Cardiovascular System

Regulation of cardiac output

Intrinsic and extrinsic factors

October 22, 2019 (6th week – Winter Semester 2019/2020)
Cardiac Output

- the amount of blood pumped by each ventricle in one minute.

- **Cardiac Output** = Heart Rate * Stroke Volume
  - HR is the number of heart beats per minute
  - SV is the amount of blood pumped out by a ventricle with each beat [SV = EDV – ESV]

- is around 5L/min (70 beats/min × 70 ml/beat = 4900 ml/min) and varies with demands of the body.

- **Cardiac reserve** is the difference between resting and maximal CO
Stroke Volume

SV is the difference between end-diastolic volume (EDV) and end-systolic volume (ESV).

SV is the amount of blood pumped out by a ventricle with each beat \([SV = EDV – ESV]\).

SV is determined by extent of venous return and by sympathetic activity.

SV is influenced by two types of controls:

- Intrinsic control
- Extrinsic control

- Both controls increase stroke volume by increasing strength of heart contraction (inotropic effects)
Factors Affecting Cardiac Output

- The heart rate and stroke volume are under the dual control of:
  - (1) Regulatory mechanisms intrinsic to the heart (result from normal functional characteristics of heart - contractility, HR, preload stretch),
  - (2) Neural and hormonal pathways that are extrinsic to the heart.

- Heart rate
  - Autonomic innervation
  - Hormones (epinephrine, norepinephrine, thyroid hormone)
  - Cardiac reflexes

- Stroke volume
  - Starlings law
  - Venous return
  - Cardiac reflexes
Regulation of Cardiac Output

1) Nervous control (extrinsic)
   • Sympathetic control
   • Parasympathetic control
   • Higher centers
   • Reflexes

2) Hormonal Control (extrinsic)

3) Autoregulation (intrinsic)

4) Other factors
Regulation of Cardiac Output

- **Intrinsic regulation**: Results from normal functional characteristics
  - Starling’s law of the heart

- **Extrinsic regulation**: Involves neural and hormonal control
  - Parasympathetic stimulation
    - Supplied by vagus nerve, decreases heart rate, acetylcholine secreted
  - Sympathetic stimulation
    - Supplied by cardiac nerves, increases heart rate and force of contraction, epinephrine and norepinephrine released
Fig.: Factors Influencing Cardiac Output
Regulation of Cardiac Output

- Stroke volume usually remains relatively constant
  - Starling’s law of the heart – the more the cardiac muscle is stretched, the stronger the contraction
- Changing heart rate is the most common way to change cardiac output
Regulation of Heart Rate
Regulation of Heart Rate

- The resting HR is determined by the degree of the vagal tone.
- Vagal tone is greater in males than females, in adults than in children and in athletes than in non-trained persons.
- Physiological variations in HR are related to age, sex, physical training and metabolic rate.
Regulation of Heart Rate

- Regulation of heart rate includes 3 mechanisms:
  
a) **Nervous regulation**: Changes in HR by afferent impulses that modify the activity of the cardiac centers in the medulla oblongata.

b) **Chemical regulation**: Changes in HR due to changes in the chemical composition of blood.

c) **Physical regulation**: Changes in HR due to changes in body temperature.
(a) NERVOUS REGULATION

❤ cardiac centers in the medulla oblongata $\rightarrow$ change in their activity $\rightarrow$ changes on the HR.

1) Impulses from the right atrial receptors “Bainbridge reflex”:

- *Bainbridge reflex* $\rightarrow$ the reflex increase of HR due to increase of the RA pressure $\rightarrow$ increase of venous return and venous pressure in the RA (e.g. during muscular exercise) causes reflex heart acceleration.
(a) NERVOUS REGULATION

- The increased right atrial pressure → stimulation of stretch receptors (=volume receptors) in the atrial wall → discharge of impulses along afferent vagal fibers to the medulla oblongata → stimulation of the vasomotor centre → efferent impulses along the sympathetic nerves to the heart → increase of the HR.
(a) NERVOUS REGULATION

2) Impulses from the arterial baroreceptors of the aortic arch & carotid sinus “Mary's reflex” / baroreceptor reflex.

