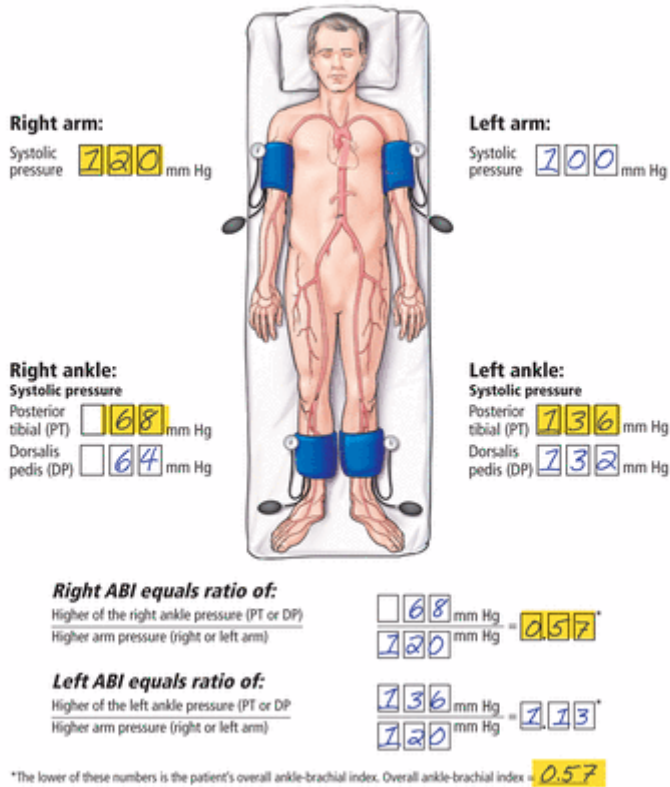
MAP and pulse pressure both decline with increasing distance from the heart.



The Ankle Brachial Index (ABI).

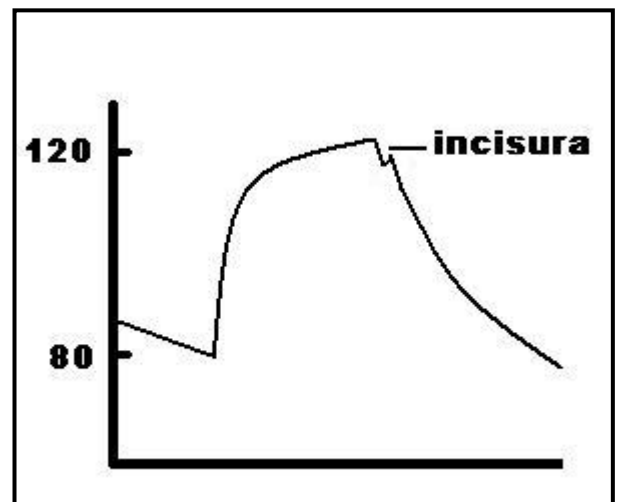
is the ratio of the [blood pressure](#) in the lower legs to the blood pressure in the arms. Compared to the arm, lower blood pressure in the leg is an [indication](#) of blocked arteries ([peripheral vascular disease](#) or PVD). The ABI is calculated by dividing the [systolic blood pressure](#) at the ankle by the systolic blood pressures in the arm. An ABPI between 0.9 and 1.2 considered normal (free from significant [PAD](#)), while a lesser than 0.9 indicates arterial disease. An ABPI value greater than 1.3 is also considered abnormal, and suggests [calcification](#) of the walls of the arteries and incompressible vessels, reflecting severe [peripheral vascular disease](#)

How to calculate the ankle-brachial index



Medical Illustrator: Joseph Pangrace CCF ©2012

[M] Pressure waves in the arteries: Since the heart is a pulsatile pump, blood enters the arteries intermittently with each heartbeat, causing pressure pulses in the arterial system. Each wave consists of initial very rapid rise in arterial pressure during ventricular systole, followed by a maintained high level of pressure, and this terminated by a sharp *incisura* or *dicrotic notch* at the end of systole, followed by a slow decline of pressure back to the diastolic level. The incisura occurs immediately before the aortic valve closure and is caused by backflow of blood from aorta to the aortic root during diastole which raises the pressure slightly again.



D-(Dicrotic-wave)

Reflective oscillatory wave occurred from the blood crash into aortic valve by blood-pressure-of-aorta.

Methods of measuring blood pressure: Blood pressure can be recorded

- Invasively (direct) by using cannula needle into the artery [usually, radial, femoral, or brachial] this is usually done by an anesthesiologist or surgeon in a hospital.

-Indirect Method [Non invasive]: are of two types.

1- Oscillometric methods.

Similar to that of the auscultatory method, but with an electronic pressure sensor [transducer] to detect blood flow, and cuff inflated & release by electronic operating pump that fitted in the wrist [elevated to heart height] or the upper arm is preferred. , instead of using the stethoscope, so may be suitable for use by untrained staff and for automated patient home monitoring.

2- The auscultatory – palpatory method.

A. Palpatory method

Feel the radial pulse of the subject by placing the three middle fingers on the radial artery against the radius bone with mild pressure of the distal finger; you can feel the radial pulse by the index finger, Raise the pressure in the cuff until disappear of the radial pulse. Start to lower the pressure slowly while you are feeling the radial pulse. Once you feel the pulsation of the radial artery, record the reading on the manometer. This reading gives you the systolic pressure. Repeat this procedure many times and record your result.[checking only systolic Bp , without used stethoscope]

B. Auscultatory method:[manometric , either mercury manometric or aneroid].

From your surface anatomy knowledge of the anticubital fossa, put the diaphragm of the stethoscope at the position of the brachial artery on medial side of biceps tendon in anticubital fossa just below the lower edge of the cuff (not underneath the cuff !). Raise the pressure until radial pulse disappearance, then lower the pressure slowly and steadily. The following phases of the character of the sound (**Korotkow or Korotkoff sounds**) will be heard by the stethoscope:

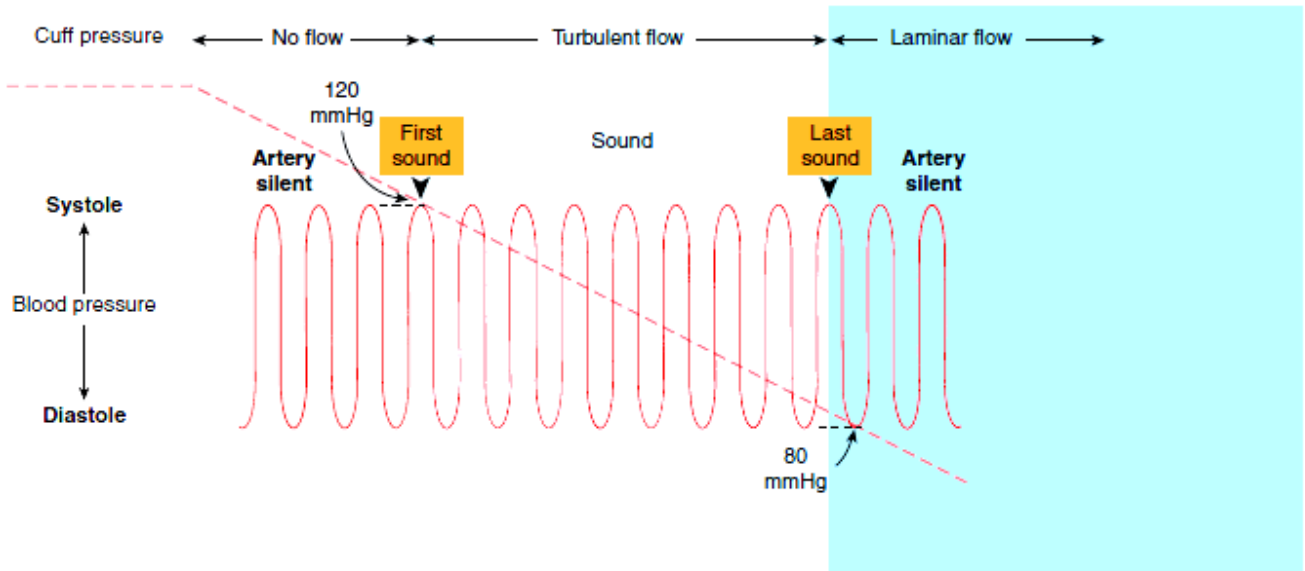
Phase 1: If the pressure is above systolic no sound can be heard . when the systolic pressure is reached, a clear loud sound is heard with each heart beat. Passes of blood flow through narrowed brachial artery ---- turbulence flow.

phase 2: When you lower the pressure more the sound becomes softer.

Phase 3: As the pressure is lowered , the sound becomes louder and banging in character.

