Anticholinergic drugs

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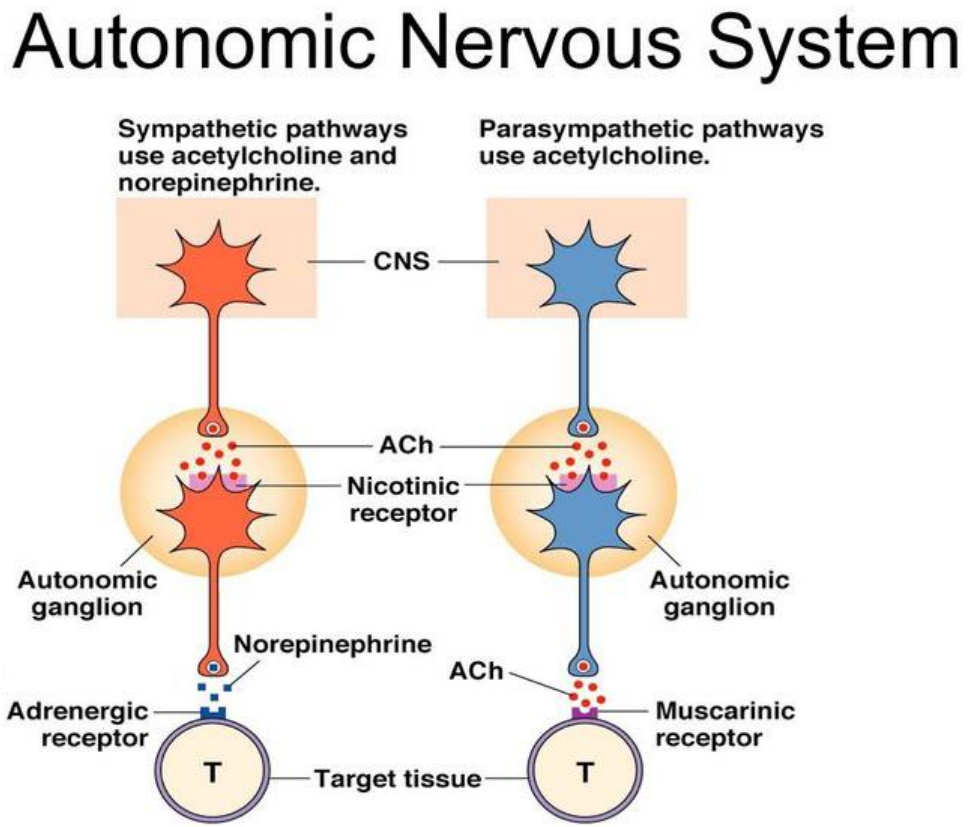
Muscarinic receptor antagonists: Atropinic or Parasympatholytic

They block actions of ACh in ANS and in the CNS exerted through muscarinic receptors. All anticholinergic drugs are competitive antagonists.

Nicotinic antagonists also block certain actions of ACh, they are generally referred to as "ganglionic blockers".

Synthetic atropine substitutes also possess significant nicotinic-blocking properties.

Many other classes of drugs like tricyclic antidepressants and anti-histamines possess significant antimuscarinic actions.



Classification

1. Natural alkaloids: Atropine, Hyoscine (Scopolamine)

2. Semisynthetic derivatives: Homatropine, Atropine methonitrate, Hyoscine butyl bromide, Ipratropium bromide, Tiotropium bromide.

3. Synthetic compounds:

(A) Mydriatics: Cyclopentolate, Tropicamide.

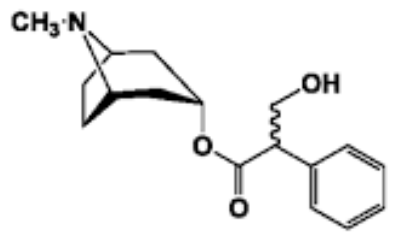
(B) Antisecretory-antispasmodics:

(i) Quaternary compounds: Propantheline, Oxyphenonium, Clidinium, Glycopyrrolate.

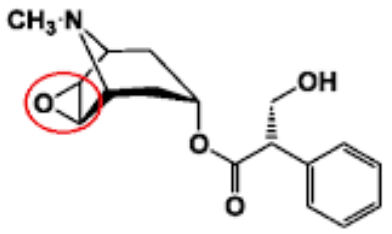
(ii) Tertiary amines: Dicyclomine, Valethamate, Pirenzepine.

