Regulation of Cardiovascular functions

- Goals:
  - Maintain normal blood pressure (heart pump + vascular resistance + blood volume)
  - Adaptation of blood pressure to special circumstances (redistribution)
    - Maintains the blood flow to the heart and brain (hemorrhage)
    - Increase blood supply to active tissues
    - Increase or decrease heat loss from the body

Discovery of acetylcholine as a neurotransmitter mediating the effects of n. vagus on the heart (1926).
Nobel Prize in physiology or medicine in 1936.

Otto Loewi
1873-1961 (88)
German pharmacologist

Sir Henry Hallett Dale
1875-1968 (93)
English pharmacologist, physiologist
• **Discovery of** vascular pressor- and chemo-receptors
• **Nobel Prize for Physiology or Medicine** (1938)

Corneille Jean François Heymans
• 1892-1968 (76)
Belgian physiologist

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**Neural mechanism: autonomic control**

• **Reflex arc:**
• Stimulus - Receptor – afferent nerve – center – efferent nerve – effector - response
Autonomic efferentation
1. Sympathetic effects

Through thoraco-lumbar sympathetic fibers

a. Sympathetic vasoconstriction ($\alpha_1$: $G_q \rightarrow IP3/DAG \rightarrow Ca^{2+} \uparrow$; tonic, induced) acting on arterioles and veins

\textbf{VASODILATION caused by decreased sympathetic activation}

b. Sympathetic adrenergic vasodilation

$\beta_2$ ($Gs \rightarrow cAMP \uparrow$): blood vessels of skeletal muscle, liver heart and lung

c. Sympathetic cholinergic vasodilation: endothel cells: $M_1$ receptor:

$IP3/DAG \rightarrow Ca^{2+} \uparrow \Rightarrow NO$ release (blood vessels of skeletal muscle: anticipatory vasodilation)

d. Sympathetic effects on the heart

$\beta_1$ ($Gs \rightarrow cAMP \uparrow$): positive chronotropy, inotropy etc.

e. Sympathetic effects on JGA: $\beta_1$ ($Gs \rightarrow cAMP \uparrow$) $\Rightarrow$ renin release $\uparrow$

f. Sympathetic effects on adrenal medulla: adrenaline, noradrenaline release $\uparrow$

Parasympathetic effects on the heart

Action mechanism:

$M_2$ receptor: $cAMP \downarrow$

Parasympathetic vasodilation:

vessels in brain [pial], choroidal, external genitals, some GI glands, lung

Action mechanism:

Endothel cells: $M_1$ receptor: $IP3/DAG \Rightarrow Ca^{2+} \uparrow \Rightarrow NO$ release

$\Rightarrow$ vasodilation

The parasympathetic activation does not influence the TPR.
**Autonomic efferentation**

2. Parasympathetic effects

**Cranial nerves:**
- Facial nerve (VII):
  - Cerebral blood vessels: vasodilation
  - Blood vessels of salivary glands: vasodilation
- Glossopharyngeal nerve (IX)
  - Blood vessels of salivary glands: vasodilation
- **Vagal nerve (X):**
  - Heart: Heart rate ↓; Conductivity ↓; Tonic inhibition of the heart
  - Blood vessels of GI glands: vasodilation
  - Pulmonary blood vessels: vasodilation

**Sacral parasympathetic nerves:**
- N. Pelvic: Blood vessels of external genitalia: vasodilation
EFFERENTATION

PARASYMPATHETIC

Preganglionic

Postganglionic

Ach—Nikotinic R

Ach—Muscarinic R

(VIP, NO)

atropine

Adrenal medulla

Adr (NA)

atropine

SYMPATHETIC

Preganglionic

Postganglionic

Ach—Muscarinic R

(NPY)

NA

α1 R

β1 R

β2 R

Ach—Nikotinic R
Neural mechanisms

3. Sensory efferentation

Primary chemosensitive neurons:
Axon reflex (CGRP, SP => vasodilation)

