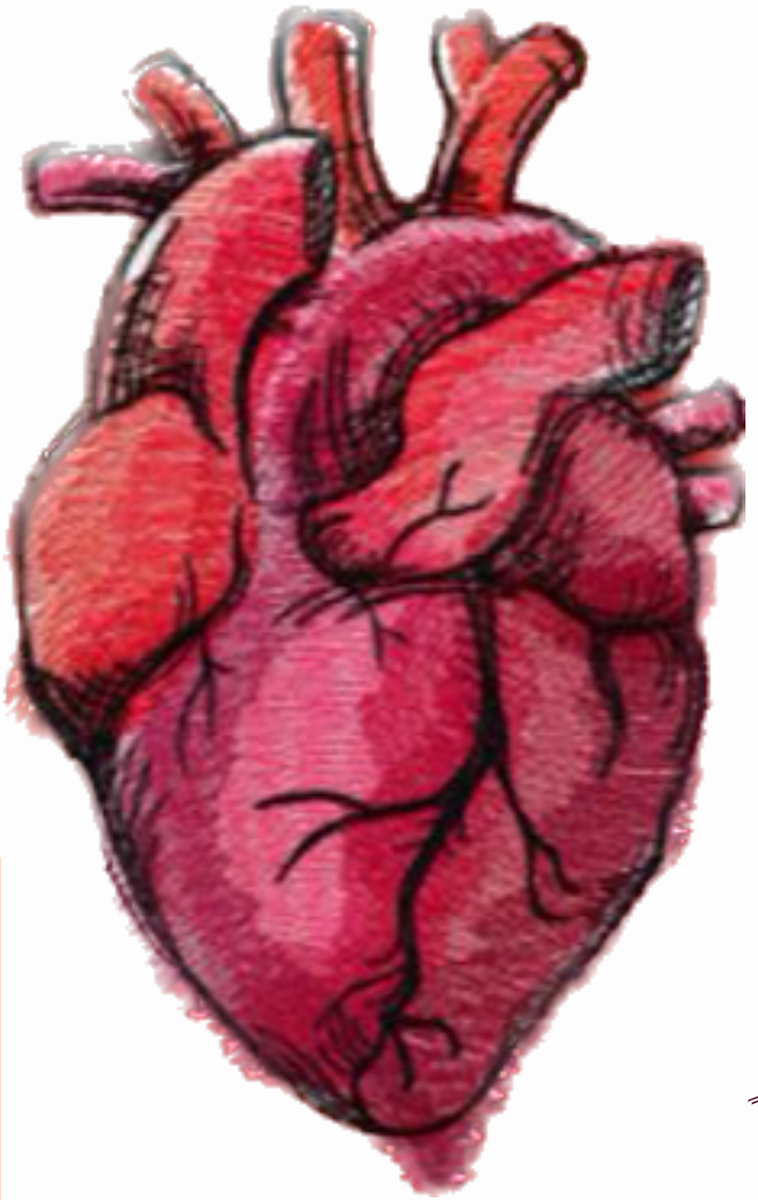


النادي الطبي

CARDIOVASCULAR SYSTEM

SUBJECT : physiology

LEC NO. : 11

DONE BY : Abdullah Bani Mustafa

وَقُل رَّبِّ زِدْنِي عِلْمًا

SCAN ME!

Regulation of organ blood flow

Prof. Said Khatib

Regulation Of Blood Flow To Tissues

Relevant Weekly Objectives:

- Explain the nervous and hormonal mechanisms designed to regulate the blood flow to tissues.

Lecture Objectives:

By the end of the lecture the students should be able to:

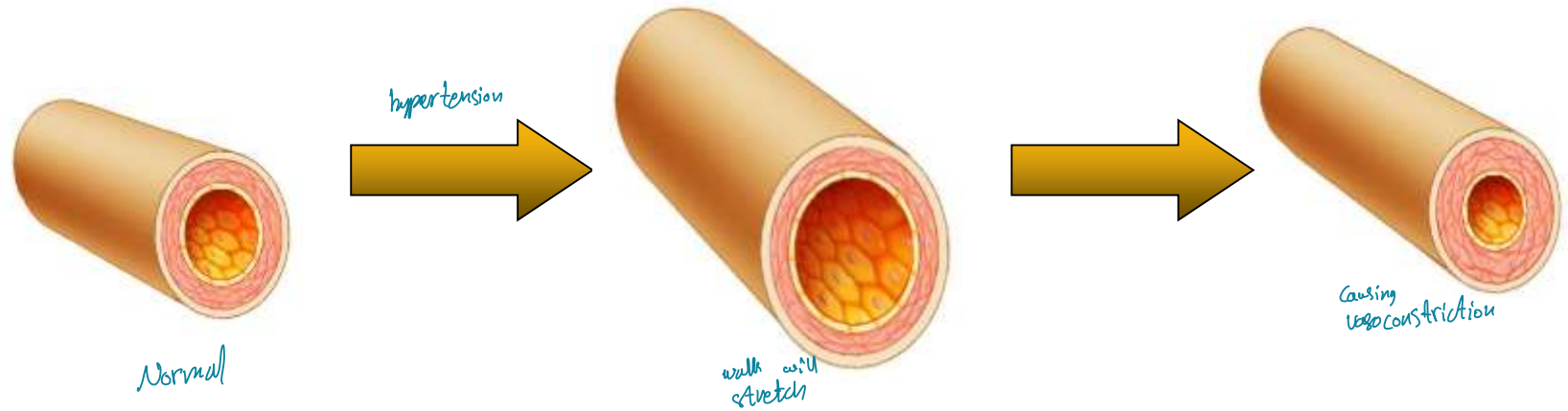
- Describe the pre-capillary regulatory mechanisms, local metabolites and other factors controlling capillary blood flow level.
- Describe the role of arteriolar smooth muscles and local metabolites in controlling local blood flow.
- Describe the Endothelium dependent mechanisms of local blood flow regulation.
- Explain the role of autonomic nervous system on blood flow regulation and the effects of circulating hormones on blood flow control.

