ANS Pharmacology summary:

1) Introduction:

- ANS Receptors:
  
  **A1:**
  - Found in: blood vessels, kidney, liver, pregnant uterus, male sexual organs, intestinal smooth muscle.
  - Causes vasoconstriction, decreased rennin secretion, uterine contraction.

  **A2:**
  - Inhibits release of norepinephrine.
  - Affects vascular smooth muscle, inhibits insulin secretion, platelet aggregation (BP reduce).

**M1:** Neurons and Parietal cells

**M2:** Heart

**M3:** Bladder, Exocrine glands, Smooth muscles

Neuromuscular Junction (blocked by: Tubocurare)

Ganglia, (blocked by: Hexamethonium)

Adrenal Medulla

**1- Muscarinic**

- M1: Neurons and Parietal cells
- M2: Heart
- M3: Bladder, Exocrine glands, Smooth muscles

**1- Nicotinic**

Neuromuscular Junction (blocked by: Tubocurare)

Ganglia, (blocked by: Hexamethonium)

Adrenal Medulla

**1- Alpha**

**A1:**
- Found in: blood vessels, kidney, liver, pregnant uterus, male sexual organs, intestinal smooth muscle.
- Causes vasoconstriction, decreased rennin secretion, uterine contraction.

**A2:**
- Inhibits release of norepinephrine. affects vascular smooth muscle, inhibits insulin secretion, platelet aggregation (BP reduce).

**2- Beta**

**B1:** heart and kidneys (increased heart rate)

**B2:** affects lungs, liver, blood vessel vasodilation, decreased motility and tone ... (bronchodilation)
**Fibers**  | **Receptors**  | **Neurotransmitters**

- Exceptions: only symp (adrenal medulla / sweet gland / pilomotor muscle)
  (only pregan.) (Only ACH)
ANS drugs:
- produce their effect either by: **mimicking** (Agonist) or **altering** the function of the system (antagonist)
- Always keep this RULE in ur mind: most drugs work in receptors, so we can classify them according to the receptors :D

---

**Cholinergic drugs**: produce effects that mimic the effects of the endogenous Acetylcholine (also called cholinomimetic or parasympathomimetic)

**Classification of Cholinergic Drugs**

- **General Effects of Cholinergic Drugs**:
  1. **CVS**: Bradycardia / BP↑
  2. **GIT**: salivation ↓ / motility and secretion↑ / Relaxation of sphincters
  3. **Eye**: Miosis / Fixed Accommodation
  4. **Urinary**: urination
  5. **RS**: Bronchospasm / secretion
  6. **Sweating**
  7. **Production of tears**
  8. **CNS effect**: tremors / convulsions
  9. **Muscles**: Twitching and contraction / Paralysis (at high doses)

---

**1) Agonist**
- Act on muscarinic receptors

**INDIRECT ACTING** (reversible)
- Ambenonium
- Demecarium
- Donepezil
- Edrophonium
- Galantamine
- Neostigmine
- Physostigmine
- Pyridostigmine
- Rivastigmine
- Tacrine

**DIRECT ACTING**
- Acetylcholine
- Bethanecol
- Carbachol
- Cevimeline
- Pilocarpine

**Choline Esters Alkaloids**

---

**Inhibit Acetylcholinesterase**
- Echotoephate
- REACTIVATION OF ACETYLCHOLINE ESTERASE
- Pralidoxime

---

**2) Antagonist**

**KEY**: atropine .. ipratropium .. scop (IFMSA!)
= at trip with scop
* success tu bo victory

---

**Antimuscarinic Agents**
- Atropine
- Cyclopentolate
- Ipratropium
- Scopolamine
- Tropicamide

**Ganglionic Blockers**
- Mecamylamine
- Nicotine

**Neuromuscular Blockers**
- Atracurium
- Cisatracurium
- Doxacurium
- Metocurine
- Mivacurium
- Pancuronium
- Rocuronium
- Succinylcholine

**Depolarizing** (agonist)

**Non-depolarizing** (competitive antagonist)
- Tubocurarine
- Vecuronium

---

**KEY**: ABC .. pile is alkel! .. edro news at Ph by radio .. echo pray
Adrenergic drugs: produce effects that mimic the effects of the endogenous Acetylcholine (also called cholinomimetic or parasympathomimetic).

