

- **Control of Tissue Blood Flow**
- By
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- LEARNING OBJECTIVES
- ***By the end of this session, the student should be able to:***
- Enumerate the mechanisms of local control of blood flow in response to tissue needs.
- Describe the acute and long-term mechanism for regulation of tissue blood flow.
- Discuss the humoral regulation of circulation.
- Methods of Regulation

- **Vasodilator:** Lack of oxygen produces lactic acid, adenosine (degradation of ATP) which directly affect vascular tone.
- **Oxygen demand:** Lack of oxygen prevents SMC from sustaining contraction. (But smc can remain contracted with extremely low oxygen).
- **Need for other nutrients:** e.g. vitamin B, as in beriberi.
- Vasodilator Theory for Acute Local Blood Flow Regulation—Possible Special Role of Adenosine.

- According to this theory, the greater the rate of metabolism or the less the availability of oxygen or some other nutrients to a tissue, the greater the rate of formation of *vasodilator substances* in the tissue cells. The vasodilator substances then are believed to diffuse through the tissues to the precapillary sphincters, metarterioles, and arterioles to cause dilation.
- contd

- Some of the different vasodilator substances that have been suggested are *adenosine, carbon dioxide, adenosine phosphate compounds, histamine, potassium ions, and hydrogen ions.*
- Hyperemia
- **Active Hyperemia:** As a result of exercise.
 - Can increase blood up to 20-fold.
- **Reactive Hyperemia:** As a result of ischemia.

- Used as a test for coronary stenosis.
- Local Response to Pressure
- **Metabolic:**
- Increased pressure increases flow, leading to increased oxygen, tending to constrict the vessels.
- **Mechanical:**
- Stretch receptors in smooth muscle cause vascular constriction. Might lead to positive feedback.
- Special Mechanisms of Control

- **Kidney (tubuloglomerular feedback):** fluid composition in the distal tubule is detected by the macular densa. Excess fluid causes reduced flow rate.
- **Brain:** Oxygen, CO₂ and Hydrogen Ion play a dominant role.
- **Control of Large Vessel Tone**
 - **EDRF (NO):**
 - Produced by endothelial cells.
 - An EC response to shear stress.
 - Also produced in response to acetylcholine, bradykinin, ATP.
 - Potent vasodilator.

- Leads to post-stenotic dilatation.
- *Has other purposes:*
Neurotransmitter, platelet inhibitor, inhibits cell proliferation
- Humoral control of blood flow
- Humoral control of the circulation means control by substances secreted or absorbed into the body fluids—such as hormones and locally produced factors.
- Vasodilators
- **Bradykinin:** Causes arteriole dilation and increased capillary permeability.

- Kallerikin -> Kallikrein* (acts on) alpha₂-globulin (releases) kallidin -> bradykinin (inactivated by) carboxypeptidase (or) converting enzyme
- Regulates flow to skin, salivary glands, gastrointestinal glands.
- Vasodilators (continued)
- Serotonin (5-hydroxytryptamine or 5HT):
 - Found in platelets (potentiator of platelet activation).
 - Neurotransmitter.
 - May be vasoconstrictor or vasodilator.
 - Role in circulation control not fully understood.

- Vasodilators (continued)
- Histamine:
 - Released by damaged tissue.
 - Vasodilator and increases capillary porosity.
 - May induce edema.
 - Major part of allergic reactions.
- Prostaglandins:
 - Most are vasodilators, some are vasoconstrictors.
 - Pattern of function not yet understood.
- Other Ions
- Calcium: Vasoconstrictor (smc contraction)
- Potassium: Vasodilator (inhibit smc contraction)

- Magnesium: Vasodilator (inhibit smc contraction)
- Sodium: Mild dilatation caused by change in osmolality. Increased osmolality causes dilitation.
- Acetate and Citrate: Mild vasodilators.
- Increased CO₂/pH: Vasodilation
- Vasoconstrictors
- Angiotensin:
 - 1 micro gram can cause 50 mm Hg increase in pressure.
 - Acts on all arterioles
- Vasopression:
 - Made in hypothalamus – released to pituitary from which it is

distributed to the body. Highly potent.

- Controls flow in renal tubules
- Vasoconstrictors (contd)
- **Endothelin**
- Effective in nanogram quantities.
- Probably major mechanism for preventing bleeding from large arterioles (up to 0.5 mm).
- Constricts the umbilical artery of a neonate.
- Especially effective on coronary, renal, mesenteric and cerebral arteries.

- Mechanism of Long-Term Regulation—Change in “Tissue Vascularity”
- The mechanism of long-term local blood flow regulation is principally to change the amount of vascularity of the tissues. For instance, if the metabolism in a tissue is increased for a prolonged period, vascularity increases, a process generally called *angiogenesis*
- **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
- Eg
- retinoblastosis fetalis
- Importance of Vascular Endothelial Growth Factor in Formation of New Blood Vessels
- *vascular endothelial growth factor (VEGF), fibroblast growth factor, and angiogenin*, each of which has been isolated from tissues that have inadequate blood supply. Presumably, it is

deficiency of tissue oxygen or other nutrients, or both, that leads to formation of the vascular growth factors (also called “angiogenic factors”).

THANK

YOU