I. Myogenic Mechanism

when blood pressure increases the arterioles will stretch causing an increase in tension in the walls of arterioles and it will trigger vasoconstriction

"Bayliss effect"

The smooth muscles contract or relax in response to change in wall tension



- When the lumen of a blood vessel is suddenly expanded, the smooth muscles respond by contraction in order to restore the vessel diameter and resistance; (the reverse is also true).

how the stretch result a reflux → only in smooth & cardiac muscles it's suddenly stretch Ca^{+2} channels will open & Ca^{+} concentration will be increase causing contraction of the wall of arterioles

- The stretch causes depolarization activates membrane calcium channels, which leads to increase cytosolic calcium and eventually contraction of vascular smooth muscle fibers.

Metabolic Mechanisms

vasodilator theory

Potassium ions leak out from the cells where there is a present myocardial infarction & them will accumulate around the muscular cells & this will affect the resting membrane potential & this accumulation of it will cause relaxation in the wall of the arterioles

- Increased metabolism results in:
- Availability of O2 and nutrients
- Leads to release of local metabolites:
  - **Adenosine.** → specially in cardiac muscle
  - **Potassium ions.** → outside the cell
  - **Histamine**
  - **Carbon dioxide.**
  - **Hydrogen ion.**
  - **Lactic acid.** acidosis

comes from ATP → ADP → AMP → A → very strong vasodilation on arterioles ↓ this is very common in the myocardium infarction produced by ATP causing vasodilatation in coronary arteries

} → Vasodilation → locally

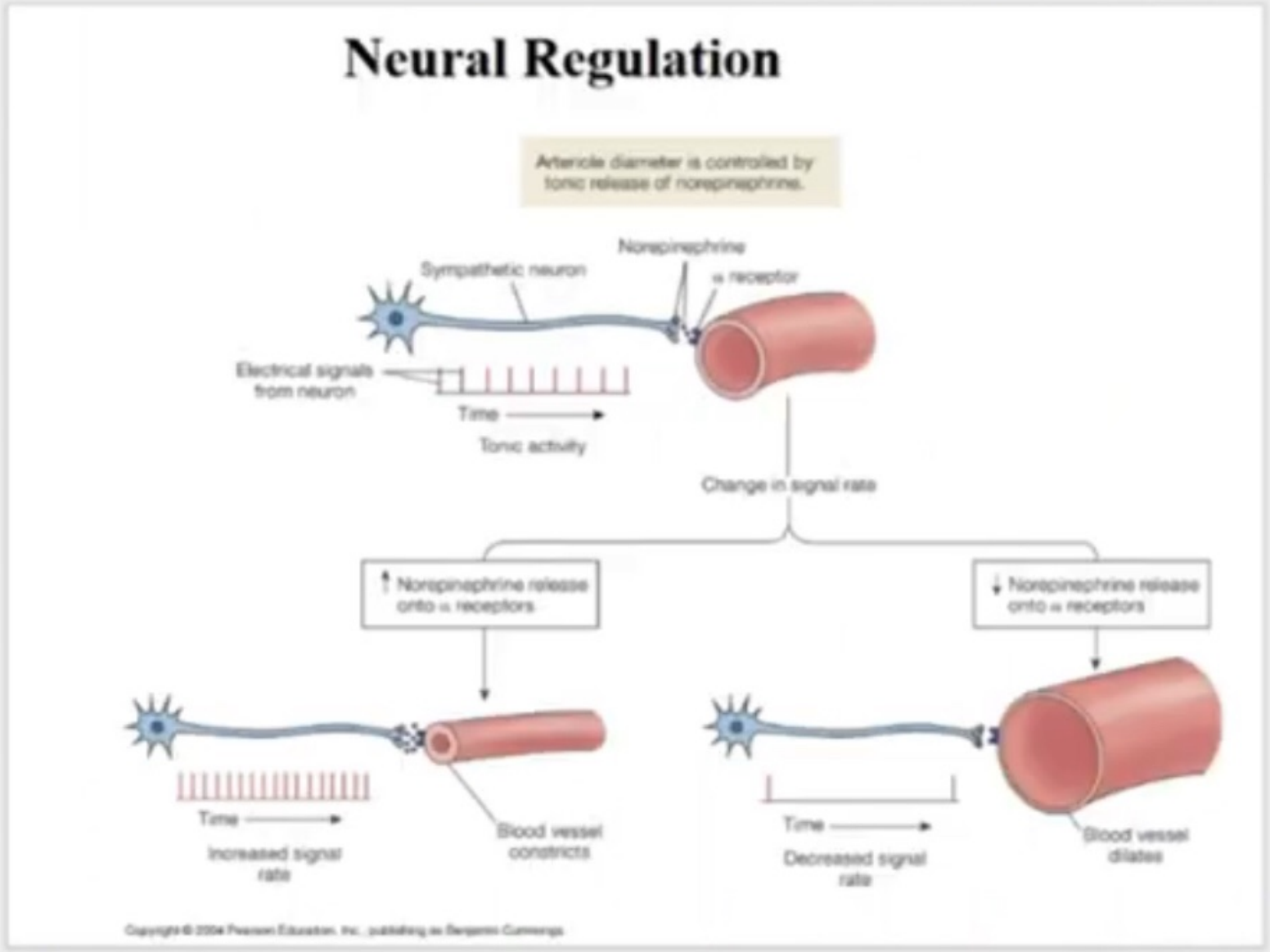
} → Vasoconstriction

- Local metabolites act as arteriolar smooth muscle relaxants (vasodilators) leading to increase blood flow.

