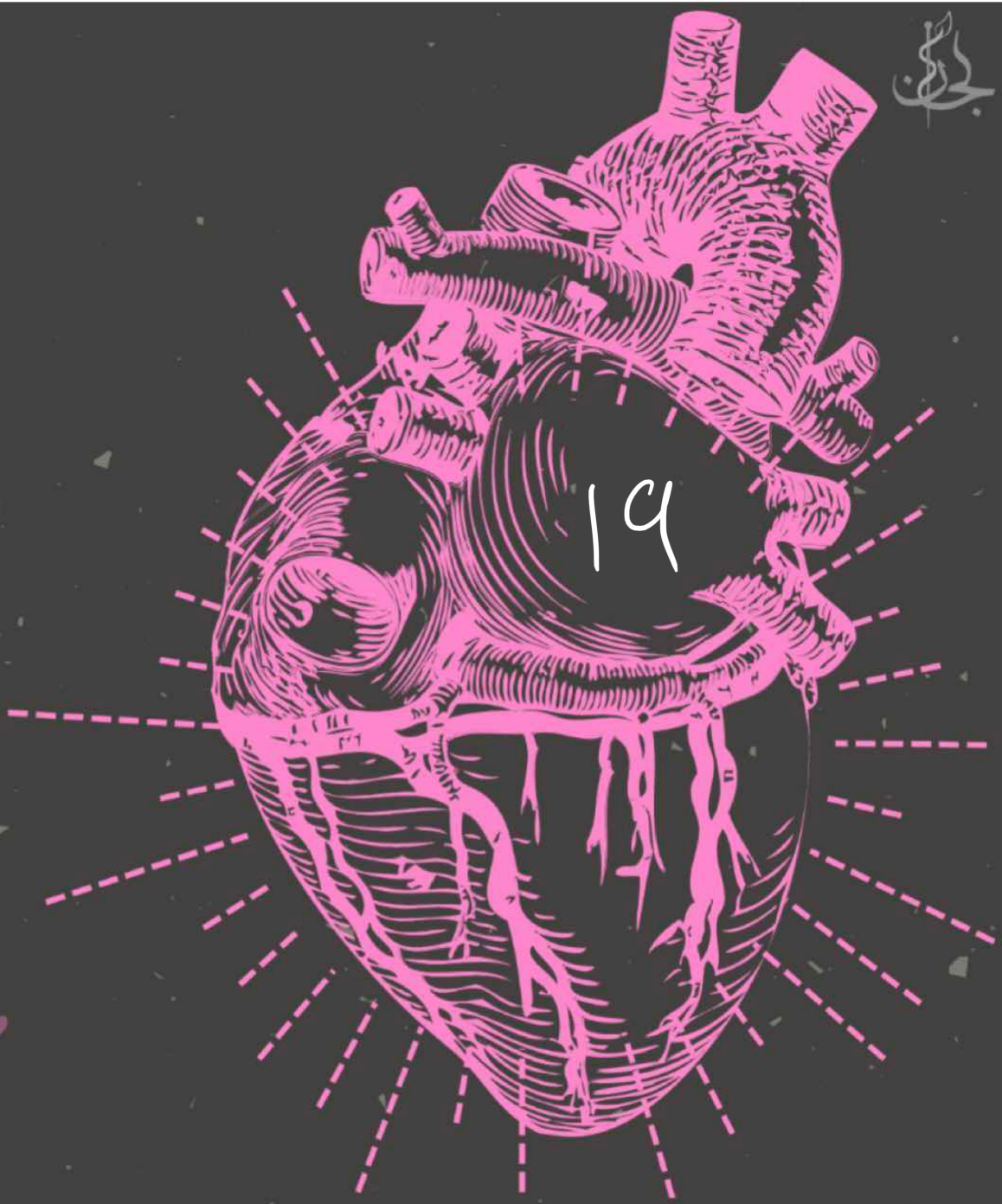
CVS



PHYSIOLOGY

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In this sheet we'll be talking about tissue blood flow control. Have fun.

Control of Tissue Blood Flow

Introduction: Each tissue regulates its own blood flow just proportional to its needs. These needs decrease or increase depending on the metabolic rate of tissues. This regulation mechanism where the tissue itself controls its blood flow is called autoregulation

-More blood needed → causing vasodilation of arterioles

-Less blood needed → causing vasoconstriction of arterioles

Why do tissues need blood supply?

