Autonomic Nervous System & Neuromuscular Junction
Review 2005
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Tips for Drug Learning

• Learn agents by drug classes
  ie. beta-blockers, Ca++-blockers etc
• Key points:
  - Clinical application
  - Mechanism of action
  - Important drug/drug interactions
    ie. MAOI and tyramine rich foods
  - Adverse drug reactions
    ie. beta-blockers – asthma
• Drugs of choice (DOC)
  ie. epinephrine (anaphylaxis)
  - Prototype drugs
    ie. propranolol, atropine
• Do not focus on dosage or trade names

ANS – Review
1. Tissues / Organs: - receptors present, tissue / organ response
2. Transmitters: - NE, Ach, synthesis, storage, release, regulation
3. Eye: - miosis, mydriasis, cycloplegia, Glaucoma: wide- vs narrow-angle, Horner’s Syndrome
4. Drugs: - receptor selectivity, mechanism of action
5. Can predict: - clinical application, side effects, toxicity, treatment of toxicity
6. General: - learn by drug classes, important adverse reactions, not dosage

Neurons of the ANS

Transmitter synthesis and release

Receptors of the ANS

Adrenoceptors
Cholinceptors

Selective agents available
Selective agents available for major groups but not for M-receptor subtypes
E. Ishac

Ciliary m. symptoms and signs?

following is the most appropriate therapy for these

salivation, diarrhea, and bradycardia while being treated

A 59-year old man develops excessive sweating and

and diarrhea for the past 6 hours. He is sweating and

A 32-year old man is brought to the emergency

department because of confusion, wheezing, vomiting

and diarrhea for the past 6 hours. He is sweating and

salivating profusely. There is generalized muscle

weakness. Which of the following substances is the most

likely cause of these findings?

A. Glutethimide
B. Heroin
C. Jimson weed (belladonna alkaloids)
D. Parathion
E. Phencyclidine (PCP)

USMLE Step 1: 2003, 2005

**ANS – Review Tissues/Organs**

**ANS Excess / Deficiency**

- Cholinergic excess: (ie. AchE inhibition or mushrooms)
  salivation, lacrimation, urination, diarrhea, emesis (slude), miosis, ↑HR, sweating, cycloplegia (paralysis)
- Cholinergic deficiency: (ie. Atropine toxicity)
  ↓GI motility, mydriasis, cycloplegia, ↓secretions, tachycardia, delirium
- Sympathetic excess: (ie. Tyr-MAOI or Pheochrom.)
  ↑BP, ↑HR, pupil dilation (mydriasis), ↓GI motility
- Sympathetic deficiency: (ie. Guanethidine-block)
  ↓BP, ↓tissue perfusion, pupil constriction (miosis)

**Terminology – ANS**

i. clammy: → PNS excess, ie. ↑secretion (sweating)
ii. wheezy: → PNS excess, ie. difficulty in breathing
  (↑bronchial resistance, ↑secretion)
iii. flushed: → PNS deficiency ie. vasodilatation,
  thermoregulation (atropine toxicity)
iv. cramps: → muscle contraction ie. abdominal
  (↑PNS)
v. palpitations: → SNS excess ie. hypertension,
  hypertensive crisis, MAOI-Tyramine
  or pheochromocytoma

**Question 1**

A 32-year old man is brought to the emergency
department because of confusion, wheezing, vomiting

and diarrhea for the past 6 hours. He is sweating and

salivating profusely. There is generalized muscle

weakness. Which of the following substances is the most

likely cause of these findings?

A. Glutethimide
B. Heroin
C. Jimson weed (belladonna alkaloids)
D. Parathion
E. Phencyclidine (PCP)

USMLE Step 1: 2003, 2005

**Drugs of Choice**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Therapeutic use</th>
<th>Notes</th>
</tr>
</thead>
</table>
| Atropine | Block parasympathetic junc. in ANS | ↓secretion, ↓salivation, ↓GI motility (through ganglionic blocking effects)
| Physostigmine | Reverse cholinesterase inhibitor in ANS | ↑secretion, ↑GI motility, ↑salivation (through direct effects on cholinergic receptors) |
| Labetalol, Carvedilol | β-blockers | ↓HR, ↓BP in CHF (both β₁- and β₂-receptors)
| Phentolamine | α-blockers | ↓BP in septic shock (α₁-receptors)
| Timolol | β₂-blockers | ↓HR, ↓BP in CHF (both β₁- and β₂-receptors), ↓vasoconstriction |
**A-M (Propranolol)**