Vascular Control by Ions

- Ca^{2+} ions – vasoconstriction. only in cardiac muscle or smooth muscle
- K^{+} ions – vasodilation.
- Mg^{2+} ions – vasodilation (often inhibits the actions of Ca^{2+} ions). it competes with Ca^{2+} & decrease Ca^{2+} entering
- H^{+} ions – increase cause vasodilation. acidosis reduce the interaction between myosin & actin
- Anions – acetate and citrate cause vasodilation.
- CO_2 – vasodilation, particularly important in the brain. because in the brain the sympathetic activity is almost absent

Neural Regulation



Neural Regulation

Neural Regulation

- **Sympathetic nerves:**
  - **Sympathetic vasoconstrictor nerves:**
    - Supplies vascular smooth muscle in all tissues.
    - System for regulating arterial blood pressure rather than blood flow to individual tissues.
    - Mediator: noradrenaline through a adrenergic receptors.
  - **Sympathetic vasodilator nerves:**
    - Some tissues have a specific vasodilator supply e.g. skeletal muscles.
    - Mediator adrenaline through ß adrenergic receptors & Ach through muscarinic receptors.
- **Parasympathetic nerves:**
  - In tissues which need sudden increase in blood flow (salivary gland, sweat glands and external genitalia).

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Humoral Regulation of Blood Flow

- The release of **vasoactive substance** from tissues into the tissue fluids and blood under certain conditions act to regulate blood flow.
- Some are released by gland and others are formed locally.

  - Vasoconstrictors

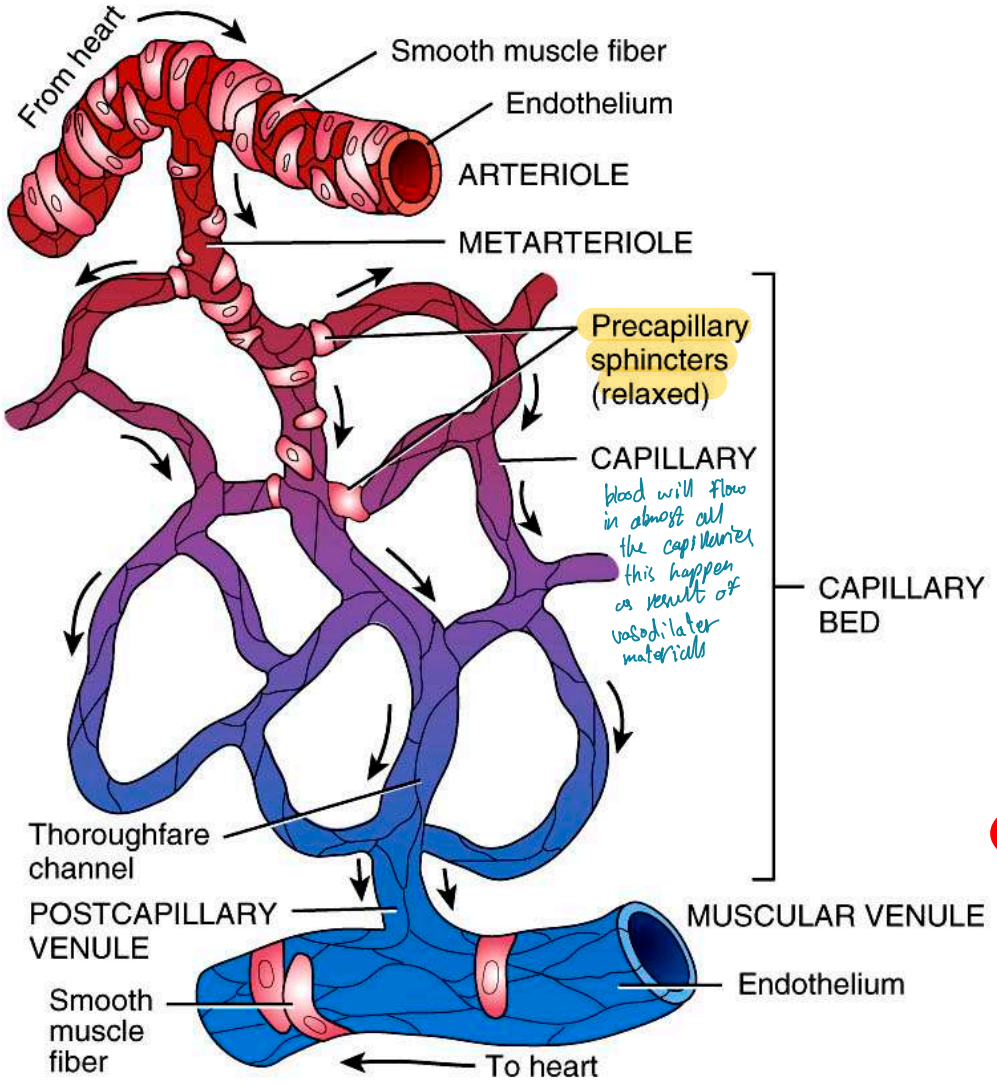
    Norepinephrine and epinephrine (they are neurotransmitters) } systemic
    Angiotensin II
    Vasopressin (ADH)
    Endothelins — local

