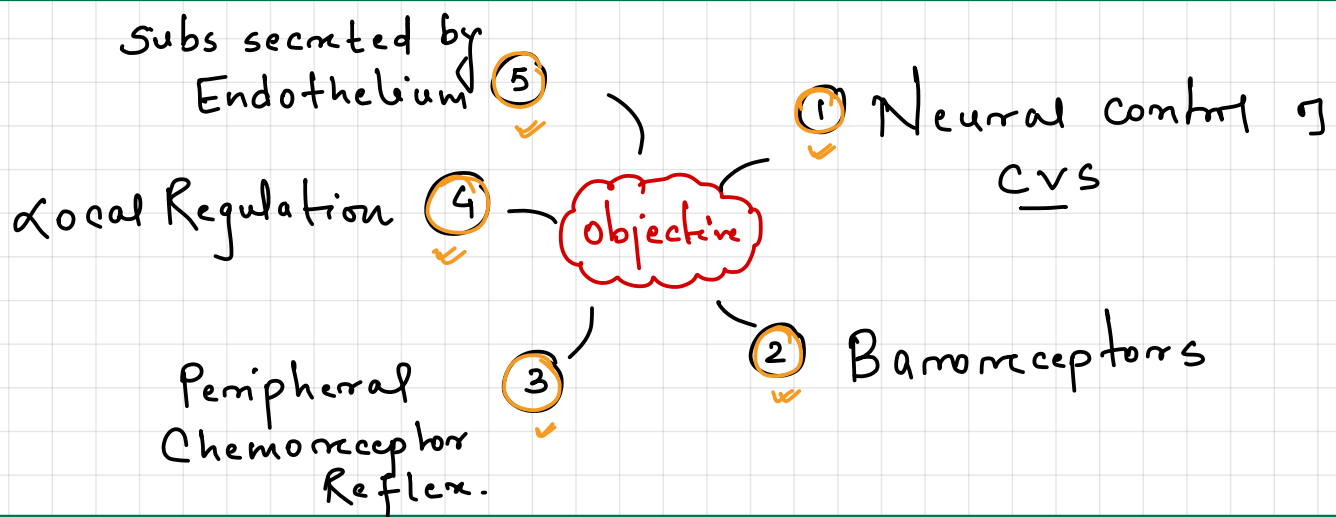


Cardiovascular Regulatory Mechanism



Objective
①

Neural Control of CVS

- Vasoconstrictors & Vasodilators

Innervation of Heart

- Release of Norepinephrine from postganglionic sympathetic nerve activates β_1 -adrenoceptors in heart, notably on SA node, AV node, His-Purkinje system.
- Stimulation of sympathetic nerves leads to;
 - (a) Heart Rate $\uparrow$ (chronotropy)
 - (b) Rate of transmission in the cardiac tissue $\uparrow$ (dromotropy)
 - (c) Force of ventricular contraction $\uparrow$ (inotropy)

Vasoconstriction

Local factors

Decreased local temperature
Autoregulation

Endothelial products

Endothelin-1
Locally released platelet serotonin
Thromboxane A_2

Circulating neurohumoral agents

Epinephrine (except in skeletal muscle and liver)
Norepinephrine
Arginine vasopressin
Angiotensin II
Endogenous digitalis-like substance
Neuropeptide Y

Neural factors

Increased discharge of sympathetic nerves

Vasodilation

Increased CO_2 and decreased O_2
Increased K^+ , adenosine, lactate
Decreased local pH
Increased local temperature

Nitric oxide
Kinins

Prostacyclin

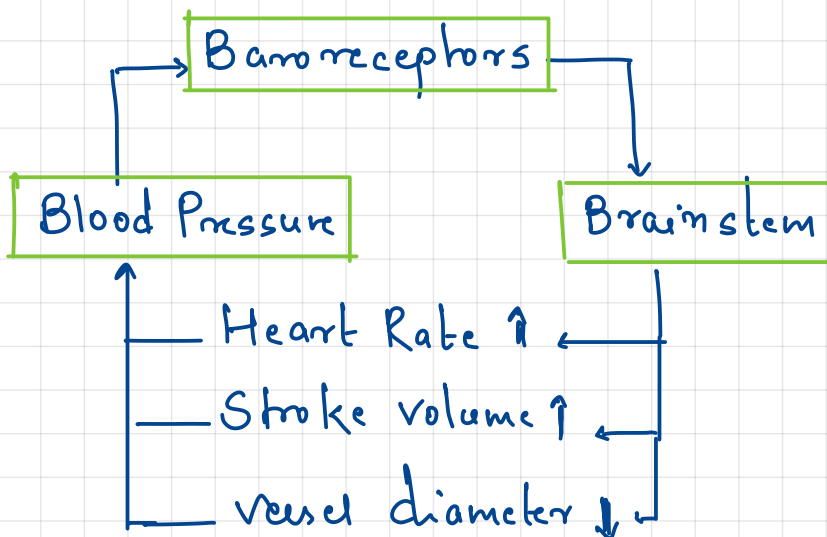
Epinephrine in skeletal muscle and liver
Calcitonin G-related protein
Substance P
Histamine
Atrial natriuretic peptide
Vasoactive intestinal polypeptide

