Adrenergic Drugs
Sympathetic Nervous System

Many adrenergic drugs are active in the CNS

This fact sheet, and accompanying lecture, focuses on the peripheral nervous system. The adrenergic receptors are the same in the CNS as in the PNS.

If the parasympathetic nervous system was concerned with rest and ...digestion, then we can think of the sympathetic nervous system as being concerned with fight and/or flight. It is, of course, more complicated than that. All cells have a basal level of activity and it is generally accepted that it is the sympathetic nervous system that maintains that “tone” in the viscera as well as all other smooth muscle.

The adrenergic receptors, like the cholinergic receptors, do not need to be innervated. This is especially true of Beta receptors, they tend to respond better to Epinephrine, a hormone released from the modified sympathetic neurons that make up the Adrenal Medulla (a gland atop the kidneys). For instance, the Beta receptors in the lungs are mostly non-innervated β 2 receptors that relax bronchial smooth muscle.

β 2 receptors respond to EPINEPHRINE. In humans, there are often as many β 2 as β 1 in both the heart and lungs.

Adrenergic Receptors

<table>
<thead>
<tr>
<th>Type</th>
<th>Effect</th>
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<tbody>
<tr>
<td>Alpha 1</td>
<td>Smooth &amp; cardiac muscle contraction</td>
</tr>
<tr>
<td>Alpha 2</td>
<td>Opposite of alpha-1; block insulin secretion from pancreas</td>
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<tr>
<td>Beta 1</td>
<td>Increased heart rate, renin secretion from kidney</td>
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<tr>
<td>Beta 2</td>
<td>Bronchodilation, vasodilation; increased glucagon secretion from pancreas</td>
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**Sympathomimetic Bronchodilators = β2 agonists**

The Beta-2 agonists are used to treat asthma and Chronic Obstructive Pulmonary Diseases (COPD).

**Albuterol** *(Proventil® HFA)* is a top-selling drug worldwide used as a metered inhaler or tablet for asthma, primarily. HFA refers to the propellant. It is fairly selective for beta 2 receptors.

**Terbutaline** *(Brethaire)* is an older bronchodilator also available in a SC formulation.

Both Albuterol and Terbutaline are short-acting bronchodilators used to treat asthma attacks.

**Salmeterol** is a long-acting beta-2 agonist (LABA) and because the LABA drugs are associated with rebound bronchoconstriction, salmeterol must be co-formulated with a corticosteroid, like fluticasone. This combination is sold as “Advair.” The corticosteroid acts as an anti-inflammatory, thus helping maintain an open airway.

Corticosteroids may be used alone in asthma/COPD maintenance therapy. We cover them with Autocoids and Lungs.

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**General β2 Agonist Issues**

- Promote glycogenolysis (raising blood glucose)
- Cause tachycardia (use caution in heart and hyperthyroid patients)
- Lower seizure threshold
- Potential rebound bronchoconstriction
- Hypokalemia (with frequent use)
- Incompatible with MAOIs, TCA, β blockers and diuretics
Adrenergic Drugs

The adrenergic agonists are important drugs. The alpha-1 agonists are used to treat shock and shock-like conditions as well as congestion associated with colds and allergies. The alpha-2 agonists have uses treating hypertension, chronic pain and Attention Deficit Hyperactivity Disorder (ADHD). The β2 agonists are used to treat asthma and chronic obstructive pulmonary diseases (COPD).

Drugs with mixed alpha & beta agonist effects

**Dobutamine** *(Dobutrex)* is a synthetic catecholamine that mainly activates β1 receptors. It mimics epinephrine, but lasts longer and is used to treat heart failure and shock.

**Dopamine** is available as a generic, and is used to treat shock and heart failure.

**Epinephrine** is a naturally occurring catecholamine like dopamine. It is used to treat anaphylactic shock, severe bronchospasm, open angle glaucoma, to inhibit uterine contractions and to prolong local and regional anesthesia (among some of its uses). It is also used to resuscitate patients in cardiac arrest.

**Norepinephrine** is a third naturally occurring catecholamine. It is used in specific cases of hypotension and as an adjunct to treat cardiac arrest.

The CNS stimulants like **Amphetamine** and **methylphenidate** will be covered with ADHD.

Drugs with alpha 2 agonist effects

The α2 agonists are used mainly as anti hypertensives, to treat Attention Deficit Hyperactivity Disorder (ADHD), or as an adjunct in chronic pain treatment.

**Clonidine** *(Catapres)* is used to treat hypertension and is an adjunct to treat chronic pain when combined with an opiate.

Another common α2 agonist is **Guanfacine** *(Tenex, Intuniv)* used to treat hypertension *(Tenex only)* and ADHD *(Intuniv only)*. This is an example of a drug with two trade names used for different purposes.
Drugs with alpha 1 & 2 agonist effects

The mixed α1 & 2 agonists are typically used as over-the-counter (OTC) decongestants.

