		Cholinergic Drug	*Mechanism*	*Therapeutic Use*
Agonists	ACh-Esterase Inhibitors	**Edrophonium**	competitive antagonist (short half life)	diagnose myasthenia gravis
		Donepezil	competitive antagonist (long half life)	Alzheimer's
		Physostigmine	carbamyolation	treat acute glaucoma by causing miosis which moves iris away from canal of Schlemman reverse anticholinergic poisoning
		Neostigmine		treatment of myasthenia gravis restore GI motility and urinary flow following surgery
		Pyridostigmine		treatment of myasthenia gravis
		Organophosphates (Sarin)	phosphorylation (irreversible)	toxic nerve gas in biochemical warfare insecticide
	Muscarinic	**Bethanecol**	agonist resistant to ACh-Esterase	restore GI motility and urinary flow following surgery
		Carbechol	muscarine agonist	Treat acute glaucoma by causing miosis which moves iris away from canal of Schlemman
		Pilocarpine	muscarine agonist	Treat acute glaucoma by causing miosis which moves iris away from canal of Schlemman stimulate salivation in pts with xerostomia CF Chloride Sweat Test
		Nicotine		smoking cessation therapy
Antagonists	ACh-EsteraseReactivators	**Pralidoxime**	displaces organophosphate from irreversible phosphorylated active site on Ach-Esterase	reverse cholinergic poisoning due to organophosphates
	Muscarinic	**Atropine**	competitive inhibitor (long half-life)	reverse cholinergic poisoning
		Benzatropine		reduce tremors in Parkinson's disease
		Tropicamide	competitive inhibitor (short half-life)	mydriasis (but in doing so there is an increase in intraocular pressure which can precipitate narrow angle glaucoma) cycloplegia (lose accommodation)
		Scopolamine		motion sickness
		Ipratropium Bromide		bronchodilator and decreases bronchial secretions therefore effective for asthma and bronchitis
	Ganglionic Nicotinic	**Trimethaphan** **Hexamethonium** **Decamethonium**	competitive antagonist with the end effect on an organ depending on which system (Sym or Para) is the more dominant	Primary Sympathetic in Artery/Vein thus resulting in hypotension Primary Parasympathetic in Heart/Iris/GI thus resulting in tachycardia, mydriasis, decreased GI motility

	Neuromuscular Nicotinic	**Succinylcholine** (depolarizer)	unusual mechanism b/c this drug is an agonist that actually antagonizes, there is initial stimulation resulting in fasciculations but after a while the effect stops the muscle is a constant depolarized state so additional ACh can't elicit an AP in addition nicotinic receptors become desensitized after awhile THUS THE END EFFECT IS ANTAGONISM	adjuvant for anesthesia relax muscle for orthopedic procedures and intubation, and electroshock therapy (order of paralysis: face/fingers/toes > limbs/neck > intercostals muscles > diaphragm) N.B. prolonged apnea N.B. can cause malignant hyperthermia when there is exists the combination of succinylcholine + halothane + ryanodine receptor mutation resulting in hyperthermia and muscle rigidity N.B. potential hyperkalemia b/c of tissue damage
		D-Tobucurarine **Vecuronium** (non-depolarizer)	true competitive antagonist	adjuvant for anesthesia relax muscle for orthopedic procedures and intubation, and electroshock therapy N.B. prolonged apnea N.B. drug interactions with inhalational anesthetics, antibiotics, CCB by increasing their effects

βB (Beta-Blockers)

β1>2 Blockers "Cardioselective" (best for the pts that have relative contraindications to bb noted below)
Atenolol (Tenormin) used for HTN/ischemia but rarely used, +chlorthalidone (Tenoretic)
Esmolol (Brevibloc) b/c very short half life (10min) used only to treat acute SVTs
Metoprolol Tartrate (Lopressor) +HCTZ (Lopressor HCT) BID dosing, used for HTN/ischemia
Metoprolol Succinate (Toprol XL) QD dosing, used for HTN/ischemia and CHF
Betaxolol (Kerlone)
Bisoprolol (Zebeta) +HCTZ (Ziac) CHF
Acebutolol (Sectral)

β1=2 Blockers "Non-Cardioselective"
Propranolol (Inderal) used to treat mainly migraine, systemic catecholamine effects (hyperthyroidism, anxiety, pheo), portal HTN, SVTs
Timolol (Blocadren) as an ointment used to treat chronic glaucoma + HCTZ (Timolide)
Nadolol (Corgard) + bendroflumethiazide (Corzide)
Pindolol (?)
Sotalol (Betapace)
Penbutolol (Levatol)
Propranolol (?)