(C) Vasicoselective: Oxybutynin, Flavoxate, Tolterodine.

(D) Antiparkinsonian: Trihexyphenidyl (Benzhexol), Procyclidine, Biperiden.

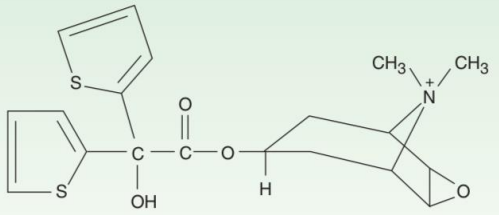


Atropine



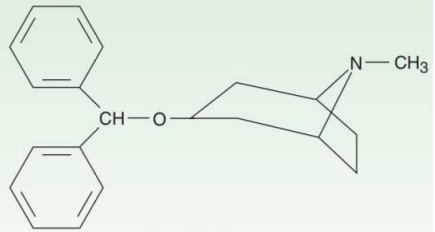
Scopolamine

Quaternary amine for use in asthma:



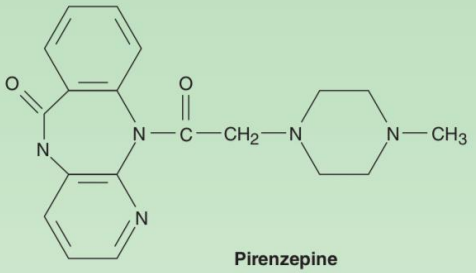
Tiotropium

Tertiary amine for Parkinson's disease:

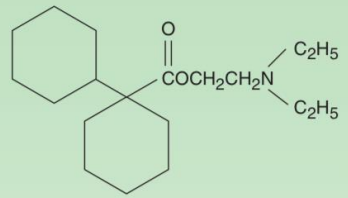


Benztropine

Tertiary amines for peripheral applications:



Pirenzepine
(peptic disease)



Dicyclomine
(peptic disease, hypermotility)

Natural alkaloids

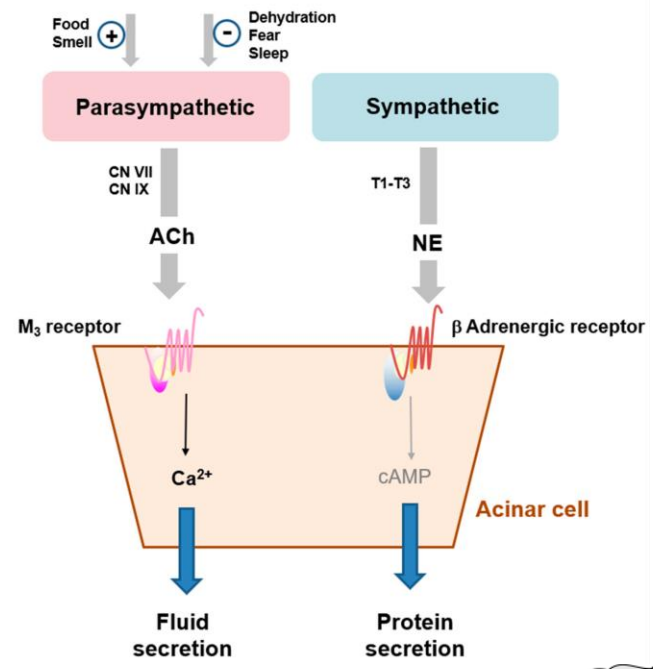
They are found in plants of the Solanaceae family. Atropine in Atropa belladonna and Datura stramonium.

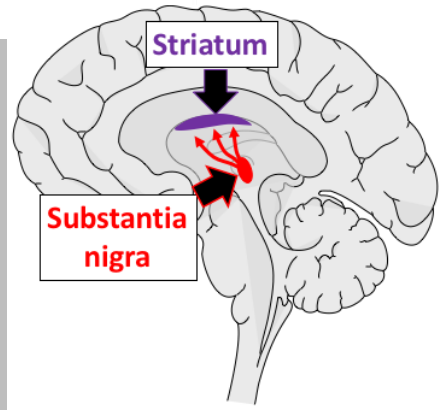
Atropine is the prototype drug of this class, is highly selective for muscarinic receptors.