  - Vasodilators

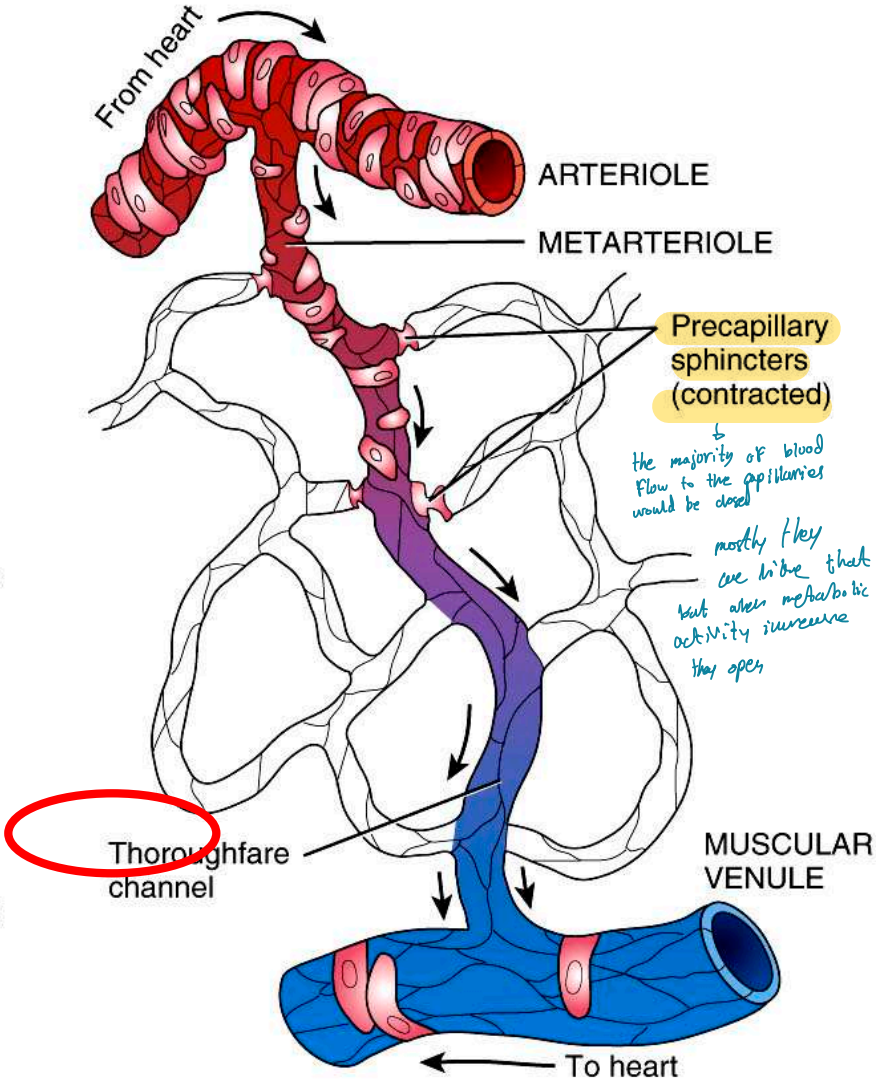
    Bradykinin local
    Serotonin local
    Histamine local
    Prostaglandins local

Precapillary sphincters

Local factors effect both arterioles & precapillary sphincters



(a) Sphincters relaxed: blood flowing through capillaries



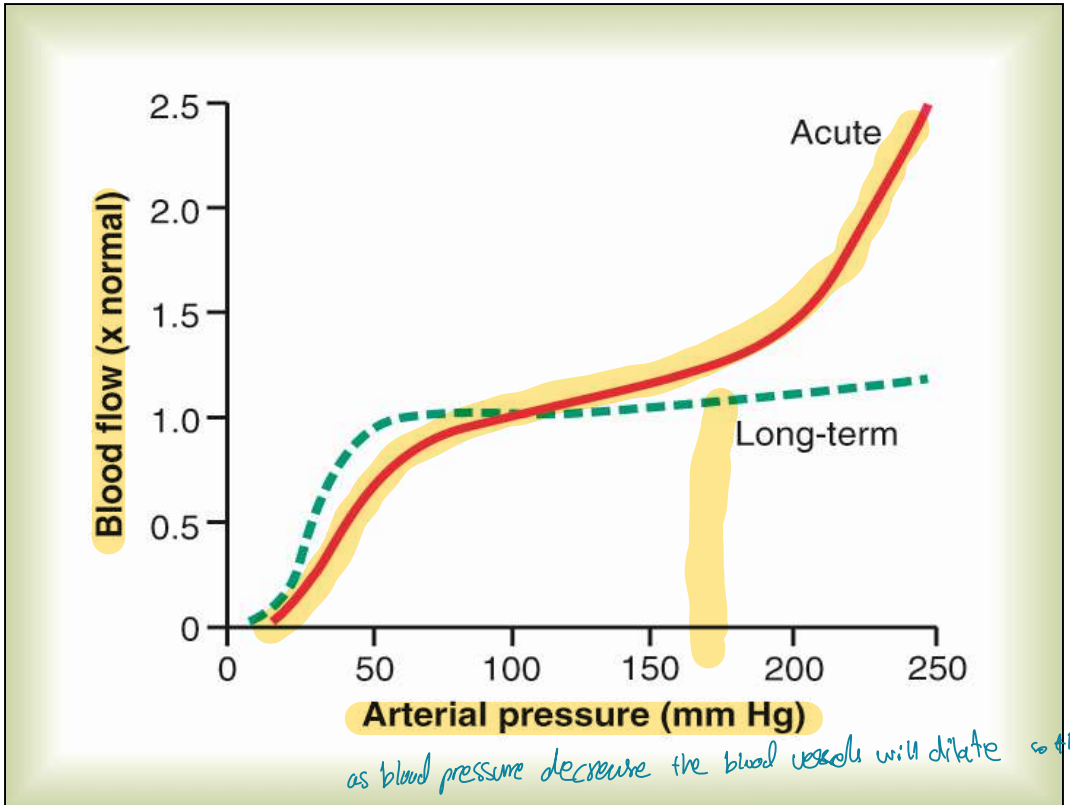
(b) Sphincters contracted: blood flowing through thoroughfare channel

Autoregulation of Blood Flow

when blood pressure changes

brain, heart & kidneys are the only organs that have auto-regulation so the blood flow will never stop for these 3 organs — very vital for survival

- It is the ability of an organ to maintain a **constant blood flow** despite changes in blood pressure. it will never stop
- occurs in the absence of neural or hormonal influences and therefore is intrinsic to the organ.



as blood pressure decrease the blood vessels will dilate so the blood flow stay the same

Blood Flow autoregulation theories:

Myogenic Mechanism.