Decreased discharge of sympathetic nerves
Activation of β_2 -adrenoceptors on the vasculature of skeletal muscles of the limbs

- Release of Acetylcholine from postganglionic parasympathetic (vagus) nerve activates muscarinic receptors in heart, on SA and AV nodes & Atrial muscle.
- Stimulation of Vagus nerve reduces ;
 - (a) Heart Rate
 - (b) Transmission through AV node
 - (c) Atrial Contractility.

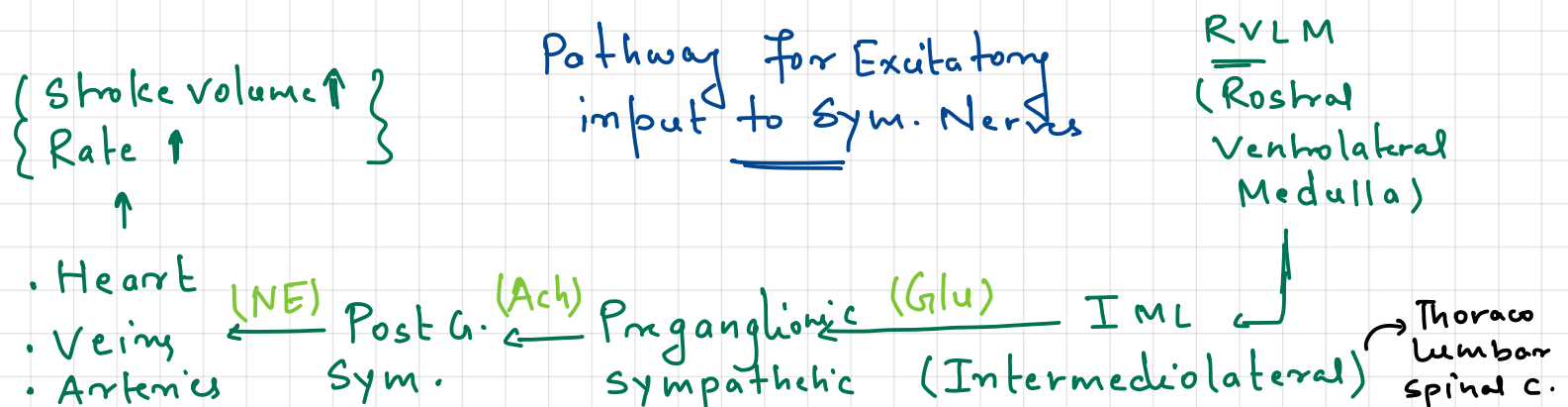
Central Neural Control of CVS :

- Neural influence of CVS is by Brain stem, forebrain and insular cortex.
- Simplified Flowchart:



- One of the major sources of excitatory input to sympathetic nerves controlling the vasculature
 ↓
 Group of Neurons near the pial surface of Medulla in the Rostral Ventrolateral medulla (RVLM)

Simplified neural pathway :-



- This pathway is responsible for BP rise & Tachycardia.
- RVLM also receives input from other brain regions and from Arterial baroreceptors and the carotid & Aortic chemoreceptors.

TABLE 32-2 Factors affecting the activity of the RVLM.

Direct stimulation
CO ₂
Hypoxia
Excitatory inputs
Cortex via hypothalamus
Mesencephalic periaqueductal gray
Brainstem reticular formation
Pain pathways
Somatic afferents (somatosympathetic reflex)
Carotid and aortic chemoreceptors
Inhibitory inputs
Cortex via hypothalamus
Caudal ventrolateral medulla
Caudal medullary raphe nuclei
Lung inflation afferents

TABLE 32-3 Factors affecting heart rate.

