

PNS

- Preganglionic – Long
- ACh+NR @ Ganglion
- ACh+MR @ Organ
- Salivation
- Lacrimation
- Bradycardia
- Miosis
- Erection
- Diarrhea

SNS

- Preganglionic – Short
- ACh+NR @ Ganglion
- NE+AR @ Organ
- Mydriasis
- Bronchial dilation
- Tachycardia
- Dilation of muscle arterioles
- Sphincter Contraction
- Ejaculation

ENS

- Enteric system modulated by PNS & SNS

Somatic

- No Ganglion
- ACh+NR @ Organ

Adrenal

- ACh+NR @ Adrenal
- Releases NE + Epi

ACh

- Release stimulated by Ca^{2+}
- Metabolized by AChE

Muscarinic Receptors

- M1, M3, M5 > G_q > PLC > IP3 + DAG > PKC
- M2, M4 > G_i > inhibits adenylyl cyclase >

↓cAMP; M2 increase K^+ conductance

Nicotinic Receptors

- Activates ligand channel > depolarization

Norepinephrine

- Exocytosis postganglionic nerve in SNS
- Released from adrenal gland
- Metabolized by COMT/MAO

Epinephrine

- Released from adrenal gland

α_1	↓GI Tone, Mydriasis, ↑PVR, ↑Bladder Sphincter Tone	G_q
α_2	↓NE, ↓Lipolysis, ↓Insulin, ↓Aqueous Humor, ↓ACh	G_i
β_1	↑HR, ↑Contractility, ↑Lipolysis, ↑Renin	G_s
β_2	↓PVR, bronchodilation, ↑Glu, ↓Uterine Tone	G_s
β_3	↑Lipolysis, Bladder Relaxation	G_s

Desensitization

Direct Acting Cholinergic Agonists

I. Drugs

- Bethanechol > Post-op atonic bladder
- Carbachol > Glaucoma
- Cevimeline > Dry Mouth
- Pilocarpine > Glaucoma, Dry Mouth

II. Activity: Stim. Nicotinic & Muscarinic

III. Adverse Effects

- D.U.M.B.E.L.L.S.

Centrally Acting Cholinergic Agonists

I. Drugs

- Donepezil > Alzheimer's Dementia
- Galantamine > Alzheimer's Dementia
- Rivastigmine > Alzheimer's Dementia

II. Activity: Stim. Nicotinic & Muscarinic

III. Adverse Effects

- Nausea & Diarrhea
- Delays but does not stop Alzheimer's

Reversible Cholinesterase Inhibitors

I. Drugs

- Edrophonium > Dx Myasthenia Gravis
- Physostigmine > Cholinergic Tox Reversal
- Neostigmine > NM Blocker antidote, Tx Myasthenia Gravis
- Pyridostigmine > Tx Myasthenia Gravis

II. Activity: Reversibly Inhibits AChE

III. Adverse Effects

- D.U.M.B.E.L.L.S.

Irreversible Cholinesterase Inhibitors

I. Drugs

- Echothiophate > Chronic Glaucoma
- Malathion > Insecticide
- Parathion > Insecticide
- Sarin > Chemical Nerve Agent

II. Activity: Irreversible binds AChE

III. Adverse Effects

- D.U.M.B.E.L.L.S.

Antimuscarinics (Non-GU/Bladder)

I. Drugs

- Atropine > Induces mydriasis/cycloplegia; GI: antispasmodic; ↑HR; Tox: Antidote for cholinergic toxicity
- Benztrapine > Parkinson's; Tx EPS from anti-psychotics
- Cyclopentolate > Mydriasis, Cycloplegia
- Dicyclomine > Antispasmodic, N&V Preg
- Scopolamine > Motion sickness
- Ipratropium > Bronchospasm, COPD
- Tiotropium > COPD

II. Activity: Blocks muscarinic & SNS cholinergic

III. Adverse Effects

- Blind as a Bat, Red as a Beet, Dry as a Bone, Hot as Hades, Mad as a Hatter, Constipation, Urinary Retention

Antimuscarinics (GU/Bladder)

I. Drugs

- Darifenacin > Overactive Bladder
- Fesoterodine > Overactive Bladder
- Oxybutynin > Overactive Bladder
- Solifenacin > Overactive Bladder
- Tolterodine > Overactive Bladder
- Trospium > Overactive Bladder

II. Activity: Blocks muscarinic & SNS cholinergic

III. Adverse Effects

- Blind as a Bat, Red as a Beet, Dry as a Bone, Hot as Hades, Mad as a Hatter, Constipation, Urinary Retention

Nicotine

I. Activity: Dose dependent; initially stimulates, then paralysis at high doses

II. Addictive

- A. ↑Dopamine, NE, ACh, Glutamine, Serotonin, β-endorphin, GABA

III. Adverse Effects

- A. High Doses: Medullary paralysis -> Central resp paralysis & hypotension
B. Withdrawal: Irritable, Anxious, HA Tremor, Irritability, diarrhea, ↑HR, ↑BP

IV. Cessation: Bupropion, Varenicline, Nicotine

Depolarizing Neuromuscular Blockers

I. Drugs

- A. Succinylcholine > Skeletal muscle paralysis, Intubation

II. Activity: Depolarizes NM Junction

- A. Phase 1: Fasciculations resulting from stimulation
B. Phase 2: Receptor repolarizes but is not sensitive to stimulation (paralysis)

III. Adverse Effects

- A. Apnea
B. Malignant Hyperthermia
1. Uncontrolled SM contraction -> ↑O₂ needs and metabolites, ↑Temperature
2. Tx: Dantrolene (decoupler), cooling
3. Autosomal Dominant
C. Hyperkalemia: Burns, Crush, Stroke, Renal Failure, Cong. Myopathy