**β-Labetalol, Carvedilol**

**Epinephrine**

- **α-Blockers**
  - Open angle (wide, chronic) – treated with beta-blockers and other agents
  - Closed-angle (narrow-angle) – dilated iris can occlude outflow

**Increased intraocular pressure:** Untreated → blindness

**Glaucoma:**
- **Open angle** (wide, chronic) – can occlude outflow
- **Closed-angle** (narrow-angle) – dilated iris can occlude outflow

**Glaucoma treatment**
1. α-Agonist: T-Outflow
2. β-Blocker: ↓Secretion
3. β-Blocker: ↓Secretion
4. α-Agonist: ↓Secretion
5. Prostaglandin: T-Outflow
6. Carbonic acid inhibitors: ↓Secretion

**Hypertension, angina, arrhythmias, CHF**

**Glaucoma**

**Prostaglandins:**

**M-Agonists:**

2-Agonist:

**β-Agonist:**

- Physiologically counters the effects of released histamine (ie. bronchospasm, asthma, diabetes agonist activity (ISA). CI: heart failure (unstable CHF, depression, pheochromocytoma)

**Hypertensive crisis:**

- Tyramine effect, pheochromocytoma

**Acute hypersensitivity reaction:**

- ie. bee attack

**Reverse toxic effects of AchE inhibitors:**

- ie. neostigmine, physostigmine, or organophosphates

**Pralidoxime**

- Reversible AchE inhibitor, can cross CNS

**Reverse atropine toxicity**

**Physostigmine**

- A very useful group, differ in selectivity (α1-receptors) to maintain BP but dilates renal vessels

**Renal vasoconstriction:**

- →↑outflow

**Emergency glaucoma**

**Pilocarpine**

**A-H-Action, partial agonist**

**Destruction of Sympathetic innervation to the iris**

- Loss of postganglionic fibers
- Loss of preganglionic fibers

**Horner’s Syndrome**

- Loss of parasympathetic innervation left unopposed

**Horner’s Syndrome** (note sagging left eyelid and miosis)
**Question 3**

The circles represent the size of the pupils of a patient's right and left eyes, both without treatment and with two different treatments. Which of the following is compatible with the findings shown for the left eye?

A. Blockade of \( \alpha \)-adrenergic rec.
B. Blockade of \( \beta \)-adrenergic rec.
C. Blockade of muscarinic rec.
D. Inhibition of cholinesterase
E. Sympathetic denervation


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**Question 4**

Which of the following drugs applied topically produces mydriasis without producing cycloplegia?

A. Atropine
B. Neostigmine
C. Phentolamine
D. Phenylephrine
E. Pilocarpine


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**Drugs of Choice**

<table>
<thead>
<tr>
<th>Agent</th>
<th>Therapeutic use</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dantrolene</td>
<td>Inhibits calcium release from SRM</td>
<td>Malignant hyperthermia</td>
</tr>
<tr>
<td>Neostigmine</td>
<td>Reverse toxic effects of AChE inhibitors</td>
<td>Regenerate AChE enzyme</td>
</tr>
<tr>
<td>Atropine</td>
<td>M-agonist causes ↑ outflow</td>
<td>Emergency glaucoma</td>
</tr>
<tr>
<td>Timolol</td>
<td>( \beta )-blocker, most common agent used for chronic glaucoma</td>
<td>Glaucoma</td>
</tr>
<tr>
<td>Propranolol</td>
<td>( \beta )-blockers</td>
<td>Hypertensive crisis or hypertensive crisis</td>
</tr>
<tr>
<td>Dopamine</td>
<td>( \alpha )-( \beta )-agonist, physiologically counters the effects of released histamine</td>
<td>Acute hypersensitivity reaction</td>
</tr>
<tr>
<td>Anticholinergics</td>
<td>( \alpha )-methyl-p-tyrosine</td>
<td>Tyramine Interaction with MAO inhibitors</td>
</tr>
<tr>
<td>Pralidoxime</td>
<td>Reversible AchE inhibitor</td>
<td>Pheochromocytoma</td>
</tr>
</tbody>
</table>

