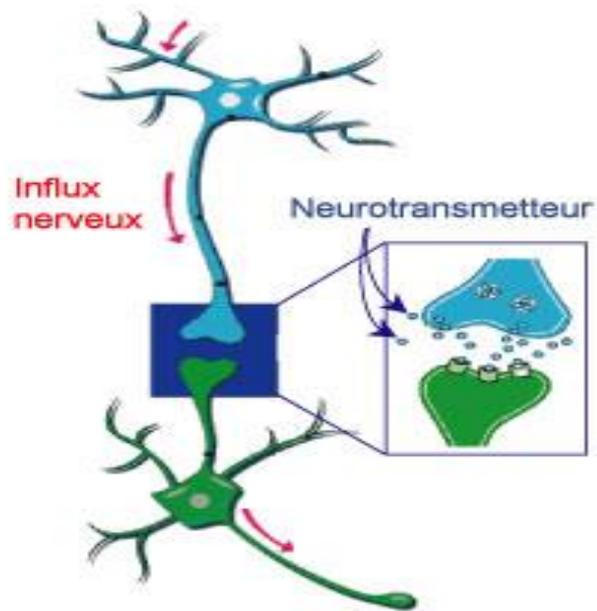


Cholinergic Antagonist Drugs



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Cholinergic Antagonist Drugs



- **Anti-muscarinic drug**: Atropine-like drugs, Hyoscine (Scopolamine)
- **Anti-nicotinic drugs**
 - a) **Ganglion blockers**: Used in experimental pharmacology. E.g. Nicotine, Trimethapan.
 - b) **Neuro-muscular blockers**: Used in surgery to produce complete muscle relaxation.

Anti-muscarinic anti-cholinergic drugs



- ❑ Natural agents:
 - **Atropine, Hyoscine**
- ❑ Semi-synthetic
 - **Homatropine**
- ❑ Synthetic
 - **Ipratropium, Pirenzepine, Propantheline**

Anti-muscarinic

❑ Atropine (Hyoscyamine)

- Alkaloids obtained from *Atropa Belladonna*,
- Considered as prototype for parasympatolytics



❑ Hyoscine (Scopolamine)

- Obtained from *Hyocyamus niger* plant (*Datura Stramonium*)



Note: Antihistamines, phenothiazides and some antidepressants have anti-muscarinic effects

Clinical pharmacology of anti-muscarinic drugs

Mechanism of action:

- **Reversible blockade** of **M** receptors
- **Exocrine glands** are most **sensitive**
- **Gastric secretion** is the **least** affected
- **Heart** is **intermediate**

Note: Atropine blocks all 3 subtypes receptors
(M₁, M₂, M₃)

Pharmacokinetics

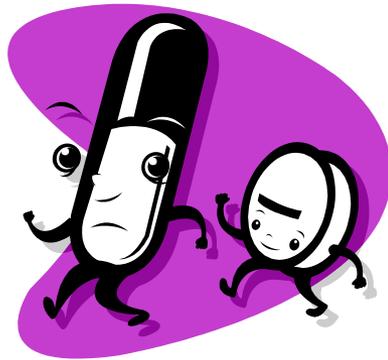
□ Absorption:

- **Natural and most tertiary amines: good**
- **Wide distribution and cross BBB**
- **Quaternary amines: poorly absorbed and poor crossing BBB (Ipratropium)**

□ Atropine $t_{1/2}$: 2hrs

□ **Partly metabolized and partly excreted unchanged**

Routes of administration



Oral



Parenteral



Topical (suppositories)



**Some by inhalation
(Ipratropium)**

Pharmacodynamics

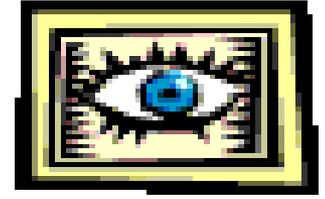
- ❑ **Exocrine glands: at low doses reduced secretions**
 - Salivary
 - Bronchial
 - Sweet glands