Phase 4: Then the sound becomes soft and muffled. The point at which the sound begins to fade is taken as the diastolic pressure.

Phase 5:The sound will disappear completely (sometimes this is taken as the diastolic pressure).because the blood flow become silent [laminar blood flow]



■ **Figure 14.30** The indirect, or auscultatory, method of blood pressure measurement. The first Korotkoff sound is heard when the cuff pressure is equal to the systolic blood pressure, and the last sound is heard when the cuff pressure is equal to the diastolic pressure. The dashed line indicates the cuff pressure.

The exact cause of Korotkoff sounds is still debated but they are believed to be caused mainly by blood jetting through the partly occluded vessel. The jet causes turbulence in the open vessel beyond the cuff, and this sets up the vibrations heard through the stethoscope.

The cardiovascular center [CVC], located in **the medulla oblongata**. The outputs from the CVC are sympathetic and parasympathetic nerve fibers. Both types of these fibers are under tonic discharge. CVC (figure 7.11 A) consist of:

- The cardioacceleratory center projects to sympathetic neurons in the T 1 –T 5 level of the spinal cord. These

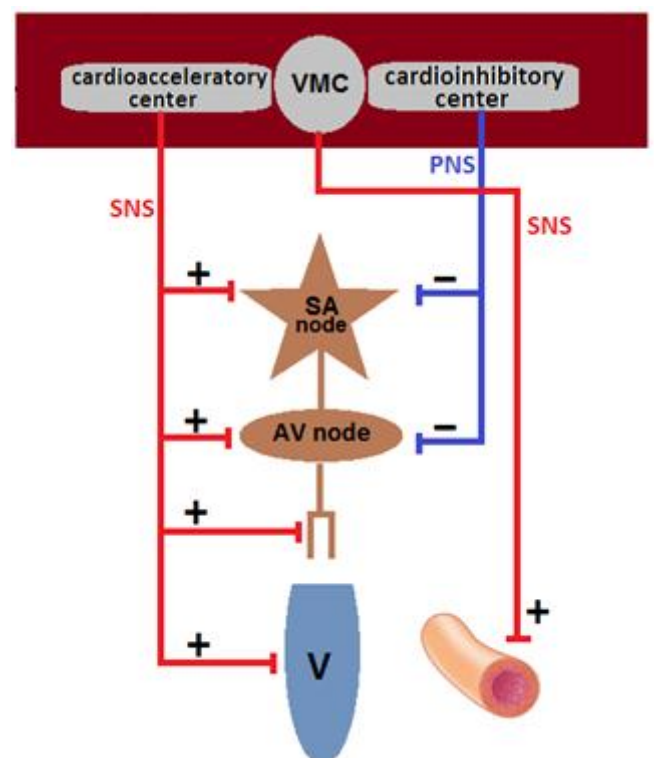


Figure 7.11 A: Medullary cardiovascular centers.

preganglionic neurons, in turn, synapse with postganglionic neurons in the cervical and upper thoracic sympathetic trunk. From there, postganglionic fibers run through the cardiac plexus to all parts of the heart and innervate the SA and AV nodes, **with a strong representation to the ventricular muscle, and coronary arteries.** The sympathetic nerves are distributed to all parts of the heart.

- The cardioinhibitory center sends impulses to the parasympathetic dorsal vagus nucleus in the medulla, which in turn sends inhibitory impulses to the heart via branches of the vagus nerves. Most parasympathetic postganglionic motor neurons lie in ganglia in the heart wall and their fibers project most heavily **to the SA and AV nodes and to lesser extent to the muscle of the two atria, and far very few to the ventricular muscle.**

The vasomotor center (VMC) that controls the diameter of blood vessels. The vasomotor center transmits impulses at a fairly steady rate along sympathetic efferent called vasomotor fibers. These fibers exit from the T 1 through L 2 levels of the spinal cord and innervate the smooth muscle of blood vessels, mainly **arterioles.** As a result, the arterioles are almost always in a state of moderate constriction, called vasomotor tone. These sympathetic nerves release norepinephrine from their endings that interacts with α -adrenergic receptors on the smooth muscle cells to cause contraction and thus arteriolar constriction.

CVC are subjects of various stimuli that modify their activities. In general, stimuli that increase the heart rate also increase blood pressure, whereas those that decrease the heart rate lower blood pressure. However, there are **exceptions**, such as the production of hypotension and tachycardia by stimulation of atrial stretch receptors and the production of hypertension and bradycardia by increased intracranial pressure.

The VMC is controlled by higher center where received impulse from cerebral cortex & limbic system , hypothalamus , reticular activating system , and also from baroreceptors & chemoreceptors

There are descending tracts to the CVC

A-from the cerebral cortex (particularly the limbic cortex) that relay in the hypothalamus. These fibers are responsible for the blood pressure and heart rate changes produced **by emotions such as sexual excitement and anger** (figure 7.11 B).

B-Heart rate varies with respiration, heart rate increase during inspiration and decreases during expiration which result from variations in vagal tone that affect the SA node and it is commonly seen in children and in athlete. Inhalation

temporarily suppresses vagal activity, causing an immediate increase in heart rate. Exhalation then decreases heart rate and causes vagal activity to resume.

C- Pain usually causes a rise in blood pressure via afferent impulses in the reticular formation converging in the vasomotor center. However, prolonged severe pain may cause vasodilation and fainting. The activity in afferents from exercising muscles probably exerts a similar pressor effect via pathway to the VMC (figure 7.11 B). The pressor response to stimulation of somatic afferent nerves from exercising muscles is called the somatosympathetic reflex.

D- Baroreceptor are stretch receptors located in the **carotid sinuses** (dilations in the internal carotid arteries, which provide the major blood supply to the brain), in the **aortic arch**, and in the walls of nearly every large artery of the neck and thorax. These receptors are **high-pressure receptors**.

Baroreceptors are also located in the walls of the right and left atria at the entrance of the superior and inferior venae cavae and the pulmonary veins, as well as in the pulmonary circulation. These receptors are **low-pressure receptors**. The low-pressure baroreceptors are involved with the regulation of blood volume. The blood volume determines the mean pressure throughout the system, in particular in the **venous side** where most of the blood is held. The low-pressure baroreceptors **have both circulatory and renal effects**; they produce changes in hormone secretion, resulting in profound effects on the retention of salt and water; they also influence intake of salt and water. An **increase in systemic arterial pressure** causes the walls of the arterial regions to stretch. When stretched, high-pressure baroreceptors send a rapid stream of impulses along sensory nerve fibers to the cardiovascular center causing inhibition of the vasomotor and cardioacceleratory centers while stimulation of cardioinhibitory center. **A fall in pressure below the normal range**, by contrast, causes a decrease in the frequency of action potentials produced by these sensory nerve fibers and consequently causing excitation of the vasomotor and cardioacceleratory centers while inhibition of cardioinhibitory center. Although baroreceptors respond to short-term changes in blood pressure, they quickly adapt to prolonged or chronic episodes of high or low pressure.

Peripheral

E-chemoreceptors (figure 7.11 B) act principally to detect variation of the **oxygen** concentration in the **arterial blood**, whilst also monitoring arterial **carbon dioxide** and **pH**. They are located in the **aortic body** and **carotid body**, on the **transverse aortic arch** and on the **common carotid artery**, respectively.