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**Pheochromocytoma**

- **Tumor:** ↑ synthesis, ↑ release of NE & EPI into the circulation.
- **Result:** ↑ BP, ↑ HR → hypertensive crisis
- **Treatment:** - surgical removal for solid tumor
- \( \alpha \) - \( \beta \)-blocker, i.e. Labetatol, Carvedilol
- \( \alpha \)-blocker i.e., phenoxymenzamine or phentolamine
- inhibitor of tyrosine hydroxylase i.e. \( \alpha \)-methyl-p-tyrosine
- \( \beta \)-blocker only after \( \alpha \)-blockade

**Rule of Ten**

10% Pheochromocytomas are:
- Malignant
- Extra-Adrenal
- In Children
- Familial
- Recur (within 5 to 10 years)
- Present after stroke

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**Tyramine Interaction with MAO Inhibitors**

Can cause hypertensive crisis (↑BP, ↑HR)

- Aged cheese & red wine are rich in tyramine

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**Parkinson's Disease**

- General population: 1:1000, over 60: 1:75
- Tremor, stiffness, or clumsiness, usually involving one side difficulty walking, fatigue, depression
- Progressive destruction of the dopaminergic nigrostriatal pathway
- Elevated cholinergic activity

- **Treatment:**
  - MAO inhibitors:
  - Dopamine agonists: bromocriptine
  - L-Dopa
  - Anticholinergics: benztropine
  - Decarboxylase inhibitor: carbidopa
  - Amantadine: Inhibit D-uptake, M-rec, NMDA-block, release dopamine
**Drugs of Choice**

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<thead>
<tr>
<th>Agent</th>
<th>Therapeutic use</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epinephrine</td>
<td>Increases sympathetic activity in low doses.</td>
<td>—</td>
</tr>
<tr>
<td>Doxazosin</td>
<td>Block β-receptors. β1-selective agents preferred</td>
<td>—</td>
</tr>
<tr>
<td>Diuretics</td>
<td>Contraindications: CAH, CHF, significant side effects.</td>
<td>—</td>
</tr>
<tr>
<td>Caution in Congestive Heart failure:</td>
<td>β-blockers can precipitate latent heart failure by removing compensatory increase in sympathetic effects on heart. Note CI: unstable CHF, depression, significant bradycardia or bronchospasm.</td>
<td>—</td>
</tr>
</tbody>
</table>

**Beta-Adrenoceptor Blocking Agents (-olol)**

(Drugs A-M are β1-selective exp. Labetalol & Carvedilol)

<table>
<thead>
<tr>
<th>Selection</th>
<th>Partial β1-Agonist Activity</th>
<th>Membrane Action</th>
<th>Lipid Solubility</th>
<th>Elimination Half-life</th>
<th>Appropriate/Benzodiazepinoids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metoprolol</td>
<td>Yes</td>
<td>Yes</td>
<td>Low</td>
<td>1–2 h</td>
<td>10</td>
</tr>
<tr>
<td>Labetalol</td>
<td>No</td>
<td>No</td>
<td>Low</td>
<td>0.5–1.5 h</td>
<td>10</td>
</tr>
<tr>
<td>Nebivolol</td>
<td>Yes</td>
<td>Yes</td>
<td>Low</td>
<td>1–2 h</td>
<td>10</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>No</td>
<td>Yes</td>
<td>Low</td>
<td>1–2 h</td>
<td>10</td>
</tr>
<tr>
<td>Atenolol</td>
<td>No</td>
<td>Yes</td>
<td>Low</td>
<td>1–2 h</td>
<td>10</td>
</tr>
</tbody>
</table>

*Some agents affect β2-receptors. Labetalol and Atenolol have additional intrinsic sympathomimetic action.*