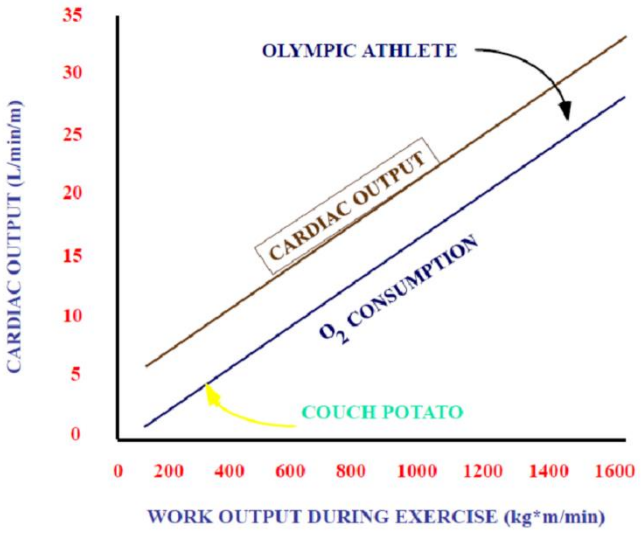
1) Delivery of oxygen to tissues

2) Delivery of nutrients such as glucose, amino acids, etc.

3) Removal of carbon dioxide, hydrogen, and other metabolites from the tissues

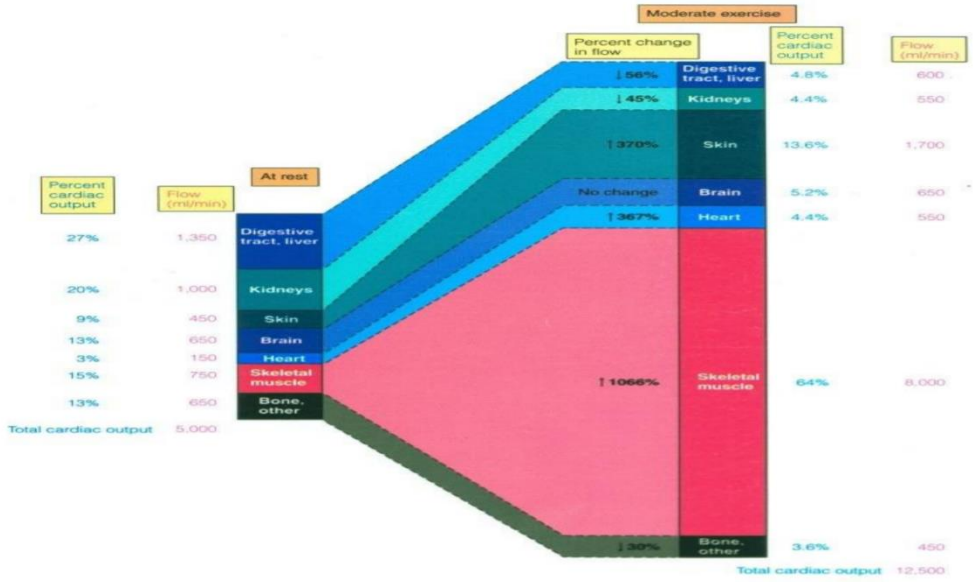
4) Transport various hormones and other substances to different tissues

Remember: There is a linear positive relationship between cardiac output and O2 consumption. During exercise, there will be an increase in the metabolic rate of the tissues, which causes an increase in the O_2 consumption. So, to compensate that increasing demand, we will have more blood flow to the tissues, meaning more cardiac output.
-Athletes have high O_2 consumption compared to lazy people (couch potatoes).



-We have also talked about the figure below that represents cardiac output during rest and exercise. Cardiac output during rest is around 5L, but during exercise it might reach 12L. During rest, skeletal muscles do not receive much blood. However, during exercise, most of blood (more than 8L) is going to the skeletal muscles.

Blood flow to the heart also increases. Skin blood flow will increase as well but this time it is for the sake of body temperature control, not O_2 delivery. On the other hand, flow to the GI tract decreases dramatically.



Remember: The heart is one of the most O_2 – consuming organs in the body. You may say: oh yeah but thyroid gland and adrenal glands have higher numbers in this table. Keep in mind that these are tiny glands with small masses, so they receive much more blood than what they actually need. What about kidneys? It receives blood for filtration and NOT for O_2 supply.