Phenylephrine (NeoSynephrine PE) has many other uses. It is used for its vasoconstrictive properties as a decongestant, in hemorrhoid preparations, in ophthalmic drops and as an injection to treat shock.

Phenylephrine injection
Phenylephrine ophthalmic solution
Phenylephrine Monograph

Oxymetazoline (Afrin), on the other hand, is only used as a topical nasal spray as a nasal decongestant. It is available OTC in hundreds of products including combination products. It has a potent rebound (runny nose) if used chronically.

Drugs with mixed beta 1 & 2 agonist effects

Isoproterenol (Isuprel) is used to treat heart block, but has serious limitations to its use. It is also used to prevent bronchospasm during surgery due to anesthetic agents.

Drugs with mixed β1 & 2 blocking effects

The β blockers are primarily for angina or hypertension, but may be used to treat migraine, anxiety and other conditions.

Propranolol (Inderal) is an old drug with a lot of uses and indications. It is indicated for hypertension (HTN), angina, hypertrophic subaortic stenosis, arrhythmias, pheochromocytoma, migraine and essential tremor. It is used as an anxiolytic to treat stage fright and is being investigated as a potential “cure” for Post-traumatic Stress Disorder.

Extended release capsules: http://www.drugs.com/pro/propranolol.html

Drugs with selective β1 blocking effects

Atenolol (Tenormin) and Metoprolol (Lopressor, Toprol) target the β1 receptor important in the heart and kidneys.
Metoprolol is one of the top selling drugs in the world. It comes as two different salts that are not bioequivalent. Lopressor is the tartrate and Toprol is the succinate salt. The succinate is stronger than the tartrate, but, in this case, manufacturers market the extended release succinate in a bioequivalent dosage (23.75 mg of the succinate = 25 mg of the tartrate). They call this product, “25 mg” (or “50 mg” for that strength, and so forth). On the 200 mg Toprol-XL product display panel shown, each tablet only contains 190 mg of Metoprolol succinate, which is EQUIVALENT to 200 mg of Metoprolol tartrate. The AstraZeneca display panel shown is from drugs.com/pro/Toprol-xl.html, but the same holds for generic Metoprolol succinate products.

**Drugs with non-selective α/β blocking effects**

**Labetalol** ([Normodyne](#)) is another antihypertensive, but is generally only used in cases of severe hypertension or hypertensive crisis.

**Drugs with non-selective α blocking effects**

**Phentolamine** ([Regitine, Oraverse](#)) is a nonspecific α blocker. It has an extremely short duration, usually less than 30 minutes. It has two important uses, (1) pheochromocytoma-related hypertensive crisis control and prophylaxis; and (2) to reverse the effects of extravasated norepinephrine. If you miss the blood vessel, and inject a catecholamine like norepinephrine into tissues, severe vasoconstriction can lead to tissue necrosis. Because phentolamine reverses the effects of catecholamines, it is also used to reverse the effects of local anesthetics that contain epinephrine. The product named [Oraverse](#) is for this purpose and is used almost entirely by dentists (oral surgeons).

**Drugs with selective α-1 blocking effects**

**Doxazosin** ([Cardura](#)) and **Tamsulosin** ([Flomax](#)) are selective alpha-1 inhibitors. This class of drugs is associated with profound hypotension when the patient first starts taking them. As a practical matter, patients should be started on a low dose, titrated up, and told to take their medication just before going to bed. The orthostatic hypotension can be so profound as to cause syncope, something patients need to be strongly cautioned about. This is particularly true for Doxazosin. This class of drugs also can cause priapism.

Doxazosin has an indication for HTN, but is no longer recommended for this due to increased risk of heart failure.
### Adrenergic drug incompatibilities

**Sympathomimetics should not be given with:**
- MAOIs (monoamine oxidase inhibitors)
- COMT-I (catechol O-methyl transferase inhibitor)
- Antidepressants
- Antipsychotics
- Beta blockers

**Sympatholytics should not be given with:**
- Sympathomimetics

Beta Blockers can increase responsiveness to allergen challenge and decrease the response to epinephrine used to treat anaphylaxis (because they are blocking the receptor!).

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### Homework and Exercises

1. Read the “START HERE” announcement in Laulima for updates and instructions.
3. Review the Powerpoints and listen to the audio from the face-to-face lecture. You may opt to watch the appropriate videos for this lecture. Review any handouts available for this lecture in the Course Index.
5. Use “Chat,” “Discussions and Private Messages” or the lecture “Forum” to ask questions and find answers or to seek assistance.
6. Complete the online quiz in Laulima Tasks, Tests and Surveys.

If you have any questions, email me at abeale@hawaii.edu

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All images, except the Metoprolol product display panel and the photo of the author with her much beloved dog, are from the National Library of Medicine image collection.