Heart rate accelerated by:
Decreased activity of arterial baroreceptors
Increased activity of atrial stretch receptors
Inspiration
Excitement
Anger
Most painful stimuli
Hypoxia
Exercise
Thyroid hormones
Fever
Heart rate slowed by:
Increased activity of arterial baroreceptors
Expiration
Fear
Grief
Stimulation of pain fibers in trigeminal nerve
Increased intracranial pressure

Objective
②

Baroreceptors :

- Stretch receptors in the walls of Heart & Blood Vessels.
- Baroreceptors are present in the
 - (a) Adventitia of vessel within a small dilation of Internal Carotid Artery
 - (b) In the wall of Arch of Aorta.

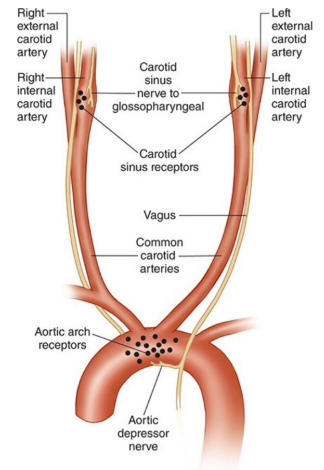


FIGURE 32-4 Baroreceptor areas in the carotid sinus and aortic arch. One set of baroreceptors (stretch receptors) is located in the carotid sinus, a small dilation of the internal carotid artery just above the bifurcation of the common carotid into external and internal carotid branches. These receptors are innervated by a branch of the glossopharyngeal nerve, the carotid sinus nerve. A second set of baroreceptors is located in the wall of the arch of the aorta. These receptors are innervated by a branch of the vagus nerve, the aortic depressor nerve.

* Baroreceptor $\xrightarrow{\text{(Glu)}}$ NTS (Nucleus of Tractus solitarius) $\xrightarrow{\text{(Glu)}}$ CVLM (caudal ventrolateral Medulla) $\xrightarrow{\text{(GABA)}}$ RVLM

Inhibitory signal

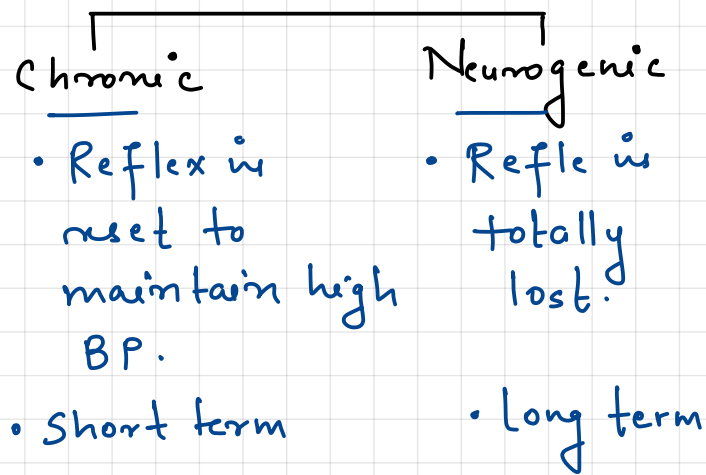


Inhibits Tonic discharge of Sym. Nerves and Inc. Vagal Tone.

• Cardiac Output ↓ • Hypotension • Vasodilation • Bradycardia • Venodilation

- Changes in Heart Rate and BP that occurs on standing up or lying down are due for most part to **Baroreceptor Reflexes**.
- Baroreceptors are very important in short term control of Arterial pressure.
- Activation of Reflex allows Rapid Adjustments in BP in response to ;
 - (a) Change in Posture
 - (b) Blood Volume
 - (c) Cardiac Output
 - (d) Peripheral Resistance during Exercise.

