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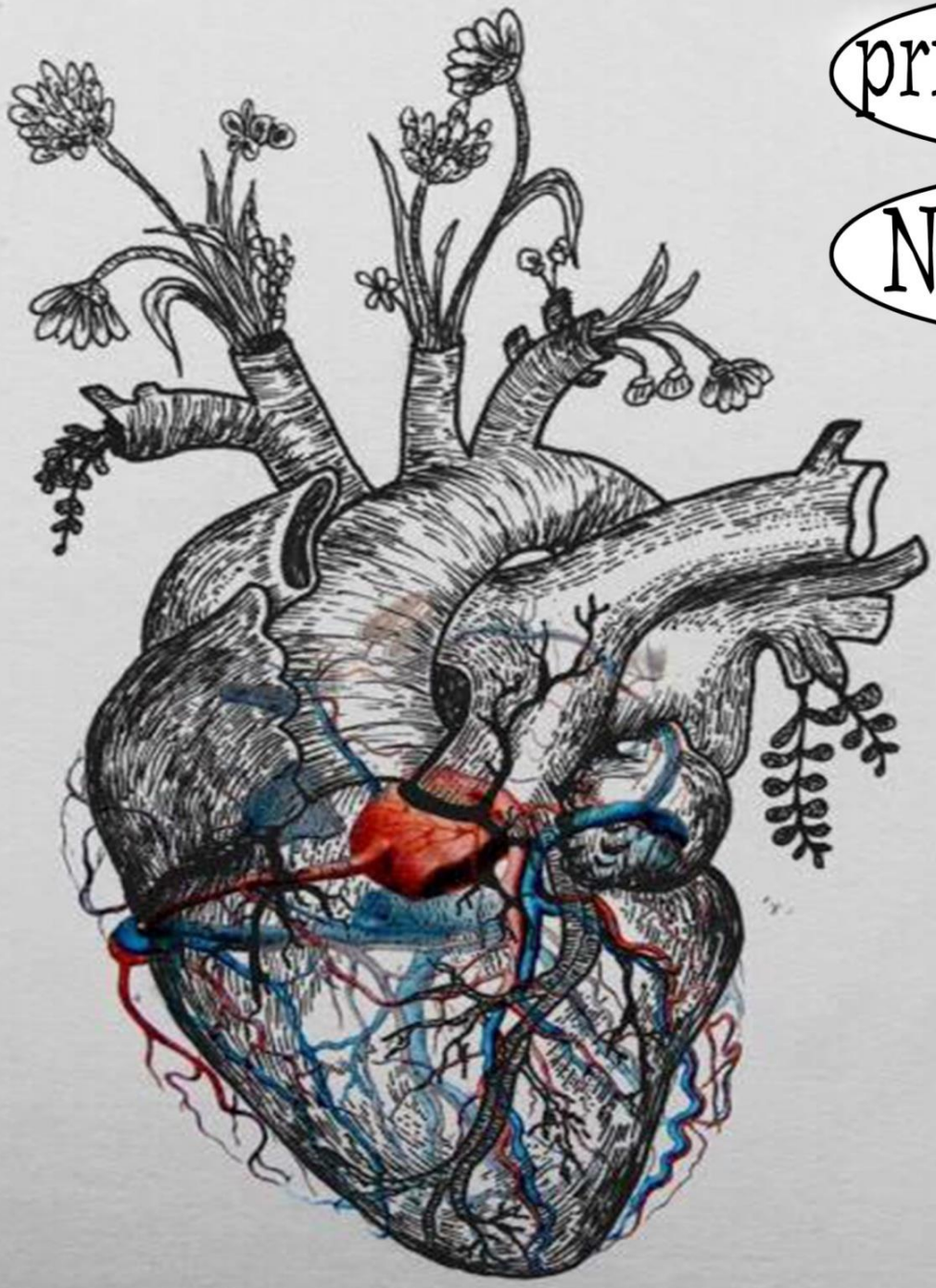

CVS

Physiology #10

sub-system

lecture: Local Blood flow to tissues

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Local Blood Flow to Tissues

Why do we need to regulate the blood flow??

