Phenylephrine

- Pure alpha receptor agonist
- Decreases CO and renal perfusion
- No B1 or B2 effects
- Longer lasting than epinephrine
- Can cause a reflex bradycardia
- Useful as a mydriatic

Isoproterenol

- Synthetic catecholamine that acts on beta 1 and 2 receptors
- Stimulates heart, dilates blood vessels in skeletal muscle and causes bronchodilation
- No alpha stimulation
- Used in heart blocks (when pacemaker not available) and as a bronchodilator

Beta2-selective agonists

Salbutamol, Terbutaline, Metaproterenol, Albuterol, Salmeterol , Ritodrine.

- Bronchodilation
- Cardiac effects observed only at high doses
- Not metabolized by MAO or COMT
- Longer duration of action than isoproterenol (salmeterol is the longer)
- Administration: Oral, parenteral, local (inhaled)
- Uses: Asthma, COPD; Terbutaline used as tocolytic (prevent premature labor)

A selective β_3 agonist has potential weight loss effects through modulation of lipolysis as well as for the treatment of overactive bladder

Anti-adrenergics

- Sympatholytic
- Block or decrease the effects of sympathetic nerve stimulation, endogenous catecholamines and adrenergic drugs

Antiadrenergics—mechanisms of action and effects

- Can occur by blocking alpha 1 receptors postsynaptically
- Or by stimulation presynaptic alpha 2 receptors. Results in return of norepineprhine to presynaptic site. Activates alpha 2 resulting in negative feedback. Decreases release of additional norepinephrine.

Alpha-Adrenergic Agonists and blocking agents

- Alpha 2 agonists inhibit release of norepinephrine in brain; thus, decrease effects on entire body
- Results in decrease of BP
- Also affects pancreatic islet cells, thus some suppression of insulin secretion

Alpha 1 adrenergic blocking agents

- Act on skin, mucosa, intestines, lungs and kidneys to prevent vasoconstriction
- Effects: dilation of arterioles and veins, decreased blood pressure, pupillary constriction, and increased motility of GI tract

Alpha 1 adrenergic blocking agents

- May activate reflexes that oppose fall in BP such as fluid retention and increased heart rate
- Can prevent alpha medicated contraction of smooth muscle in nonvascular tissues
- Thus, useful in treating BPH as inhibit contraction of muscles in prostate and bladder

Benign prostatic hyperplasia (BPH)

Alpha 1 antagonists

- Minipress (prazosin)—prototype.
- Hytrin (terazosin) and Cardura (doxazosin)—both are longer acting than Minipress.

- **Minipress (prazosin hydrochloride) is an alpha-adrenergic blocker used to treat hypertension (high blood pressure).**
- **Initial Dose** 1 mg two or three times a day

- Generic Name: prazosin hcl
- Brand Name: Minipress
- Drug Class: Alpha Blockers, Antihypertensives
- Common side effects of Minipress include:
- Headache,
- Drowsiness,
- Tiredness,
- Weakness,
- Blurred vision,
- Nausea,
- Vomiting,
- Diarrhea, or
- Constipation as your body adjusts to the medication

- **What is Hytrin?**
- Hytrin (terazosin) is in a group of drugs called alpha-adrenergic blockers. Hytrin relaxes your veins and arteries so that blood can more easily pass through them. It also relaxes the muscles in the prostate and bladder neck, making it easier to urinate.
- Terazosin is used alone or with other drugs to treat high blood pressure (hypertension). Lowering high blood pressure helps prevent strokes, heart attacks, and kidney problems. This medication works by relaxing blood vessels so blood can flow more easily.
- Terazosin is also used in men to treat the symptoms of an enlarged prostate (benign prostatic hyperplasia-BPH).
- It does not shrink the prostate, but it works by relaxing the muscles in the prostate and part of the bladder. This helps to relieve symptoms of BPH such as difficulty in beginning the flow of urine.

- **CARDURA**
- Generic Name: doxazosin mesylate
- Brand Name: Cardura
- Drug Class: BPH, Alpha Blockers
- What is Cardura?
- Cardura is a prescription medicine used to treat the symptoms of hypertension (high blood pressure) or to improve urination in men with benign prostatic hyperplasia (enlarged prostate). Cardura may be used alone or with other medications. Cardura is an alpha blocker.
- The safety and effectiveness has not been established in children.
- What are the possible side effects of Cardura?
- Cardura may cause serious side effects including:
- a light-headed feeling, like you might pass out
- severe ongoing stomach pain or bloating
- new or worsening chest pain
- trouble breathing
- an erection that is painful or lasts 4 hours or longer

Indications for use

- Alpha 1 blocking agents are used for treatment of hypertension, BPH, in vasospastic disorders, and in persistent pulmonary hypertension in the newborn
- May be useful in treating pheochromocytoma
- May be used in Raynaud's or frostbite to enhance blood flow

- **What is Raynaud's phenomenon?**
- Raynaud’s phenomenon is a problem that causes decreased blood flow to the fingers. In some cases, it also causes less blood flow to the ears, toes, nipples, knees, or nose. This happens due to spasms of blood vessels in those areas. The spasms happen in response to cold, stress, or emotional upset.

What is Frostbite phenomenon?