**Contraindications** for adrenergic agonist:
- Cardiac dysrhythmias, angina pectoris (B1)
- Hypertension
- Hyperthyroidism
- Cerebrovascular disease
- Distal areas with a single blood supply such as fingers, toes, nose and ears
- Renal impairment use caution

1- Adrenergic Agonists

1- Adrenergic Antagonists (sympatholytic drugs)

- **Indications**
  - Emergency drugs in treatment of acute cardiovascular, respiratory and allergic disorders (anaphylaxis)
  - For vasoconstrictive and hemostatic purposes (local anesthetics, shock)
  - Inhibition of uterine contractions
  - Phenylephrine may be used to treat nasal congestion

DIRECT-ACTING
- Albuterol
- Clonidine
- Dobutamine*
- Dopamine*
- Epinephrine*
- Fortetol
- Isoproterenol*
- Metaproterenol
- Methoxamine
- Noradrenaline
- Phenylephrine
- Prazosin
- Salbutamol
- Terbutaline

INDIRECT-ACTING
- Amphetamine
- Cocaine
- Tyramine

DIRECT and INDIRECT ACTING (mixed action)
- Ephedrine
- Pseudoephedrine

\( \alpha \)-BLOCKERS
- Aliiuzosin
- Doxazosin
- Phenoxylbenzamine
- Phentolamine
- Prazosin
- Tamsulosin
- Terazosin
- Yohimbine

\( \beta \)-BLOCKERS
- Acebutolol
- Atenolol
- Carvedilol
- Esmolol
- Labetalol
- Metoprolol
- Nadolol
- Pindolol
- Propranolol
- Timolol

Drugs affecting neurotransmitter uptake or release
- Guanethidine
- Reserpine

*Act on skin, mucosa, intestines, lungs and kidneys to prevent vasoconstriction

Effects:
- dilation of arterioles and veins
- decreased blood pressure
- pupillary constriction
- increased motility of GI tract

KEY: (PNT Es MAA Pin CaLabe)

PNT: (FEB0 09/24, 09/24)

*remains: clonidine, dobutamine, isoproteranol... mmmmmmm
(clon do but is not protected)
Agonist: will produce the same effect!

Antagonist (blockers): will produce the reverse effect! or will just block the effect.

- Blood vessels, kidney, liver, pregnant uterus, male sexual organs, intestinal smooth muscle.
- Causes vasoconstriction

- $\alpha_2$ agonists are used in hypertension to reduce the blood pressure. (clonidine)
- $\alpha_1$ agonist this will result in hypertension.

- Affects heart and kidneys
- Stimulating of $\beta_1$ will result in tachycardia

- Affects lungs, liver, blood vessel vasodilatation, decreased motility and tone, present in the bronchi, there stimulation results in dilation (relaxation)... (given to pregnant)
### 1- Adrenergic Agonists

<table>
<thead>
<tr>
<th>DRUG</th>
<th>RECEPTOR SPECIFICITY</th>
<th>THERAPEUTIC USES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epinephrine</td>
<td>(\alpha_1, \alpha_2) (\beta_1, \beta_2)</td>
<td>Acute asthma, Treatment of open-angle glaucoma, Anaphylactic shock, In local anesthetics to increase duration of action</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>(\alpha_1, \alpha_2) (\beta_1)</td>
<td>Treatment of shock</td>
</tr>
<tr>
<td>Isoproterenol</td>
<td>(\beta_1, \beta_2)</td>
<td>As a cardiac stimulant</td>
</tr>
<tr>
<td>Dopamine</td>
<td>Dopaminergic</td>
<td>Treatment of shock, Treatment of congestive heart failure, Raise blood pressure</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>(\beta_1)</td>
<td>Treatment of congestive heart failure</td>
</tr>
<tr>
<td>Oxymetazoline</td>
<td>(\alpha_1)</td>
<td>As a nasal decongestant</td>
</tr>
<tr>
<td>Phenytoin</td>
<td>(\alpha_1)</td>
<td>As a nasal decongestant, Raise blood pressure, Treatment of paroxysmal supraventricular tachycardia</td>
</tr>
<tr>
<td>Methoxamine</td>
<td>(\alpha_1)</td>
<td>Treatment of supraventricular tachycardia</td>
</tr>
<tr>
<td>Clonidine</td>
<td>(\alpha_2)</td>
<td>Treatment of hypertension</td>
</tr>
<tr>
<td>Metaproterenol</td>
<td>(\beta_2 &gt; \beta_1)</td>
<td>Treatment of bronchospasm and asthma</td>
</tr>
<tr>
<td>Albuterol</td>
<td>(\beta_2)</td>
<td>Treatment of bronchospasm (short acting)</td>
</tr>
<tr>
<td>Terbutaline</td>
<td>(\beta_2)</td>
<td>Treatment of bronchospasm (long acting)</td>
</tr>
<tr>
<td>Salmeterol</td>
<td>(\beta_2)</td>
<td>Treatment of bronchospasm (long acting)</td>
</tr>
<tr>
<td>Formoterol</td>
<td>(\alpha_1, \beta, \text{CNS})</td>
<td>As a CNS stimulant in treatment of children with attention deficit syndrome, narcolepsy, and appetite control</td>
</tr>
<tr>
<td>Amphetamine</td>
<td>(\alpha_1, \beta, \text{CNS})</td>
<td>As a CNS stimulant in treatment of children with attention deficit syndrome, narcolepsy, and appetite control</td>
</tr>
</tbody>
</table>