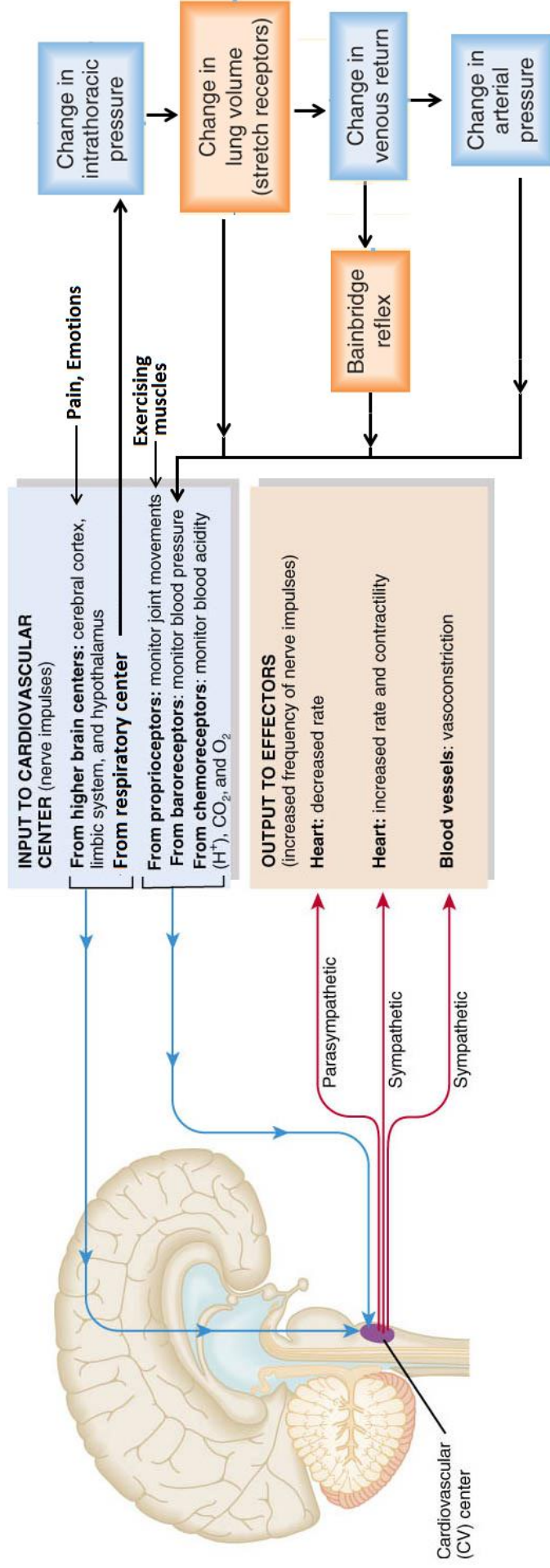


Figure 7.11 B: Medullary cardiovascular centers.

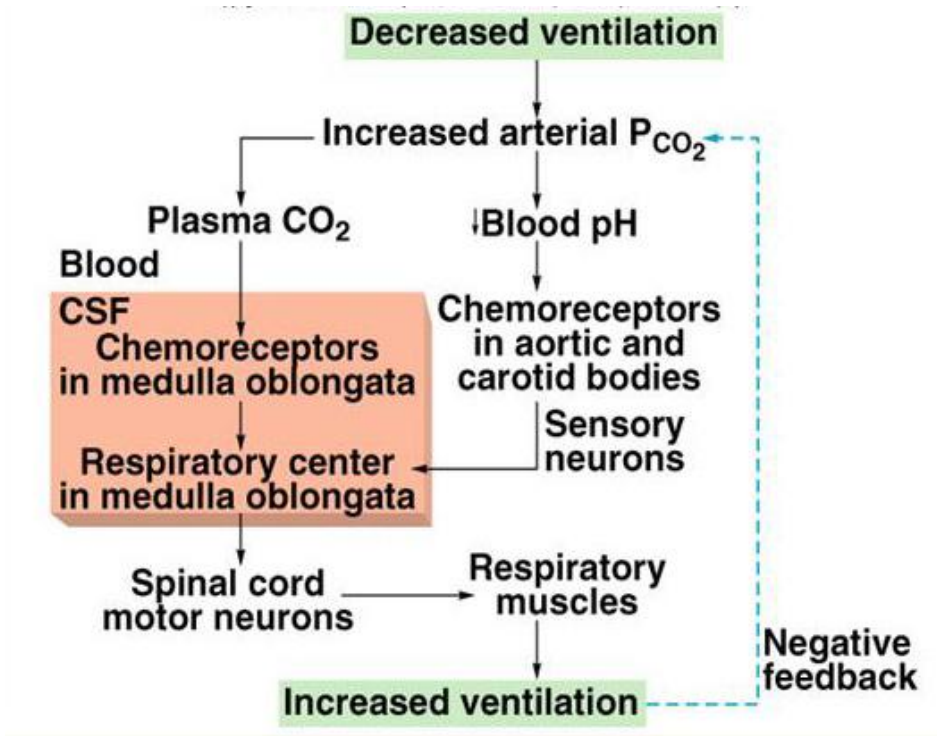
Under certain conditions, during the “**Alarm or Defense pattern of stimulation**”, the hypothalamus [a] activate the sympathetic vasodilator system to the muscles to increase their blood flow, and at the same time [b] stimulates the vasomotor center intensely, causing intense vasoconstriction throughout the remainder of the body and an intense increase in heart activity. The arterial blood pressure rises, cardiac output increases, the heart rate increases, and the circulation is ready to supply nutrients to the muscles if there be need. Also, impulses are transmitted simultaneously throughout the central nervous system to cause a state of generalized excitement and attentiveness.

Vasovagal Syncopial Attacks.

Some times, during intense emotional experiences, the muscle vasodilator system becomes powerfully activated by the hypothalamus so that blood flow through the muscles increases several fold in association with an intense vagal stimulation of the heart, causing the heart rate to slow markedly. This overall effect is called vasovagal syncope (emotional fainting). The arterial pressure falls instantly, which in turn reduces the blood flow to the brain and causes the person to lose consciousness. resulting in simultaneous enhancement of parasympathetic nervous system[vagal tone] and withdrawal of sympathetic nervous system tone. if the person does not fall into a fully flat, supine position, and the head remains elevated above the trunk, a seizure may result from the blood's inability to return quickly to the brain. Fainting occurs with the loss of oxygen to the brain.

Occurs in. Typical triggers for vasovagal episodes include:

- Prolonged standing or upright sitting
- Standing up very quickly (Orthostatic hypotension)
- Stress directly related to trauma
- Any painful or unpleasant stimuli, such as:
 - Trauma (such as hitting one's funny bone)
 - Watching or experiencing medical procedures (such as Venipuncture)
 - High pressure on or around the chest area after heavy exercise
- Severe menstrual cramps
- Sudden onset of extreme emotion
- Lack of sleep
- Dehydration
- Hunger
- Being exposed to high temperatures
- Pressing upon certain places on the throat, sinuses, and eyes (also known as vagal reflex stimulation when performed clinically)



The control of blood flow to the tissues: the circulatory system is able to control the blood flow through different tissues. This is achieved by local and systemic (nervous and humoral) mechanisms:

1-Local mechanisms: These include:

[A] Short-term blood flow control.

Autoregulation . have two theories

-Myogenic theory — local response to S.M of arterioles

-Metabolic theory --- have two examples;

[i] Active hyperaemia

[ii] Reactive hyperaemia.

[B] Long-term blood flow control.---- [new blood vessels formation]

2-Systemic mechanisms: These include:

[i] Nervous mechanisms.

[ii] Humoral mechanisms.

[1] Local mechanisms:

[A] Short-term blood flow control:

Autoregulation: The capacity of tissues to regulate their own blood flow at nearly normal levels despite marked changes in arterial pressure. This mechanism is very efficient and acts within a few minutes after the local tissue conditions or the blood pressure have changed. The possible theory for autoregulation is

The myogenic theory: When high arterial pressure, the blood flow to the tissue increases causes stretches the vessel, this in turn causes the smooth muscle of the vessel wall to contract with consequent vascular constriction and reduces the blood flow back near normal. Conversely, at low pressures, the degree of stretch of the vessel is less, so that the smooth muscle relaxes and allows increased flow.

Immediate **Increase** blood flow--- distension & stretching wall blood vessels--- contraction smooth muscle of vessels----- decrease blood flow----- return blood flow to normal.

Decrease blood flow---- decrease stretching on wall of blood vessels---- relax muscles—-increase blood flow

Metabolic Theory. Have two Examples.

[i] Active hyperaemia: The blood flow to an organ is proportional to its metabolic activity. When any tissue becomes highly active, such as a muscle during exercise, a gastrointestinal gland during a hypersecretory period, the rate of blood flow through the tissue increases. The possible explanation underlying this phenomenon is **The Metabolic theory:** When the rate of tissue metabolism or the oxygen demand by the tissue is increased, or the blood pressure is decreased, the local tissue blood flow is increased to cope with the tissue demands. The possible explanation for this mechanism is as follows: A greater rate of metabolism or a less local blood flow due to low blood pressure (i.e., less oxygen available to the tissue) will cause an excessive local formation of a vasodilator substance that induces a local vasodilatation of precapillary sphincters, metarterioles, and arterioles. Consequently, vasodilation occurs and an increase in local blood flow will take place. Some of these vasodilator substances are an increase in local concentrations of CO₂, lactic acid, adenosine (in cardiac muscles and not in skeletal muscles), adenosine phosphate compounds, histamine, K⁺ ions, and H⁺, or a decrease in local concentrations of O₂ and nutrients (such as glucose or vitamins like thiamine, niacin, and riboflavin that are required for smooth muscle contraction). In addition, **local increase in temperature** exerts a direct vasodilator effect while a drop in tissue temperature causes vasoconstriction. Local liberation of serotonin from platelets at an **injured blood vessel** in part causes intense vasoconstriction.

. i.e increase the Bp ----- increase blood flow ---- increase O₂ & nutrient to the tissues---- causes vasoconstriction of blood vessels----- so return of blood flow to normal despite the increased pressure.