- **Frostbite** is an injury caused by freezing of the skin and underlying tissues. In the earliest stage of frostbite, known as frostnip, there is no permanent damage to skin. Symptoms include cold skin and a prickling feeling, followed by numbness and inflamed or discolored skin. As frostbite worsens, skin may become hard or waxy-looking

Raynaud phenomenon causing lingual pallor and dysarthria

Raynaud phenomenon results from reduced blood flow in response to cold or emotional stress, causing discoloration and paresthesias of the fingers and toes, and occasionally other parts of the body. It is frequently associated with autoimmune rheumatic diseases. Lingual Raynaud phenomenon has not been reported to be a predictor of worse prognosis from the underlying autoimmune rheumatic disease.
Dysarthria can occur during these episodes, although no hypothesis about its mechanism has been proposed.

Alpha 1 antagonists cont.

- Tamsulosin Used in BPH. Produces smooth muscle relaxation of prostate gland and bladder neck. Minimal orthostatic hypotension.
- Tolaxoline used for vasospastic disorders. PuImonary hypertension in newborns. Can be given sub Q, IM or IV.
- Phentolamine Used for extravasation of potent vasoconstrictors (dopamine, norepinephrine) into subcutaneous tissues

Indications for use

- Alpha 2 agonists are used for hypertension—Catapres
- Epidural route for severe pain in cancer
- Investigationally for anger management, alcohol withdrawal, postmenopausal hot flashes, ADHD, in opioid withdrawal and as adjunct in anesthesia

Alpha 2 agonists

- Catapres (clonidine). PO or patch.
- Tenex (guanfacine)
- Aldomet (methyldopa). Can give IV. Caution in renal and hepatic impairment.

Beta adrenergic blocking medications

- Prevent receptors from responding to sympathetic nerve impulses, catecholamines and beta adrenergic drugs.

Effects of beta blocking drugs

- Decreased heart rate
- Decreased force of contraction
- Decreased CO
- Slow cardiac conduction
- Decreased automaticity of ectopic pacemakers

Effects of beta blocking drugs

- Decreased renin secretion from kidneys
- Decreased BP
- Bronchoconstriction
- Less effective metabolism of glucose. May result in more pronounced hypoglycemia and early s/s of hypoglycemia may be blocker (tachycardia)
- Decreased production of aqueous humor in eye
- May increase VLDL and decrease HDL
- Diminished portal pressure in patients with cirrhosis

Beta blocking medications

- Mainly for cardiovascular disorders (angina, dysrhythmias, hypertension, MI and glaucoma)
- In angina, beta blockers decrease myocardial oxygen consumption by decreasing rate, BP and contractility. Slow conduction both in SA node and AV node.

Beta blockers

- Possibly work by inhibition of renin, decreasing cardiac output and by decreasing sympathetic stimulation
- May worsen condition of heart failure as are negative inotropes
- May reduce risk of “sudden death”

Beta blockers

- Decrease remodeling seen in heart failure
- In glaucoma, reduce intraocular pressur by binding to beta-adrenergic receptors in ciliary body, thus decrease formation of aqueous humor

Beta blockers

- Propranolol (Inderal) is prototype
- Useful in treatment of hypertension, dysrhythmias, angina pectoris, MI
- Useful in pheochromocytoma in conjunction with alpha blockers (counter catecholamine release)
- migraines

Beta Blockers

- In cirrhosis, propranolol may decrease the incidence of bleeding esophageal varices
- Used to be contraindicated in heart failure, now are standard
- Known to reduce sudden death
- Often given with ACEIs

Angiotensin-converting-enzyme inhibitors (ACE inhibitors (ACEIs)) are a class of medication used primarily for the treatment of high blood pressure and heart failure.[1][2] They work by causing relaxation of blood vessels as well as a decrease in blood volume, which leads to lower blood pressure and decreased oxygen demand from the heart.

Receptor selectivity

- Acetutolol, atenolol, betaxolol, esmolol, and metoprolol are relatively cardioselective
- These agents lose cardioselection at higher doses as most organs have both beta 1 and beta 2 receptors
- Byetta is new agent that is cardioselective

Cardioselective Beta Blockers

Metoprolol
Atenolol
Nebivolol
Bisoprolol
Acebutolol
Betaxolol
Esmolol

β Receptor Locations
β1 = Heart (1 heart)
β2 = Lungs (2 lungs)

Non-Receptor selectivity

- Carteolol, levobunolol, metipranolol, nadolol, propranolol, sotalol and timolol are all non-selective
- Can cause bronchoconstriction, peripheral vasoconstriction and interference with glycogenolysis

Dopamine receptors

Five subtypes of dopamine receptor have been cloned.
D1: CNS excitatory and blood vessels vasodilatation and natriuresis.
D2: CNS inhibitory and inhibits prolactin release
D3: limbic system associated with emotional and cognitive behavior
D4: autoreceptor (presynaptic)
D5: highest mounts in the hippocampus and hypothalamus

Dopamine receptors agonists

Dopamine is a catecholamine neurotransmitter found in neurons of both the central and peripheral nervous systems.
Uses: treatment of cardiogenic and septic shock and in chronic refractory congestive heart failure.
Short half life.
Overdose causes excessive sympathomimetic activity.

Dopamine receptors agonists

Dobutamine

- Dopamine derivative
- Available as a racemic mixture
- positive inotropic effect on heart with little chronotropic effect
- Metabolized by COMT and conjugation, not sensitive to MAO
- Short half-life (~2 min)
- Administered: Parenteral
- Use: Acute heart failure, shock