Cardiovascular Physiology III.

48. Short-term control mechanisms of arterial blood pressure.
49. Long-term control of arterial blood pressure.

Ferenc Domoki, November 13 2018.

Control of circulation

Systemic control
Major goal: to maintain constant perfusion pressure ($\Delta P$) chiefly by regulating mean arterial blood pressure (MABP)

Local control
Major goal: to maintain adequate blood flow to meet locally the metabolic and functional needs of the tissue. Hemostasis, and immune functions also affect local blood flow.
Systemic control of the circulation

1. Renal and hormonal regulation of MABP through pressure diuresis and volume regulation
2. Neural regulation of MABP via reflexes of the autonomic nervous system

REGULATION OF MEAN ARTERIAL BLOOD PRESSURE

\[ \Delta P = Q \times R \]

Q (cardiac output): Volume / time

Total Peripheral Resistance: diameter of arterioles

\[ \Delta P = MABP - CVP \]

CVP \approx 0 \text{ mmHg}

HEART (Contractility, rate)
VENOUS RETURN (ECV and blood volume, venous constriction (compliance)
1. Renal and hormonal regulation of MABP = volume regulation

- Urine output increases drastically with increasing MABP = PRESSURE DIURESIS
- Increased urine output will lead to decreased blood pressure (see next diagram)
- Pressure diuresis is modified by hormonal regulation of renal function to adapt to change in salt and fluid intake (osmo- and volume-regulation)

INTEGRATED BLOOD PRESSURE REGULATION

CNS control: Fast Adaptable

Renal & hormonal control: Slow Powerful
BLOOD PRESSURE (MABP) REGULATION BY VOLUME REGULATION: PRESSURE-DIURESIS

BLOOD PRESSURE  \rightarrow URINE OUTPUT

CARDIAC OUTPUT  \uparrow

EXTRACELLULAR AND BLOOD VOLUME

VENOUS RETURN  \rightarrow MEAN FILLING PRESSURE

INCREASES  \rightarrow DECREASES

BLOOD PRESSURE REGULATION BY VOLUME REGULATION: HORMONES

ATRIAL NATRIURETIC HORMONE (ANH)

BLOOD PRESSURE  \rightarrow URINE OUTPUT

RENIN-ANGIOTENSIN-ALDOSTERON AXIS VASOPRESSIN

INCREASES  \rightarrow DECREASES
Pressure diuresis is modulated by hormonal effects

- ANH increases diuresis thus decreases MABP
- The renin-angiotensin-aldosterone axis (RAS) decreases diuresis thus increases MABP
- Vasopressin (AVP) decreases diuresis thus increases MABP
- Details of these hormone systems: renal physiology

Direct vasoactive effects of these hormones

- Under pathological conditions (shock) and/or at high supraphysiological concentrations, these hormones can directly affect TPR:
  - ANH causes vasodilation (NPR1 receptor, also GC-A, cGMP ↑ coupling), MABP ↓
  - Angiotensin-2 causes vasoconstriction (AT1 receptor, IP3/DAG/Ca^{2+} ↑ coupling), MABP ↑
  - Vasopressin causes vasoconstriction (V1 receptor, IP3/DAG/Ca^{2+} ↑ coupling), MABP ↑
Systemic control of the circulation

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2. Neural regulation of MABP via reflexes of the autonomic nervous system

Otto Loewi identified acetylcholine as a neurotransmitter mediating the effects of n. vagus on the heart (1926).
For the discovery of chemical transmission of nerve action, Otto Loewi and Sir Henry Hallett Dale shared the Nobel Prize in physiology or medicine in 1936.
REGULATION OF MEAN ARTERIAL BLOOD PRESSURE

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- **Q** (cardiac output): Volume / time
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- **VENOUS RETURN** (ECV and blood volume, venous constriction (compliance))
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\[ \Delta P = \text{MABP-CVP} \]

\[ \text{CVP} \approx 0 \text{ mmHg} \]

SYSTEMIC NEURAL REGULATION OF CIRCULATION: EFFERENTS

- **Vasomotor center**
- **Vessels**
- **Vagus**
- **Heart**
- **Vessels**

- **Sympathetics** have an exclusive role in the regulation of TPR.!!!!!
SYSTEMIC EFFECTS OF CATECHOLAMINES ON CIRCULATION

β-1 Stimulation of the heart

α-1 Contraction of veins

Increased venous return

Increased cardiac output

α-1 Contraction of arterioles

α-1 / β-2 Less strong contraction of arterioles in skeletal muscle

Increased TPR

INCREASED BLOOD PRESSURE

Components of the resting tone in arteriolar smooth muscle

RESTING TONE = BASAL TONE + NEUROGENIC TONE

Systemic hormones

Myogenic tone

Sympathetic vasoconstrictor tone

Local vascular (endothelial) factors

Local tissue humoral factors
Sympathetic vasoconstrictor innervation of vascular smooth muscle: role of noradrenaline (α-1 metabotropic receptor) AND ATP (P2X1 ionotropic receptor) cotransmission!

• Not all vessels have significant sympathetic vasoconstrictor tone! Cerebral and coronary vessels are the most important exemptions!

Sympathetic vasoconstrictor system

• Sympathetic nerves carry large number of vasoconstrictor nerve fibers and only a few vasodilator fibers.

• Sympathetic vasoconstrictor effect is most powerful in the kidneys, gut, spleen, and skin, less potent in skeletal muscle and the brain.

• Sympathetic system maintains normal sympathetic vasoconstrictor tone by continuously firing at a rate of 0.5-2.0 imp/sec. Thus, blood vessels maintain vasomotor tone.

• Not all vessels have significant sympathetic vasoconstrictor tone! Cerebral and coronary vessels are the most important exemptions!
2018.11.19.