NOTE.

Blood flow to the tissue remains relatively constant despite a reduction in arterial pressure [autoregulation]

[Auto regulation of tissue blood flow in response to an increase in arterial pressure occurs as a result of excessive delivery of nutrients such as O₂ to the tissues, the increase in tissue O₂ causes constriction of arterioles and returns blood flow to normal levels.

Reduction perfusion to tissue----- decrease O₂ & increase CO₂ --- increase arteriolar diameter & decrease vascular resistance ---- to increase perfusion.

[ii] Reactive hyperemia: Is an increase in blood flow to an organ that occurs after a period of occlusion of flow. When the blood supply to a tissue is blocked for a few seconds to several hours and then is unblocked, the flow through the tissue usually increases to **about five times normal and last in proportion to the duration of occlusion**. This phenomenon is called reactive hyperemia. Recent evidence suggests the possible role of NO [nitric oxide] in reactive hyperemia.

[B] Long-term blood flow control: It acts within hours, days, and weeks which gives a more complete regulation. The mechanism of long-term local blood flow regulation is almost certainly a function of change in the degree of vascularity of the tissues. That is, if the arterial pressures falls to 60 mm Hg and remains at this level for many weeks, or the metabolism of the tissue increases, Lead to

- 1- Angiogenesis [new blood vessels formation from wall of venules , capillaries & some time from arterioles from ischemic tissues].
- 2- Development of collateral circulation [opening of non - functioning blood vessels]vascular channels **are normally found** but they are closed so **in hypoxia** & metabolic vasodilator of the ischemic segment lead to the opening of these non - functioning blood vessels.

[2] Systemic mechanisms:

[i] Nervous mechanisms: either **direct nervous sympathetic stimulation to the smooth muscles of blood vessels or indirect through adrenal medulla** .These mechanisms for regulation of tissue blood flow operate through autonomic nervous system which is controlled by VMC.

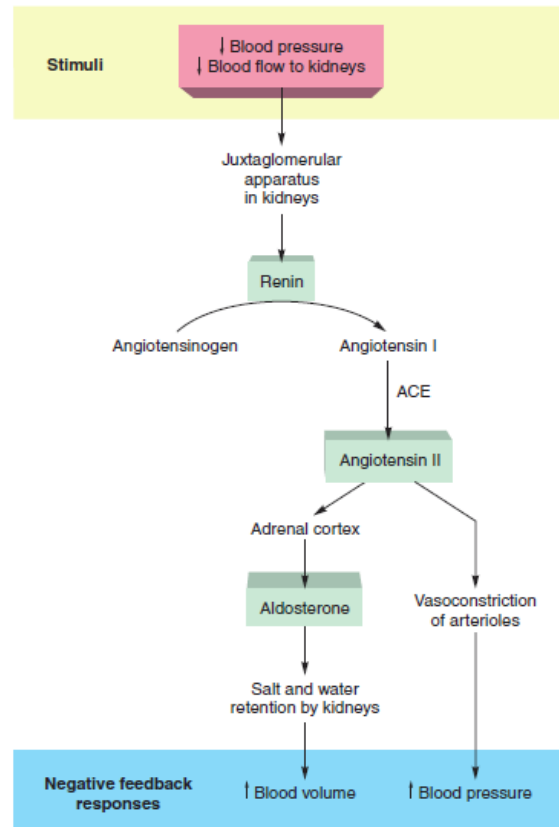
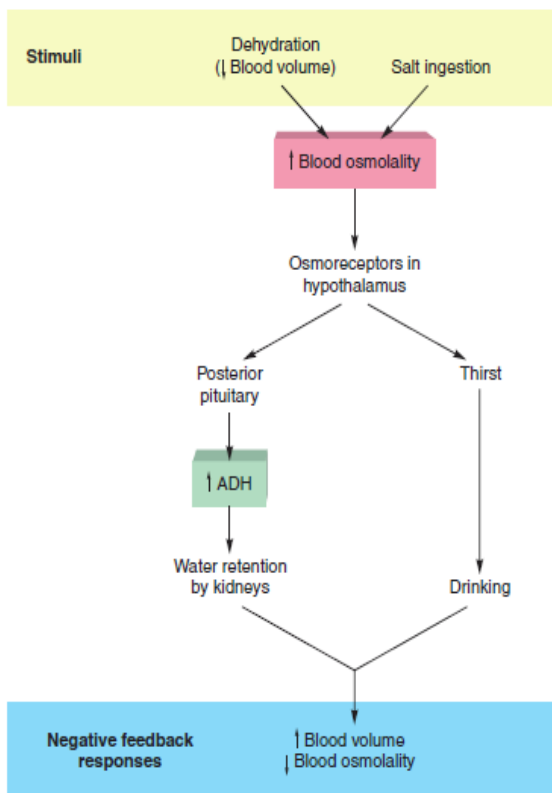
[ii] Humoral mechanisms: Humoral regulation of the circulation means regulation of tissue blood flow by substances in the body fluids, such as by hormones, ions, or so forth. Among the most important of the humoral factors that affect circulatory function are the following:

[A] Vasoconstrictor agents:

[I] Epinephrine and Norepinephrine: Norepinephrine has vasoconstrictor effects in almost all vascular beds of the body, and epinephrine has similar effects except it has a mild vasodilator effects in skeletal muscles.

[II] Angiotensin: Is one of the most powerful vasoconstrictor substances known. A decrease in arterial pressure will cause a decrease in blood flow to the kidneys. The reduction of renal blood flow will stimulate the juxtaglomerular cells (cells that are located in the walls of the afferent arterioles) secrete renin into the blood. In addition, sympathetic nerve signals directly to the juxtaglomerular cells can also cause these cells to release renin. The renin in turn acts on one of the plasma proteins (angiotensinogen) to form angiotensin I which is converted by the lung enzyme into angiotensin II. Angiotensin II has a number of important effects on the circulation related to arterial pressure control, but the most important is to constrict the blood vessels everywhere in the body.

[III] Vasopressin: It is also called antidiuretic hormone (ADH). It is formed by the hypothalamus but is transported down the center of the nerve axons to the posterior pituitary gland, where it is eventually secreted into the blood. It is even more powerful than angiotensin II as a vasoconstrictor. When the BP falls low, the same or the closely related signals that excite the sympathetic nervous signals also excite the hypothalamus to secrete large quantities of vasopressin by way of posterior pituitary gland. It also stimulates the kidney to decrease the excretion of water which helps increase the blood volume any time the BP remains low for any period of time. The increased blood volume then helps bring the BP back to normal (long-term acting BP regulation mechanism)



[B] Vasodilator agents;

N.B:

The endothelium-derived relaxing factor

This is a powerful V.D. substance that is secreted by the vascular endothelium, and is chemically nitric oxide (NO). Many substances act through releasing this EDRF (e.g. acetylcholine, bradykinine, substance P and VIP). It is also a transmitter in the CNS and is released by the parasympathetic nerves in the penis (helping erection).

Substances released by the vascular endothelium

1. EDRF
2. Endothelins
3. Prostacyclin
4. Thrombomodulin
5. Interleukins
6. Platelet derived growth factor (PDGF)
7. Endothelial cell growth factor
8. Von Willebrand factor

[II] Atrial natriuretic peptide (ANP): It is released from the atria in response to an increase in atrial pressure and causes relaxation of vascular smooth muscle, dilation of the arterioles, and decreased total peripheral resistance. It also increases excretion of salt and water by the kidney, which reduces blood volume and attempts to bring arterial pressure down to normal. It also inhibits renin secretion.

[C] Ions and other chemical factor:

[I] Ca⁺⁺ ions: An increase in Ca ion concentration causes vasoconstriction.

[II] K⁺ ions: An increase in K ion concentration causes vasodilatation due to inhibition of smooth muscle contraction.

[III] Mg⁺⁺ ions: An increase in Mg ion concentration causes vasodilatation by inhibiting smooth muscle contraction.

[IV] Na⁺ ions: An increase in Na ion concentration causes arteriolar dilatation due to an increase in osmolality of the fluid (as it also occurs when the blood glucose concentration is increased). Decreased osmolality causes arteriolar constriction.

[V] Acetate and citrate: They are the only anions that have vasodilator effect.

[VI] [H⁺]: An increase in hydrogen ion concentration causes dilatation of the arterioles. A slight decrease in hydrogen ions concentration causes arteriolar constriction, but an intense decrease causes dilatation.

[VII] CO₂: An increase in CO₂ concentration causes moderate vasodilatation in most tissues and marked vasodilatation in the brain. However, CO₂, acting on the vasomotor center, has an extremely powerful indirect vasoconstrictor effect that is transmitted through the sympathetic vasoconstrictor system.

