8. Regulation of diameter of Arteriols.

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Arterioles are the terminal branches of the arterial system

• **Characters of arterioles:**

1)Loss of elastic elements and **increase smooth ms. layer**.

2) Have **great resistance** to blood flow (so the blood pressure drops from 80 to 30 mmHg) and act as sphincter between arterial system and venous system.

3) Have **sympathetic** VC fibres and some **parasympathetic** VD fibres.

4) They are sensitive to chemicals of blood as the blood gases, hormones, metabolites & pH.

5) The endothelium in their walls can **synthesize chemical mediators** .

6) The only site at which arterioles can be seen is the retina.

• **Functions of arterioles**:

1. Determination of the **peripheral resistance** : They are called the resistance vessels because they control the peripheral resistance and the arterial blood pressure.

2. They **control the blood flow** to the tissues : by changing their diameter .

- **Factors regulate arteriolar diameter:**

I. Local regulatory mechanisms

1) O2 Tension :

-The **normal** (PO2) produces **partial vasoconstriction** and this is maintained by **VC tone**.

-**Decreased O2 tension** leads to direct **vasodilator effect** on the arteriolar **smooth muscles, except** for the **pulmonary vessels** which constrict due to O2 lack.

-O2 lack is the most potent vasodilator in the heart , while CO2 excess is the most potent vasodilator inside the CNS

-When the metabolic activity of a tissue decreases the PO2 is increased leading to VC.

-If the metabolic activity of a tissue is increased the PO2 is decreased leading to VD.

2) Metabolites :

When the tissue becomes **hyperactive** → increase CO2 tension ,acidosis, osmolality, K+, and adenosine→ VD.

Active hyperemia:

The **increase in blood flow** at the **active tissues** by vasodilation produced by accumulation of metabolites.

Reactive hyperemia:

The **increase in blood flow** of a tissue produced by **accumulation of metabolites** due to temporary occlusion of its blood supply.

3) Intrinsic Mechanism (Autoregulation):

- It is the ability of a tissue to regulate its blood flow according to its need.

Mechanism:

1-Myogenic theory: When the blood flow increases to a tissue →stretching the vascular smooth muscles → their depolarization → vascular smooth muscle contraction → decreased the blood flow to normal.

2-Metabolic theory: If the blood flow to an organ is **decreased**, vasodilator **metabolites accumulate** producing VD which will increase the blood flow to wash the metabolites and remove their effect.

4) Local vasoconstrictor substances:

Injured arteries and arterials constrict powerfully due to **serotonin** release from blood platelets.

5) Local temperature:

- Drop in the tissue temperature has a direct V.C. effect.

- Increase in the tissue temperature causes V.D.

6) Substances released by the endothelium :

A-Thromboxane A2 and Prostacyclin: Both are formed **from archadionic acid**

- Prostacyclin: released from endothelium, causes VD and inhibition of platelets aggregation.

- Thromboxane A2: released from platelets and cause VC and increase platelet aggregation**.**

***Aspirin (acetyle salicylic acid)** → irreversible inhibition of cyclooygenase enzyme and resynthesis of this enzyme by platelets needs long time while the life span of platelets is only 6-7 days so there is decrease in formation of thromboxane A2 → VD and inhibition of platelets aggregation.

-So aspirin is used to prevent clot formation.

B- Endothelins

- Three types are now known, each is a polypeptide (21 amino acid) formed in the endothelial cells.
- Released by stretching the vessels.
- It is a potent V.C.
- Endothelins has two types of receptors in the vascular walls.
- **Actions:**

• Positive inotropic effect on cardiac muscle.
• Vasoconstriction of the coronaries.
• Stimulate aldosterone and catecholamine release
• Decrease renal blood flow and increase renal vascular resistance.
• Strong contraction of the vascular smooth muscles especially veins (the most potent one).

C- Endothelium-derived-relaxing factor (EDRF):

• It is identified as nitric oxide (NO) and synthesized from **arginine amino acid**.

• It increases cGMP → vasodilation.

• It is released by endothelium under the effect of bradykinin, substance P, vasoactive intestinal peptide (VIP) as a mediator for their vasodilator effects.