**VASOMOTOR CENTERS**

1. **SPINAL CORD**

   Sympathetic vasomotor tone is LOST after transection of the spinal cord (MABP falls: spinal SHOCK), but retained if the medulla remains connected. The ORIGIN of the sympathetic tone resides in the MEDULLA.

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**INTEGRATED BLOOD PRESSURE REGULATION**

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VASOMOTOR CENTERS

2. MEDULLA

Rostral ventrolateral Medulla (RVLM) generator of sympathetic tone

Caudal ventrolateral medulla (CVLM)

Inhibition of RVLM + stimulation of cardiac parasympathetic tone

NTS= nucleus tractus solitarii: AFFERENTATION

Baroreceptor zones and nerves

- Carotid sinus – ramus caroticus nervi glossopharyngei (Hering’s nerves)
- Aortic arch – rami cardiaci nervi vagi (n. depressor in other species)

Heinrich Ewald Hering 1866-1948
The baroreceptors are primary sensory neurons, morphologically they are pseudounipolar neurons, functionally they are interoceptive mechanoreceptors.

The cell bodies in sensory ganglia of cranial nerve IX and X.

Peripheral nerve arborize in the medial-adventitial border in the wall of the carotid arteries (sinus caroticus) and the aorta.

RESPONSE PROPERTIES OF ARTERIAL BARORECEPTORS

- Nerve endings respond to mean pressure, pulse pressure (i.e. SABP-DABP), and rate of change of pressure (dP/dt)
- Actually, they respond to pressure-induced changes in wall tension: carotid massage can interfere with the receptors.
BAROREFLEX PATHWAYS IN THE MEDULLA OBLONGATA

*Sympathetic NS*

1. Initial input to nucleus of the tractus solitarius (NTS)
2. Excitatory connection to caudal ventrolateral medulla (CVLM)
3. Inhibitory connection to rostral ventrolateral medulla (RVLM)

BAROREFLEX PATHWAYS IN THE MEDULLA OBLONGATA

*Parasympathetic NS*

1. Initial input to nucleus of the tractus solitarius (NTS)
2. Excitatory connection to dorsal motor nucleus of the vagus (dmnX)
3. Excitatory connection to nucleus ambiguus (nA)
BAROREFLEX CONTROL OF SNA AND PSNA

- ↑ baroreceptor input → ↓ SNA
- ↑ baroreceptor input → ↑ PSNA

Baroreceptor control system

Source: Mehlerman St, Nafz U: Cardiovascular Physiology. 6th Edition: http://www.accessmedicine.com
Postural change:

Standing up is causing a DEACTIVATION of baroreceptors that stimulates sympathetic tone on the heart, arterioles and veins.

NOTE: everything changes EXCEPT mean arterial blood pressure – homeostatic regulation!

SIGNIFICANCE OF CAROTID SINUS REFLEX

- Prompt defense against oscillations in blood pressure (buffering).
- Normal blood flow to the brain (standing up).
- The reflex is active in the normal range of blood pressure (60-180 mmHg).
- The baroreceptors adapt: The reflex cannot correct chronic alterations in blood pressure.
- Carotid sinus is more sensitive than the receptors in the aortic arch.
„Low pressure“ – „cardiopulmonary“ baroreceptors: sensors of blood volume and venous return

Weak depressor reflexes can be evoked from all low pressure baroreceptor areas. Right atrial stretching may elicit increased heart rate in some species (Bainbridge reflex). Stimulation results in inhibition of vasopressin secretion contributing to blood volume regulation.

Systemic blood pressure control during adaptation, stress and emergency situations
These factors also affect baroreceptor sensitivity

- response to exercise (central command)
- sense of danger (fighting/defense reaction)
- central ischemic response
- ↑ intracranial pressure (Cushing reflex)
- ↑ PCO₂, ↑ PCO₂ in arterial blood
- ↓ central venous pressure (cardiopulmonary baroreflexes)
- cutaneous pain

![Diagram of baroreceptor sensitivity](image)

CheMORECEPTOR REFLEXES

**HYPOXIA**

- Hypercapnia
- Acidosis

**HYPERCAPNIA**

- Acidity

![Diagram of chemoreceptor reflexes](image)

**MEDULLA**

Pressor area

- n. IX

- Glomus caroticum
- Carotid sinus

- A. carotis communis

- Glomus aorticum
- Aortic arch

**Ventral surface of medulla**

- Pons

**Sympathetic vasoconstriction**

- Blood pressure rises.

- Heart rate does NOT increase, in contrast, it slows down!
GLOMUS CAROTICUM (CAROTID BODY) AND GLOMUS AORTICUM (AORTIC BODY)

- The aortic and carotid bodies receive their own blood supply.
- These organs have the highest blood flow per mg tissue in the body.

Some details of glomus cell physiology are still unresolved: a modern view supports multiple transmitters
MEDULLARY CHEMOSENSITIVE AREAS

\[
\text{CO}_2 + \text{H}_2\text{O} = \text{H}_2\text{CO}_3
\]

\[
\text{H}^+ \quad \text{HCO}_3^- \quad \text{Pressor area}
\]

Chemosensitive neuron

Blood flow to the brain

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
CNS ischemic reflex
(Cushing reaction)
INTEGRATED CONTROL OF BLOOD PRESSURE

1-30 sec  1-30 min  1-16 hours  1-16 days

Autoregulation  Angiotensin-Vasopressin: vasoconstriction  Transcapillary fluid shift

Correction power (gain)

Change in pressure
CNS ischemic r.
Baroreceptor r.
Chemoreceptor r.

Kidney: Pressure-volume control
Vasopressin: Fluid control
Angiotensin-Aldosterone: Na-fluid control

Long-term control is achieved through volume regulation.