Regulation of arterial blood pressure (BP): The basic relationship between arterial BP, cardiac output, and total peripheral resistance is: Arterial BP = C.O x total peripheral resistance. There are two main mechanisms for regulation of BP and these are:

[A] Rapidly acting mechanism (short-term regulation), which are rapid to begin acting, they begin to act within seconds and become fully active within a minute or so, and lose their capability for pressure control after few hours or a few days (adaptations mechanisms). None of them able to bring the arterial BP all the way back to normal. These mechanisms include:

Nervous pressure control mechanisms which include:

- [I] The baroreceptors feedback mechanism,
- [II] The central nervous system ischemic mechanism,
- [III] The chemoreceptor mechanism.

[B] INTERMEDIAT acting Mechanisms which begin to react within minutes and become fully active within 30 minutes to several hours and include:

- [I] The hormonal mechanism which include norepinephrine-epinephrine, vasopressin, and renin-angiotensin vasoconstrictor mechanisms.
- [II] Stress relaxation mechanism,
- [III] Capillary fluid shift.

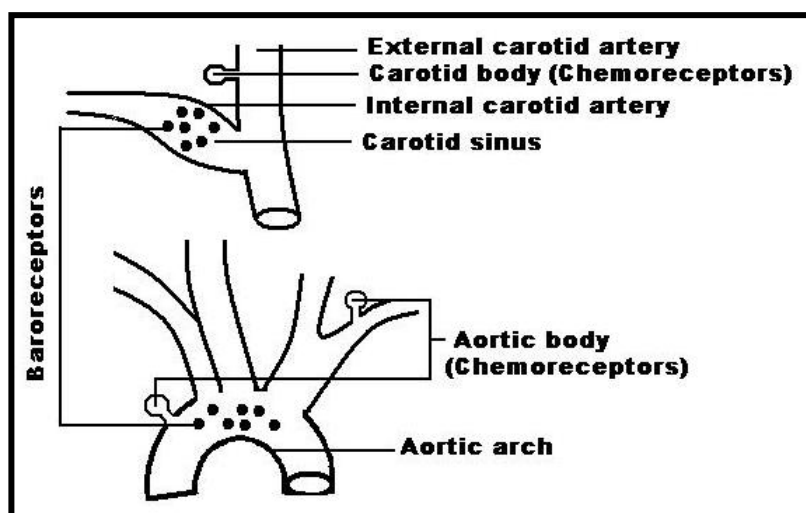
[C] Slow acting mechanism (long-term regulation), which are slow to begin acting and control the arterial BP over a period of days, weeks, months, and years. Their effectiveness becomes steadily greater with time (non adapting mechanisms), and able to bring the pressure all the way back to normal.

These mechanisms include.

- 1-renal-body fluid-mechanisms
- 2- the rennin angiotensine- aldosteron system.

[A] Rapidly acting mechanism (Short-term regulation):

1-The baroreceptors feedback mechanism:
This reflex is mediated by the baroreceptors located in the



carotid sinus at the bifurcations of the common **carotid arteries**, and their afferent nerve fibers pass to the **glossopharyngeal nerves**, and by the baroreceptors which are located along the **arch of the aorta**, and their afferent nerve fibers pass through the **vagi**.

This reflex is extremely rapid in response to change in arterial BP and is initiated by stretch receptors (baroreceptors) located in the walls of the large systemic arteries and veins (low pressure receptors that detect venous pressure changes as a result of blood volume changes).

A rise in pressure stretches the baroreceptors and causes them to transmit signals into the nucleus of tractus solitarius which is the sensory termination of both the vagal and glossopharyngeal nerves at central nervous system.

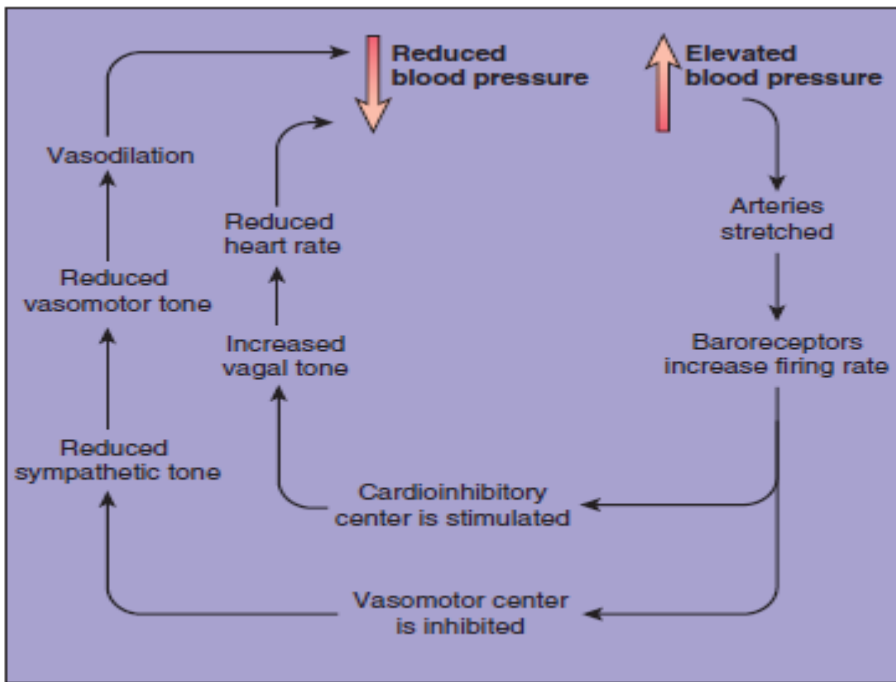
From this nucleus an inhibitory signals pass to the vasoconstrictor area of the VMC and an excitatory signals pass to the vagal (parasympathetic) center.

The feedback signals are then sent back through autonomic nervous system to the circulation to cause vasodilatation (decrease peripheral resistance), a decrease in heart rate and contractility. All will reduce arterial blood pressure downward toward the normal level.

The ability of the baroreceptors to maintain relatively constant arterial pressure is extremely important when a person sits or stand after having been lying down. Immediately upon standing, the arterial pressure in the head and upper part of the body obviously tends to fall, and marked reduction of this pressure can cause loss of consciousness. Fortunately, however, the falling pressure at the baroreceptors elicits an immediate reflex, resulting in strong sympathetic discharge throughout the body, and this minimizes the decrease in pressure in the head and upper body.

Baroreceptors adapt in one to two days to whatever pressure level they are exposed to. Therefore, they are of little or no importance in long-term regulation of BP.

Q1 –what occurs to person move from a supine to standing position?



Strong pressure on the neck over the bifurcations of the carotid arteries in human being can excite the baroreceptors of the carotid sinus, causing the arterial pressure to fall as much as 20 mm Hg in normal person and even a more marked reduction in BP and even stop the heart completely in older atherosclerotic patients which lead to fainting (carotid sinus syncope).

2-The central nervous system ischemic mechanism:

It acts when the BP decrease to or less than **60 mmHg** this will lead to decrease blood flow to VMC [ischemia] and accumulation of CO₂ which is a powerful stimulants to VMC to elevate BP by generalized vasoconstriction and increasing myocardial contractility. If ischemia not relieved within 3-10 minutes after maximum elevation of BP the VMC neurons become totally inactive and circulatory failure is the end result.

3-chemoreceptor mechanism: Whenever the arterial pressure falls below critical level, the chemoreceptors become stimulated because of diminished blood flow to the aortic and carotid bodies and therefore diminished availability of O₂ and excess CO₂ and H⁺ ions are not removed by the slow flow of blood. The signals from the chemoreceptors are transmitted to VMC to excite it, and this elevate the BP back toward normal level whenever it falls too low. Chemoreceptors mechanism start to operate when the arterial oxygen [po₂] falls **below 80** . also stimulation of respiratory center cause stimulation of the phrenic & costal nerves lead to increase rate & depth of respiration----- wash out of co₂.

[B] Intermediate acting mechanism.

1-Thenorepinephrine-epinephrine, vasopressin, and renin-angiotensin vasoconstrictor mechanisms: As described before.

2-Stress relaxation mechanism: A pressure change is associated with the same pressure changes in the most of the blood storage areas (veins). This causes vessels gradually to adapt to a new size, thereby accommodating the amount of blood that is available. Thus, following massive transfusion, the arterial pressure rises markedly at first, but because of relaxation of the circulation during the next 10 – 60 minutes the BP returns nearly to normal even though the blood volume may be as great as 30% above normal. Conversely, following prolonged bleeding, the reverse stress-relaxation mechanism can cause the blood vessels gradually to tighten around the amount of blood that is left, thereby again re-establishing nearly normal circulatory dynamics.