Can't we just have high blood flow to all of our tissues?? (Why don't we have constant, high, and enough blood flow to all of our tissues permanently???)

Because this leads to a high **load on heart**. The heart can't tolerate this load. So we must shift the blood flow from one type of tissue to another **depending on the need of the tissue (metabolic rate of the tissue).**

Lecture objectives :-

1. Describe the local mechanism that controls blood flow to tissues, including acute and long-term control.
2. Discuss the metabolic and myogenic theory for control of blood flow
3. Discuss the changes that can develop in long-term regulation, including tissue vascularity, angiogenesis, and collateral circulation.
4. Discuss humoral regulation of blood flow, by vasoconstrictor and vasodilator agents.

LECUTRE'S OBJECTIVES IN COURSE

e.g.: During exercise blood flow to the muscles increases, while blood flow to GIT decreases.

We have two mechanisms of regulation:

1. **Acute control**: used in sudden short term changes. Ex: exercise, anxiety, & during eating a meal. **Rapid changes** within seconds to minutes.

2. **Long Term Control**: ex. People who live at high altitude. **Slow** controlled changes over days, weeks, or even months.

The Acute Regulation

Rapid changes in local vasoconstriction or vasodilation of vessels.

I. **Vasodilator theory**: Vasodilator theory states that the greater the rate of metabolism or the less availability of oxygen or some other nutrients to a tissue, the greater the formation of vasodilator substances in those tissue cells.

Oxygen and nutrients are believed to diffuse into the tissues where a high metabolic rate is present to increase blood flow. Lack of oxygen is the stimulus. It stimulates the tissues to secrete vasodilators.

Lack of oxygen →**vasodilator** → vasodilation → ↑ blood flow

Vasodilator substances:

- CO_2
- Hydrogen ion (H^+)
- Histamine
- Adenosine
- adenosine phosphate compounds
- Bradykinin
- Nitric oxide

II. **Oxygen lack theory**: Smooth muscles of blood vessels need oxygen to contract. So if there is no oxygen there will be no contraction (vasodilatation).

Cyclic opening and closing of the precapillary sphincters is called **vasomotion**.

Which means: lack of oxygen → smooth muscles can't contract (no enough oxygen) → vasodilation →↑blood flow.

During exercise skeletal muscles will have hypoxia because they use all of their oxygen. This will cause vasodilatation. But the GIT will be inactive so there will be abundancy of oxygen which will cause vasoconstriction. Exactly the opposite will happen after a meal.

After a meal (ex: mansaf)	Exercise
GIT → vasodilatation. skeletal muscles → vasoconstriction.	GIT → vasoconstriction. skeletal muscles → vasodilatation.

Both mechanisms **(vasodilator theory & Oxygen lack theory)** act ***together***. They work at the same time. These mechanisms are called the ***metabolic mechanisms***. The next two topics are examples of the metabolic mechanisms.

Now if we apply pressure on an arm, this causes reduction (almost absolutely) of the venous return. This causes congestion of the arm tissue and a bluish color due to hypoxia. When you remove the pressure the venous return goes back to normal. We call that **reactive hyperemia**. This leads to

- ➔ Increase in blood
- ➔ Change in color
- ➔ Warm skin because metabolism is high

We need to check this point ☺

Reactive hyperemia is the process in which blood flow is drastically increased after a blockage. When blood supply to a tissue is blocked whether for a few seconds or for hours, **reactive hyperemia will occur once the blockage is removed.** The flow will be approximately 4-7 times the normal blood flow and its duration is directly proportional to duration of the blockage. This compensates the period that the tissue wasn't supplied by blood.

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Active hyperemia: like when we do exercise or when any tissue needs more blood. (GIT after meal) This is because the tissue becomes active.

- ❖ ↑ metabolism
- ❖ ↓ oxygen in tissue
- ❖ vasodilatation
- ❖ ↑ blood flow

Active = ↑ activity of tissue

Reactive = reaction to the blockage (obstruction) of blood flow (happens after reperfusion)

During exercise most of the GIT capillaries will be closed (by precapillary sphincters), but not all of them, why? Because tissue needs continuous blood supply even it is at rest.