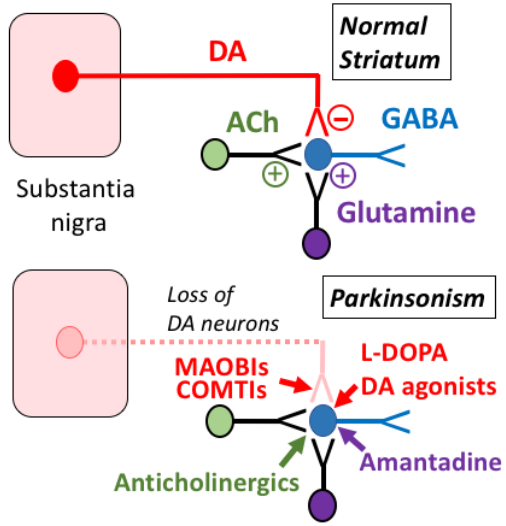
Atropine stimulates many medullary centers—vagal, respiratory, vasomotor.

By blocking the relative cholinergic overactivity in basal ganglia, it suppresses tremor and rigidity of parkinsonism.

Atropine and glycopyrrolate are occasionally employed to prevent salivation during dental procedures and oral surgery.

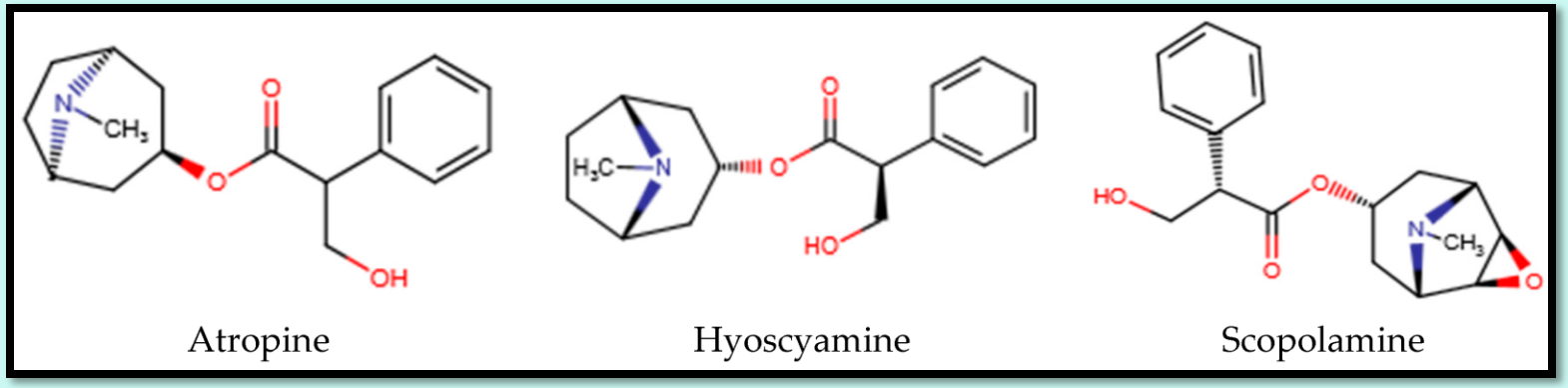






Natural alkaloids

- Hyoscine in Hyoscyamus niger. The levo-isomers are much more active than the dextroisomers. Atropine is racemic while scopolamine is l-hyoscine.
- Hyoscine differs from atropine in producing depressant (drowsiness, amnesia, fatigue) effects at low doses.
- Hyoscine butyl bromide and atropine methonitrate are quaternary derivatives that do not produce CNS effects and are used mainly for colics and GIT disorders.