#### Catecholamines
- Rapid onset of action
- Brief duration of action
- Not administered orally
- Do not penetrate the blood-brain barrier

#### Noncatecholamines
- Compared to catecholamines:
  - Longer duration of action
  - All can be administered orally

**Direct acting**

**Indirect**

**Mixed**
2- Adrenergic Antagonist (beta blockers)

**Contraindications**
- Heart block
- Heart failure
- Diabetes (caution)
- B2 in pregnant
- B2 in Asthma patients

**Effects of beta blocking drugs**
- Decreased heart rate
- Decreased force of contraction
- Decreased CO
- Slow cardiac conduction
- Decreased automaticity of ectopic pacemakers
- Decreased renin secretion from kidneys
- Decreased production of aqueous humor in eye

<table>
<thead>
<tr>
<th>DRUG</th>
<th>RECEPTOR SPECIFICITY</th>
<th>THERAPEUTIC USES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Propranolol</td>
<td>$\beta_1, \beta_2$</td>
<td>Hypertension, Glaucoma, Migraine, Hyperthyroidism, Angina pectoris, Myocardial infarction</td>
</tr>
<tr>
<td>Nadolol</td>
<td>$\beta_1, \beta_2$</td>
<td>Glaucoma, Hypertension</td>
</tr>
<tr>
<td>Timolol</td>
<td>$\beta_1, \beta_2$</td>
<td></td>
</tr>
<tr>
<td>Acebutolol</td>
<td>$\beta_1$</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Atenolol</td>
<td>$\beta_1$</td>
<td></td>
</tr>
<tr>
<td>Esmolol</td>
<td>$\beta_1$</td>
<td></td>
</tr>
<tr>
<td>Metoprolol</td>
<td>$\beta_1$</td>
<td></td>
</tr>
<tr>
<td>Pindolol</td>
<td>$\beta_1, \beta_2$</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Carvedilol</td>
<td>$\alpha_1, \beta_1, \beta_2$</td>
<td>Hypertension, Congestive heart failure</td>
</tr>
<tr>
<td>Labetalol</td>
<td>$\alpha_1, \beta_1, \beta_2$</td>
<td></td>
</tr>
</tbody>
</table>

prototype

[Non-cardioselective]

