ADRENERGIC BLOCKING DRUGS – ADRENERGIC ANTAGONISTS

Block responses caused by adrenergic nerve stimulation.

I. Types of adrenergic receptor blocking drugs.

A. Adrenergic receptor Blocking Drugs (Adrenergic Receptor Antagonists).
   Bind to adrenergic receptors but do not stimulate the receptor to cause a response. Since antagonist drugs are bound to the receptor they prevent binding of the neurotransmitter norepinephrine or of agonist drugs and the subsequent response caused by these agents.

B. Adrenergic Neuron Blocking Drugs.
   Inhibit the activity of adrenergic nerves.

II. Selectivity* of adrenergic receptor antagonists for adrenergic receptor types.

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<td>PROPRANOLOL</td>
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<td>NADOLOL</td>
<td>CARVEDILOL</td>
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<td>PHENTOLAMINE</td>
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<td>PHENOLYBENZAMINE</td>
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<td>α₁</td>
<td>α₂</td>
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<td>TERAZOSIN</td>
<td>PRAZOSIN</td>
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<td>DOXAZOSIN</td>
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*Absolute versus relative selectivity of adrenergic receptor antagonists.

Labetalol- Blocks > 1 adrenergic receptor type.

Propranolol, Pindolol, Nadolol, Carvedilol- Other similar drugs = timolol, levobunolol, carteolol, phenbutolol. Intrinsic sympathomimetic activity (pindolol).

Phentolamine, Phenoxybenzamine- In contrast to other adrenergic receptor blocking drugs, phenoxybenzamine causes a non-competitive or irreversible blockade of α-adrenergic receptors.

Terazosin- Other similar drugs = doxazosin, prazosin.

Atenolol, Metoprolol, Acebutolol, Esmolol - Other similar drugs = betaxolol etc.

III. Responses* of effector organs to adrenergic receptor blocking drugs.
The effects listed above depend on the level of sympathetic tone. Some of these effects reflect unmasking of opposing parasympathetic input to these structures.

IV. \( \alpha \)-Adrenergic receptor antagonists.

1. Epinephrine Reversal

2. Therapeutic uses of \( \alpha \)-adrenergic receptor antagonists.
   Treatment of hypertension- Terazosin, labetalol.

   Treatment of benign prostatic hyperplasia- Terazosin, doxazosin, saw palmetto?.

   Treatment of peripheral vascular disease- Phentolamine, phenoxybenzamine.

   Treatment of impotence- Phentolamine plus papaverine for erectile dysfunction.
Yohimbine?

3. Adverse effects of α-adrenergic receptor antagonists.

   Cardiovascular - Reflex tachycardia -
   - Sodium retention -
   - Orthostatic (postural) hypotension - This is most often seen following initial doses of terazosin, doxazosin and prazosin. This is called the “first dose effect”.

   Genitourinary - Impairment of ejaculation in males.

V. β-Adrenergic receptor antagonists.

1. Therapeutic uses of β-adrenergic receptor antagonists.
   Treatment of essential hypertension- Propranolol, labetalol, atenolol.
   \[ \text{↓ release of rennin} \]
   \[ \text{↓ cardiac output} \]
   Effects in the CNS

   Treatment of angina pectoris- Propranolol, atenolol, nadolol.

   Treatment of cardiac arrhythmias- Propranolol, esmolol.

   Treatment of heart failure- Carvedilol.

   Prevention of recurrent myocardial infarction- Atenolol, propranolol.

   Treatment of glaucoma- Timolol.

   Reduced muscle tremor- Propranolol.

2. Adverse effects.
Central nervous system - lethargy, depression, fatigue, altered sleep patterns.

Respiratory - Wheezing, bronchoconstriction in patients with respiratory disease.

Cardiovascular - Bradycardia, atrioventricular (AV) nodal block.
- Decreased cardiac work.

Rebound effects after abrupt cessation of drug treatment.

VI. Adrenergic Neuron Blocking Drugs. These drugs inhibit the activity of adrenergic nerves.

1. Drugs that reduce sympathetic nerve outflow from the CNS.

   Clonidine, guanabenz, α-methyldopa

   A. Mechanism of action.
   These drugs stimulate α₂-adrenergic receptors in the brainstem causing a reduction in sympathetic nerve outflow from the CNS to blood vessels. Reduced vascular sympathetic tone causes a reduction in blood pressure.

   B. Therapeutic uses.
   - Treatment of hypertension
     - Clonidine decreases withdrawal symptoms during opioid or nicotine withdrawal.

   C. Adverse effects.
   - CNS effects – sedation, fatigue, sleep disturbances
   - Impaired ejaculation
   - Clonidine - dry mouth.

2. Drugs that block the storage of norepinephrine in the storage vesicle of adrenergic nerves.
   Reserpine, Guanethidine
A. Mechanism of action.
- Inhibits the storage vesicle uptake mechanism that transports norepinephrine and dopamine into the storage vesicle.
- Since catecholamines cannot enter the storage vesicle the vesicle becomes depleted of norepinephrine.
- Reserpine acts on both central and peripheral nerves and also blocks storage of serotonin, histamine and dopamine in nerves.

B. Therapeutic uses.
- Treatment of hypertension.

C. Adverse effects.
- Increased gastrointestinal motility, diarrhea.
- Orthostatic (postural) hypotension.
- Sodium and water retention.
- Reserpine also causes CNS effects - sedation, nightmares, depression and suicidal tendencies.

3. Drugs that inhibit norepinephrine release.
   **Guanethidine**, Guanadryl

A. Mechanism of action.
- Inhibits the process whereby the storage vesicle moves to and binds to the neuronal membrane.
- May cause an initial release of norepinephrine but over time also depletes the storage vesicle of norepinephrine.
- Are polar molecules and therefore do not enter into the CNS.

B. Therapeutic uses.
- Used to treat hypertension.

C. Adverse effects.
- Increased gastrointestinal motility, diarrhea.
- Orthostatic (postural) hypotension.
- Sodium and water retention.