REGULATION OF CARDIOVASCULAR SYSTEM

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- Intrinsic
  - Coupling of cardiac and vascular functions
    - Autoregulation of vessel diameter
- Extrinsic
  - Neural
    - short term
  - Hormonal
    - long term
Autoregulation of Blood Flow through Organs and Tissues

**AUTOREGULATION**

- Constant blood flow in a tissue or organ in the face of changing perfusion pressure
  - Matches blood flow to demand of tissues as long as mean arterial pressure is normal
AUTOREGULATION OF BLOOD FLOW IN AN ORGAN

- FLOW (Q) cm³/s = ΔP / R

- However, for a particular organ
  - No change in blood flow when MAP is 60 - 140 mmHg (Autoregulation)
    - due to automatic contraction & relaxation of arterioles and sphincters

As long as the BP is adequate, the blood flow through an organ is controlled within the organ.

A pre-capillary sphincter regulates the flow of blood through the capillaries in an organ.
Autoregulation of vessel diameter

**AUTOREGULATION**

- Constant blood flow in a tissue or organ in the face of changing perfusion pressure
  - Operates when MAP = 60 - 140 mmHg
  - Matches blood flow to demand of tissues as long as mean arterial pressure is normal

- Can be explained by:
  1. Myogenic hypothesis
  2. Metabolic hypothesis
  3. Tissue pressure hypothesis
  4. Flow velocity dependent dilatation
MYOGENIC (BAYLISS) HYPOTHESIS

- Stretch of vascular smooth muscle $\Rightarrow$ contraction
- Decreased tension in smooth muscle $\Rightarrow$ relaxation

$\Rightarrow$

- $\uparrow$ arterial pressure (+ associated $\uparrow$ blood flow) $\Rightarrow$
  stretch of arteries & arterioles $\Rightarrow$
  constriction of vessels $\Rightarrow$
  $\uparrow$ resistance $\Rightarrow$
  $\downarrow$ blood flow

MYOGENIC (BAYLISS) HYPOTHESIS [contd.]

- Mechanism:
  Stretch of smooth muscle $\Rightarrow$ $\uparrow$ intracellular [Ca++] $\Rightarrow$ activation of contraction

  - Response is enhanced by catecholamines & sympathetic stimulation (extrinsic control)
  - Response is inhibited by NO & metabolic products (intrinsic control)
METABOLIC HYPOTHESIS

- Dilatation of arterioles ←
  - ↓ metabolic substrate (e.g. O₂)
  - ↑ metabolic products (e.g. CO₂, H⁺)
  - ↑ Temperature
  - Adenosine, Lactate, K⁺, Prostacyclin, NO, Bradykinins, Histamine

TISSUE PRESSURE HYPOTHESIS

- This mechanism applies to an organ enclosed by a rigid capsule (e.g. kidney)

- ↑ Blood flow →
  - ↑ Perfusion pressure →
  - ↑ capillary filtration →
  - ↑ Interstitial (tissue) pressure →
  - Compression of small vessels →
  - ↓ blood flow
**FLOW VELOCITY DEPENDENT DILATATION**

↑ Blood flow velocity →
↑ shear stress on endothelium →
release of NO (EDRF) →
vessel dilatation → ↓ velocity of flow

[N.B. Velocity = Volume Flow / Cross-sectional area of vessel]

**ENDOTHELIAL & PLATELET FACTORS**

- Relaxing factors:
  - Nitric Oxide (EDRF)
  - Prostacyclin

- Contracting factors:
  - Endothelin-1 (EDCF)
  - Thromboxane A₂ & Serotonin from platelets
**NITRIC OXIDE**

- Released by:
  1. Norepinephrine stimulation of α2 receptors => opposes direct norepinephrine vasoconstrictive effect on vascular smooth muscle
  2. Acetylcholine (e.g. released by parasympathetic nerves onto arterioles in penis)
  3. Histamine, bradykinin & calcium channel stimulation
  4. ↑ Blood flow velocity
     - N.B. Viagra → ↑ NO → Activates Guanylyl Cyclase → ↑ cGMP → Arteriolar smooth muscle relaxation → ↑ penile blood flow