Variations in Tissue Blood Flow

	Per cent	ml/min	ml/min/ 100 gm
Brain	14	700	50
Heart	4	200	70
Bronchi	2	100	25
Kidneys	22	1100	360
Liver	27	1350	95
Portal	(21)	(1050)	
Arterial	(6)	(300)	
Muscle (inactive state)	15	750	4
Bone	5	250	3
Skin (cool weather)	6	300	3
Thyroid gland	1	50	160
Adrenal glands	0.5	25	300
Other tissues	3.5	175	1.3
Total	100.0	5000	---

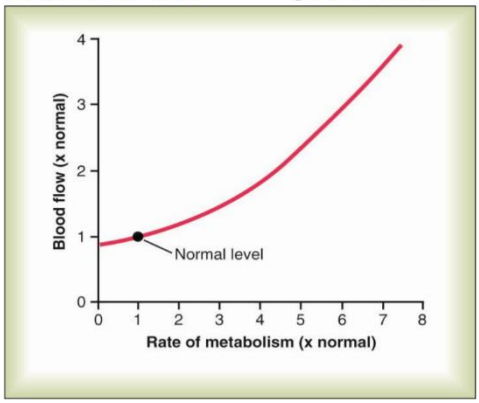
Acute Control of Local Blood Flow

The control is happening at the level of the tissue. The blood flow will change if we have:

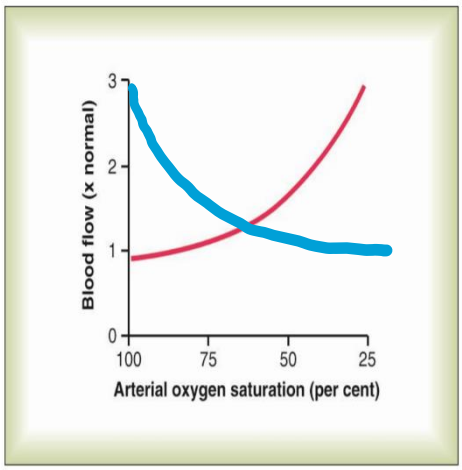
1- Changes in tissue metabolism: Increases in tissue metabolism lead to an increase in blood flow. More metabolism → more oxygen needed → more blood flow→ increase in the **CO** because it is the sum of all blood flow in the tissues.

2- Changes in the O_2 availability in tissues: Decreased oxygen availability to tissues increases tissue blood flow as you can see in this figure. When the rate of metabolism increases, decreased PO_2 and increased PCO_2 are witnessed.

↑ Tissue Metabolism ⟶ ↑ Blood Flow



↓ Tissue Oxygen Concentration ⟵ ↑ Blood Flow



Note: The x-axis is going in a descending way from 100 to 25. If it was the opposite, the curve will flip like THIS
If the numbers are normal but pCO_2 is plotted on the x-axis instead of pO_2, the curve will also look like THIS. So please pay attention to numbers and variables.

Ohm's law

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

We can explain this acute control by two theories:

A- *The vasodilator theory:* if we want to change the flow, the most important factor is to change the resistance either by vasodilation (decreasing resistance) or vasoconstriction (increasing resistance). Remember that resistance is mostly affected by **radius *r***.

So, what does this theory say?

-When there is an increase in the metabolism of the tissues, there is a release of certain substances which are considered vasodilators. As a result, we will have a decrease in resistance and consequently an increase in the blood flow. At first, scientists thought that only one of these local vasodilators can cause dilation but then they found that they must work together and one of them cannot do anything by itself. These vasodilators include: Adenosine, CO_2, Lactic acid, ADP compounds,

Histamine, K^+ ions, H^+, prostacyclin, bradykinin and Nitrous oxide (NO) with the last two being the most important ones in heart tissue.

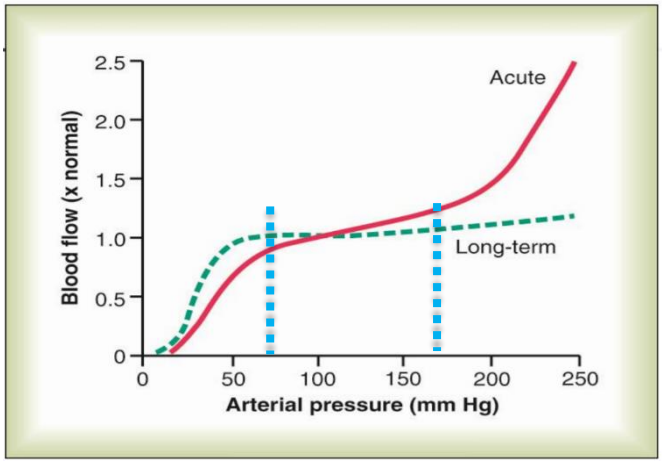
Remember: Adenosine is formed as a result of energy consumption.
ATP → ADP → AMP → Adenosine

B- *Oxygen Demand Theory:* As we said before, when there is an increase in metabolism, there is an increase of O_2 demand and O_2 supply won't be enough anymore. This causes vasodilation and thus increasing blood flow.
Very important in the heart.