• Its deficiency as in cases of **endothelium injury** → loss of its vasodilator effect and the vasoconstrictors as thromboxane A2 becomes predominant causing VC, atherosclerosis, hypertension and impotence (failure of erection by VD in male genital organs).

II. Central (or systemic) regulation

A. Neuronal Regulatory Mechanisms

(1) Vasoconstrictor fibers (V.C.):

a. Sympathetic V.C.:

-The sympathetic noradrenergic fibers arise from the lateral horn cells; of the thoraco-lumbar segments of the spinal cord .

-They discharge **continuously**, leading to generalized partial V.C which is called sympathetic vasoconstrictor tone.

b. Parasympathetic vasoconstrictor fibers:

-**No** vasoconstrictor parasympathetic fibers are known

-Parasympathetic stimulation to the **heart** causes **coronary vasoconstriction** by decreasing the metabolic activity and elevation of O2 tension, together with decreasing metabolites which lead to **coronary vasoconstriction**.

(2) Vasodilator fibers (V.D.):

(a) Sympathetic vasodilator fibers:

-All the sympathetic innervations to blood vessels cause **V.C, except in:**

(i) Coronary vessels:

This occurs **indirectly** by increasing heart rate and the metabolic activity of the heart →↓ O2, tension and accumulation of metabolites → VD (metabolic theory of autoregulation).

(ii) Skeletal muscles:

-The sympathetic (V.D.) fibers are **cholinergic** (secrete acetylcholine).

-They start to operate and dilate the skeletal muscle blood vessels **even before the start of the exercise** and so help to increase the skeletal muscle blood flow during exercise.

-This system can be activated by **sudden strong emotions** → widespread vasodilatation → severe hypotension→ brain ischemia → syncope.

(iii) The splanchnic areas:

-The blood vessels of these areas are richer in (B) adrenergic receptors than (alpha) receptors, and (B) receptors in turn produce VD.

(iv) Sweat glands:

- **Sympathetic cholinergic** VD fibers supply blood vessels of the sweat glands. Their activity is controlled by the **heat loss center** in the **anterior hypothalamus**.

(b) Parasympathetic vasodilator fibers:

-The **only** parasympathetic fibers which are definitely vasodilator are those which supply the **genital** organs (sacral out-flow).

-However, the parasympathetic fibers in the facial and Gloss pharyngeal nerves (7th, 9th) cranial nerves which supply the salivary glands produce (V.D) by **increasing metabolic activity** of these glands during active secretion.

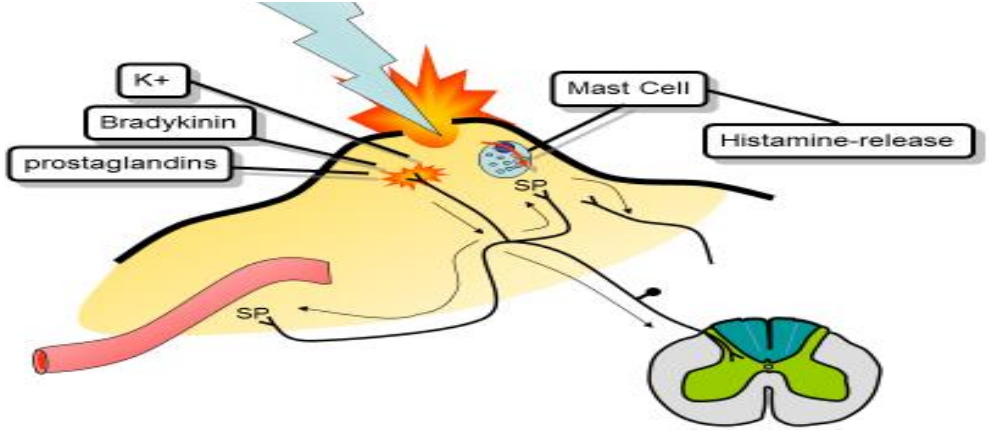
(c) Antidromic vasodilator impulses:

-When pain receptors are stimulated by pain stimuli, (e.g. inflammation or scratching the skin with a pin) produces dilatation of the adjacent blood vessels.

- **Mechanism: local axon reflex**: Stimulation of pain receptors initiates impulses travel along sensory nerve fibers toward CNS until they reach a branch, they travel a long it (**antidromically**).