Metabolic Mechanism

Autoregulation of blood flow

(two theories)

Myogenic theory

- when high arterial pressure stretches the vessel, this in turn causes reactive vascular constriction (increases resistance), which reduces blood flow nearly back to normal.

Metabolic theory

- due to increase of pressure, increased blood flow provides too much oxygen and nutrients to the tissues.
- The excess 0_2 causes constriction and the flow returns nearly to normal despite the increased pressure.

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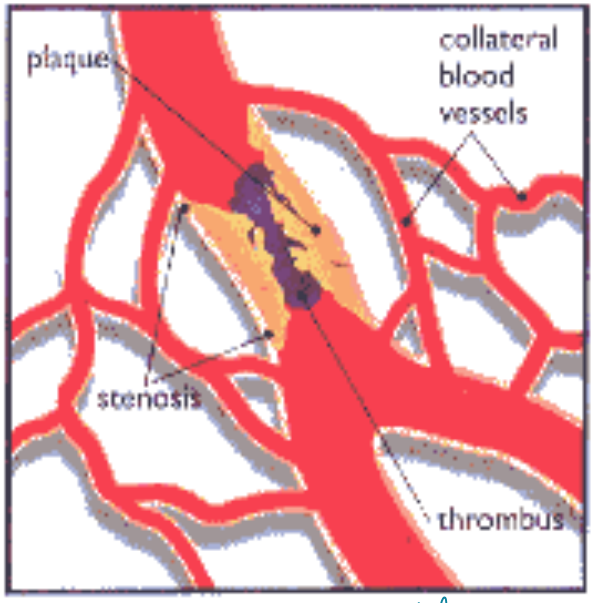
Collateral Circulation

It is the development of new blood vessels that *reroute* blood flow around the blockage. this happen when the artery is blocked so the blood continue to reach the organ to provided it with nutrients

When a blood vessel is blocked:

1) Within few minutes after blockage, dilation of the small vascular loops (Collaterals) that already connect the vessel above the blockage to the vessel below occurs.
2) further opening of these collaterals occurs within the following hours, so that within 1 day as much as half the tissue needs (O2 & nutrients) may be met, and within a few days often all the tissue needs.



this occurs through a process called angiogenesis which describe the formation of collateral blood vessels by pass the clot or the clouser of any vessel it's prominent in cardiac muscle , hardly in the skeletal muscle , because of these collateral which build over the years in cardiac muscle that is why elderly who are (70s-80s have higher chance of survival than other age groups in case of myocardial infarction

Cerebral Circulation

entirely controlled by local metabolic factors not the sympathetic
↳ this is due to the function of the brain, so in case of a vicious sympathetic stimulation the blood flow won't be cut by the vasoconstriction so we survive

- In an adults cerebral blood flow (**CBF**) is 750 ml/min (15% Cardiac Output).
- CBF is controlled by local metabolites:
  1. CO_2 is the most important vasodilator:
     - CO_2 diffuses to vascular cells, forms H_2CO_3 which gives (H^+).
     - Intracellular H^+ causes vasodilatation.
     - Increase in blood flow, removes excess CO_2 and H^+.
  2. **Decrease in PO_2 (hypoxia) increases cerebral blood flow.**
- Many vasoactive substances do not affect cerebral circulation, do not cross the blood-brain barrier.

the circle of willis

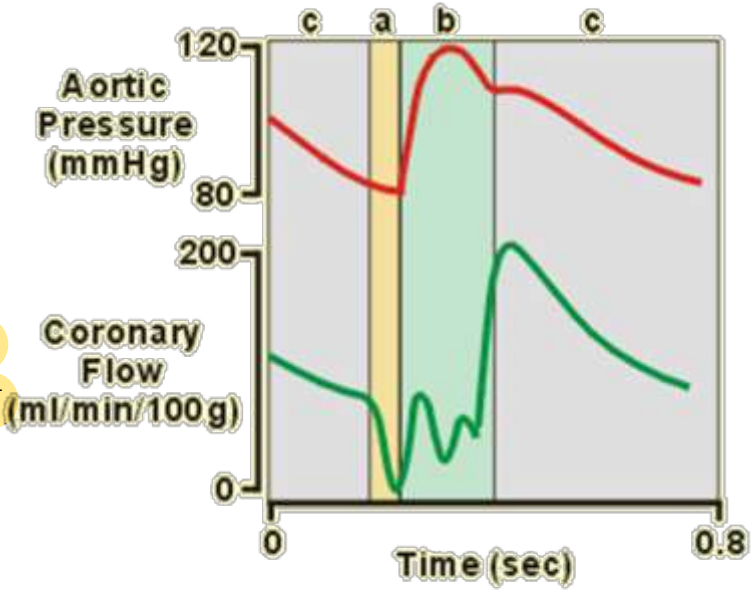
due to the tight junction between the endothelial cells of their capillaries

Sympathetic
mostly vasodilation in case of α receptors
vasodilation in case of β receptors such as in the heart also in the skeletal muscle during exercise only !!