**Beta-Blockers: Contraindications**

- **Supersensitivity:** Rebound effect with β1-blockers, less with β2-blockers with partial agonist activity (ie. pindolol). Gradual withdrawal
- **Asthma:** Blockade of pulmonary β2-receptors. β1-selective agents preferred
- **Diabetes:** Compensatory hyperglycemic effect of EPI in insulin-induced hypoglycemia is removed by block of β2-ARs in liver. β1-selective agents preferred
- **Caution in Congestive Heart failure:** β-blockers can precipitate latent heart failure by removing compensatory increase in sympathetic effects on heart. Note CI: unstable CHF, depression, significant bradycardia or bronchospasm

**Hypertension (JNC VII – 2003)**

- **BP Classification**
  - Normal: <120 and <80
  - Pre-hypertension: 120–139 or 80–89
  - Stage 1 Hypertension: 140–159 or 90–99
  - Stage 2 Hypertension: ≥160 or ≥100

*Requires three measurements (repeat visits) BP lowest in the morning → during the day

**β-Blockers**: - Frontline agents
  - Hypertensive crisis, special circumstances
  - a1-Agonists: Useful, not frontline ie. Clonidine
  - Reserpine: Resistant hypertension, significant side effects, rarely used
  - Guanethidine: Resistant hypertension, significant side effects, rarely used

**Question 5**

The histograms show changes in HR and bronchial resistance produced by the administration of epinephrine alone, drug X alone, and epinephrine together with drug X. Drug X is most likely to be?

- A. Isoproterenol
- B. Metoprolol
- C. Nadolol
- D. Pindolol
- E. Propranolol

**Hypertension (JNC VII – 2003)**

<table>
<thead>
<tr>
<th>BP Classification</th>
<th>SBP mmHg</th>
<th>DBP mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>&lt;120</td>
<td>&lt;80</td>
</tr>
<tr>
<td>Pre-hypertension</td>
<td>120–139</td>
<td>80–89</td>
</tr>
<tr>
<td>Stage 1 Hypertension</td>
<td>140–159</td>
<td>90–99</td>
</tr>
<tr>
<td>Stage 2 Hypertension</td>
<td>≥160</td>
<td>≥100</td>
</tr>
</tbody>
</table>

*Requires three measurements (repeat visits) BP lowest in the morning → during the day

**β-Blockers**: - Frontline agents
  - Hypertensive crisis, special circumstances
  - a1-Agonists: Useful, not frontline ie. Clonidine
  - Reserpine: Resistant hypertension, significant side effects, rarely used
  - Guanethidine: Resistant hypertension, significant side effects, rarely used
**Deadly Nightshade**
Approx 5,000 per yr

Mainly atropine
Devil's apple
Stink weed
Devil's cherries

**Datura**

Mainly scopolamine & hyoscyamine
Thorn apple
Jimson weed

**Myasthenia gravis**
Autoimmune disease

- 110,000 (250,000 USA)
- Antibodies to NMJ nicotinic receptors leads to degradation
- Simplified synaptic folds
- Normal nerve terminal and transmitter
- Widened synaptic junction