- *Mary's reflex* (Mary's Law) states that “the heart rate is inversely proportional to the arterial blood pressure “ provided that other factors affecting HR remain constant.

Thus, increase of ABP → decrease of HR
decrease of ABP → increase of HR
(a) NERVOUS REGULATION

![Heart symbol]  ↑ ABP → stimulation of the arterial baroreceptors in the aortic arch and carotid sinus → afferent impulses along the buffer nerves → stimulation of cardio-inhibitory centre (CIC) → ↑ vagal tone and in turn decrease of HR.

![Heart symbol]  ↓ ABP (as in haemorrhage) → decrease of number of impulses from the arterial baroreceptors to the CV centers in the medulla oblongata → inhibition of the CIC and stimulation of the vasomotor centre (VMC) → increase of HR.
(a) NERVOUS REGULATION

3) Impulses from the respiratory centre and the lungs: "Respiratory sinus arrhythmia" = a regular increase in HR during inspiration and decrease in HR during expiration. It occurs during deep respiration.

- The increase in HR during inspiration may be due to inhibition of the depressor area (CIC) and decrease of the vagal tone by the following mechanisms:

  a) During inspiration, the activity of the inspiratory centre irradiates inhibitory impulses to CIC.

  b) During inspiration, expansion of the lungs → stimulation of stretch receptors in the wall of the alveoli → discharge of impulses along afferent pulmonary vagal fibers → inhibition of CIC.

  c) During inspiration, the venous return to the heart is increased → stimulation of the stretch receptors in the right atrium → discharge of impulses along afferent vagal fibers → inhibition of CIC.
4) Impulses from the higher centers (cerebral cortex & hypothalamus):

- Certain areas in the cerebral cortex can influence heart rate through their effects on the hypothalamus and the cardiac centers in the medulla oblongata e.g.

- During emotions & muscular exercise, impulses from the cerebral cortex → stimulation of the vasomotor centre → increase of HR.

- The conditioned reflexes which mediated via the cerebral cortex → increase or decrease of HR in response to visual or auditory stimuli.

- The hypothalamus also contain nuclei which can modify HR e.g. during sleep or emotions.
5) Impulses from other parts of the body:

a) Skeletal muscles (Alam – Smirk reflex):
   - During muscular activity, the proprioceptors of the active muscles discharges impulses along afferent nerve fibers to the medulla oblongata → stimulation of the vasomotor centre (VMC) → increase of HR to supply the active muscles with more blood.

b) Trigger areas (eyeball, ear, larynx, epigastrium, testicles...):
   - If painful stimuli (e.g. heavy blows) are applied to one of the trigger areas, this leads to reflex decrease of HR (bradycardia). Slight or moderate (semantic or visceral) pain usually causes increase of heart rate. However, severe pain (specially visceral pain) is usually associated with decrease of HR.
(b) CHEMICAL REGULATION

❤ Effect of changes in PO2 and PCO2:
This includes the effect of changes in blood gases (O2 and CO2), the effect of some hormones (thyroxin, adrenaline & noradrenalin) and the effect of some autonomic drugs (e.g. adrenaline & atropine).

❤ *Hypoxia*:
- Slight or moderate hypoxia → ↓ PO2 in blood → increase of HR due to stimulation of the peripheral chemoreceptors in the aortic and carotid bodies → stimulation of the vasomotor centre in the medulla oblongata = “chemoreceptor reflex”.

