Basic Mechanisms of Circulatory Control

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Major Physiologic Mechanisms Regulation Blood Pressure

• Rapidly Induce Reflexes: Act very rapidly, within seconds or minutes:
  (1) Baroreceptor,
  (2) Chemoreceptor
  (3) CNS ischemic response.

• Responses of Intermediate Time Course: Develop their major response 30 minutes to a few hours:
  (1) Stress-relaxation
  (2) Capillary fluid-shift
  (3) Renin angiotensin system

• Long-Term Mechanisms: Develop over one day and strengthen further to dominate longer term BP control:
  (1) Powerful renal pressure natriuresis
  (2) Regulation of aldosterone.
Major physiologic mechanisms regulating blood pressure

-Time course and strength (in terms of feedback gain) of:
- BP corrective mechanisms
- after a sudden change in arterial pressure is applied (indicated by $\Delta$)
Clinical Testing and Stimulation of Baroreceptors

• The function of the baroreceptors can be tested by:

  * monitoring changes in heart rate:
    - as a function of increasing arterial pressure
    - during infusion of phenylephrine (α-adrenergic agonist)

  * monitoring changes in pulse and BP:
    - in response to brief periods of straining (forced expiration against a closed glottis):
      “Valsalva maneuver”
The Chemoreceptor Reflex

• Normally the chemoreceptor reflex:
  - plays very little or no role in BP control.

• The chemoreceptor reflex only becomes significant:
  - at times of hypotension (BP < 60 mm Hg)
  - with consequence hypoxia.

• If pO₂ falls enough:
  - (+) chemoreceptors of the carotid and aortic bodies
  - the reflex (+) respiration and
  - causes some (+) of the vasomotor center
  - increasing COP and TPR.
The CNS Ischemic Response Reflex

• The reflex is excited by:
  - ischemic phenomena (raised pCO$_2$ and acidosis more than hypoxia) in the area of the medullary vasomotor area i.e brainstem damage because of local disease.
  - systemic hypotension (BP < 50 mm Hg)
  - and/or ischemia.

• The reflex is the most powerful stimulus of the SNS:
  - causing profound vasoconstriction.
Stress-Relaxation and Capillary Fluid-Shift Mechanisms

• The increase in capillary bed hydrostatic pressure:
  - shifting the Starling force equilibrium
  - favor fluid movement from the circulation into ISF.

• The capillary fluid–shift mechanism:
  - reduces circulatory filling, preload, COP, and BP.

• Stress-relaxation and capillary fluid-shift:
  - limit rapid BP rises.
The wall of the afferent arteriole within the JG apparatus acts as an:
- integrator of signals for activation of renin release.

Renin is the rate-limiting factor in activation of the RAS.

Factors that activate renin release include:
- decrease arterial blood pressure (ABP),
- hypovolemia,
- decrease in sodium delivery to the proximal renal tubule,
- β-adrenoreceptor sympathetic stimulation.
RAS has an influence on long-term BP regulation:
- it interacts with: Renal pressure-natriuresis system and aldosterone-$\text{Na}^+$ retention pathway.
Renin Angiotensin System

• Plays an important role in the origin of raised BP by:
  - being inappropriately active in the face of elevated BP

• The RAS is activated when there is:
  - arterial disease/narrowing afferent to glomeruli
  - a population of nephrons with reduced perfusion.
**Renin Angiotensin System**

- Reduced delivery of NaCl to macula densa as in:
  - glomerular disease with less filtration for normal afferent flow.
  - diabetes where the proximal Na\(^+\) reabsorption is greater than normal

- In both renal or renal arterial disease:
  - Renin release predispose to HTN.
  - (-) renal pressure natriuresis predispose to sustained HTN.
Na⁺ homeostasis normally determines ECF volume and BP.

The renal pressure natriuresis mechanism:
- entraining Na⁺ excretion to maintain normotension.

- sustained HTN occurs if pressure natriuresis is (-).
In response to increased BP:
- a pressure rise is transmitted from the systemic circulation to the glomeruli of the nephrons across the afferent vascular resistance.

Effectiveness of the renal pressure natriuresis is impaired if transmission of pressure is limited by:
- RA stenosis
- Experimental in the clipped kidney in Goldblatt HTN models
Renal Pressure Natriuresis

• Increased pressure reaching the nephrons:
  - enables an increase in $\text{Na}^+$ and water filtration at the glomeruli.

• Changes in renal $\text{Na}^+$ handling:
  - a reduced fractional reabsorption of $\text{Na}^+$ ($\text{FR}_{\text{Na}}$)
  - increased natriuresis.

• Aldosterone is the principle regulator of $\text{Na}^+$ reabsorption in the late DCT-CD.
• The aldosterone-responsive distal nephron:
  - receives from 2% to 3% of filtered Na\(^+\)
  - plays an important role in maintaining Na\(^+\) balance
  - regulates Na\(^+\) reabsorption over a 100-fold range
    (0.02% to >2% of filtered Na\(^+\)) to match requirements.

• The pathway by which aldosterone upregulates Na\(^+\) reabsorption in kidney:
  - is key in regulating Na\(^+\) balance and
  - highly implicated in BP control.
Other Blood Pressure Control Mechanisms

• Additional BP control systems:
  - the natriuretic peptide,
  - ET, and
  - NO systems

• The natriuretic peptide and ET systems:
  - may be less critical than the RAS in normal BP control
  - they modulate the renal-pressure natriuresis system

• ANP and ET play important roles in certain contexts:
  - the volume-expanded state for ANP
  - renal ischemia for ET