**Diagnosis:** Edrophonium (Tension, short acting) is used for diagnosis and determination of maintenance dose

**Treatment:** Neostigmine has direct (stimulates receptor) and indirect actions (inhibition of AchE). No CNS activity.

**Drugs of Choice**

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<tr>
<th>Agent</th>
<th>Therapeutic use</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Edrophonium</td>
<td>Autoimmunobility reversal in host attack</td>
<td>1:10,000 (250,000 USA) – antibodies to NMJ nicotinic receptors leads to degradation</td>
</tr>
<tr>
<td>Edrophonium</td>
<td>Muscle weakness; reverse junction reversal in elderly patients; dilates most vessels; (Edrophonium, USA) – initial recomimmunization</td>
<td></td>
</tr>
<tr>
<td>Thymol</td>
<td>Muscarine</td>
<td>Gallamine, thymol or gallamine agent used to close glands, accelerate gastric emptying</td>
</tr>
<tr>
<td>AChI poisoning</td>
<td>AChI poisoning; antihistamine, GI, CNS, muscle relaxant, antiemetic; anti-inflammatory, anti-allergic</td>
<td>AChI poisoning, antihistamine, GI, CNS, muscle relaxant, antiemetic; anti-inflammatory, anti-allergic</td>
</tr>
<tr>
<td>Atropine</td>
<td>Emergence of nausea, vomiting, diarrhea, CNS, muscle relaxant, antiemetic; anti-inflammatory, anti-allergic</td>
<td>AChI poisoning, antihistamine, GI, CNS, muscle relaxant, antiemetic; anti-inflammatory, anti-allergic</td>
</tr>
<tr>
<td>Physostigmine</td>
<td>Reverse atropine toxicity; irreversible inhibitor; use cases CNS</td>
<td>Reverse atropine toxicity; irreversible inhibitor; use cases CNS</td>
</tr>
<tr>
<td>Pralidoxime</td>
<td>Atropine-competitive</td>
<td>Reverses competitive ACh competitive; use cases CNS</td>
</tr>
<tr>
<td>Pilocarpine</td>
<td>M-agonist causes ↑ outflow</td>
<td>Emergency glaucoma; pilocarpine</td>
</tr>
<tr>
<td>Amines</td>
<td>M-agonist causes ↑ outflow</td>
<td>Emergency glaucoma</td>
</tr>
<tr>
<td>Timolol</td>
<td>β-blockers</td>
<td>Glaucoma</td>
</tr>
<tr>
<td>Dopamine</td>
<td>Alpha-β-agonist, physiologically counters the effects of released histamine (ie. bronchospasm, pain)</td>
<td>Acute hypersensitivity, respiratory collapse; pressor agent (α1-receptors) to maintain BP but dilates renal vessels (D1-receptors, NE → renal vasoconstriction)</td>
</tr>
</tbody>
</table>

**Acetylcholinesterase & Irreversible Inhibition**

DFP, Isoflurionate, Malathion, Parathion

2-PAM Pralidoxime
No CNS action

Aging
30-40 min

Nerve gas
sec / min

Parathion, Malathion (produgs)
4 – 6 hr

**US Military 2-PAM / Atropine Injector**

2.5 mg Atropine, 600mg 2-PAM

**Wild Mushrooms - Amanita**

10,000 cases per year

Muscarine poisoning
5,000 mushroom species
100 “bad”, 10 “deadly”
**Drugs of Choice**

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</thead>
<tbody>
<tr>
<td>Epinephrine</td>
<td>Block hyperadrenergic receptors &amp;, base release</td>
<td>α-agonist, pharmacologically reversed for effects of released hormones (eg, stress)</td>
</tr>
<tr>
<td>Dantrolene</td>
<td>Inhibits calcium release from SR</td>
<td>Malignant hyperthermia</td>
</tr>
<tr>
<td>Atropine</td>
<td>Reverse toxic effects of AchE inhibitors (neostigmine, physostigmine, organophosphates, mushroom poisoning)</td>
<td>Reverse AchE inhibition</td>
</tr>
<tr>
<td>Pralidoxime</td>
<td>Reversible AchE inhibitor, can cross CNS</td>
<td>Regenerate AchE enzyme</td>
</tr>
<tr>
<td>Pilocarpine</td>
<td>M-agonist causes ↑ outflow</td>
<td>Emergency glaucoma</td>
</tr>
<tr>
<td>β-Blockers</td>
<td>A-M β₁-selective</td>
<td>Hypertension, angina, arrhythmias, CHF, tremor, migraine, hyperthyroidism, panic stress</td>
</tr>
<tr>
<td>Labetalol, Carvedilol</td>
<td>β₁-β₂-blockers (α-β-blockers) can reduce both BP &amp; HR, or α-β-blockers, phenoxybenzamine, phentolamine only reduce BP</td>
<td>Hypertensive crisis (ie. tyramine effect, pheochromocytoma)</td>
</tr>
<tr>
<td>Timolol</td>
<td>β₂-blocker, most common agent used for chronic glaucoma</td>
<td>Glaucoma</td>
</tr>
<tr>
<td>Dopamine</td>
<td>α-β-agonist, physiologically counters the effects of released histamine (bronchospasm, ↓ BP)</td>
<td>Acute hypersensitivity reaction (ie. bee attack)</td>
</tr>
</tbody>
</table>

