Special Circulations

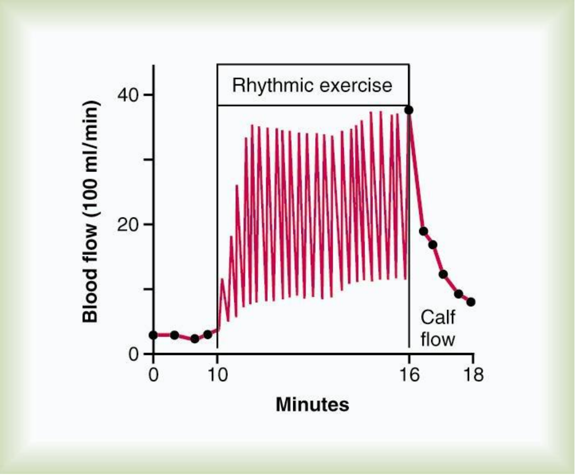
Objectives

- Describe the control of blood flow to different circulations (Skeletal muscles, pulmonary and coronary).
- Point out special hemodynamic characteristics pertinent to each circulation discussed.

- You know that the tissues' blood flow is basically regulated by a local control, with other few exceptions (by nervous system).

Blood flow in skeletal muscles

- During relaxation of the body, and although they constitute about 40% of the body weight, skeletal muscles' blood flow is about 1 liter/min which is minimal. This, however, changes during exercise. There are two types of exercise; isotonic and isometric. In the first, the length of the muscle changes and the tension is constant, and in the second, the length is constant and the tension changes. We are concerned about the isotonic (rhythmic) exercise (e.g. jogging/raising an object while moving parts of the body) in which there is an alteration between contraction/relaxation (here we mean by relaxation the part of skeletal muscle'smechanical phases during exercise that is different from the "relaxation" term used while describing the exercising state of the body). During relaxation of the muscle, there is increase in blood flow, while during contraction; there is decrease in blood flow because the vessels are constricted.But in any case, the blood flow does not decrease less than the basal line(relaxation of the body) even when the exercising muscles are in their relaxation phase (notice the chart). Notice that the **average** blood flow (average line between the contraction/relaxation phases) during exercise is much greater than in the relaxing state of the body.



Local regulation

- The main contributor in the increase in blood flow during isotonic exercise is the local vasodilation. There is an increase in metabolic rate and oxygen consumption during exercise to produce and consume ATP (thus more adenosine consumption). Also, there is more CO_2 production and thus, more vasodilators. The mean arterial pressure does not increase during exercise (the heart rate is what increases), because the local vasodilation causes the resistance to reduce and overcome the increased cardiac output, thus preserving the blood pressure from increasing. This occurs in the isotonic contraction, and the increased flow **due to increased metabolic rate** is called **active hyperemia**.

- On the other hand, isometric contraction (e.g. keeping the weight lifted in front of your head) causes a significant increase in the blood pressure (much greater than the effect of the heart rate), because the vessel's wall is compressed due to the great continuous increase in tension in the muscle fibers surrounding the vessel. The vasodilators accumulate in the ECF and cannot be washed out due to the compression. After releasing the exercise's effect, the compression on the arteries is relieved and the vasodilators that were collected during exercise cause the flow to greatly spontaneously increase. This is called **reactive hyperemia**. When the vasodilators are washed away, the blood flow returns to normal levels.

- Reactive hyperemia is different the reperfusion injury (e.g. after thrombotic occlusion) that causes damage to the cells, particularly to the mitochondria.

- The blood flow may increase in variable amounts depending upon many factors. For example, athletes may have their cardiac output increase up to 35 liters/min (or maybe up to 20-folds) during exercise. Most of thisblood is directed towards the muscles and the heart, and next are the lungs, and significantly decreased blood goes to the GIT.

- In the skeletal muscles, the increased demand of oxygen is overcome by increasing the extraction ratio (which is different from the heart where the increased demand is only overcome by increasing the blood flow because the extraction ratio is already at its maximal level - 75%). The arterial blood contains about 15-16g of hemoglobin per 100 ml; each 1 gram of Hb carries about 1.34g of oxygen. Thus, there are about 20 grams of oxygen per 100 ml of blood (the venous blood carries about 15 grams of oxygen per 100 ml of blood). During relaxation, the extraction ratio in the skeletal muscles is about 25%, thus, about only 5 grams of oxygen are extracted by the muscle. However, the extraction ratio is increased during exercise up to 75%.
- In the capillaries, the density increases; the precapillary sphincter opens (the vasomotion - that is achieved by means other than smooth muscles since they are not present in the capillary wall - is being towards the opening of the capillaries not towards the closure), and the flow is increased.