Hypertension



Valsalva Maneuver :

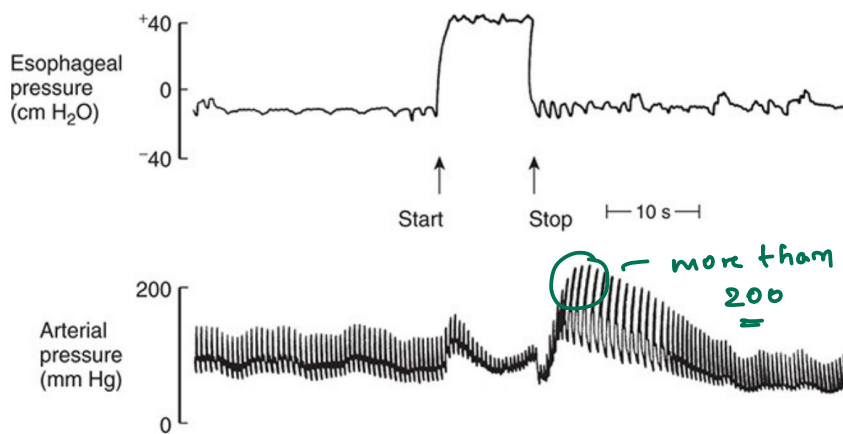


FIGURE 32-6 Diagram of the response to straining (the Valsalva maneuver) in a healthy man, recorded with a needle in the brachial artery. Blood pressure rises at the onset of straining because increased intrathoracic pressure is added to the pressure of the blood in the aorta. It then falls because the high intrathoracic pressure compresses veins, decreasing venous return and cardiac output. (Used with permission of M McIlroy.)

- In patients whose sympathetic nervous system is not functional, this heart rate change still occurs because baroreceptor & vagi are intact.

- Valsalva maneuver occurs regularly during coughing, defecation and heavy lifting.

- The BP $\uparrow$ because the intrathoracic pressure is added to pressure in Aorta.

Objective
③

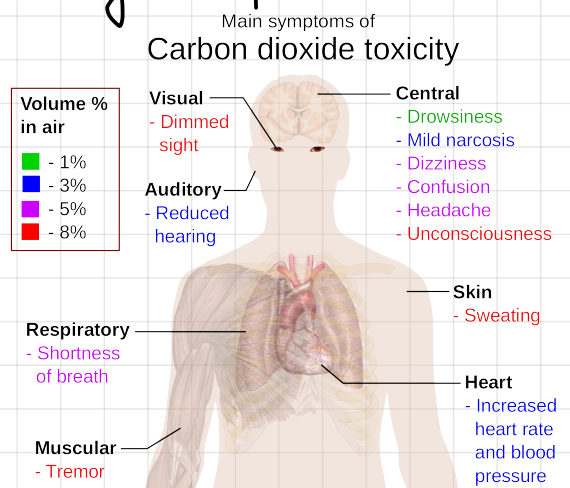
Peripheral Chemoreceptor Reflex:

- Present in Carotid and aortic bodies
- Activated by Reduction in Arterial partial pressure of O_2 , partial pressure of CO_2 and pH.
- Chemoreceptors are mainly for Respiration however their activation leads to vaso constriction.
- A direct effect of chemoreceptor is to increase vagal nerve activity.
- Both carotid and Aortic bodies increase sensory discharge during hypoxia.

Central Chemo receptors:

- Works like peripheral chemoreceptor but detects CO_2 concentration in Cerebrospinal fluid around brain.
- Located near Ventrolateral medullary surface

- Hypercapnia (Retention of CO_2) directly stimulates RVLM but the direct peripheral effect of hypercapnia is vasodilation.



- Activation of Central Chemo-receptor due to compromised blood flow, induces a rise in systemic arterial pressure. (Cushing Reflex) →

- The Cushing reflex is a result of cerebral ischemia caused by intracranial pressure
- Cerebral ischemia at the medullary vasomotor center induces initial activation of the sympathetic nervous system
- This activation will lead to increase in heart rate, arterial blood pressure, and myocardial contractility in an effort to improve cerebral perfusion



CARDIAC REFLEXES

Local Regulation

Auto Regulation

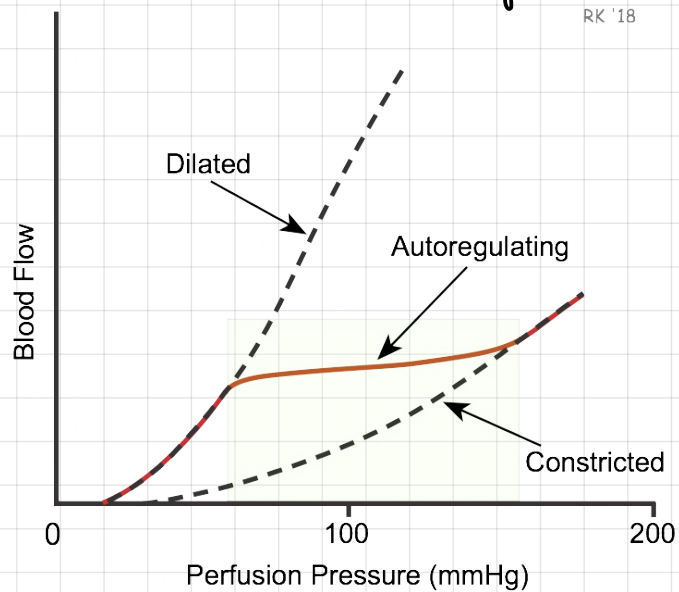
- Capacity of tissue to regulate their own blood flow is autoregulation.

