Pharmacology of the Cardiovascular System

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Main classes (‘frontline agents’)

Diuretics (1st of equals)
Beta-blockers
Calcium blockers
ACE inhibitors / ARBs

 Sites of Action of Antihypertensive Agents

*Figure 11-3. Sites of action of the major classes of antihypertensive drugs.*
Baroreceptor Reflex Arc

Oppose direct changes in BP, not HR, not pulse pressure

Increase stretch → increase firing of baroreceptors

Cardiovascular - 1

Blood Pressure = Cardiac Output X TPR
Cardiac Output = Heart rate X Stroke volume

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Response</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>alpha₁</td>
<td>vasoconstriction</td>
<td>↑ TPR  ↑ BP</td>
</tr>
<tr>
<td>beta₁</td>
<td>↑ heart rate</td>
<td>↑ CO  ↑ BP</td>
</tr>
<tr>
<td>beta₂ **</td>
<td>vasodilation</td>
<td>↓ TPR  ↓ BP</td>
</tr>
<tr>
<td>M₂ (vagus)</td>
<td>↓ heart rate</td>
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** not innervated
# Cardiovascular - 2

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<tr>
<th></th>
<th>Resting</th>
<th>After ↑BP</th>
<th>After ↓BP</th>
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<tr>
<td>alpha₁</td>
<td>++++</td>
<td>o</td>
<td>++++++</td>
</tr>
<tr>
<td>beta₁</td>
<td>+</td>
<td>o</td>
<td>+</td>
</tr>
<tr>
<td>beta₂</td>
<td>+</td>
<td>++</td>
<td>o</td>
</tr>
<tr>
<td>vagus</td>
<td>++</td>
<td>+++</td>
<td>o</td>
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Note: Athletic individual has low HR (high vagal tone)
Lance Armstrong resting HR 32 bpm

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## Neurons of the ANS

- **Parasympathetic**
  - Cardiac and smooth muscle, gland cells, nerve terminals
  - Sweat glands

- **Sympathetic**
  - Cardiac and smooth muscle, gland cells, nerve terminals
  - Renal vascular smooth muscle
  - Skeletal muscle

- **Somatic**
Cardiovascular Actions – Low dose

α₁ β₁ (β₂) β₁ β₂ α₁ β₁ β₂

Blood Pressure = Cardiac Output X TPR
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** not innervated
Cardiovascular – High dose – PE, EPI, ISO

**FIG. 8D**

- **Phenylephrine**
  - $\alpha$-agonist
- **Epinephrine**
  - $\alpha$- and $\beta$-agonist
- **Isoproterenol**
  - $\beta$-agonist

**Phenylephrine $\alpha$-agonist, Epinephrine $\alpha$-$\beta$-agonist, Isoproterenol $\beta$-agonist**

**Cardiovascular Actions – Epinephrine Reversal**

**FIG. 8E**

- **Phentolamine**
  - $\alpha$- antagonist
  - ↑ PP, ↓ BP, ↑ HR (reflex)
- **Epinephrine before Phentolamine**
- **Epinephrine after Phentolamine**

*Effects of intravenous phentolamine, a $\alpha$-blocker, on blood pressure and heart rate in response to a $\alpha$-agonist (phenylephrine) or a $\alpha$-$\beta$-agonist (epinephrine), showing a reflex increase in heart rate due to alpha-blockade.*

*In the presence of phentolamine, epinephrine now causes ↓ BP.*
Cardiovascular Summary

http://www2.courses.vcu.edu/ptxed/ptx/cv_ans.htm

α1  ↑TPR  ↑BP
β1  ↑HR  ↑BP
β2 **  ↓TPR  ↓BP
M2  ↓HR  ↓BP
M **  ↓TPR  ↓BP

Key Diagrams
NE, PE, EPI, ISO
α-blocker, β-blocker

NE + atropine
NE + α-blocker
NE + β-blocker
PE + atropine
EPI + α-blocker
EPI + β-blocker

Postural (Orthostatic) Hypotension

• Venous return falls, blood pressure falls (>20mmHg SBP, >10mmHg DBP)

  • Sympathetic activity increases
  • Constriction of great veins
  • Constriction of arteries (↑ TPR)
  • Increase in heart rate (> 20bpm)

Reflex mediated

no reflex  reflex

BP (mmHg)
95  100  95

HR
55  95

BP
55  95

HR
100  100

BP
195  105