Severe hypoxia → decrease of HR (bradycardia) due to direct depression of the SA node.
**Hypercapnia:**

- *Slight or moderate hypercapnia* → \( \uparrow \)PCO2 in blood → increase of heart rate due to:
  - Direct stimulation of the vasomotor centre in the medulla oblongata.
  - Stimulation of the peripheral chemoreceptors in the aortic and carotid bodies → stimulation of the vasomotor centre (=chemoreceptor reflex”.
- *Severe Hypercapnia* (=marked Co2 excess in blood) → decrease of HR due to direct depression of the SA node.
2) Effect of hormones (thyroxin, adrenaline & noradrenalin):

❤️ **Thyroxin:**
- Thyroxin increases heart rate due to
  a) Direct stimulation of the SA node and increase of its sensitivity to catecholamine.
  b) Increase of metabolic rate.

❤️ **Adrenaline:**
- Adrenaline (like sympathetic) causes increase in HR due to direct stimulation of the SA node.

❤️ **Noradrenalin:**
- Noradrenalin is a strong vasoconstrictor agent → generalized vasomotor constriction → ↑ABP. Increase of ABP → decrease of HR (Marey’s Reflex).
3) Effect of autonomic drugs:

- Parasympatholytic drugs (e.g. atropine) → increase in HR
- Sympathomimetic drugs (e.g. adrenaline) → increase in HR
(c) PHYSICAL REGULATION

• **Increase in body temperature** (hyperthermia or fever) → increase in HR due to:
  
  a) Direct stimulation of the SA node.
  
  b) Stimulation of the vasomotor centre in the medulla oblongata by impulses discharged by the hypothalamus (thermo-regulatory centre).

• **Decrease in body temperature** (hypothermia):
  
  - → bradycardia
Heart acceleration (140/min or more) during muscular exercise due to:

1) Emotional Effect → stimulation of the vasomotor centre.
2) Chemoreceptor reflex
3) Bainbridge Reflex
4) Proprioceptor reflex
5) Secretion of adrenaline from the adrenal medulla → direct stimulation of the SA node.
6) Sympathetic over activity → stimulation of sympathetic nerves of the heart.
7) Increase of the body temperature → stimulation of the SA node.
Regulation of Heart Rate

- Increased HR:
  - Sympathetic nervous system
    - Crisis
    - Low blood pressure
  - Hormones
    - Epinephrine
    - Thyroxine
  - Exercise
  - Decreased blood volume
Regulation of Heart Rate

- Decreased HR:
  - Parasympathetic nervous system
  - High blood pressure or blood volume
  - Decreased venous return
  - In Congestive Heart Failure the heart is worn out and pumps weakly. Digitalis works to provide a slow, steady, but stronger beat.
Fig.: Modulation of Heart Rate by the Nervous System

- Sympahtetic stimulation and adrenaline deploarize the autorhythmic cell and speed up the depolarization rate, increasing the HR.

- Parasympathetic stimulation hyperpolarizes the membrane potential of the autorhythmic cell and slows depolarization, decreasing the HR.
SA node that establishes baseline

HR is modified by ANS:

- **Sympathetic stimulation**
  - Supplied by cardiac nerves
  - Epinephrine and norE released
  - Positive inotropic effect
  - Increases heart rate (chronotropic) and force of contraction (inotropic)

- **Parasympathetic stimulation**
  - Supplied by vagus nerve
  - Acetylcholine secreted
  - Negative inotropic and chronotropic effect
Fig.: Reflex Control of Heart Rate
Higher Centers of Autonomic Nervous System

- medulla oblongata
- hypothalamus
- thalamus
- cerebral cortex
Fig.: Medulla Oblongata Centers Affect Autonomic Innervation

- receives input from higher centers, monitoring blood pressure and dissolved gas concentrations
- **Cardio-acceleratory center** activates sympathetic neurons
- **Cardio-inhibitory center** controls parasympathetic neurons (nucl. vagus, nucl. ambiguus)
Hypothalamus, Thalamus, Cerebral cortex