3-Capillary fluid shift: When the arterial pressure changes, this is usually accompanied by a similar change in capillary pressure. This causes fluid to begin moving across the capillary membrane between the blood and the interstitial fluid compartment. Within a few minutes to an hour a new state of equilibrium usually will be achieved in favor of increase blood volume with consequent increase in BP.

Increase BP--- increase capillary pressure --- fluid move from circulation to tissue thus reduction blood volume --- decrease BP.

Decrease BP --- decrease capillary pressure – fluid move from interstitial space to intravascular by osmosis ---- increase blood volume---- increase BP.

[C] Slow-acting mechanism (long-term regulation):

1-The renal-body fluid system for arterial pressure control:

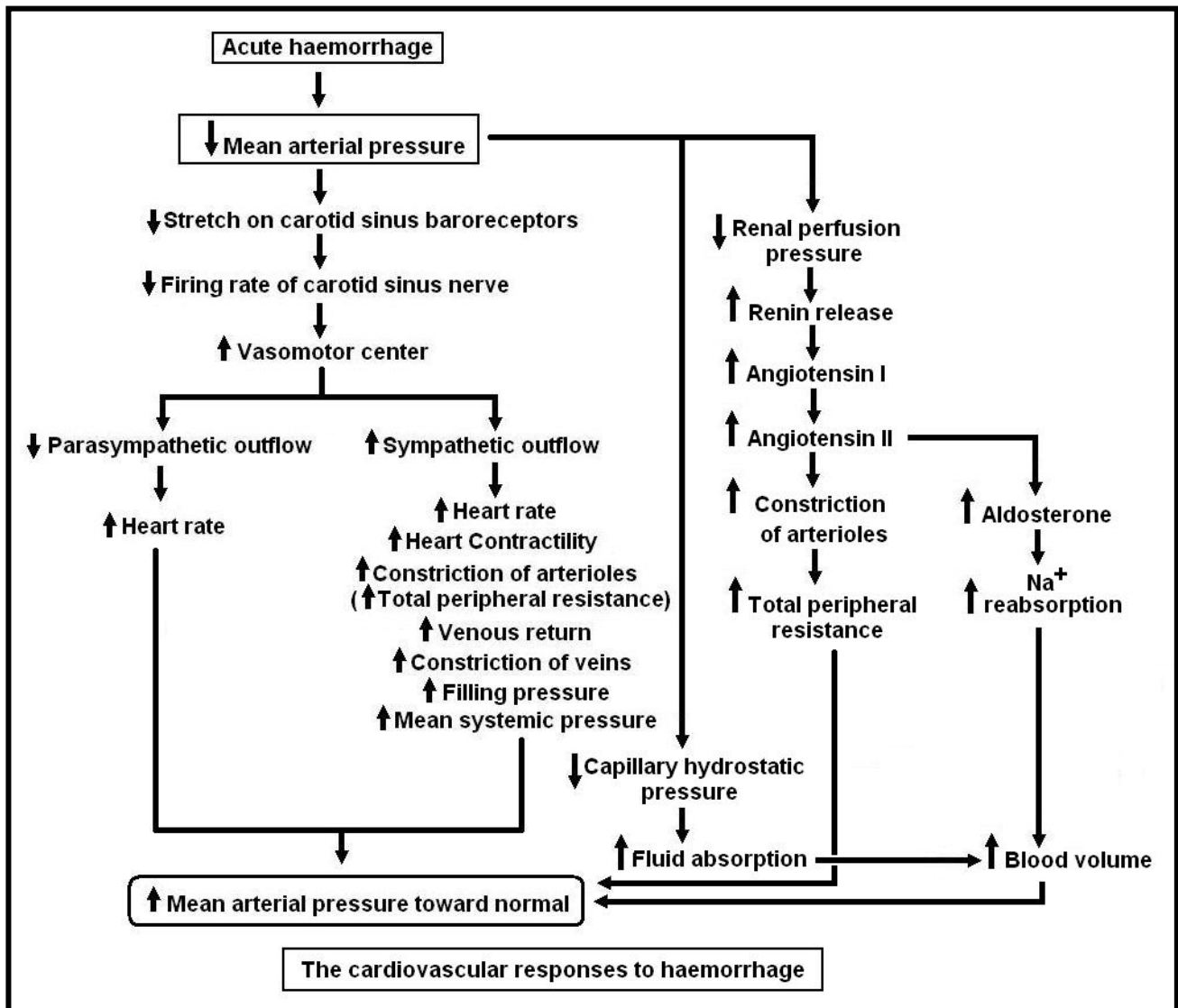
When the arterial pressure rises, the rise in pressure directly causes the kidney output of water and salt to increase markedly (pressure diuresis and pressure natriuresis). This in turn causes decreased extracellular fluid volume and decreased blood volume. The decreased in blood volume decreases the C.O by the heart, which returns the arterial pressure back to normal, and vice versa.

2-The renin-angiotensin-aldosterone system for arterial pressure control: This system operate as short-term and as long-term mechanism for regulating the arterial BP. When the arterial pressure falls too low, the renal blood flow decreases, and this trigger the release of renin as described before with consequent formation of angiotensin which has an immediate vasoconstrictor effect (short-term regulation) and long-term effects through:

[1] Angiotensin directly affects the kidneys to cause salt and water retention in the body.

[2] Angiotensin causes the adrenal glands to secrete aldosterone, which in turn directly affects the kidneys to cause salt and water retention.

Both these effects cause an increase in the extracellular fluid volume, with consequent increase in venous return and thus the C.O causing an increase in the arterial BP.



Circulation through special regions:

The pulmonary circulation: The vessels have much larger diameter and they are more distensible than their counterpart systemic vessels. Both these criteria give the pulmonary vessels a very large compliance to accommodate most of the stroke volume output of the right ventricle. The pressure in the pulmonary artery is about 25/8 mm Hg (with a mean arterial BP of 15 mm Hg). About 9% of the total blood is present in the lungs which can act as a blood reservoir. About half of this blood can be shifted to the systemic circulation when high pressure is built up in the lungs such as when blowing air out so hard or when there is haemorrhage.

The pulmonary circulation is able to accommodate greatly increased blood flow due to (1) high compliance of the pulmonary vascular bed and due to (2) opening of more and more of dormant capillaries. Both are important to conserve the energy of the right heart and to prevent a significant rise in pulmonary capillary pressure and therefore to prevent the development of pulmonary edema during the increased cardiac output such as in exercise. Furthermore, When one entire lung is removed, the flow of blood through the remaining lung usually is well within the limits of compensation as long as the patient

remains inactive. However, the patient thereafter has far less pulmonary circulation reserve than does the normal person, for if the cardiac output increases to more than 150-200 per cent above normal.

(3) The very low mean pulmonary capillary pressure (7 mm Hg) in comparison with the mean systemic capillary pressure (15 mm Hg) is the essential factor that prevents the development of the pulmonary edema. For the pulmonary edema to develop (as occurs in left heart failure), the mean capillary pressure must rise high enough to overcome the plasma colloid osmotic pressure. In addition, (4) the enlargement of the pulmonary lymphatic with consequent increase in lymph flow from the interstitial spaces that is associated with chronic elevation of pulmonary capillary pressure, gives another safety factor against the development of pulmonary edema.

An increase in the pulmonary vascular resistance with consequent increase in the pulmonary artery pressure can occur in:

[A] Heavy exercise of patients with one lung is removed.

[B] In patients with massive (closing pulmonary artery) or diffuse pulmonary embolism (blood, air, or fat emboli that close pulmonary capillaries).

[C] In emphysema [alveolar hypoxia] because the enlarged and damaged alveoli causing also a damage to the adjacent capillaries and impair gas exchange with air, consequently the air inside these alveoli is suffering from low oxygen (alveolar hypoxia), so that the adjacent blood vessels come continually under the influence of the local hypoxic stimulus, resulting in chronic vasoconstriction.

An increase in the pulmonary vascular resistance results in so called pulmonary hypertension which can cause right heart failure.

The cerebral circulation: The normal blood flow through the brain tissue of the adult averages **15%** of the total resting cardiac output. Local blood flow regulatory mechanism is much the same as that existing in many other circulatory areas of the body.

An increase in either the CO₂ or H⁺ ion concentration (the most important local vasodilators for the cerebral circulation) increases cerebral blood flow, whereas a decrease in O₂ concentration increase the flow.

The blood flow in each individual segment of the brain changes in response to changes in local neuronal activity of that segment. For example, simple clapping the hand causes an immediate increase in blood flow in the motor cortex of the opposite side of the brain.