Coronary Circulation

auto-regulation so the blood flow to the heart will never stop.
the major factor that effect the coronary blood flow circulation is the metabolic products
sympathetic can effect the coronary circulation but NOT Vasoconstriction instead vasodilation why? → because of the β_1 receptors which cause vasodilation

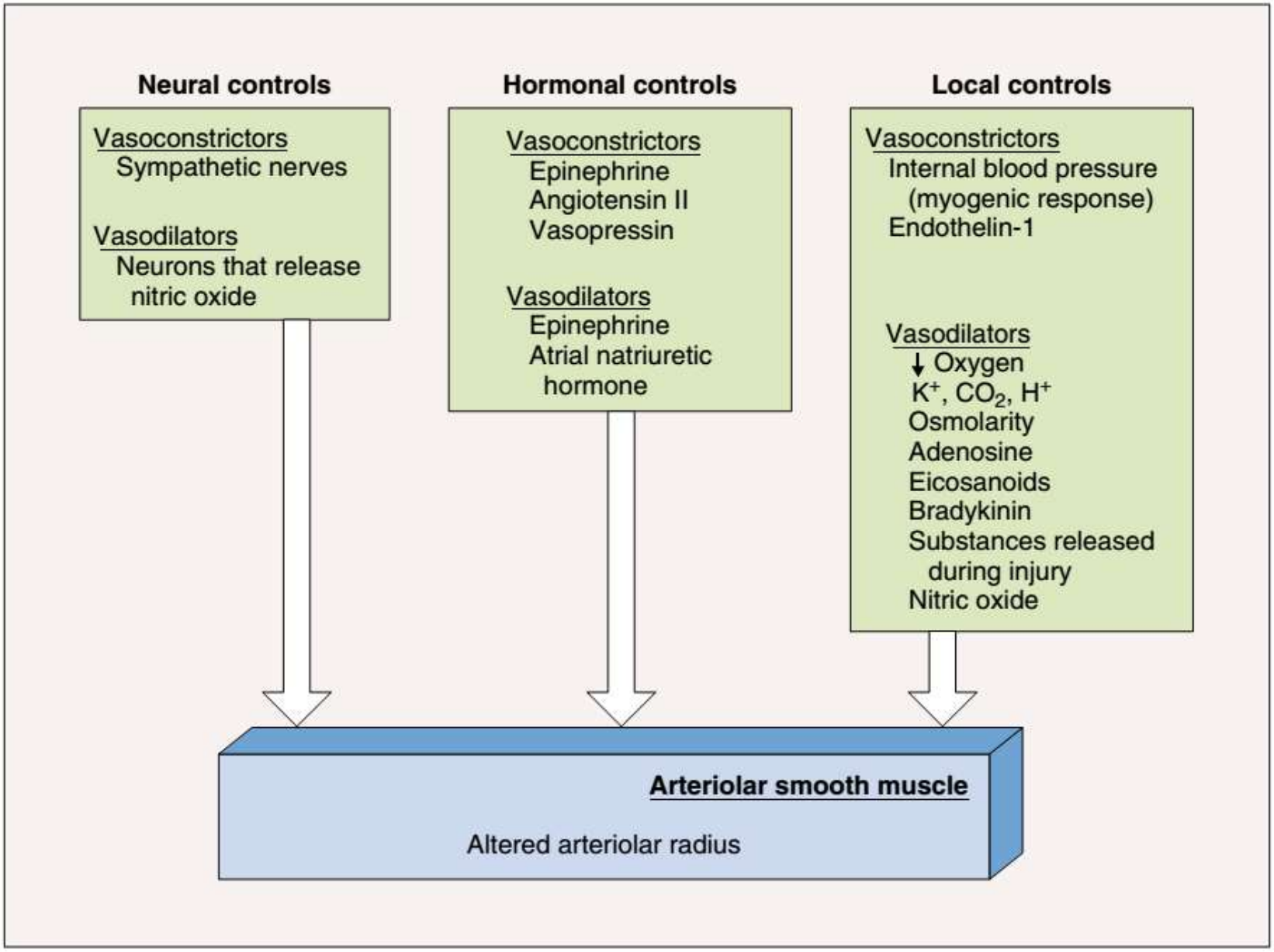
- Coronary blood flow is 250 ml/min (5% of COP).
- Blood supply is interrupted by systole (sub-endocardium).
- Has to cope with increased demand during exercise.
- **Control of coronary circulation:**
  - **Metabolic:**
    - Coronary blood flow is controlled primarily by local metabolites (e.g. Adenosine, K^+, H^+ $C0_2$).
    - Shows excellent active hyperaemia.
  - **Neural:**
    - Sympathetic stimulation causes vasoconstriction through α-adrenergic receptors.
    - β -adrenergic receptors cause dilation and also stimulate myocardial contraction.
    - Sympathetic stimulation increases oxygen consumption and increases metabolites, therefore causes dilation rather than constriction.



Pulsatile nature of left coronary artery blood flow. Flow is lower during phases of isovolumetric contraction (a) and ejection (b) than during diastole (c).

from the graph just know that blood flow of the coronary arteries increase during diastole & decrease during Systole because they are compressed during the contraction of myocardium vice versa

Summary


Neural controls
Vasoconstrictors
Sympathetic nerves
Vasodilators
Neurons that release nitric oxide
Hormonal controls
Vasoconstrictors
Epinephrine
Angiotensin II
Vasopressin
Vasodilators
Epinephrine
Atrial natriuretic hormone
Local controls
Vasoconstrictors
Internal blood pressure (myogenic response)
Endothelin-1
Vasodilators
↓ Oxygen
K^+, CO_2, H^+
Osmolarity
Adenosine
Eicosanoids
Bradykinin
Substances released during injury
Nitric oxide
Arteriolar smooth muscle
Altered arteriolar radius