- A pointed object is drawn moderately over the skin:
- 0. White reaction: vasoconstriction
- Triple response
- 1. Red reaction: capillary opening (vasodilation)
- 2. wheal (swelling): increased permeability (capillary, postcapillary venules)
- 3. Flare (redness spreading): surrounding arteriolar dilation

AXON-REFLEX: NEUROGENIC INFLAMMATION
Receptors, afferent nerves (IX, X)

- **Baroreceptors**: stretch receptors
  - High-pressure receptors:
    - Carotid sinus
    - Aortic arch
  - Low-pressure receptors:
    - right and left atria
    - at the entrance of superior and inferior venae cave and pulmonary veins
    - Pulmonary circulation

- **Chemoreceptors**
  - Peripheral: carotid and aortic bodies (glomerus)
  - Central: medulla
Location of Baroreceptors

Decreased           Normal                      Enhanced

Karotissinuserv

Decreased           Normal                      Enhanced
FUNCTION OF CAROTIC AND AORTIC BODIES

- They have own vessels.
- Rich blood supply

**HYPOXIA**
- K-accumulation
- Depolarisation
- Opening of voltage-gated L-type Ca²⁺ channels
- Dopamine-release
- Impulse in IX/X nerves

Glomus cell

**O₂-sensitive K-channels**
Maintains the resting potential.

Nerve terminal of n. IX és n. X

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Central chemosensitive area

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Vasomotor centers

SPINAL CORD

MEDULLA:
Pressor area: rostral ventrolateral medulla (RVLM)
Depressor area: Caudal medulla

Hypothalamus
Cerebral cortex
1. Spinal cord

**Figure:**
- **Title:** VASOMOTOR CENTERS
- **Diagram:** Illustration of the spinal cord with a lesion labeled 'Lesion'. There is a graph showing changes in arterial pressure (mm Hg) over time (Seconds) with peaks and valleys indicated by the graph line. The graph has labels for 'Total spinal anesthesia' and 'Injection of norepinephrine'.
2. Medulla

NTS = nucleus tractus solitarii: AFFERENTATION

Pressor: Rostral ventrolateral medulla
Depressor: Caudal medulla

FUNCTION OF VASOMOTOR CENTERS

Hypothalamus, cortex
Medulla
Heart
Vessels
Spinal cord

Pressor TONIC ACTIVITY

Heart inhibition

IX
X

Baroreceptors

NTS
• **Pressor area:**
  – activation of sympathetic preganglionic neurons =>
    tonic activation of heart + vasoconstriction (mainly)

• **Depressor area:**
  – direct inhibitory effect on the heart by vagal activation
  – inhibition of pressor area
  – inhibition of sympathetic preganglionic neurons
Tone in blood vessels

Tone: continuous contraction of smooth muscle cells in the wall of blood vessels

1. **Basal tone**: Independent of the nervous system (primarily myogenic origin).
   Brain, heart (coronary) > kidney, skeletal muscle > splanchnic, skin, pulmonary.

2. **SYMPATHETIC OR VASOMOTOR TONE**: is maintained by constant sympathetic activity
   Splanchnic, skin > skeletal muscle > kidney > brain, heart (coronary).

- TPR is determined by sympathetic activity.
- Vasoconstriction: increased sympathetic activity => Blood pressure ↑.
- Vasodilation: decreased sympathetic activity => Blood pressure ↓.

<table>
<thead>
<tr>
<th>Organ</th>
<th>Basal</th>
<th>Vasomotor</th>
<th>Sympathetic activation</th>
</tr>
</thead>
<tbody>
<tr>
<td>coronary</td>
<td>++++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>brain</td>
<td>++++</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>muscle</td>
<td>++</td>
<td>++</td>
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</tr>
<tr>
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<td>+++</td>
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<td>splanchnic</td>
<td>+</td>
<td>++</td>
<td>++++</td>
</tr>
<tr>
<td>skin- acral</td>
<td>-</td>
<td>+++</td>
<td>++++</td>
</tr>
<tr>
<td>skin- non-acral</td>
<td>+</td>
<td>+++</td>
<td>++++</td>
</tr>
</tbody>
</table>
Important reflexes

1. Carotis sinus reflex, aortic arch baroreceptor reflex

Carotis sinus reflex, aortic arch baroreceptor reflex

Carotis sinus receptors: BP ↑
Aortic arch receptors: BP ↑

Depressor
Pressor

Heart rate ↓
Heart contractility ↓
Vasodilation

ETC:
• Respiration ↓
• muscle tone ↓
• Vasopressin ↓
• Drowsiness

BP ↓: Opposite changes.