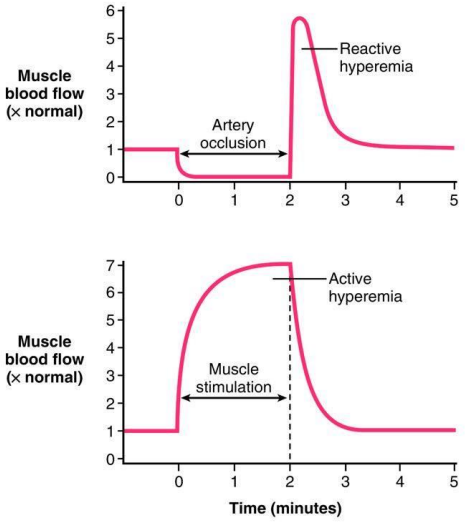

Figure 17-4. *Reactive hyperemia* in a tissue after temporary occlusion of the artery supplying blood flow and *active hyperemia* following increased tissue metabolic activity.

Autoregulation

In any tissue of the body, a rapid increase in arterial pressure causes an immediate rise in blood flow. However, within a minute or two, the blood flow in most tissues returns almost to the normal level, even though the arterial pressure is kept elevated. This return of flow toward normal is called autoregulation.

Autoregulation: regulation of **blood flow** by contraction of the smooth muscles of blood vessels (vasoconstriction) when there is a sudden increase in blood pressure. (not hypertensive patients)

Autoregulation works better when the pressure is between 50 (or 70 in the book, not that much difference) and 175. Look at the two horizontal lines. Between these two values the flow won't change more than 30%. Sudden increase between these values **smooth muscles will adapt** to these changes.

Would that happen when we exercise? NO because there is a real need for oxygen in this condition, which leads to more consumption of oxygen → vessels can't vasoconstrict (metabolic theory).

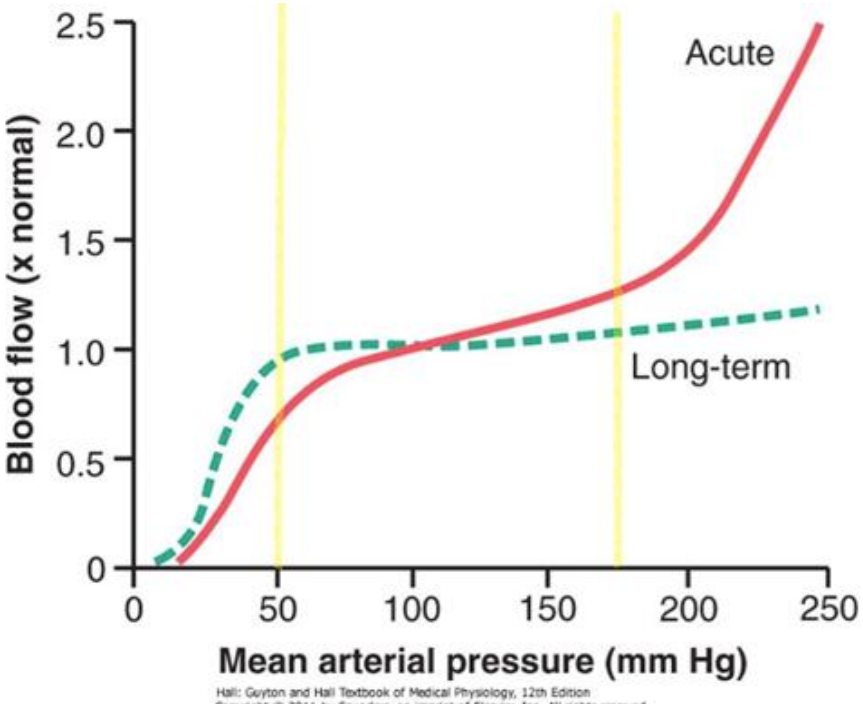

Figure 17-4 Effect of different levels of arterial pressure on blood flow through a muscle. The *solid red curve* shows the effect if the arterial pressure is raised over a period of a few minutes. The *dashed green curve* shows the effect if the arterial pressure is raised slowly over a period of many weeks.