- Involved in the cardiac response to environmental temperature changes, exercise, or during excitement, anxiety, and other emotional states
- stimulated by increase in arterial pressure (stretch)
- Effect: negative chronotropic and inotropic
- regulate the heart when BP increases or drops
- involved in short term regulation of BP

Fig.: Baroreceptor reflex

- aortocarotic receptors
- ↑ BP → negat. chronotopic and inotrop. effect
Peripheral chemoreceptors
-- carotic bodies (glomus caroticus)
-- aortic body (arcus aortae)
-- response to ↓ O₂, ↓ pH, ↑ CO₂
→ posit. chronotr. and inotrop. effect
- Stimulated by muscle and joint movement
- Effects: increase heart rate during exercise
Regulation of Stroke Volume
Intrinsic Control of Stroke Volume

The end-diastolic volume (EDV) depends on:

- Filling pressure
- Filling time
- Ventricular compliance
Intrinsic Control of Stroke Volume

The end-systolic volume (ESV) depends on:

- Preload
- Afterload
- Heart rate
- Contractility
INCREASING HEART RATE INCREASES CONTRACTILITY

Normal Heart Rate

Fast Heart Rate

Ca++

Ca++

Ca++

Ca++

Ca++

Ca++
Fig.: Intrinsic Factors Affecting Stroke Volume

- **Contractility**
  - cardiac cell contractile force due to factors other than EDV

- **Preload**
  - amount ventricles are stretched by contained blood - EDV

- **Venous return**
  - skeletal, respiratory pumping

- **Afterload**
  - back pressure exerted by blood in the large arteries leaving the heart
The Frank–Starling law of the heart (also known as Starling's law or the Frank–Starling mechanism):

*the greater the volume of blood entering the heart during diastole (end-diastolic volume), the greater the volume of blood ejected during systolic contraction (stroke volume) and vice-versa*

A heterometric mechanism controlling SV:

*initial length of myocardial fibers determines the initial work done during the cardiac cycle (optimum 2.2 μm)*

- Figure
Preload is the critical factor controlling SV.

Slow heartbeat and exercise increase venous return to the heart, increasing SV.

Blood loss and extremely rapid heartbeat decrease SV.
Extrinsic Factors Influencing Stroke Volume

Contractility is the increase in contractile strength, independent of stretch and EDV.

Increase in contractility comes from:
- Increased sympathetic stimuli ($\Rightarrow \uparrow [\text{Ca}^{2+}] = \text{the homeometric mechanism controlling SV}$)
- Hormones - epinephrine and thyroxine
- Ca$^{2+}$ ($\Rightarrow$ the homeometric mechanism controlling SV)
- and some drugs

$\Rightarrow$ Intra- and extracellular ion concentrations must be maintained for normal heart function.
Sympathetic stimulation releases norepinephrine and initiates a cAMP second-messenger system.
Fig.: Modulation of Cardiac Contractions
Hormonal regulation

*Extracardial regulation*

- epinephrine, norepinephrine – posit. chronotrop.,
inotrop., dromotropic, bathmotropic effect
- acetylcholin – negat. Chronotrop. and inotrop. effect
- glucagon, thyroxin, T3 - posit. chronotrop., inotrop. effect
- insulin – posit. inotropic effect
- progesteron - negat. chronotrop., inotrop. and
bathmotropic effect
Other Factors

- Blood level of ionic calcium, sodium, and potassium
  - Hypercalcemia (high plasma Ca^{++}): positive inotropic
  - Hypernatremia (high plasma Na^+): negative chronotropic
  - Hyperkalemia (high plasma K^+): negative chronotropic

- Age, gender, exercise, and body temperature
Fig.: Regulation of Cardiac Output

Baroreceptor reflex

↑ BP inhibits sympathicus
and ↓ HR

Bainbridge’s reflex

↑ intravascular volume
↑ HR independent of BP

Starling mechanism

Dependance of the SV on
the end-diastolic volume
Fig.: Regulation of Cardiac Output