Local axon reflex doesn't involve the CNS.

- When they reach the **arterioles**, cause releasing of **Substance P** which has a vasodilator effect on the arterioles thus the area of inflammation become **red.**



B- Hormonal Regulation

1. Circulating Vasoconstrictor Substances:

a. Catecholamines:

- **Noradrenaline**: has a potent VC effect on the blood vessels through acting via **α** receptors.

- **Adrenaline:** causes VD of blood vessels in skeletal muscles and liver (especially in small doses) by acting on **B2** adrenergic receptors.

b-Renin- angiotensin-system:

Decreased blood pressure (dehydration, salt restriction, haemorrhage) →↓renal blood flow→ renal ischemia → + juxtaglomerular apparatus secret **renin** which act on alpha globulin in the plasma **angiotensinogen** producing **angiotensin I** which is converted to **angiotesin II** by the angiotensin convertase enzyme in the lung. Angiotesin II has the following **effects:**

1-Strong arteriolar **VC** (50 times as NOR) leading to increased peripheral resistance and blood pressure.

2-Stimulation of **aldosterone release** from the suprarenal gland.

3-Stimulation of **ADH** (vassopressin) secretion from the pituitary gland

4-Stimulate **NA** release from postganglionic sympathetic fibres.

5-Stimulate **thirst sensation** → ↑water intake → ↑Bl.volume →↑ Bl.pr.

6- Stimulate **salt and water retention by the kidney** → Increase blood volume and blood pressure.

(all above effects → ↑ Bl. pressure).

-Some of angiotebnsion -II → angiotension III

c. Vasopressin (Antidiuretic Hormone) (ADH):

- This is a potent V.C. hormone secreted by the posterior pituitary gland.

- It plays important role in acute hemorrhage.

Mechanism of action:

(1) It acts on V1 receptors (in vascular smooth muscle) to increase Ca+2 concentration in smooth muscle fibers → V.C.→ ↑blood pressure.

(2) It acts on V2 receptors in the nephrons → increase the permeability of the cells to water, urea, and some other solutes→ increases the extra-cellular fluid volume→ increase in the arterial blood pressure.

2-Circulating Vasodilator Substances:

a- Kinins:

-They are polypeptide and potent vasodilator.

-They are plasma kinin (bradykinin) and tissue kinin (kalidin)

- They are synthesized from precursor **kininogen** by kallikrein enzymes in plasma or tissue

Actions of kinins:

1) VD by release of endothelium derived relaxing factor → marked decrease in blood pressure.
2) Contraction of smooth muscles as in respiratory system.
3) Stimulation of pain receptors.
4) Increase capillary permeability.
5) Act as mediator for **VD** in active salivary glands.
6) Positive chemotaxis effect (attract **WBCs**).

b. Atrial Natriuretic Peptide:

- ANP is secreted from the **Atria**; (others are secreted from the bain and heart ventricles)

- They are secreted **when**:

(1) NaCl intake is increased

(2) The blood volume is increased

(3) Immersion in water up to the neck with increase VR.

(4) Increased CVP.

(5) Increased inta-ventricular pressure.

- It **decreased** in rising from supine to erect position.

Actions of ANP:

1) Natriuresis: (loss of Na+ in urine)

2) Vasodilators of blood vessels that decrease ABP.

3) ↓ Aldosterone secretion and ↓ Vasopressin hormone secretion.

5) ↓ Renin release causes decrease angiotensin II formation.

Factor	VC	VD
I. Local regulatory mechanisms	Increased O2 Serotonin, Cool, Thromaxane A2, Endothelins	Decreased O2, Increased CO2 increase CO2 tension, acidosis, K+, and ↑ adenosine Warm, Prostacyclin, EDRF
II. Central (or systemic)	Sympathetic V.C (sympathetic vasoconstrictor tone)	(a) Sympathetic VD fibers (1) Coronary vessels (2) Skeletal muscles (3) The splanchnic areas (4) Sweat glands (b) Parasympathetic vasodilator fibers (c) Antidromic vasodilator impulses
B- Hormonal Regulation	a. Catecholamines: NOR- EPI b-Renin- angiotensin-system C-Vasopressin (ADH)	a. Kinins b. Atrial Natriuretic Peptide

Thank You