β1=2 Weak Blockers "Intrinsic Sympathomimetic Activity – ISA" (not good for CHF, partial beta agonist in that they stimulate the beta receptor to which they are bound yet they inhibit stimulation by more potent endogenous catecholamines there in effect they are weak blockers)
Penbutolol (Levatol), Pindol (Visken) used for HTN/ischemia but rarely used
Acebutolol (Sectral) used to treat acute SVTs
Carteolol (Cartol) as an ointment used to treat chronic glaucoma

β1=2,α1 Blockers "Beta/Alpha Blockers" (best for pts who are in a hyper-catecholamine state 2/2 amphetamine/cocaine/MAOI use, clonidine withdrawal, pheochromocytoma, these patients are stimulating both alpha and beta and if you use any other BB there will be unopposed alpha resulting in severe vasoconstriction and thus MI, CVA, APVD, NB "-a/ilol" not "-olol", has minimal metabolic SEs therefore good in pts w/ DM)
Carvedilol (Coreg) used for HTN/ischemia and CHF
Labetalol (Trandate) used for HTN/ischemia and HTN emergency b/c can be given IV

Nevivolol (Bystolic) new BB that apparently is better than Coreg

- Coreg and Toprol XL are proven in CHF b/c they are long acting
- Labetalol can be titrated up to 2400mg, metoprolol is fast acting, esmolol is short acting

Mechanism

- -β1
- -/+β2
- -α1
- decreased heart remodeling (CHF)
- decreased aqueous humor secretion (chronic glaucoma)
- decreased CNS vasodilation (migraines)
- decreased sympathetic effects (hyperthyroidism, anxiety, pheo)
- decreased RAS effects by decreasing renin secretion
- decreased HR/SV (SVTs, ischemia, and mild HTN despite the inhibition of beta 2)
- reset baroreceptors
- release of vasodilatory prostaglandins
- CNS antihypertensive effects

Side Effects & Containdications

CNS (esp the more lipophilic the BB like propranolol)

- fatigue, malaise, sedation
- sleep alteration w/ nightmares
- even though ejaculation is alpha mediated pts on BB exhibit sexual dysfunction specifically decreased
- depression

CV

- bradycardia ± heart block especially worrisome in acutely decompensated CHF
- orthostatic hypotension
- claudication symptoms b/c the increase in BP from inhibiting beta2 is enough to cause an immediate local problem despite the decrease in BP from inhibiting beta1
- decreased exercise capacity

Pulm

- bronchospasm especially worrisome in acutely decompensated asthma

GI

- D/N/V/GERD

GU

- libido

Endo

- decreases hepatic gluconeogenesis resulting in hypoglycemia (use cautiously in diabetics b/c more prone to hypoglycemia and when it occurs symptoms of hypoglycemia ie sympathetic hyperactivity is not as pronounced so called “hypoglycemic unawareness”)
- dyslipidemia (refer)

Skin

- hair thinning

	α1	α2	β1	β2	Overall Effect
clonidine (Catapres) guanfacine (Tenex) longer acting than clonidine therefore less rebound effects methyldopa (Aldomet) Fenoldopam (Corlopam) has less alpha2 stimulation but more dopamine stimulation		+			• α2 is primarily found on cells that secrete NEpi acting as a negative feedback mechanism, clonidine specifically acts on the pre-synaptic NEpi neuron in the brain that acts on the adrenal medulla to secrete Epi (circulating catecholamine) thereby decreasing circulating catecholamines • Uses: (1) acute hypertensive urgency/emergency (2) decrease the physical symptoms (not mental symptoms hence that is why you need methadone) of heroin withdrawal (3) decrease the symptoms of amphetamines, cocaine, et al (4) ADHD, insomnia, tic syndrome, et al (5) neuropathic pain (6) hot flashes in menopause (7) migraine headaches • SEs: rebound hypertension/tachycardia/diaphoresis, bradycardia, constipation, dry mouth, dizzy, drowsy, sexual dysfxn, rash if tansdermal formed used, +Coomb's hemolytic anemia and +ANA and hepatitis in methyldopa
Beta Blockers			-	-	(refer)
Phenoxybenzamine (Dibenzyline) Phentolamine (Regitine)	-	-			• Directly blocks alpha mediated vasoconstriction therefore profound effects on blood pressure unlike beta blockers but the problem is that there is a reflex tachycardia which is profound enough that the overall effect on BP is minimal • Use: pheochromocytoma (phenoxy) and acute HTN crisis (phento) • Phenoxy irreversibly blocks (therefore long lived) while phento reversibly blocks (therefore short lived) • "first dose effect" greater decrease w/ the first dose than w/ subsequent doses
-zosin doxazosin (Cardura) prazosin (Minipress) terazosin (Hytrin)	-				• Use: HTN in pts with BPH • SEs: extensive orthostatic hypotension resulting in HA, dizziness, and even syncope (esp w/ first dose), dyslipidemia • "first dose effect" as above