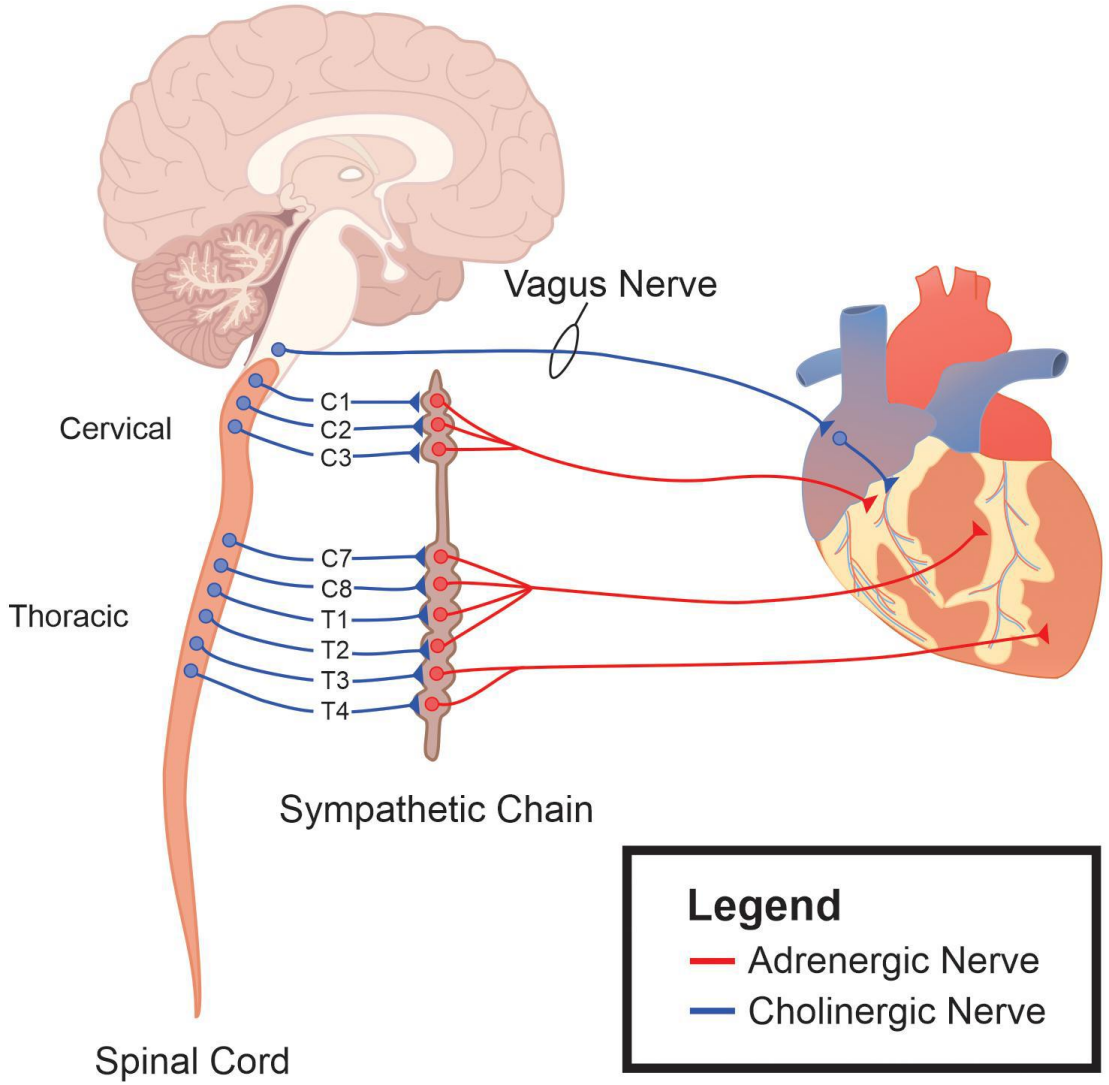
Mechanism of action of Atropine

Heart: Atropine causes tachycardia prominently due to the blockade of M2 receptors on SA node through which vagal tone decreases HR.

Atropine does not have any consistent or marked effect on BP.

The sensitivity of different organs and tissues to atropine varies and can be graded as:

Saliva, sweat, bronchial secretion > eye, bronchial muscle, heart > smooth muscle of intestine, bladder > gastric glands, and smooth muscle.



Atropine substitutes

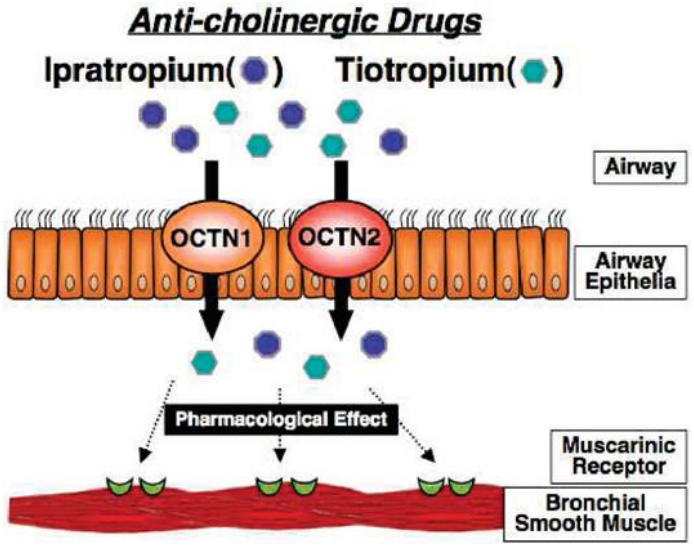
Many semisynthetic derivatives of belladonna alkaloids:

