Pharmacology of the Cardiovascular System

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Main classes
- Beta-blockers
- Diuretics
- Calcium blockers
- ACE inhibitors/ARBs

Sites of Action of Antihypertensive Agents

Baroreceptor Reflex Arc
Oppose direct changes in BP, not HR, not pulse pressure

Increase stretch → increase firing of baroreceptors

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

Cardiovascular - 1

<table>
<thead>
<tr>
<th>Receptor</th>
<th>Response</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>alpha&lt;sub&gt;1&lt;/sub&gt;</td>
<td>vasoconstriction</td>
<td>↑ TPR ↑ BP</td>
</tr>
<tr>
<td>beta&lt;sub&gt;1&lt;/sub&gt;</td>
<td>↑ heart rate</td>
<td>↑ CO ↑ BP</td>
</tr>
<tr>
<td>beta&lt;sub&gt;2&lt;/sub&gt; **</td>
<td>vasodilation</td>
<td>↓ TPR ↓ BP</td>
</tr>
<tr>
<td>M&lt;sub&gt;2&lt;/sub&gt; (vagus)</td>
<td>↓ heart rate</td>
<td>↓ CO ↓ BP</td>
</tr>
<tr>
<td>M (vascular) **</td>
<td>vasodilation</td>
<td>↓ TPR ↓ BP</td>
</tr>
</tbody>
</table>

** not innervated

Cardiovascular - 2

Resting: BP 120/80 mmHg HR 70 bpm
No tone: BP 60/40 mmHg HR 75 bpm

<table>
<thead>
<tr>
<th></th>
<th>Resting</th>
<th>After ↑BP</th>
<th>After ↓BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>alpha&lt;sub&gt;1&lt;/sub&gt;</td>
<td>++++</td>
<td>o</td>
<td>++++++++</td>
</tr>
<tr>
<td>beta&lt;sub&gt;1&lt;/sub&gt;</td>
<td>+</td>
<td>o</td>
<td>++</td>
</tr>
<tr>
<td>beta&lt;sub&gt;2&lt;/sub&gt;</td>
<td>+</td>
<td>++</td>
<td>o</td>
</tr>
<tr>
<td>vagus</td>
<td>++</td>
<td>+++++</td>
<td>o</td>
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</tbody>
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Note: Athletic individual has low HR (high vagal tone)
Lance Armstrong resting HR 32 bpm
Cardiovascular Actions – Low dose

Cardiovascular function
- Norepinephrine: +++
- Isoproterenol: 0+
- Epinephrine: ++

Cardiovascular Summary
- Systolic blood pressure: +++ 0+ ++
- Diastolic blood pressure: ++ - - -
- Total peripheral resistance: +++ - - - - -
- Heart rate: (chronotropic effect) - ++ +
- Stroke output: (inotropic effect) + ++ ++
- Cardiac output: -0 +++ +++)
- Mean blood pressure: ++ - -+0-

0 = no effect; + = increased; - = decreased. Symbols indicate the approximate magnitude of the response.

Cardiovascular Actions – High dose

Phenylephrine
- α-agonist, PP constant

Epinephrine
- α-β-agonist, ↑ PP

Isoproterenol
- β-agonist, ↑ PP

Epinephrine Reversal
- Phenolamine
  - α-antagonist, ↑ PP, ↓ BP, ↑ HR (reflex)

In the presence of phenolamine, epinephrine now causes ↓ BP

Cardiovascular Summary

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

Cardiovascular - 1

BP = CO X TPR  CO = HR X Stroke volume

Receptor          Response                Effect
alpha$_1$       vasoconstriction       ↑ TPR  ↑ BP
beta$_1$        ↑ heart rate            ↑ CO  ↑ BP
beta$_2$ **      vasodilation           ↓ TPR  ↓ BP
M$_2$ (vagus)   ↓ heart rate            ↓ CO  ↓ BP
M (vascular) **  vasodilation           ↓ TPR  ↓ BP

** not innervated  Reflex opposes BP change

NE  α1 β1 β2 (weakest)  (mainly α)
EPI α1 β1 β2 (β at low dose, α dominate at high dose)
ISO β  (equal at low dose, β2 dominate at high dose)