**Endothelin-1**

- Released from damaged endothelium
- Effects include:
  - Vasoconstriction
  - +ve Inotropic and +ve Chronotropic effects
  - In kidneys:
    - ↓ GFR
    - ↓ & ↑ Na+ reabsorption via different mechanisms
REGULATION OF CARDIOVASCULAR SYSTEM

- Intrinsic
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- Extrinsic
  - Neural
    - for short term regulation of changes in B.P. (e.g. due to changes in posture)
  - Hormonal
    - for long term changes involving control of fluid and electrolytes

Neural Feedback Control of CVS

Central Nervous System (Brain & Spinal Cord)

Sensor

Physiological factor e.g. blood pressure

Effector Organs & Systems

Afferent Impulses

Efferent Impulses
NEURAL CONTROL SYSTEM: SENSORS

1. Arterial Baroreceptors
2. Cardiopulmonary Baroreceptors
3. Chemoreceptors
4. Pulmonary Receptors

Orthostatic or Postural Hypotension

- Sudden fall in BP (usually > 20/10 mmHg) on standing up
- ?→ faintness, dizziness, light-headedness
- Occurs more commonly in the elderly
Orthostatic Hypotension - Pathophysiology

- Suddenly standing up ➔
- pooling of blood in veins (1/2 – 1 litre) ➔
- failure of BP control mechanisms to function.
ARTERIAL BARORECEPTOR REFLEX: SENSORS & AFFERENTS

- Carotid & Aortic Sinuses
  - Sensors = Mechanoceptors => Respond to stretch
  - Carotid baroreceptors dominate over the aortic baroreceptors
  - Carotid sensors are more sensitive to changing pressure than to sustained pressure
  - Threshold of baroreceptors is increased in hypertension

- Afferents to CNS via:
  - Vagus nerve (cranial nerve X)
  - Glossopharyngeal nerve (cranial nerve IX)

ARTERIAL BARORECEPTOR REFLEX: INTEGRATIVE CENTRES - FUNCTIONAL DESCRIPTION

- Set point for MAP ~ 100 mmHg
- Pressor area
  - Dorsolateral medulla
  - Stimulation ----> Pressor Response i.e.
    - ↑ heart rate (+ve Chronotropic & Dromotropic effects)
    - ↑ Myocardial contractility (+ve Inotropic effect)
    - Vasoconstriction
- Depressor area
  - Caudal & Ventromedial to Pressor area
    - Inhibits pressor area
    - Direct effects on target organs to oppose pressor effects
ARTERIAL BARORECEPTOR REFLEX: EFFERENT FIBRES & EFFECTS

- Sympathetic Activation →
  - ↑ Contractility
  - ↑ Heart Rate, no beat-to-beat effect, however shifts the baseline bias for more direct vagal effect
  - ↑ Total peripheral resistance
  - ↑ Venomotor tone
  - ↑ Release of epinephrine & norepinephrine from adrenal gland

- Sympathetics innervate entire vascular tree

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ARTERIAL BARORECEPTOR REFLEX: EFFERENT FIBRES & EFFECTS [CONT.D]

- Parasympathetic Activation →
  - ↓ Heart Rate (i.e. -ve Chronotropic & Dromotropic effects)
    - Vagus has a beat-to-beat influence on SA node (heart rate)
  - ↓ Contractility (i.e. -ve Inotropic effect)
    - Effect on atria > ventricle

- Parasympathetics innervate some vessels e.g. coronary (constrict), cerebral (dilate), genital (dilate) circulations
  - Do not innervate vessels of skin & skeletal muscles
NEURAL CONTROL REFLEXES:
SENSORS