- Most blood flow occurs between contractions (during relaxation phases of the rhythmic contraction).
- Decreased oxygen during exercise also affects vascular smooth muscle **directly** (vasodilation). Other vasodilators include: **adenosine**, K^+, osmolality, and nitric oxide (EDRF).

Nervous regulation

- Sympathetic effect causes vasoconstriction (mainly by norepinephrine) in order to maintain the cardiac output (protection against a probably high oxygen demand that may exceed the cardiac pumping ability).

- In animals, muscles have **β**-receptor vasodilators that are not significant in humans (except for the liver). The main vasodilator in humans is adenosine. **α**-receptors are also important for vasoconstriction in order to maintain the cardiac output in its required amounts.

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Blood flow to the brain

- The main vasodilator in the brain is CO_2. When it accumulates, it also stimulates the vasomotor center as well as the chemosensitive areas that also stimulate the respiration (stimulating the central chemoreceptors that are different from the peripheral chemoreceptors located in the carotid sinus and the aortic arch). The peripheral chemoreceptors are sensitive **mainly** to the lack of oxygen besides the increase in CO_2 but the central ones are sensitive to CO_2 and H^+ (H^+ is produced by carbonic anhydrase enzyme that is present in plenty amounts in the brain (**$CO_2 \alpha H^+$**)much more than oxygen lack. Actually, hydrogen ions are the main stimuli in the brain because - and although they cannot cross the BBB -almost all CO_2 is converted to hydrogen ions inside the brain. This means that the brain is highly sensitive to changes in pH.

- Blood flow to brain should be kept constant (as neurons are intolerant to ischemia like the myocardium). Myogenic theory applies here; when the mean arterial pressure decreases, vasodilation occurs, and when the MAP increases, vasoconstriction occurs to keep the blood flow constant. The decrease in MAP is limited to 60 mmHg; if it drops to less than that, ischemia occurs causing syncope (fainting). Ischemia induces CNS ischemic response that causes extremely massive sympathetic effect trying to save the brain. On the other hand, the increase in MAP is limited to 160 mmHg and more than that is dangerous (brain edema or fatal bleeding).Between 60-160 mmHg, the blood flow is constant.This mechanism is called **autoregulation** of the brain.

Blood flow to the skin

- It is suggested that the skin is the only part of the body in which the blood flow's regulation is achieved by nervous means.
- Its importance is due to the fact that it is the main regulator of temperature. The flow is considerably regulated based on temperature changes in addition to supplying nutrients to the cells.
- It is controlled by sympathetic system. When the sympathetic is stimulated, this causes vasoconstriction, and this causes less blood flow to the skin, less heat production and thus, preserving temperature (white skin in the winter). However, if the sympathetic is inhibited, vasodilation occurs and causes more blood flow to the skin, more heat loss, more sweating, and thus, lowering the temperature (red skin in the hot weather).
- Sympathetic control is initiated by temperature receptors (T receptors) and by the CNS.
- The skin constitutes a blood reservoir.
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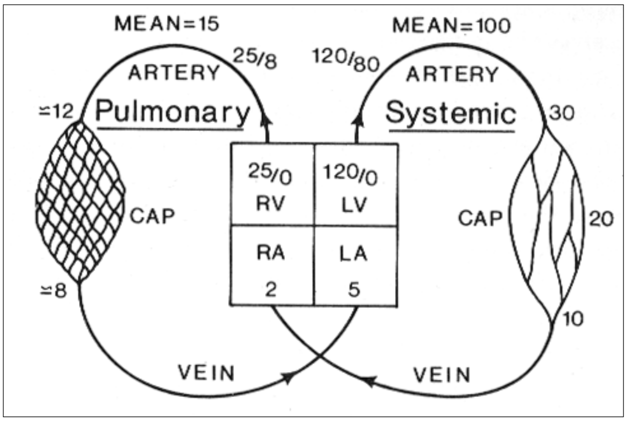
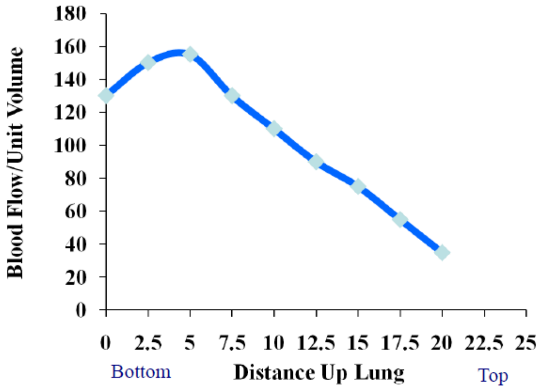
Pulmonary circulation