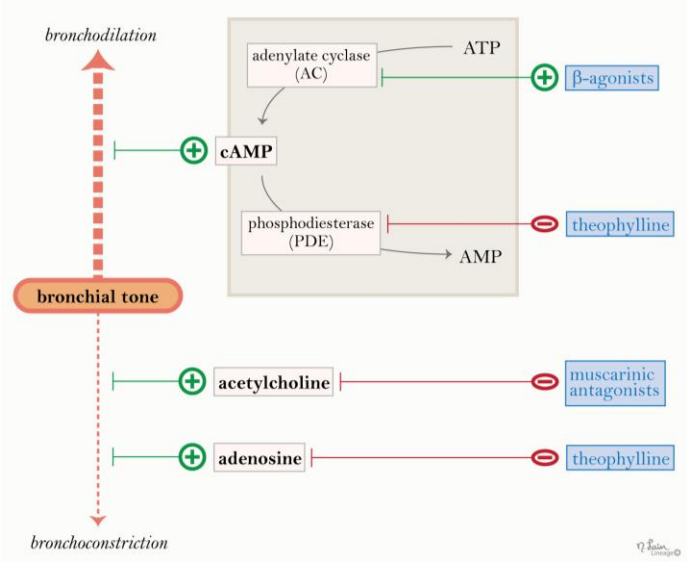
Ipratropium bromide is given by inhalation in bronchial asthma and chronic obstructive pulmonary disease (COPD).

Unlike atropine, it does not depress mucociliary clearance by bronchial epithelium.

Tiotropium bromide is along acting and more broncho-selective congener of ipratropium.

Inhaled ipratropium bromide and tiotropium bromide are useful in COPD and as an adjuvant to inhaled β2 agonists in severe bronchial asthma .





Atropine substitutes

Glycopyrrolate acts rapidly, used parenterally before and during anesthesia.

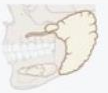
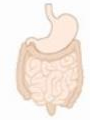
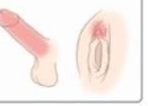
Dicyclomine has antiemetic properties used in morning and motion sicknesses.

Valethamate has antispasmodic properties used to hasten dilation of the cervix during labor.

Oxybutynin, tolterodine, and flavoxate have smooth muscle relaxant properties used in urge incontinence.

Homatropine, cyclopentolate, and tropicamide are mydriatic, and cycloplegic, have quicker action than atropine.

Trihexyphenidyl, procyclidine, and biperiden have central antimuscarinic action, used in parkinsonism.

Parasympathetic nervous system		
M_3	Miosis Focus on near objects	
M_3	↑ Serous salivary secretion	
M_2	↓ Heart rate, conduction velocity, atrial contractility	
M_3	Bronchoconstriction	
M_3	↑ Gastric acid secretion Dilation of sphincters ↑ Motility	
M_3	↑ Insulin and exocrine secretion	
M_3	↑ Glycogenesis ↓ Glucose production	
M_3	↓ Sphincter muscle tone Detrusor muscle contraction	
M_3	Erection ♀♂	

Ganglionic stimulants

- Selective nicotinic agonists:
- Nicotine (small dose), Lobeline, Dimethyl phenyl, piperazinium iodide (DMPP), Tetramethyl ammonium(TMA), Varenicline.
- Nonselective/muscarinic agonists:
- Acetylcholine, Carbachol, Pilocarpine, Anticholinesterases, MCN 343-A

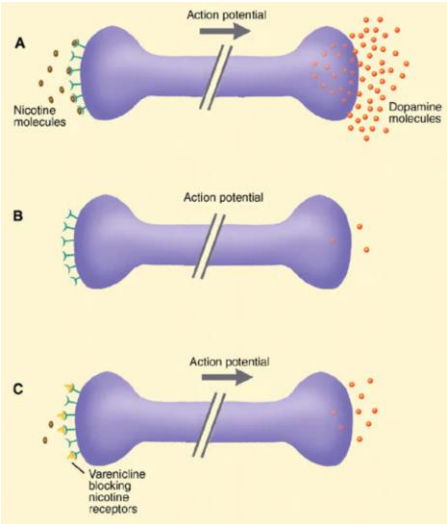
Nicotine and Varenicline

Nicotine: from Nicotiana tabacum is important in the context of smoking or chewing tobacco.