1. Arterial Baroreceptors
2. Cardiopulmonary Baroreceptors
3. Chemoreceptors
4. Pulmonary Receptors

CARDIOPULMONARY BARORECEPTOR REFLEX

- Sensors located in
  - Atria
  - Ventricles
  - Pulmonary vessels
- Vagal & sympathetic afferents
- Efferents from medulla
- Stimulation by ↑Blood Volume →
  - ↑ heart rate (Bainbridge reflex)
  - ↓ sympathetic stimulation of kidneys → ↑ renal blood flow & ↑ urine flow
- Hormonal response via release of atrial natriuretic hormone

When starting Heart rate is low
- Cardiopulmonary reflex dominates → high heart rate

When starting HR is high
- Baroreceptor reflex dominates → low heart rate
NEURAL CONTROL REFLEXES: SENSORS

1. Arterial Baroreceptors
2. Cardiopulmonary Baroreceptors
3. Chemoreceptors
4. Pulmonary Receptors

CHEMORECEPTOR REFLEX

- Peripheral chemoreceptors (Carotid bodies & Aortic bodies)
  - Main stimulus = ↓ O₂ (may result from ↓ MAP)
  - Stimulation → Pressor response
- Central chemoreceptors in medulla
  - Main stimuli = ↑ CO₂, ↑ H⁺; may result from cerebral ischaemia or changes in peripheral circulation
  - Acute Stimulation →
    - ↑ Ventricular contractility & TPR (← Sympathetic stimulation) i.e. Pressor response.
    - ↓ Heart rate (← Parasympathetic stimulation)
  - Chronic Stimulation → Depressor response → ↓ CO
NEURAL CONTROL REFLEXES:
SENSORS

1. Arterial baroreceptors
2. Cardiopulmonary baroreceptors
3. Chemoreceptors
4. Pulmonary receptors

PULMONARY REFLEXES

- Respiration → Rhythmic changes in heart rate (12 cycles per min = 12/60 s = 0.2 Hz)
  - via CNS discharge thro’ ANS efferents
- Respiration → Rhythmic changes in diameter of arterioles → Traube - Hering waves (= Tonic B.P. Oscillation at respiratory frequency)
  - cp. Mayer waves (0.1Hz) i.e < respiratory frequency
- Inflation of lungs (e.g. During mechanical ventilation) → Activation of lung stretch receptors → ANS afferents →
  - ↑ Heart rate
  - systemic vasodilatation
  - ↓ B.P.
- Collapse of lungs → Opposite effects i.e. ↓ Heart rate, reflex vasoconstriction, ↑ B.P.
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Angiotensin II →

- Vasoconstriction (via AT1A receptors on blood vessels)
- Thirst
- Aldosterone release (via AT1B receptors in adrenals)
  \[ K^+ & Na^+ \text{ excretion by kidneys} \rightarrow \uparrow \text{Blood Volume} \rightarrow \uparrow \text{B.P.} \]

- Vasopressin (ADH)
  (from Posterior Pituitary)
  \[ \text{Water Excretion (via V2 receptors in kidneys)} \rightarrow \uparrow \text{blood vol.} \]

Vasoconstriction (via V1 receptors on blood vessels)
Atrial natriuretic peptide/hormone →

- Vasodilatation
- Na⁺ & water excretion
- ↓ thirst

N.B. ANF & Angiotensin II have opposite effects, however they both inhibit renin secretion, as does vasopressin.

HORMONAL CONTROL

- **Epineprine**
  - Effects on heart similar to norepinephrine
  - In skeletal muscle
    - ↓ Concentration → arteriolar dilatation
    - ↑ Concentration → arteriolar constriction
HORMONAL CONTROL

- The following hormones ↑ heart rate or contractility
  - THYROID HORMONES
  - GLUCAGON
  - INSULIN
  - ADRENOCORTICOIDS
SHORT v/s LONG TERM EXTRINSIC REGULATION OF B.P.

- **Short - term regulation of B.P.**
  (e.g. Due to changes in posture)
  - Involves neural reflexes

- **Long - Term regulation of B.P.**
  - Involves control of fluid and electrolytes by hormones