Extra: This theory is related to the sympathetic control of blood vessel diameter. Aka. Vasomotor tone.

Autoregulation of Blood Flow During Change in Pressure

It is the ability of a tissue to maintain blood flow relatively constant over a wide range of arterial pressures. As you can see in the figure, for example, the blood flow to the tissue is almost (not 100%) constant along with varying blood pressure from 60 to 180.



How can we explain this regulation? Again we have two theories:

A- Metabolic theory: it is basically the same as the vasodilator theory.
B- Myogenic theory: states that when the pressure decreases, the stretch at the blood vessels decreases that will cause decrease in the permeability of smooth muscles to Ca^{+2}, and this will cause vasodilatation as well as increased blood flow.

Certain tissues have other mechanisms such as the kidneys which depend on a feedback loop between tubules and arterioles. The blood flow to the brain is controlled by CO_2 and H^+ (so it's somewhat related to the metabolic theory)

We can explain the myogenic theory using LaPlace's law

Laplace's law

$$Tension = Distending\ Pressure \times Radius$$

So, if we have high pressure, we have high tension. In order to return this tension to its normal value we reduce the radius by vasoconstriction. Makes sense, right?

For the first while yes. But, unfortunately, on the longer term, it won't make sense anymore because we will enter a vicious circle (حلقة مفرغة). Increased pressure will cause vasoconstriction which causes further increase in pressure and so on. So, we can say that myogenic theory in not accurate 100% and works to a certain extent only.

Long-Term Regulation of Blood Flow

We might need this type of regulation in chronic increased metabolism such as in ***hyperthyroidism.*** *Long-term regulation can be achieved by:*

A- Change in tissue vascularity:

This can be done by changing the size and number of vessels. Oxygen is an important stimulus for regulating tissue vascularity. The development of new blood vessels is called angiogenesis.

Angiogenesis occurs due to angiogenic factors that could be released from:

1) Ischemic tissues (ischemia is the main stimulus for angiogenesis)

2) Rapidly growing tissues (in tumors)

3) Tissue with high metabolic rates

**Most angiogenic factors are small peptides such as vascular endothelial cell growth factors (VEGF), fibroblast growth factor (FGF), and angiogen.*

Clinical correlation: The blood vessels of the eye are fully developed by the time of delivery. However, some babies are born pre-term, and they are put in neonatal incubator. In this incubator, ***the O_2 concentration is 100%.*** *After 3-4 weeks the baby will get out from the incubator and go home. But, after a month or two, his parents might bring him back to you, saying that he cannot see. What could have happened to that baby? When this baby was in the incubator, he adapted to 100% O_2 concentration. As he got out and faced 21% O_2 concentration which is the atmospheric O2 conc., his body will consider this (20% O_2 conc.) as if there is ischemia, and that will cause the stimulation of blood vessels formation in the front of the retina, end up with a blind baby. This process is called retro-lental hyperplasia. There is no treatment, but we can prevent this case from happening by Weaning (gradual decrease in incubator's O_2 before the baby gets out) from 100% to 90% to 80% and so on until we reach 20%.*

B- Development (opening) of collateral circulation

If a specific blood vessel that supplies a certain tissue is **blocked** for any reason leading to decreased blood supply to that tissue, collateral circulation develops and opens in a chronic manner (it takes a long time). This explains why MI is fatal in young people. These people have no history of ischemia or partial blocks, so their bodies have not developed collateral circulation yet. However, adults can survive MI because they most likely have been exposed to a partial block before in their lives.

Humoral Regulation of Blood Flow

A- Vasoconstrictor agents:

- Norepinephrine and epinephrine → systemic
- Angiotensin → systemic
- Vasopressin → systemic
- Endothelin → local

B- Vasodilator agents:

- Nitric oxide
- Bradykinin → local
- Serotonin
- Histamine
- Prostaglandins

They are both produced by endothelial cells. The balance between them is determined by tissue's need of O_2

Local and systemic

The doctor talked about muscle and skin circulations but I didn't mentioned them here because they are explained in the next sheet

Good Luck!!