Anti-Cholinergic Drugs

- Parasympatholytic Drugs
- Antagonists.
- Block the action of cholinergic drugs at M.R / N.R

Anticholinergic drugs

- Antimuscarinic agents
- Antinicotic agents
  - N_N blocker (Ganglionic blocker)
  - N_M blocker (Neuro-muscular blocker)

I - Anti-Muscarinic Agents

blocks the Muscarinic receptor mediated action of Ach on heart, CNS, Smooth muscle, exocrine glands.

Ach (Agonist) → Muscarinic Receptor ← Atropine (Antagonist)

Prototype → most imp drug of any class.

Atropine:

- Prototype drugs of Parasympatholytic drugs.
- 4m Atropine belladona.
- Highly selective on Muscarinic R.
- levo is more active than dextro-isomers.
- Its Synthetic dwt has nicotinic blocking.

① Natural Alkaloids :- Atropine, Hyoscine (Scopolamine) → Non-selective
↓
Reversible antagonist of muscarinic R

② Semi-Synthetic Derivatives

- Atropine methonitrate
- Homatropine
- Hyoscine butyl Br
- Ipratropium Br, Tiotropium Br — 4° → Used in COPD & Asthma → Contraindicated in Urinary Retention

③ Synthetic Drugs :

ⓐ Mydriatics :- Cyclopentolate (3° amine), Tropicamide (Shortest acting) / (By Aldol condensation) (Also Homatropine, Hyoscine)

ⓑ Anti-Secretory & Anti-spasmodics :

4° comp (Amino alcohol esters)	3° amines. (CVP) (No nitrotinic activity)
- Propantheline / Methantline (xanthene-9-carboxylate deriv)	- Dicyclomine
- Oxyphenonium	- Valethamate
- Clidinium	- Pirenzepine
- Cimetropium Br	
- Isopropamide	
- Glycopyrrolate. (Preanaesthetic agent) (Has pyrrolidine ring)	

Peptic ulcer

- In peptic ulcer. - Pirenzepine, Telenzepine
- Antispasmodic - Dicyclomine, Oxybutynin, Fluvoxate.

-

(c) Anti Parkinsonism: (BBPT) (Amino Alcohol ethers)

- Procyclidine (by Mannich condensation)
- Trihexyphenyl (Benzhexol)
- Biperiden (amino alcohol) - COI in epilepsy & Blurred vision
- Benztropine (both muscarinic & nicotinic blocker)

(d) Vasico-Selective. (Act on blood vessels)

- Oxybutin
- Fluvoxate (Piperidine) & (chromane ring)
- Darifenacin → M_3 R (amino amide)
- Solifenacin → M_3 R
- Tolterodine
  ↳ Prodrug is fesoterodine. (in UTI)

MQ Recep

M_1 Selective R

Pirenzepine, Telenzipine, Dicyclomine.

M_2 Selective R (GTHM) (M_2 - all aimes)

- Galamine, Tripitramine, Himbecine, Methotramine, AF-DX-116.

M_3 selective R

- Darifenacin (in overactive bladder) → has Dihydrobenzfuran ring
- Solifenacin
- Tolterodin
- Oxybutin.

* Papaverine is the standard for comparison for musculotropic antispasmodics.

- M_1 R → memory & cognitive behaviour control tremors & rigidity of Parkinsonism
- on GIT (M_3 R) → ↓ the secretion of HCl
  ↓ the motility
  ↓ the Sphincter

- On Eye (M_3 R)
  - passive mydriasis
  - cycloplegia (paralysis of - relax of ciliary body)
  - loss of light reflex.

- On lungs: (M_3 R)
  cause bronchodilation, used in asthma.

- Urinary bladder: (M_3 R) (Hyoscamine) as antispasmodic in UTI
  - less urine output.
  - ↓ tone of detrusor muscle
  - ↑ tone of trigone & sphincter

- Heart: (M_2)
  low doses - Bradycardia
  - Tachycardia

Miosis

- Contraction of Sphincter pupilae (circular) (Muscaric agonist Anticholinesterase)
- Relaxation of dilator pupillae. (α_1 Adr antagonist) Adr. neuron blocker.

Mydriasis

- contraction of dilator pupilae (Radial) (α_1 Adr agonist)
- Relaxation of Sphincter pupillae (circular) (Atropine) (Antimuscarinic Ganglionic blocker)

Uses of Atropine:

"ATROPA"

→ A - As Mydriatic - Cycloplegic (In Iris & Corneal inflammation)
T - Traveller's Diarhoea
R - Rapid (early) onset mushroom poisoning
O - organophosphate poisoning & carbamet. ---) (As Antidote)
P - Preanaesthetic medication
A - Arrhythmias (brady-arhythmia)

In delayed mushroom poisoning - thioticacid, Silbirin.

Adverse effects of Atropine

"DHATURA"

D - Dry Mouth
H - Hot dry skin.
A - Accomodation of paralysis
T - Tachycardia
U - Urinary retention
R - Respiratory Depression
A - Ataxia (lack of voluntary constriction)

Anti-Nicotinic Receptor Antagonists

I- Autonomic Ganglia (N_N)

- clusters of neuronal cell bodies & their dendrites.
- Junction betn autonomic neuves originating frm the CNS & autonomic neuves innervating their target organs.

① Ganglionic Stimulants

- Agents that mimic neural transmission by stimulation of the nicotinic receptors on post ganglionic autonomic neurons.

Ganglionic Stimulants

Selective Nicotinic agonist

- Nicotine (small dose)
- Lobeline
- Dimethyl Phenyl Piperazinium (DMPP) *
- Varenicline
- Tetramethyl ammonium

Non-Selective Nicotinic/muscarinic agonists

- Ach
- Carbachol
- Pilocarpine
- Anticholinesterase

② Ganglionic Blockers (Ganglioplegic)

- Inhibits the transmission both pre & post ganglionic neurons in ANS, acts as nicotinic receptor antagonist.

Ganglionic Blockers

Competitive blockers (HPT MP)

↳ 4° NH_4 Comp *
- Hexamethonium
- Pentolinium

↳ Amines
- Mecamylamine
- Pempidine

- Mono sulfonium Comp (short acting)
- Trimethaphan camphor sulphonate

Persistent depolarizing blockers (opens for long time) & large dose of Nicotine

Anticholinesterase

Decamethonium

- trace of OH group ↑ the anti-muscarinic activity

Atropine:

- Atropine stimulates CNS but scopolamine (in lie detector) CNS depressant.

Scopolamine + morphine — Temporary amnesia (Twilight sleep)

Amino-alcohol esters:

- Clidinium Br: Has quinuclidinium moiety
  - In peptic ulcer & hyperchlorhydria
  - contraindicated in glaucoma & Prostate hypertrophy.

- Cyclopentolate: in High IOP patients.

- Dicyclomine (3°) - Binds more to M_1 & M_3 than M_2 & M_4

Glycopyrrolate (4°) → more to M_1.
→ Does not enter CNS but cause ganglionic blockade.

Amino-alcohol ethers:

- Antihistamine & Antiparkinsonian.

Benztropine: Anticholinergic, antihistaminic & local anaesthetic.
Has sedative effect.

Orphendrine: → Diphenhydramine without sedative effect

Diphenhydramine.