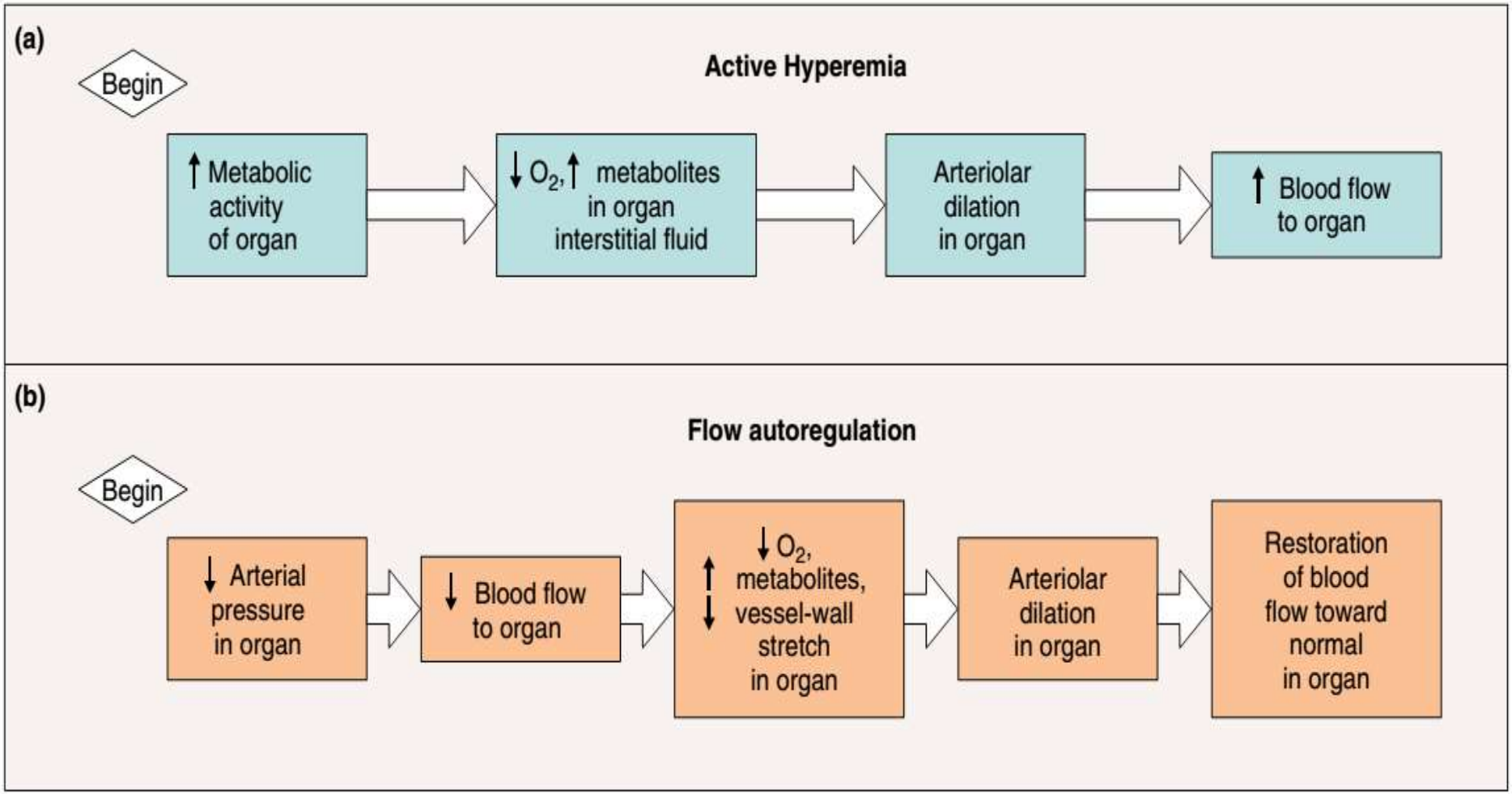


FIGURE 14–39

Local control of organ blood flow in response to (a) increases in metabolic activity, and (b) decreases in blood pressure. Decreases in metabolic activity or increases in blood pressure would produce changes opposite those shown here.

End

- One of the most fundamental principles of circulatory function is **the ability of each tissue to control its own local blood flow in proportion to its metabolic needs**.
- the very large blood flows in some organs—for example, several hundred milliliters per minute per 100 grams of thyroid or adrenal gland tissue
- large blood flow through the kidneys—1100 ml/min. This extreme amount of flow is required for the kidneys to perform their function of cleansing the blood of waste products.

- Conversely, most surprising is the low blood flow to all the *inactive muscles* of the body, only a total of 750 ml/min, even though the muscles constitute between 30 and 40 per cent of the total body mass.
- Yet, during heavy exercise, muscle metabolic activity can increase more than 60-fold and the blood flow as much as 20-fold, increasing to as high as 16,000 ml/min in the body's total muscle vascular bed (or 80 ml/ min/100 g of muscle).
- Why not simply allow a very large blood flow all the time through every tissue of the body, always enough to supply the tissue's needs whether the activity of the tissue is little or great? The answer is equally simple:To do this would require many times more blood flow than the heart can pump.
- Therefore, the blood flow to each tissue usually is regulated at the minimal level that will supply the tissue's requirements

- *adenosine is the most important of the local* vasodilators for controlling local blood flow.
- whenever the heart becomes ischemic OR more active than normal and the heart's metabolism increases an extra amount, this, causes increased utilization of oxygen, followed by (1) decreased oxygen concentration in the heart muscle cells with (2) consequent degradation of adenosine triphosphate (ATP), which (3) increases the release of adenosine.
- a combination of several different vasodilators could increase the blood flow sufficiently.

Oygen lack theory: Oxygen (and other nutrients as well) is required as one of the metabolic nutrients to cause vascular muscle contraction.Therefore, in the absence of adequate oxygen, it is reasonable to believe that the blood vessels simply would relax and therefore naturally dilate.

