Cardiac Output and Energy Demand

The blood only holds a certain amount of oxygen

During exercise, the body and tissues need more oxygen and nutrients to generate the required ATP

The only way to increase the oxygen supply is to increase the blood supply = increase cardiac output

Cardiac Output = SV x HR

• increase Stroke Volume
• increase Heart Rate
Heart Rate Adjustment

ParaSympathetic branch

Reaches heart via the vagus nerve

Releases acetylcholine which increases K+ permeability in pacemaker cells. This causes
  • a hyperpolarization
  • also slows the time before the slow depolarization phase reaches threshold

It thus reduces HR!
Heart Rate Adjustment

**Sympathetic branch**

Releases norepinephrine and binds adrenergic receptors in SA node.

Stimulates a G-protein system with increases in cAMP.

This results in an increased permeability to calcium in the SA-node cells.

This increases the rate of upward drift, reaching threshold at a faster rate and hence results in an increased HR.

The Vasomotor center or the Medullary CardioVascular Center contains the automatic headquarters for cardiac control. It functions by means of vagus control over sympathetic tone.

Increased incoming impulses from baroreceptors (thus indicating higher BP) results in:
- decreased outgoing sympathetic activity
- this results in vasodilation

Impulses from baroreceptors also reach the cardiac center where they stimulate the vagus nerve, reducing heart rate and contractile force.
**Heart Rate Adjustment**

Drugs that affect Heart rate:

- Circulating epinephrine have a similar effect as norepinephrine (tachycardia)
- Calcium blockers and beta blockers cause bradycardia
- Muscarinic antagonists, such as atropine, block vagus activity and thus results in tachycardia
- Hyperthyroidism induces tachycardia and hypothyroidism induces bradycardia.
- Hyperkalemia induces bradycardia or can even stop SA nodal firing. Hypokalemia increases the rate of phase 4 depolarization and causes tachycardia.

---

**Adjustment of Stroke Volume**

Stroke Volume = Volume ejected by a ventricle per beat

\[
SV = EDV - ESV
\]

**SV increases by adjusting**

- **EDV**
- **ESV**

---

<table>
<thead>
<tr>
<th>Phase</th>
<th>Atrioventricular valves</th>
<th>Aortic and pulmonary valves</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Open</td>
<td>Open</td>
</tr>
<tr>
<td>2a</td>
<td>Closed</td>
<td>Closed</td>
</tr>
<tr>
<td>2b</td>
<td>Open</td>
<td>Closed</td>
</tr>
<tr>
<td>3</td>
<td>Closed</td>
<td>Open</td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Adjustment of Stroke Volume

The events that affect stroke volume are named:

- Preload
- Contractility
- Afterload

Optimal-length sarcomere: lots of actin-myosin overlap and plenty of room to slide.

Long sarcomere: actin and myosin do not overlap much, so little tension can be developed.

Preload Effect

Cardiac muscle, just like skeletal muscle, exhibits a length-tension relationship.
Preload Effect

Increase of $\text{EDV} = \text{PRELOAD}$

- Cardiac muscle, just like skeletal muscle, exhibits a length-tension relationship.
- The overlap of actin and myosin filaments in myocardial sarcomeres is less than optimal.
- This allows for additional stretching of the cardiac muscles with better contraction performance.
- This stretching is caused by the returning blood into the ventricles, = ventricular filling or venous return.

Preload Effect

The greater the ventricular filling or venous return,
  - the more stretching
  - the greater the $\text{EDV}$ and
  - the greater the Stroke volume
  - and also the better the contraction

The amount of ventricular filling prior to contraction is called preload;
  - the higher the preload, the higher the $\text{EDV}$
Preload Effect

The preload effect is known as the Frank-Starling Effect

The preload effect is influenced by

• exercise
• heart beat

Exercise results in increased venous return

Low heart rate allows for more time to fill the ventricles before it is pumped out again and thus increases EDV

According to the equation, CO should increase constantly with increased SV and HR. A heart rate over 180 will actually result in a decrease in increase Cardiac Output. Why?

Cardiac Output = SV x HR
**Contractility Effect**

- Contractility = strength of contraction at a given pre-load
- Contractility usually increases by means of increased calcium in myocardial cells.

| Contractility increase = decreased ESV |

Components that increase contractility are called **positive inotropic agents**

- Examples: digitalis, epinephrine, glucagon, thyroid hormones
- Epinephrine (adrenaline) is a catecholamine released into the bloodstream by adrenal glands via sympathetic stimulation.

---

**Contractility Effect**

Heart has mostly $\beta_1$ receptors that bind epinephrine, norepinephrine

$\beta_1$ receptors work with G proteins to increase cAMP, PK A

- PK-A causes opening of calcium channels in cell membrane
- Also results in additional calcium release from SR

![Graph showing contractility effect](image)
**Contractility Effect**

- Blood vessels in the heart itself (coronary vessels) have mostly $\beta_2$ receptors.
- Binding of epi and norepi to these $\beta_2$ receptors results in vasodilation (relaxation) of the smooth muscles in these blood vessels.

This allows for better blood flow to the myocardial cells when the pumping of the heart is increased.

---

**Afterload Effect**

The greater the AORTIC pressure, the harder the heart has to work to eject blood from the ventricle to open the semilunar valve.
- the result is thus that, at a similar contractility, more blood remains in ventricle
- This translates into an increase in ESV
- And thus a decrease in CO
To increase SV, increase:
- End-diastolic volume,
- Norepinephrine delivery from sympathetic neurons,
- Epinephrine delivery from the adrenal medulla.

To increase HR, increase:
- Norepinephrine delivery from sympathetic neurons,
- Epinephrine delivery from adrenal medulla (reduce parasympathetic).

It is not possible, under normal circumstances, to increase one but not the other of these determinants of cardiac output.

Summary on Stroke Volume

Increased by sympathetic stimulation
- Increased by E, NE, glucagon, thyroid hormones
- Contractility of muscle cells
  - Cont = ↑ EDV
  - Cont = ↑ ESV
- Increased by vasodilation
  - AL = ↓ ESV
- Decreased by vasoconstriction

Decreased by parasympathetic stimulation
- contractility of muscle cells
  - Cont = ↓ EDV
  - Cont = ↓ ESV
- Increased by vasodilation
  - AL = ↑ ESV
- Decreased by vasoconstriction

STROKE VOLUME (SV)
- EDV = ↑ SV
- ESV = ↓ SV
- EDV = ↓ SV
- ESV = ↑ SV
Summary on Cardiac Output

(a) Factors affecting heart rate

- Atrial reflex
- Autonomic innervation

(b) Factors affecting stroke volume

- Preload
- Contractility
- Afterload

Heart rate

Changes in peripheral circulation

Blood volume

Skeletal muscle activity

Venous return

End-diastolic volume

End-systolic volume

STROKE VOLUME

Cardiac output

Copyright © 1994 Pearson Education, Inc., publishing as Benjamin Cummings.