There are two proposed views to explain the mechanism of autoregulation, the **metabolic theory and the myogenic theory**. The ***metabolic theory*** follows the basic principles of blood flow regulation. When the arterial pressure becomes too great, the excess flow provides too much oxygen and nutrients to the tissues (so the muscles can contact), in turn "washing out" the vasodilators released by the tissues. The increase in oxygen and decrease in vasodilator substances leads to vasoconstriction which will fight back the increased pressure thus causing blood flow to tissues to return back to its normal state. The ***myogenic theory*** is based on the observation that a sudden stretch of the small blood vessels (logically increase the pressure leads to stretch of vessels) causes the smooth muscles of the vessel walls to contract. The reaction opposes the action of the increased arterial pressure therefore causing vasoconstriction and aiding the return to the normal blood flow state.

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In sudden decrease in blood pressure the reaction must be vasodilatation, but in physiology reduction of blood pressure is very rare except in **postural** hypotension (when we stand up suddenly, and it lasts for a minute or two). {Not important}

In arterial rupture we usually lose the patient, because arterial side has low volume with high blood pressure. So losing blood from artery causes severe hypotension. However venous bleeding has less severity because veins have more volume and less pressure so we can save the patient.

Endothelial Derived Relaxing Factor (EDRF) = Nitric oxide

- Released from endothelium.
- Secreted mainly from small and medium arteries rather than large arteries.
- Causes vasodilatation, and it is very potent (powerful) vasodilator.
- Its metabolism time is only for few seconds.

Some scientists used it as drug for hypertension, what was the feedback from the patient for this drug? The patient feels that his/her sexual activity increased. Nowadays this drug is called Viagra or Cialis (manufactured nitric oxide), the metabolism for these drugs is much longer than nitric oxide. Now they use Cialis (sildenafil) to increase the erection (sexual activity) for 72 hours, but Viagra lasts for only 4 hours.

Nitric oxide is a strong vasodilator, so why do patients develop hypertension?! Actually people who develop hypertension will have a thickened endothelium that can't excrete normal amounts of nitric oxide. This may be due to atherosclerosis.

People who use antihypertensive drugs are advised not to take nitric oxide analogs with antihypertensive drugs, because it exacerbates hypotension.

Short duration and other side effects (the patient will feel warm) not convenient to the patient. That's why it isn't used as an antihypertensive.

In atherosclerosis nitric oxide analogs are not that much useful. This is because the arteries are very rigid so even with nitric oxide the vasodilation is not that much useful. **Beta-blockers are much useful**, because they at least prevent vasoconstriction.

Q: Does vasoconstriction cause an increase in flow ?

A: No, this is definitely wrong, because the diameter of the vessel is reduced so the flow will be reduced. Unlike velocity which will increase when we reduce the diameter.

We finished acute regulation of the blood pressure.

Long Term Control

Happens when the metabolic demands of a tissue changes. So the need changes in the vessels. Like people who live at high altitude, they have permanent hypoxia. So how do they adapt to this condition?

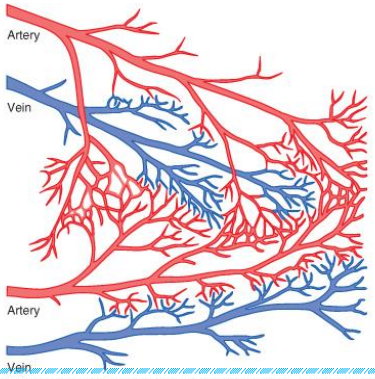
By persistent dilation of blood vessels. This is a ***structural change*** of the blood vessel. Which is the first mechanism of long term blood flow control.

Second one is ***angiogenesis*** which is formation of **new blood vessels**. Like when there is a tumor. This tumor is a new tissue so it needs blood vessels to supply them by nutrients which will stimulate angiogenesis. This happens due to hypoxia in these new tissues.