Cerebral blood flow is **autoregulated extremely well between the pressure limits of 60-140 mm Hg** without a significant change in cerebral blood flow. In persons with hypertension, this autoregulatory range shifts to even higher pressure levels (such as 200 mm Hg). If the arterial pressure falls below 60 mm Hg, cerebral blood flow then becomes severely compromised, and if the pressure rises above the upper limit of autoregulation, the blood flow rises rapidly and can cause severe overstretch of the cerebral blood vessels, and even brain edema.

Under normal condition, **the sympathetic nervous system plays a minor role in regulating cerebral circulation**. However, sympathetic nervous system role in cerebral blood flow regulation becomes an important and significant only when the autoregulatory mechanism fails to compensate enough. For instance, when the arterial pressure rises to a very high level during any states of excessive circulatory activity, the sympathetic nervous system constricts the large and intermediate-sized cerebral arteries and prevents the very high pressure from ever reaching the smaller blood vessels, thus preventing the occurrence of a vascular haemorrhage into the brain (cerebral stroke).

Vasoactive substances in the systemic circulation have little or no effect on cerebral circulation because such substances are excluded by the blood-brain barrier.

The splanchnic circulation: It consists of [A] the portal circulation (the blood flowing through intestine and spleen and then courses through the liver) and [B] the arterial blood flow into the liver. The total hepatic blood flow is about 1450 ml/min, about 29% of the C.O, (1/4 is coming from the portal circulation and 3/4 is coming from the hepatic artery. The liver and spleen are large, expandable blood reservoirs capable of supplying extra blood in times of diminished blood volume. This is achieved by

sympathetic-induced vasoconstriction of the liver and spleen's large veins and sinusoids. In general the blood flow through the splanchnic circulation is controlled in almost exactly the same way as in most other areas of the body, mainly by local regulatory mechanisms.

The liver offers a moderate amount of resistance to blood flow from the portal system to the vena cava. As a result, the pressure in the portal vein averages 8-10 mm Hg, which is considerably higher than the almost zero pressure in the vena cava. When the blood flow through the liver is impaired as it occurs in **liver cirrhosis**, the portal venous pressure is increased to very high levels and large collateral vessels develop between the splenic and the esophageal veins (**esophageal varicosities**). In addition, the high pressure in the liver sinusoids tends to push fluids out of the hepatic vascular system through the surface of the liver and then to accumulate in the peritoneal cavity as a protein-rich free fluid called **ascites**.

Skin circulation: circulation through the skin sub serves two major functions: first, **nutrition** of the skin tissues and, second, **heat conduction** from the internal structures of the body to the skin, so that the heat can be removed from the body. To perform these two functions the circulatory apparatus of the skin is characterized by two major types of vessels:

[1] the usual **nutritive** arteries, capillaries, and veins.

[2] vascular structures concerned with **heating** the skin, consisting of an extensive subcutaneous venous plexus that is supplied by inflow of blood from the skin capillaries and from arteriovenous anastomoses.

Some skin areas such as the volar surfaces of the hands and feet, the lips, the nose, and the ears, contain many arteriovenous anastomoses, which makes direct communications between the arteries and the venous plexus bypassing the capillary bed. Since the blood flow through the skin is principally regulated by nervous mechanisms rather than by local regulation, which is opposite to the regulation in most parts of the body. The thermoregulatory center in **the hypothalamus** controls blood flow in the skin in response to changes in body temperature by two mechanisms:

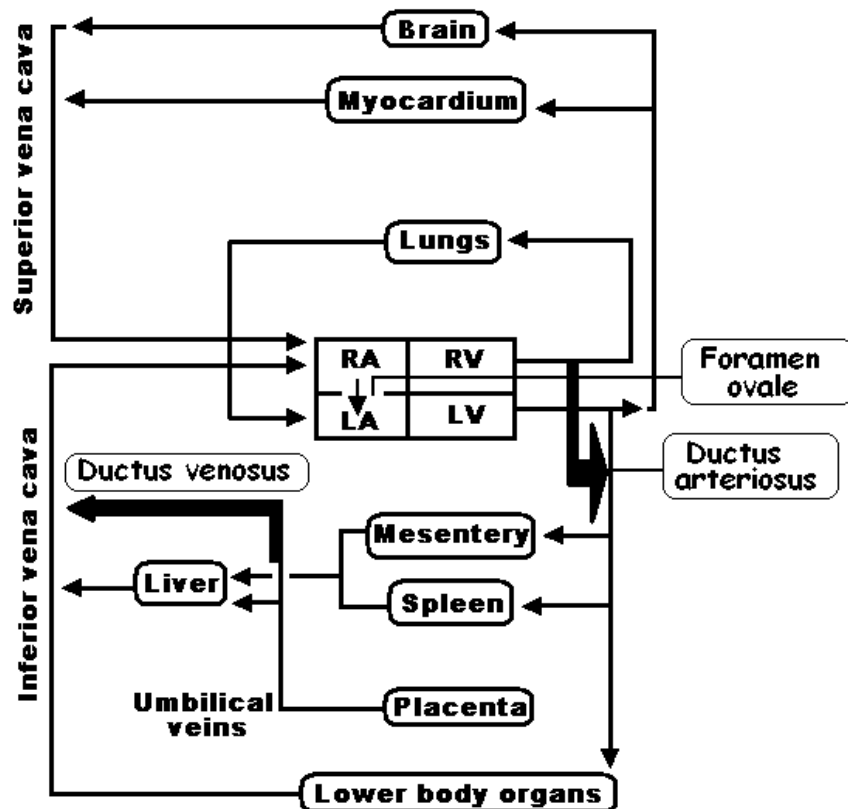
[1] A vasoconstrictor mechanism directly through noradrenergic sympathetic nerve fibers and indirectly through the effect of the adrenal catecholamine (epinephrine and norepinephrine).

[2] A vasodilator mechanism through the **cholinergic sympathetic nerve fibers that activate the sweat glands may cause a secondary vasodilatation.**

So Dynamic exercise causes a cutaneous vasoconstriction at exercise **onset** through increased vasoconstrictor activity, both in cool and warm conditions. As exercise continues, internal temperature reaches a threshold for increased **active vasodilator activity** that is elevated by exercise

Placental and fetal circulation: The blood flow of the uterus parallels the metabolic activity of the myometrium and endometrium and undergoes cyclic fluctuations that correlate well with the menstrual cycle in non pregnant women. During pregnancy, blood flow increases rapidly as the uterus increases in size. It has been suggested that estrogens act on the blood vessels to increase uterine blood flow in excess of O₂ needed.

The placenta is the lung, gastrointestinal tract, and the kidney of the fetus. Through placental villi, the nutrients and O_2 is taken up by the fetal blood and the waste products and CO_2 is discharged into the maternal circulation. Blood rich in oxygen and nutrients returns to the fetal body from the placenta in the umbilical veins. About 50% of blood flows from the umbilical veins to the inferior vena cava via **ductus venosus** while the other half flows to the portal sinus with the blood that is drained from the spleen and mesentery to enter the liver and then to the inferior vena cava. Inferior vena cava also



drains the blood from the lower part of the body. These blood streams do not mix but streamline alongside each other, with the well-saturated medial to the poorly saturated stream. About half the inferior vena cava return flows through the right atrium to the right ventricle. The remaining half, composed mainly of well-saturated blood, flows through the communication between the right and left atria, the **foramen ovale**, to the left ventricle. Thus shunting of umbilical venous blood across the ductus venosus and foramen ovale delivers high concentration of oxygen and nutrients primarily to upper body organs, which include the brain and heart of the fetus. Venous drainage from the upper body organs return to the heart in the superior vena cava. This blood, along with half the return from the inferior vena cava, is ejected by the right ventricle. Because pulmonary vascular resistance is very high in the fetus, most of right ventricular output bypass the pulmonary circulation and flows through the **ductus arteriosus** that communicates between the main pulmonary trunk and descending aorta and thus directed to the placenta. In this way, venous drainage from upper and lower body organs is shunted toward the placenta, where wastes are eliminated and oxygen and nutrients are acquired.

There are three important differences between the fetal and postnatal circulations.

[1] The fetal circulation is a parallel circuit, and the postnatal circulation is a series circuit.

[2] In fetus, the right ventricular output is double that of the left ventricular output and perfuse different portions of the peripheral circulation.

[3] By virtue of the large vascular shunts in the fetal circulation, pressures in the left and right ventricles are roughly equivalent, as are pressures in the aorta and pulmonary artery. Right atrial pressure is greater than left atrial pressure, so blood flows through the foramen ovale from the right to left atrium.