Has no clinical application of ganglionic stimulants, because no useful purpose by stimulating both sympathetic and parasympathetic ganglia.

Nicotine transdermal and nicotine chewing gum used as an aid to smoking cessation.

Varenicline: It is a Nn subtype selective nicotinic receptor partial agonist recently approved as an aid to smoking cessation.



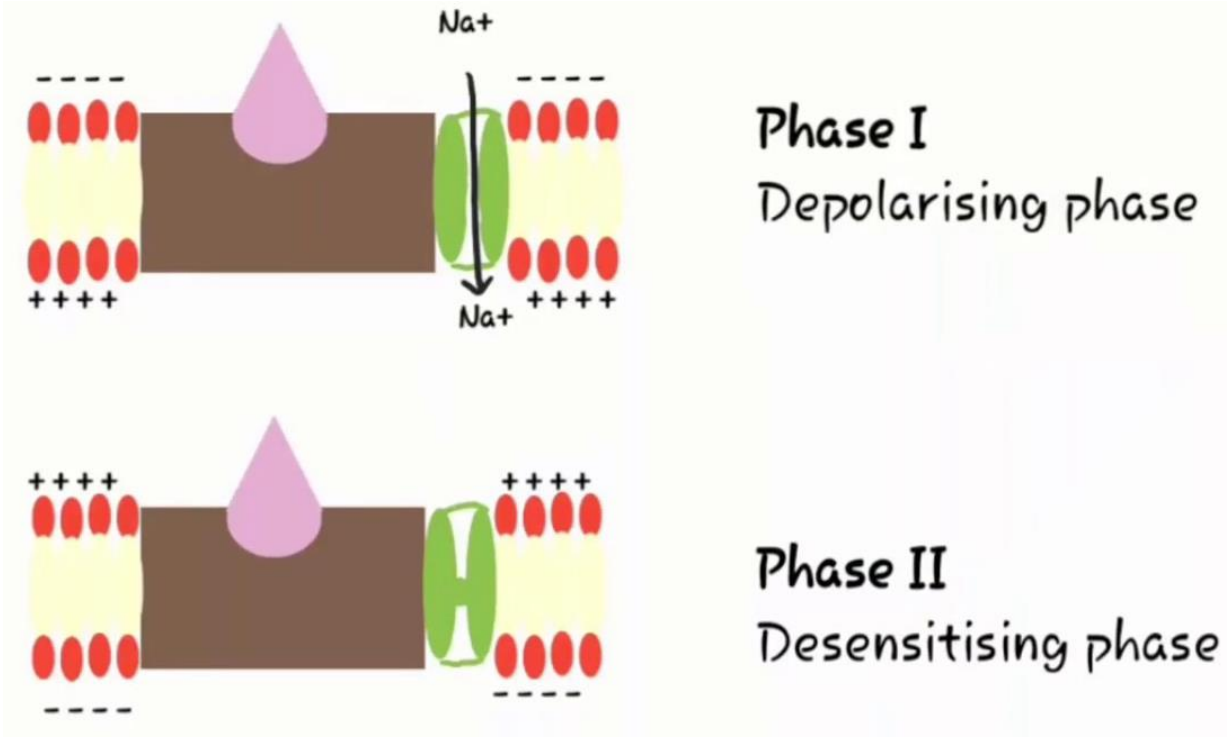
Ganglionic blockers

Competitive blockers:

Quaternary ammonium compounds, Hexamethonium, Pentolinium, Amines, Mecamylamine, Pempidine, Monosulfoniumcompound, Trimethaphan, camforsulfonate.

Persistent depolarising blockers:

Nicotine (large dose), Anticholinesterases (large dose).



Ganglionic blockers

- Competitive ganglionic blockers were used in the 1950s for hypertension and peptic ulcer.
- Have been totally replaced now because they produce several unpleasant side effects.
- There is at present no clinical relevance of ganglion blockers.