{Large tissue mass → hypoxia → secretion of **angiogenin** → angiogenesis }

Third one is development of the ***collaterals***

Collaterals: are branches of arteries that supply the same tissue. (a tissue which has two supplement of blood from two different vessels) Collaterals are present normally, but they are not opened. They open when there is a need of them. The best example is the coronary circulation. There is a connection between the branches of the coronary arteries. They open when there is a need for them, like sudden heart attack or with age. Also another important factor is exercise, which might stimulate opening of these collaterals. That's why the myocardial infraction risk is related to age. The **younger** the age is the **higher the risk of**



losing the patient is, because the **collaterals are yet not developed**. Collaterals can replace the obstructed vessel.

Collaterals can develop in **acute** (sudden blockage) or **long term** (high altitude or gradually obstruction).

Premature Birth:

For a reason or another some babies are born before full maturation. To save these babies, they must be put in incubators. Previously they gave these babies pure oxygen to help them with breathing, until surfactant is well developed they get them out of incubators. At that time the oxygen will be reduced from 100% to 21%. This stimulates the babies' tissues to form new blood vessels (angiogenesis) which causes blindness. This is due to angiogenesis in retina. Nowadays pure oxygen is not being used. The incubator is at 30% of oxygen saturation that allows the baby to breathe well and prevent side effects of pure oxygen.

Retrolental fibroplasia is the formation of new blood vessels in the retina due to sudden change in oxygen availability.

The last mechanism of controlling blood flow:

The Humoral control

Control by substances secreted or absorbed into body fluid such as hormones and locally produced factors.

1. VASOCONSTRICTOR AGENTS

- NOREPINEPHRINE AND EPINEPHRINE
- ANGIOTENSIN II: ANGIOTENSIN I is a very mild vasoconstrictor that's why we don't put it here. While ANGIOTENSIN II is a **very strong** one.
- VASOPRESSIN
- ENDOTHELIN : Very powerful vasoconstrictor, released from the injured endothelium.
- CALCIUM : stimulate smooth muscle contraction.
- INDIRECT EFFECT OF CO_2.

2.VASODILATOR AGENTS

- BRADYKININ
- HISTAMINE
- POTASSIUM, MAGNESIUM, HYDROGEN ION AND CO2

When CO2 is increased it will increase the concentration of hydrogen ions (by combination of CO_2 with water the disassociation to hydrogen ion and carbonate), which will in turn increase the acidity. This will cause vasodilation.

Hypoxia → ↑ CO_2 ($CO_2 + H_2O \rightarrow HCO_3 + H^+$) → vasodilation.

The most powerful stimulus for blood flow to the brain is H^+ then CO_2 then O_2.

CNS ischemic response.

Severe increase in CO2 will cause indirect vasoconstriction. This happens when there is a shock (bleeding mainly). There is a reduction of blood pressure and cardiac output. This means that there is low blood flow to the brain. Primarily, this will cause vasodilatation. Later on it will stimulate the sympathetic system for ***generalized vasoconstriction except in the brain.*** This will collect all of the blood all over the body to save the brain. This is called The Last Dish.

> An increase in carbon dioxide concentration causes moderate vasodilation in most tissues but marked vasodilation in the brain. Also, carbon dioxide in the blood, acting on the brain vasomotor center, has an extremely powerful indirect effect, transmitted through the sympathetic nervous vasoconstrictor system, to cause widespread vasoconstriction throughout the body.
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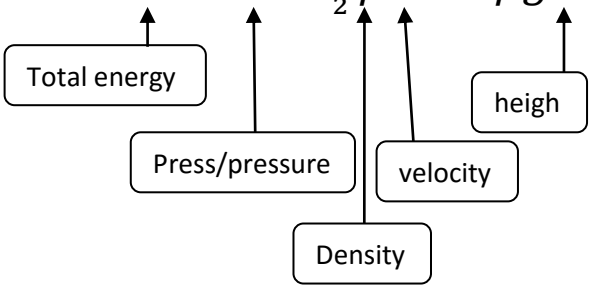
➔ **CO2**

- **Direct** = vasodilator when there is ***mild*** increase
- **Indirect** = vasoconstrictor when there is ***severe*** increase

We will talk about the shock in one lecture.

The formula is from the previous lecture :-

$$W = P + \frac{1}{2}\rho v^2 + \rho g h$$



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