Nondepolarizing Neuromuscular Blockers

I. Drugs

- A. Cisatracurium > Procedural paralysis
B. Pancuronium > Procedural paralysis
C. Rocuronium > Procedural paralysis
D. Vecuronium > Procedural paralysis

II. Activity: Blocks ions channels at endplate; small muscles affected first

Catecholamines

I. Drugs

- A. Epinephrine > Anaphylaxis, shock, Cardiac Arrest, Croup, Local anesthesia

1. Receptors: β₁, β₂
2. Effects: ↑HR, ↑BP, Dil Skl. Msc. Vasc
3. Adverse Effects: Tissue ischemia, ↑HR

- B. Norepinephrine > Shock

1. Receptors: α₁, α₂, weak β₁
2. Effects: ↑SVR
3. Adverse Effects: Tissue ischemia, ↑HR

- C. Dopamine > Cardiogenic Shock

1. Receptors: D₁, D₂, β₁, α₁
2. ↑HR, ↑BP, ↑Splanchnic Perf

- D. Dobutamine > Acute Heart Failure

1. Receptors: β₁
2. ↑HR, ↑BP

- E. Isoproterenol > Heart Block

1. Receptors: β

Peripherally Acting Alpha Agonists

I. Drugs

- A. Phenylephrine > Shock, Nasal Cong, Priapism
1. Receptors: α₁
B. Oxymetazoline > Nasal Congestion
1. Receptors: α₁, α₂
2. Adverse Effects: Rebound Nasal Cong.

Centrally Acting Alpha Agonists

I. Drugs

- A. Clonidine > HTN, Opiate W/D
B. Methyldopa > HTN in Preg

II. Activity: α₂ agonist, ↓sympathetic outflow

III. Adverse Effects: Sedation, rebound HTN

Dopamine-1 Agonist

I. Drugs

- A. Fenoldopam > HTN

II. Receptors: D-1: Dilates cardiac, renal, mesenteric arterioles

β₂ Agonists

I. Drugs

- A. Albuterol > Acute asthma, COPD
B. Terbutaline > Tocolysis (Off-label)
C. Salmeterol > Asthma Control, COPD
D. Formoterol > Asthma Control, COPD
E. Aformoterol > Asthma Control, COPD
F. Vilanterol > Overactive Bladder

II. Activity: Stim. β₂: Bronchodilation

III. Adverse Effects: Anx, tremor, ↑HR

Mixed Adrenergic Agonists

I. Drugs

- A. Ephedrine > Anes. related hypotension
1. Banned as supplement (arrhythmias)
B. Pseudoephedrine > Nasal congestion
1. Used for methamphetamine production

II. Action

- A. Release NE from nerve endings
B. Stim. α and β receptors

III. Adverse Effects

- A. ↑HR, arrhythmias, Anx, HTN

Non-Selective Alpha Blockers

I. Drugs

- A. Phenoxybenzamine > Pheo Tx, Reverse Epi
1. Covalently binds receptors
2. Inh. Ejaculation
B. Phentolamine > Pheo Tx, Reverse Epi, Clonidine W/D
1. Competitive
2. Contraindicated in CAD, Arrhythmia

II. Action: Blocks α₁ and α₂

III. Adverse Effects

- A. Postural hypotension

Alpha-1 Blockers

I. Drugs

- A. Prazosin > HTN, PTSD (off-label)
- B. Terazosin > BPH, HTN
- C. Doxazosin > BPH, HTN
- D. Tamsulosin > BPH, bladder outlet obstruction, Ureteral Stones
- E. Alfuzosin > BPH

II. Activity: Blocks α_1 receptors

III. Adverse Effects: 1st dose response (hypotension), retrograde ejaculation

Nonselective Beta Blockers

I. Drugs

- A. Propranolol > HTN, Angina, Migraine, MI
- B. Nadolol > Angina, HTN
- C. Timolol > Chronic Open Angle Glaucoma

II. Activity: Blocks β_1 and β_2 receptors

III. Adverse Effects: Bronchoconstriction (contraindicated in asthma/COPD), Arrhythmias, Fatigue, Sexual Dysfunction, Depression, Hypoglycemia

Beta-1 Blockers

I. Drugs

- A. Atenolol > Angina, HTN, MI
- B. Betaxolol > Chronic open angle glaucoma
- C. Bisoprolol > HTN, CHF
- D. Esmolol > Tachycardia, HTN Emergency
- E. Metoprolol > Angina, HTN, MI, CHF
- F. Nebivolol > HTN

II. Activity: Blocks β_1 receptors

III. Adverse Effects: Bronchoconstriction, Arrhythmias, Fatigue, Sexual Dysfunction, Depression

Beta Blockers with Partial Agonist Activity

I. Drugs

- A. Acebutolol > HTN, Angina, Ventricular Arrhythmias
- B. Pindolol > HTN

II. Activity: Blocks β_1 and β_2 receptors but also stimulates

III. Adverse Effects: Bronchoconstriction, Arrhythmias, Fatigue, Sexual Dysfunction, Depression

Nonselective β Blockers with Alpha-1 Blockade

Nonselective Beta Blockers

I. Drugs

- A. Labetalol > HTN (incl Preg), HTN Emergency
- B. Carvedilol > Angina, HTN, LV dysfunction post MI

II. Activity: Blocks β_1 , β_2 , and α_1 receptors

III. Adverse Effects: Bronchoconstriction (contraindicated in asthma/COPD), Arrhythmias, Fatigue, Sexual Dysfunction, Depression, Orthostatic Hypotension