As $F = \frac{\Delta P}{R}$, $\text{flow} \propto \frac{1}{R}$
or $R \propto \frac{1}{\text{flow}}$

- As Pressure increases, smooth muscle fibres that surround vessels constrict, to maintain similar flow.

- As Pressure ↓, R ↓ (dilation of vessel) to maintain flow.

- Kidney, Brain & Coronary circulations have great autoregulation property.
- Skeletal and splanchnic circulation show moderate and skin (cutaneous) show little to no autoregulation.



- Vasodilator metabolites that help in vasodilation of vessels in autoregulation: -

- Dec O_2 tension & pH ↓
- ↑ CO_2 also dilates blood vessels
- Temp. rise also dilates blood vessels
- K^+ ↑
- Lactate
- Histamine

(g) Adenosine → vasodilates in Cardiac muscles not in skeletal muscles.

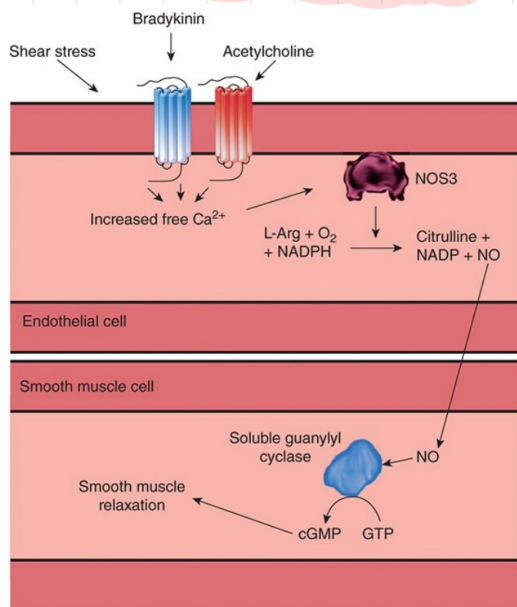
* localised Vasoconstrictor

- ↓
- Serotonin
 - Drop in temp.

Substance Secreted by Endothelium

- (1) **Prostacyclin** :
- Secreted by endothelial cells
 - Inhibits platelets aggregation
 - Promotes vasodilation.

- (2) **Nitrous oxide** :
- Endothelium-derived relaxing factor (EDRF)
 - Now known as NO.



- Synthesized by Arginine.
- NO is short lived and is inactivated by Hb.
- Also a vasodilator
- Penile erection is also produced by NO.
- NO is also imp. for antimicrobial and cytotoxic activity of immune cells.

FIGURE 32-7 Endothelial-derived NO leads to smooth muscle relaxation.

- (3) **Carbon monoxide** :
- A vasodilator in blood vessels.
 - CO is produced by Heme by the enzyme Heme oxygenase - 2 (HO-2).

- (4) **Endothelin-I** :
- A vasoconstrictor

TABLE 32-4 Regulation of endothelin-1 secretion via transcription of its gene.

Stimulators
Angiotensin II
Catecholamines
Growth factors
Hypoxia
Insulin
Oxidized LDL
HDL
Shear stress
Thrombin
Inhibitors
NO
ANP
PGE ₂
Prostacyclin

- ET₁, ET₂ & ET-3 are members of a family of three similar 21-amino acid polypeptides encoded by different genes.

- Many circulating substances affect vascular system.

Vasodilators: Kinin, VIP & ANP $\rightarrow$ secreted by heart

Vasokonstrictors hormones: Vasopressin, Norepinephrine, epinephrine and Angiotensin II
Urotensin-II (in certain diseases)

* VIP $\rightarrow$ Vasoactive intestinal peptide.

ANP $\rightarrow$ Atrial Natriuretic peptide.

BNP $\rightarrow$ B-type / Brain Natriuretic peptide

7th