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

Myogenic contraction is initiated by stretch-induced vascular depolarization, which then rapidly increases calcium ion entry from the extracellular fluid into the cells, causing them to contract. Changes in vascular pressure may also open or close other ion channels that influence vascular contraction. The precise mechanisms by which changes in pressure cause opening or closing of vascular ion channels are still uncertain, but likely involve mechanical effects of pressure on extracellular proteins that are tethered to cytoskeleton elements of the vascular wall or to the ion channels themselves.

Role of Oxygen in Long-Term Regulation. Oxygen is important not only for acute control of local blood flow but also for long-term control. One example of this is increased vascularity in tissues of animals that live at high altitudes, where the atmospheric oxygen is low.A second example is that fetal chicks hatched in low oxygen have up to twice as much tissue blood vessel conductivity as is normally true.This same effect is also dramatically demonstrated in premature human babies put into oxygen tents for therapeutic purposes. The excess oxygen causes almost immediate cessation of new vascular growth in the retina of the premature baby's eyes and even causes degeneration of some of the small vessels that already have formed.Then when the infant is taken out of the oxygen tent, there is explosive overgrowth of new vessels to make up for the sudden decrease in available oxygen; indeed, there is often so much overgrowth that the retinal vessels grow out from the retina into the eye's vitreous humor; and this eventually causes blindness. (This condition is
called *retrolental fibroplasia*.)

Cerebral blood flow autoregulation

Three different mechanisms are thought to contribute to the process of cerebral autoregulation. These are metabolic, myogenic and neurogenic.

Metabolic regulation

Metabolic regulation is driven by the balance between cerebral metabolism (demand) and oxygen delivery through cerebral blood flow (supply) and acts by means of a vasoactive substance. In principle, this is a negative feedback control system that seeks to balance cerebral blood flow to its demand.

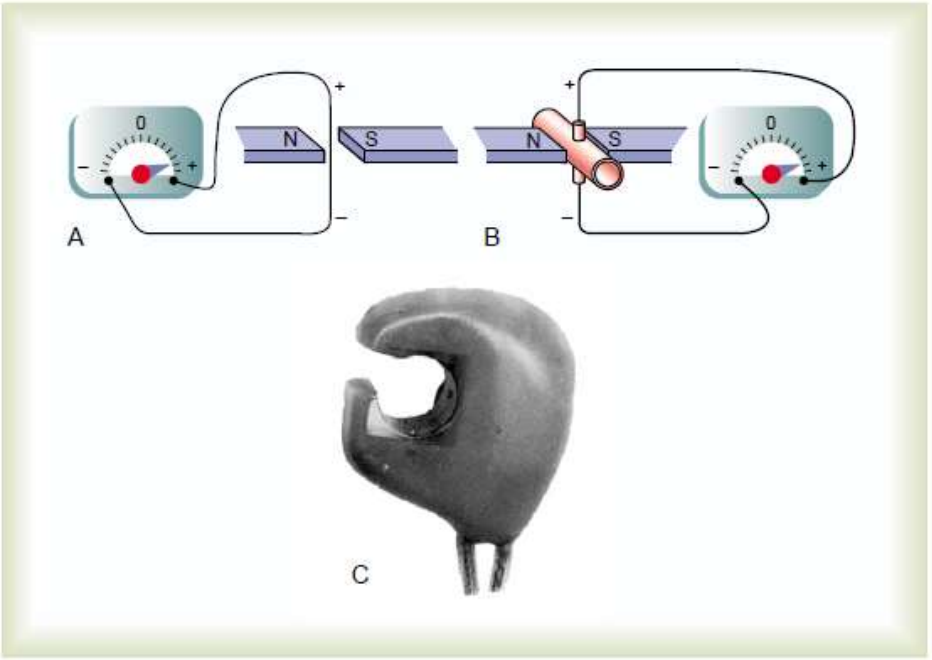
Myogenic regulation

The effect of transmural blood pressure changes are directly detected by the vascular smooth muscle in arterioles, probably via a stress sensing mechanism. Then, the calibers are adjusted accordingly to keep blood flow constant.

Neurogenic regulation

The vascular smooth muscle actuators in the resistance arterioles are controlled via sympathetic innervation, receiving the input from the appropriate brainstem autonomous control center. Nitric oxide released by parasympathetic fibers may also play a role.

Electro-magnetic flow meter - doppler



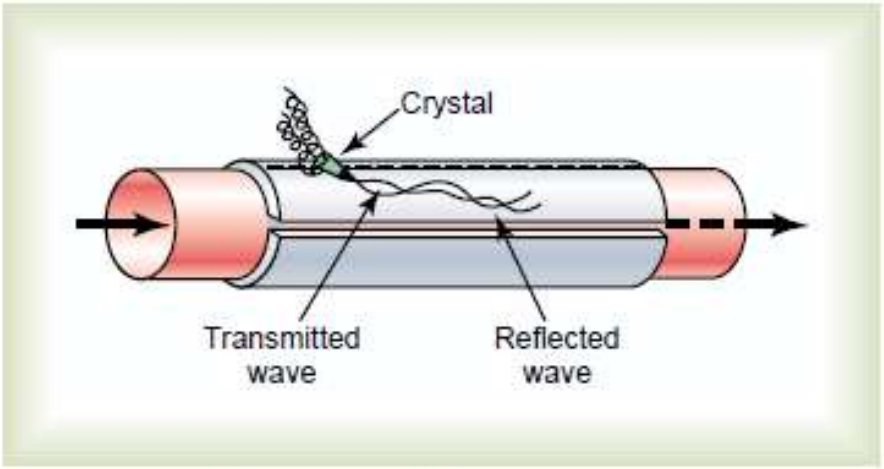


Figure 14–5

Ultrasonic Doppler flowmeter.