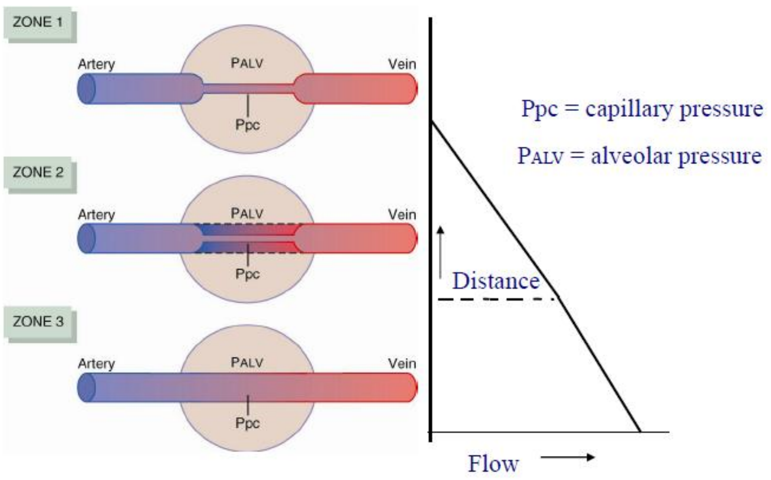


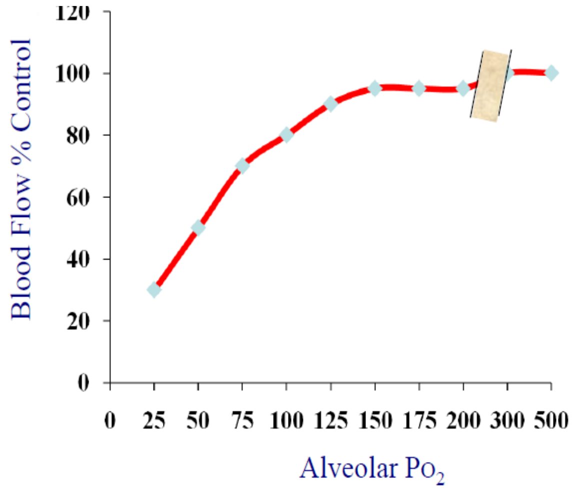
- The lungs receive as much blood as the peripheral systemic circulation (same cardiac output comes from the left ventricle **or** the right one).
- The systolic pressure of the pulmonary trunk is about 25 mmHg, while the diastolic is 5 mmHg (compared to 120/80, 120/0, 25/0 in the aorta, left ventricle, and right ventricle respectively).
- The MAP in the systemic circulation is about 100 mmHg, while in the pulmonary is **roughly** 15 (1/3*25 + 2/3*8).
- In spite of the differences in the previous pressure figures, both circulations receive the same amount of blood and this is because the **resistance** in the pulmonary vessels is about 1/6 of their counterparts in the systemic (CO = MAP/R>>> so when the MAP in the pulmonary is 1/6 of the systemic, the resistance is also 1/6, and this causes the ratio (CO) to remain constant).
- Vessels in the pulmonary circulation have the same divisions as the systemic (large arteries, medium, small, arterioles ...) but they are **shorter** and their walls are thinner.
- The relationship between oxygen level and blood flow regulation is opposite to the other tissues. When the alveolar oxygen levels are high, vasodilation of the surrounding vessels occurs in order to increase the blood going to the capillaries and getting oxygenated. But if the levels of oxygen drop and CO_2 is in high amounts inside the alveoli, vasoconstriction occurs in order to avoid wasting of the blood without getting oxygenated.
- Oxygen passes by simple diffusion, and no energy needed.

- The blood flow to the lungs is also affected by the distance from the part of the lung to the heart. The flow is high in the bottom of the lungs and is low in the higher parts of them in the standing position. This is due to gravity effect, and also because of the changes in the alveolar pressure. The alveolar pressure (P_{alv}) is high in the upper parts of the lungs, so it causes compression on the vessels and lowering of the blood flow, while the lower parts have lower P_{alv} and thus, less compression on the vessels and more blood flow. Systole/diastole phases have a role as well.