[cardioselective]
<table>
<thead>
<tr>
<th>Disease</th>
<th>Drug for therapy</th>
<th>Side effects</th>
<th>Notes</th>
</tr>
</thead>
</table>
| Glaucoma | Pilocarpine (emergency) | Fixation of accommodation, excessive sweating and salivation and CNS effects | - alkaloid, unchanged  
- Not Hydrolysed by Acetylcholin-esterase  
- Decrease salivation |
| Carbachol (Synthetic) | | | |
| Echothiophate | | | - Choline Ester as eye drops (produce miosis)  
- Not Hydrolysed by Acetylcholin-esterase  
- Muscarinic/Nicotinic Receptors  
- charged |
| Physostigmine | | | Irreversible Anticholinesterases (used for Chronic Open-Angle Glaucoma), antidote: Atropine  
(atropine is contraindicated in: Glaucoma! and prostate enlargement, and urinary retention) |
| Propranolol | ↓ cardiac output and heart rate And bronchoconstriction | | |
| nadolol / Timolol | | | |
| Eyedrops for rapid miosis before surgery | Acetylcholine (Endogenous) | | - Choline Ester  
- Hydrolysed by Acetylcholin-esterase  
- Muscarinic/Nicotinic Receptors  
- charged |
| - Postsurgical/Postparum  
Atony / Non-obstructive urinary retention / Neurogenic Atony / Megacolon  
- Atonic bladder  
- intestinal atony | Bethanechol (Synthetic) | | - Choline Ester  
- Not Hydrolysed by Acetylcholin-esterase  
- Muscarinic Receptors  
- charged |
| - Physotigimine  
- Neostigmine | | | |
<p>| Xerostomia (dry mouth syndrome) and Sjogren Syndrome | Pilocarpine | | ** Sjogren Syndrome: systemic autoimmune disease in which immune cells attack and destroy the exocrine glands that produce tears and saliva |</p>
<table>
<thead>
<tr>
<th>Condition</th>
<th>Medication</th>
<th>Side Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myasthenia Gravis</td>
<td>Edrophonium Neostigmine Pyridostigimine</td>
<td>- Diagnose Myasthenia gravis</td>
</tr>
</tbody>
</table>
| Cholinergic Crisis                            | Atropine                          | Side effects :
|                                               |                                   | - loss accommodation
|                                               |                                   | * Atropine competitively inhibits muscarinic responses to ACh                 |
| Toxicity of Organophosphate Compounds (Nerve Gases) | Antidote: Atropine Pralidoxime | Toxicity of nerve gases will produce:
|                                               |                                   | -- Runny nose, chest tightness, constricted pupil
|                                               |                                   | -- Excessive salivation, urination and defecation
|                                               |                                   | -- Muscle weakness and paralysis
|                                               |                                   | -- Coma, convulsions
|                                               |                                   | -- Death                                                                    |
| Acute Asthma                                  | Ipratropium terbutaline / albuterol | B2 agonist                                                                  |
| Prevent motion sickness                       | Scopolamine (hycosine)            | Peripheral effects similar to atropine
|                                               |                                   | More CNS effects                                                           |
| Used during surgery to relax muscles          | Turbocurarine                      | Non-depolarizing (competitive antagonist)
|                                               |                                   | Block ion channels at motor end plate
|                                               |                                   | - Increases safety of anesthetics
|                                               |                                   | - Does not cross blood-brain barrier                                       |
| endotracheal intubations                      | Succinylcholine                   | Depolarizing (agonist)
<p>|                                               |                                   | Activates receptor                                                         |
| electroconvulsive shock therapy               |                                   | ** Problem: can cause apnea (breath stop)                                   |
| Block uptake process of choline               | Hemicholinium                     |                                                                            |
| inhibit release of ACH                        | Botulinum toxin                   |                                                                            |</p>
<table>
<thead>
<tr>
<th>Condition</th>
<th>Treatment</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black widow spider</td>
<td>stimulate release of ACH</td>
<td>arrhythmia, sexual dysfunction, sexual dysfunction</td>
</tr>
<tr>
<td>Hypertension</td>
<td>All the beta blockers! remember the key! (PNT Es MAA Pin Calabe)</td>
<td>- hypertension, sexual dysfunction</td>
</tr>
<tr>
<td>Migraine</td>
<td>Propranolol</td>
<td>- postural hypotension, nasal stuffiness, nausea, and vomiting</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angina pectoris</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>Carvedilol, labetolol, dobutamine</td>
<td></td>
</tr>
<tr>
<td>nasal decongestant</td>
<td>Phenylephrine</td>
<td></td>
</tr>
<tr>
<td>BPH (benign prostatic hyperplasia)</td>
<td>Alpha 1 blockers (Tamsulosin and alfuzosin)</td>
<td>Inhibit contraction of muscles in prostate and bladder</td>
</tr>
<tr>
<td>Pheochromocytoma, (catecholaminesecting tumor of cells derived from the adrenal medulla.)</td>
<td>Phenoxybenzamine</td>
<td>postural hypotension, nasal stuffiness, nausea, and vomiting</td>
</tr>
</tbody>
</table>

Best wishes ^_^

Omar Sawas