CNS



- Central **stimulant** effects (Atropine) due to increased release of excitatory transmitters after blocking the presynaptic muscarinic receptors.
- Some may produce **sedation** (Hyoscine)
- Hyoscine blocks M receptors in vomiting centre and has **anti-emetic effect**
- **Toxic doses:** hallucination, convulsion, coma

Eye



- **Mydriasis** (dilatation of pupil)
- **Cycloplegia** (relaxation of the ciliary muscle) cause: blurred vision and impaired accommodation to near vision
- **Decreased lacrimation**
- **Increase IOP**

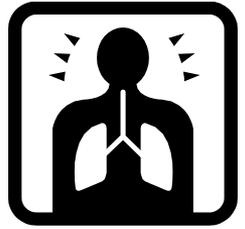
CVS



Depending in the doses

- **Central** effect (temporary & with very small doses):
 - **Decrease heart rate (due to stimulation of vagal center in the medulla)**
- **Peripheral** effect (prominent effects):
 - Blockade of cardiac M2 receptors and prevent vagal nerve action this lead to **increase heart rate**
- **ABP:**
 - **No change**

Respiratory system



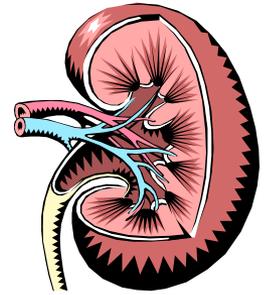
- **Bronchodilatation**
- **Reduced bronchial secretion**
- Ipratropium (quaternary amine derivate of Atropine) inhalation:
 - Useful in asthma and chronic obstructive pulmonary disease (COPD), also in patient who are unable to take adrenergic agonists.

GIT



- **Decrease salivation**
- **Decrease acid secretion**
- **Decrease motility**
- **Delay gastric emptying**
- **Prolong intestinal transit time**
- **Anti-diarrhoeal and anti-spasmodic effects**

GUT



- **Relaxation of bladder wall**
- Useful in **inflammatory spasm** and **pains** of the urinary tract
- **Risky** in patients with **BPH** (Benign Prostatic Hypertrophy)

Therapeutic uses

CNS disorders:

- **Parkinson's disease**
- Drug-induced parkinsonism as Phenothiazine (induced acute dystonias)
- Benztropine, Benzhexol: useful
- **Motion sickness:** Hyoscine oral, injection, transdermal patches

Therapeutic uses

Ocular uses:

- In **eye examination** (Tropicamide) produce mydriasis and cycloplegia
- In **iritis** (Atropine eye drop) prevent synechia (adhesion of the iris to the lens)

Note:

- Atropine eye drops effects: 7 days
- Tropicamide eye drops effects: 4-12hrs

Therapeutic uses

- **Premedication:** Hyoscine and Atropine (use as adjunct in anaesthetic procedure)
- **Bronchial asthma:** Ipratropium inh. (produce bronchodilatation)

Cardiovascular:

- **Bradycardia and heart block following AMI:** Atropine

Therapeutic uses

GI disorders:

■ Anti-diarrhoeal

- Lomotil= atropine + diphenoxylate

■ Anti-spasmodics (in intestinal colic, IBS)

- Atropine, hyoscine, clidinium, prifinium

Urinary disorders:

■ Urinary urgency with UTI

■ Renal colic

Therapeutic uses

- **Cholinergic poisoning as:**
 - Irreversible CEI insecticide poisoning
 - Chemical warfare intoxication
- **To counteract muscarinic effects**
- (nicotinic effects can not be reversed)
- Atropine IV

Adverse effects of anti-muscarinic agents



- **Dry mouth**
- **Blurred vision**
- **Tachycardia**
- **Constipation**
- **Hot flushed dry skin & hyperthermia may occur with high doses**

Contraindications



❑ Glaucoma

- Increase IOP

❑ BPH

- Bladder wall relaxation & sphincter contraction

Atropine poisoning



- Hot flushed dry skin & hyperthermia,
- Agitation, delirium, hallucination,
- Convulsions & coma
- Treatment is symptomatic

Individual drugs



- **Atropine**
- **Hyoscine**
 - Buscopan
- **Clidinium**
 - Libraxam
- **Prifinium**
 - Riabal