**Prototype Drugs**

- Propranolol
- Metoprolol
- Tubocurarine
- Succinylcholine
- Clonidine
- etc

**Neuromuscular Junction**

Succinylcholine (non-competitive):
- depolarizing (only agent), cannot reverse, short-acting, fasciculations
- atypical pseudo-AchE, hyperkalemia, malignant hyperthermia

Tubocurarine (competitive):
- non-depolarizing, reversible, long-acting, relaxed paralysis

**Neuromuscular Blocking Agents**

<table>
<thead>
<tr>
<th>Onset (min)</th>
<th>Duration (min)</th>
<th>Mode of elimination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Succinylcholine</td>
<td>1-2</td>
<td>6-8</td>
</tr>
<tr>
<td>Tubocurarine</td>
<td>4-6</td>
<td>80-120</td>
</tr>
<tr>
<td>Metocurine</td>
<td>4-6</td>
<td>80-120</td>
</tr>
<tr>
<td>Gallamine</td>
<td>4-6</td>
<td>80-120</td>
</tr>
<tr>
<td>Pancuronium</td>
<td>4-6</td>
<td>80-120</td>
</tr>
<tr>
<td>Vecuronium</td>
<td>2-4</td>
<td>30-40</td>
</tr>
<tr>
<td>Atracurium</td>
<td>2-4</td>
<td>30-40</td>
</tr>
<tr>
<td>Doxacurium</td>
<td>4-6</td>
<td>90-120</td>
</tr>
<tr>
<td>Pipecuronium</td>
<td>2-4</td>
<td>80-100</td>
</tr>
<tr>
<td>Mivacurium</td>
<td>2-4</td>
<td>12-18</td>
</tr>
</tbody>
</table>

**ANS – Cardiovascular Receptors**

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</td>
</tr>
<tr>
<td>beta₁</td>
<td>↑ heart rate</td>
<td>↑ CO</td>
</tr>
<tr>
<td>beta₂**</td>
<td>vasodilation</td>
<td>↓ TPR</td>
</tr>
<tr>
<td>M₂ (vagus)</td>
<td>↓ heart rate</td>
<td>↓ CO</td>
</tr>
<tr>
<td>M (vascular)**</td>
<td>vasodilation</td>
<td>↓ TPR</td>
</tr>
</tbody>
</table>

**not innervated**
Cardiovascular – Resting & Reflex Response

Resting: BP 120/80 mmHg  HR 70 bpm
No tone:  BP 60/40 mmHg  HR 75 bpm
vagus (-10 bpm)  beta1 (+5 bpm)

Resting   After ↑BP   After ↓BP

alpha1     ++++    o     ++++
beta1      +      o      ++
beta2      +      ++     o
vagus      ++     ++++    o

note: athletic individual has low HR (high vagal tone)

Cardiovascular Responses

Moderate/high doses:
- NE  ↑BP, ↑HR (reflex)
- EPI  ↑BP, ↑HR
- ISO  ↓BP, ↑HR
- ACH  ↓BP, ↓HR

- Epinephrine reversal (EPI response in presence of α-blocker ie. phentolamine)
- Norepinephrine in presence of atropine (↑BP, ↑HR)

Cardiovascular Actions – Low dose

Cardiovascular – High dose

Phenylephrine
α-agonist, PP constant

Epinephrine
α- β-agonist, ↑PP

Isoproterenol
β-agonist, ↑PP

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

In the presence of phentolamine, epinephrine now causes ↓BP

Question 7

A 65-year old woman on holidays is stung by a bee. She goes to the first aid station where she receives an intramuscular injection of epinephrine. A few minutes later she develops a pounding headache, and blood pressure is measured at 250/150 mmHg. Which of the following drugs might the patient have previously taken that could account for this unexpected effect?

A. atropine
B. clonidine
C. alpha-methyldopa
D. prazosin
E. propranolol
Question 8
A new agent (X) was tested for its cardiovascular actions in three anaesthetized animals.

i. Control animal
ii. Animal treated with a ganglion blocker
iii. Animal treated with a muscarinic blocker

Drug X caused a 50 mmHg rise in BP in the control animal, no change in BP in the ganglion blocker treated animal and a 75 mmHg rise in the muscarinic blocker treated animal. Drug X is a drug similar to?