CO ↓
TPR ↓
BP ↓
2. Chemoreceptor reflex

- Stimulus: hypoxia, hypercapnia, decreased pH (acidosis)
- Receptors: peripheral, central
- Center: activation of pressor area + activation of vagus center

- Response: BP ↑; HR: it would decrease (↓ !), but the hyperventilation increases it (↑)!
FUNCTION OF CHEMORECEPTOR REFLEXES

1. The major function of these reflexes is the stimulation of breathing.

2. Only very severe hypotension (below 60-80 mmHg) results in hypoxia/hypercapnia that is capable of eliciting significant vasoconstriction through chemoreceptors.

Special applications
1. Diving reflex

2. CNS ischemic reflex (Cushing reaction)
Cushing reflex

Increased intracranial pressure =>
Hypoxia + hypercapnia at brain level (ischemia) =>
activation of pressor area + vagus nerve =>
Hypertension + bradycardia

Loven reflex

- Somatic pain stimulus (local vasodilation),
- Pressor center activation
- Response: Systemic vasoconstriction (sympathetic activation)
Goltz reflex

- Stimulus:
- Strong mechanical stimulus of visceral organs (abdominal kicking)
- Activation depressor center
  - HR ↓ and BP ↓

Compensations for effects of standing

- Mean arterial pressure: ↓ 5 mmHg
- Central venous pressure: + 30%
- Heart rate: ↓ 40%
- Stroke volume: ↓ 25%
- Cardiac output: ↓ 10%
- Total peripheral resistance: ↓ 25%
- Splanchnic circulation: ↓ 25%
- Venous tone: + 100 ml
- Central blood volume: ↓ 400 ml
- Leg volume: + 600 ml
Valsalva Maneuver

Forced expiration against a closed glottis

Changes are due to the increased intrathoracic pressure:

- Decreased venous return
- Increased HR and MAP
- $\Rightarrow$ stroke

![Valsalva Maneuver Diagram]
Müller Maneuver

Forced inspiration against a closed glottis:

Changes are due to the decreased intrathoracic pressure

Stroke volume ↓, Cardiac output ↓ => baroreceptor activation => TPR ↑ => Pulse pressure ↑ HR (↑)

Bainbridge reflex

- Stimulus: increased atrial pressure
- Stretch receptor activation in the atria => afferentation: n. vagus => medulla => inhibition of vagal nerve + sympathetic activation =>
- HR ↑, if the basal HR was low
- (DOG).
Diving reflex

• Submerging the face into water => nerve V (trigeminal) activation => medulla => vagus activation (HR ↓) + pressor center activation
• This reflex puts the body into oxygen saving mode to maximize the time that can be spent under water, and includes three factors:
  • Bradycardia
  • Peripheral vasoconstriction, a decrease in blood flow to the extremities, in order to increase the supply of blood and oxygen to the vital organs, especially the brain.
  • Blood shift, the shifting of blood plasma to the thoracic cavity to avoid the collapse of the lungs under higher pressure during deeper dives.
BEZOLD-JARISH REFLEX

Activation of C-fibers in the heart (lung)

Significance: Blood pressure regulation
It may lead to hypotension during myocardial infarct.

The short- and long-lasting regulation of blood pressure

- Within seconds: pressor responses
  - baroreceptor reflex
  - chemoreceptor reflex
  - adrenal medulla secretion
- Within minutes and hours: changes in filtration at capillary level
  - renin-angiotensin
- Within hours, days: blood volume regulation (changes in renal filtration, renal reabsorption; fluid intake)
  - Renin-angiotensin-aldosterone
  - ADH