***CHECK THE FOLLOWING CHARTS**





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Blood flow to the heart

- The heart is considered as one of highest organs in terms of blood flow per 100g (the kidney is very high but that is because it is a part of its function, and the adrenal/thyroid glands are also very high because of their extremely tiny mass). The heart receives about 250 ml/min.
- At rest, the extraction ratio of the heart is at its maximum (75%); it is not 100% because the blood is moving (flowing), so if it stops, the ratio may reach 100%. The only way to meet any increase in oxygen demand is to increase the blood flow because the extraction ratio cannot be increased more than 75%.
- Aortic pressure and ventricle pumping are what mainly affect the coronary circulation.
- The two coronaries originate from the aorta just after its origin. (Do not forget to check the anatomy portion in the slides.)
- During systole, the coronaries are compressed, thus no flow is there and the stored myoglobin supplies the oxygen in this period. Vasodilators accumulate in this phase (because they cannot overcome the strong compression of the coronaries).
- During diastole, the oxygen and nutrients are being transported to the heart muscle; vasodilators that accumulated during systole cause a high transient blood flow just after systole (mainly in the early diastole phase by the mechanism of reactive hyperemia). Then the blood flow goes down after the metabolites are washed out.
- Right ventricle has less decrease in blood flow during systole than the left ventricle, supposedly because the pressure is lower in the right ventricle. This is suggested to be a contributor in the more common infarcts in the left ventricle as the decrease in blood flow during systole is greater.
- Right coronary has less increase in blood flow than the left coronary during diastole.

- In catheterization, the catheter is inserted in the femoral artery and goes upwards to reach the aorta, then the die is injected and it goes to the coronaries. An X-ray is taken and the results are monitored.

Coronary vasculature plexuses

- There are two main plexuses in the heart; the epicardial and subendocardial arterial plexuses.
- During systole, the epicardial plexus is compressed due to the high pressure in the ventricles.
- During early diastole a large amount of blood goes to the coronaries.
- The subendocardial plexus's area is more prone to infarction, particularly because it is the first to be affected by coronary occlusion as it is the last and the least to receive blood. Intraventricular pressure plays a role as well.

- We can bypass the occlusion of the coronaries by an operation called **coronary artery bypass grafting (CABG)**. A graft is taken from somewhere else (e.g. saphenous vein), and it is inserted between the aorta and a point just after the occluded part.

- The CABG operation is done when the catheterization reveals that more than 3 vessels are occluded. If less than 3, other techniques are used. One of which is angioplasty, where a balloon at the end of the catheter is inserted in the occluded part (e.g. atheroma) and is inflated to lyse the occlusion. This has recently been replaced with stents that are used in a similar way. These stents may contain additional thrombolytic agents and anticoagulants that are released slowly.

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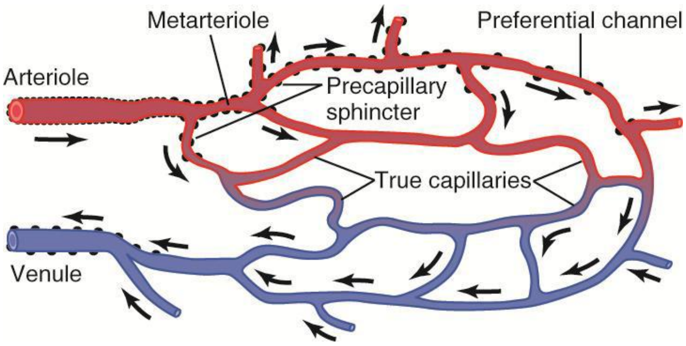
Microcirculation and Edema

Objectives

- Point out the structure and function of themicrocirculation.
- Describe how solutes and fluids are exchanged in capillaries.
- Outline what determines net fluid movementacross capillaries.

- Precapillary sphincter is important in regulation of blood flow to the capillaries; it has a vasomotion activity that is directed towards opening/closure of the capillary network.
- Remember that capillaries are unicellular in thickness, and they do not have smooth muscles in their walls unlike arterioles and large venules. There are continuous, fenestrated, and opened (discontinuous) capillaries.

- Microcirculation (in the capillaries) is important in the transport of nutrients to tissues. It is also a site of waste products removal.Over 10 billion capillaries with surface area of 500-700 square meters perform function of solutes and fluids exchange.



- Three main capillary exchange mechanisms are described:
1- Diffusion: for gases, such as oxygen and CO_2.Most plasma proteins cannot cross by diffusion; except in the sinusoids.
2- Transcytosis.
3- Bulk flow: based on pressure gradient; if the move is from the plasma towards the interstitial fluid, it is called **filtration**, and if it is from the interstitial fluid towards the plasma, it is called **reabsorption**.Reabsorption normally equals filtration with a very small extra filtrate that goes to the lymph.

- Net filtration pressure = (Blood hydrostatic pressure + Interstitial fluid osmotic pressure) - (Blood colloid osmotic pressure + Interstitial fluid hydrostatic pressure)
NFP = (BHP + IFOP) - (BCOP + IFHP)
- When we multiply NFP by the filtration coefficient (K_f), we get the filtration rate (ml/min).
- BHP and IFOP promote filtration, while BCOP and IFHP promote reabsorption.
- Edema can be caused by many factors; such as increased hydrostatic pressure or decreased plasma proteins' levels (due to liver/kidney diseases).

- "Microcirculation and Edema" slides are required, but the doctor had no time to explain all of them.