Immediately after birth, several events occur. Pulmonary ventilation and gas exchange are initiated, and the placenta is removed from the circulation. The environmental temperature decreases as the newborn leaves the warm, humid amniotic cavity for a drier, cooler environment. These events produce marked cardiovascular changes. With the initiation of pulmonary ventilation, pulmonary vascular resistance decreases drastically with consequent increase of pulmonary blood flow and a decrease of pulmonary arterial pressure. As a consequence, the quantity of blood flowing through the ductus arteriosus decreases, and pulmonary venous return to the heart increases. Left atrial pressure increases, and the foramen ovale closes functionally soon after birth. These changes reverse the blood pressure gradient

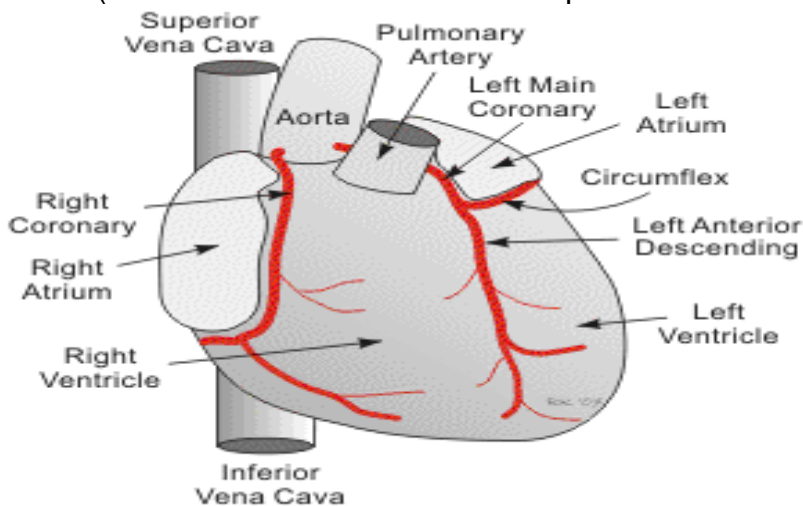
across the foramen ovale so that left atrial pressure exceeds right atrial pressure. Elimination of the placental circulation increases the systemic vascular resistance. The decrease in pulmonary vascular resistance and increase in systemic vascular resistance cause a separation of blood pressures in the aorta and pulmonary artery. With these changes, the parallel fetal circulation is transformed into a series circulation in the newborn. The foramen ovale and ductus arteriosus close within a few days after birth, and the ductus venosus closes within 7 to 10 days.

At birth, oxygen consumption increases by a factor of 2 to 3 because of the necessity of maintaining body temperature in a colder environment. In addition, heart rate and cardiac output increase.

NOTE. After birth --- ventilation—expansion of lung--- resistance to blood flow in pulmonary artery is decrease—increase blood flow to the lung.

Skeletal muscle circulation: The blood flow to the resting skeletal muscle is relatively low (3-4 ml/min/100 g) with only 10% of the capillary beds are perfused. This is sufficient to meet the basal metabolic needs of resting muscle. The blood vessels of the skeletal muscles are **controlled by extrinsic sympathetic innervation and by local metabolic factors (lactate, adenosine, and K^+)**. The blood vessels in skeletal muscles constrict in response to α_1 -adrenergic stimulation and dilate in response to β_2 -adrenergic or cholinergic stimulation. When skeletal muscle is active, neural influences on blood flow **are overridden** by powerful local metabolic control mechanism to increase the skeletal muscle blood flow as much as 25-fold in which all capillary beds are perfused. The primary regulators of skeletal muscle blood flow during exercise are **metabolic factors while at rest is sympathetic nervous system**. Vasoconstriction of skeletal muscle arterioles is a major contributor to total peripheral resistance (because of the large mass of skeletal muscle).

The coronary circulation: The coronary circulation shows considerable autoregulation, active and reactive hyperaemia. The resting coronary blood flow in the human being averages approximately 225 ml/min (about 5% of the total cardiac output)

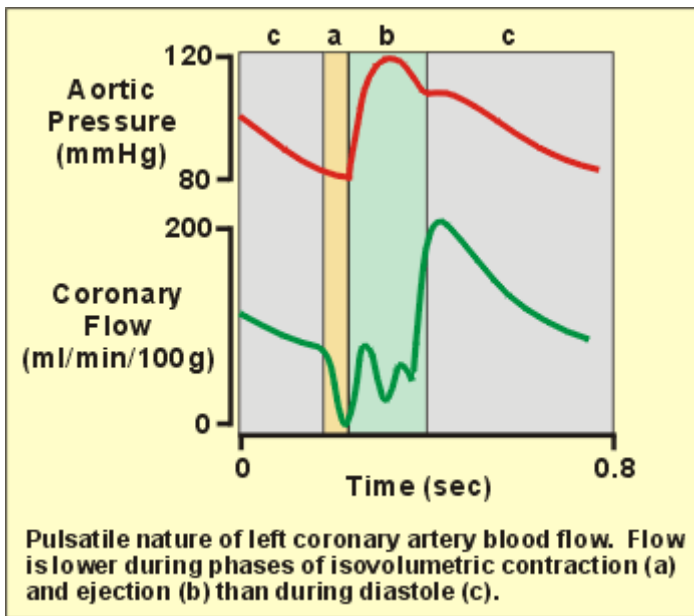


The major vessels of the coronary circulation are the left main coronary that divides into left anterior descending and circumflex branches, and the right main coronary artery. The left and right coronary arteries originate at the base of the aorta from openings called the coronary ostia located behind the aortic valve leaflets.

The left and right coronary arteries and their branches lie on the surface of the heart, and therefore are sometimes referred to as the epicardial coronary vessels. These vessels distribute blood flow to different regions of the heart. Capillary blood flow enters venules that join together to form cardiac veins that drain into the coronary sinus located on the posterior side of the heart, which drains into the right atrium.

The following summarizes important features of coronary blood flow:

- 1-Flow is tightly coupled to oxygen demand. *oxygen consumption*. whenever cardiac activity and oxygen consumption increases, there is an increase in coronary blood flow (active hyperemia) that is nearly proportionate to the increase in oxygen consumption.
- 2-Good *autoregulation* between 60 and 200 mmHg perfusion pressure helps to maintain normal coronary blood flow whenever coronary perfusion pressure changes due to changes in aortic pressure.
- 3-*Adenosine* is an important mediator of active hyperemia and autoregulation. It serves as a metabolic coupler between oxygen consumption and coronary blood flow. Nitric oxide is also an important regulator of coronary blood flow.
- 4-Activation of sympathetic nerves innervating the coronary vasculature causes only transient vasoconstriction mediated by α_1 -adrenoceptors. This brief (and small) vasoconstrictor response is followed by vasodilation caused by enhanced production of vasodilator metabolites (active hyperemia) due to increased mechanical and metabolic activity of the heart resulting from β_1 -adrenoceptor activation of the myocardium. Therefore, sympathetic activation to the heart results in coronary vasodilation and increased coronary flow due to increased metabolic activity (increased heart rate, contractility) despite direct vasoconstrictor effects of sympathetic activation on the coronaries. This is termed "functional sympatholysis."
- 5-Parasympathetic stimulation of the heart (i.e., vagal nerve activation) elicits modest coronary vasodilation (due to the direct effects of released acetylcholine on the coronaries). However, if parasympathetic activation of the heart results in a significant decrease in myocardial oxygen demand due to a reduction in heart rate, then intrinsic metabolic mechanisms will increase coronary vascular resistance by constricting the vessels.
- 6-Progressive ischemic coronary artery disease results in the growth of new vessels (termed angiogenesis) and *collateralization* within the myocardium. Collateralization increases myocardial blood supply by increasing the number of parallel vessels, thereby reducing vascular resistance within the myocardium.



7-Extravascular compression (shown to the right) during systole markedly affects coronary flow; therefore, most of the coronary flow occurs during diastole. Because of extravascular compression, the endocardium is more susceptible to ischemia especially at lower perfusion pressures. Furthermore, with tachycardia there is relatively less time available for coronary flow during diastole to occur – this is particularly significant in patients with coronary artery disease where coronary flow reserve (maximal flow capacity) is reduced.

In the presence of coronary artery disease, coronary blood flow may be reduced. This will increase oxygen extraction from the coronary blood and decrease the venous oxygen content. This leads to tissue hypoxia and angina. If the lack of blood flow is due to a fixed stenotic lesion in the coronary artery (because of atherosclerosis), blood flow can be improved within that vessel by 1) placing a stent within the vessel to expand the lumen, 2) using an intracoronary angioplasty balloon to stretch the vessel open, or 3) bypassing the diseased vessel with a vascular graft. If the insufficient blood flow is caused by a blood clot (thrombosis), a thrombolytic drug that dissolves clots may be administered. Anti-platelet drugs and aspirin are commonly used to prevent the recurrence of clots. If the reduced flow is due to coronary vasospasm, then coronary vasodilators can be given (e.g., nitrodilators, calcium-channel blockers) to reverse and prevent vasospasm.