A. Acetylcholine
B. Atropine
C. Mecamylamine
D. Epinephrine
E. Nicotine

Question 9
A new agent (Y) was tested for its cardiovascular actions in three anaesthetized animals.

i. Control animal
ii. Animal treated with a ganglion blocker
iii. Animal treated with a muscarinic blocker

Drug Y caused a 40 mmHg fall in BP in the control animal, a 50 mmHg fall in BP in the ganglion blocker treated animal and no change in BP in the muscarinic blocker treated animal. Drug Y is a drug similar to?

A. Acetylcholine
B. Edrophonium
C. Mecamylamine
D. Pralidoxime
E. Nicotine

Question 10
A 60-year old asthmatic man comes in for a check-up and complains that he is having some difficulty in voiding urine. Physical examination indicates that the man has a blood pressure of 160/100 mmHg and a slightly enlarged prostate. Which of the following medications would be useful in treating both the hypertension and the enlarged prostate?

A. prazosin
B. propranolol
C. clonidine
D. atenolol
E. isoproterenol

Question 12
A 30 yr male has been treated with several autonomic agents for 4 weeks. He is now admitted to the emergency department showing signs of drug toxicity. Which of the following signs would distinguish between an overdose of a ganglionic blocker versus a muscarinic blocker?

A. Mydriasis
B. Tachycardia
C. Postural hypotension
D. Blurred vision
E. Dry mouth, constipation

Benign Prostrate Hypertrophy (BPH)
Enlarged prostrate leads to difficulty in urination
Alpha-receptor blocker (ie Prazosin) causes prostrate relaxation
Relaxed prostrate improves urination

Actions on the Eye
Glaucoma treatment
1. α-Agonist ↑Outflow
2. M-Agonists ↑Outflow
3. β-Blocker ↓Secretion
4. α2-Agonist ↓Secretion
5. Prostaglandins ↑Outflow
6. Carbonic acid inhibitors ↓Secretion
Question 13

An asymptomatic 50-year-old woman has hypertension. Urinary excretion of catecholamines is increased. A CT scan shows a suprarenal mass. Which of the following is the most likely cause?

A. Benign neoplasm of the adrenal cortex
B. Benign neoplasm of the adrenal medulla
C. Malignant neoplasm of the adrenal cortex
D. Malignant neoplasm of the adrenal medulla
E. Diffuse hyperplasia of the adrenal cortex
F. Diffuse hypoplasia of the adrenal medulla

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Question 14

Which of the following characteristics of amphetamines is most likely to be responsible for increasing blood pressure?

- Indirect release of endogenous catecholamines
- Inhibition of catecholamine metabolism
- Metabolism to false neurochemical transmitters
- Potent alpha1-adrenergic agonism
- Potent beta1-adrenergic agonism

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Question 15

A 30-year-old woman with a 1-week history of severe diarrhea feels dizzy when she stands up. Blood pressure (supine) is 112/76 mm Hg with a pulse of 88/min; blood pressure (on standing) is 80/60 mm Hg with a pulse of 120/min. In addition to controlling her diarrhea, the most appropriate initial therapy is intravenous administration of?

A. desmopressin
B. 5% dextrose in water
C. fresh frozen plasma
D. isotonic saline
E. methoxamine
F. verapamil

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Answer C

Original workup showed high levels of the EPI metabolite and lower levels of the NE metabolite. This indicates the tumor produced almost pure EPI and little NE. This is rare but has been reported. Most Pheochromcytoma produce a mixture of EPI and NE.

A patient with a tumor like this would exhibit a dramatic 'Epinephrine reversal response' to any alpha-blocker, dropping the BP to shock levels. This is especially true if blood volume is low (i.e. dehydrated, vomiting).
Question 6

In a hypertensive patient with congestive heart failure, which of the following drugs is CONTRAINDICATED in treatment of the hypertension?

(A) Captopril
(B) Chlorothiazide
(C) Methyldopa
(D) Prazosin
(E) Propranolol