Muscle relaxant

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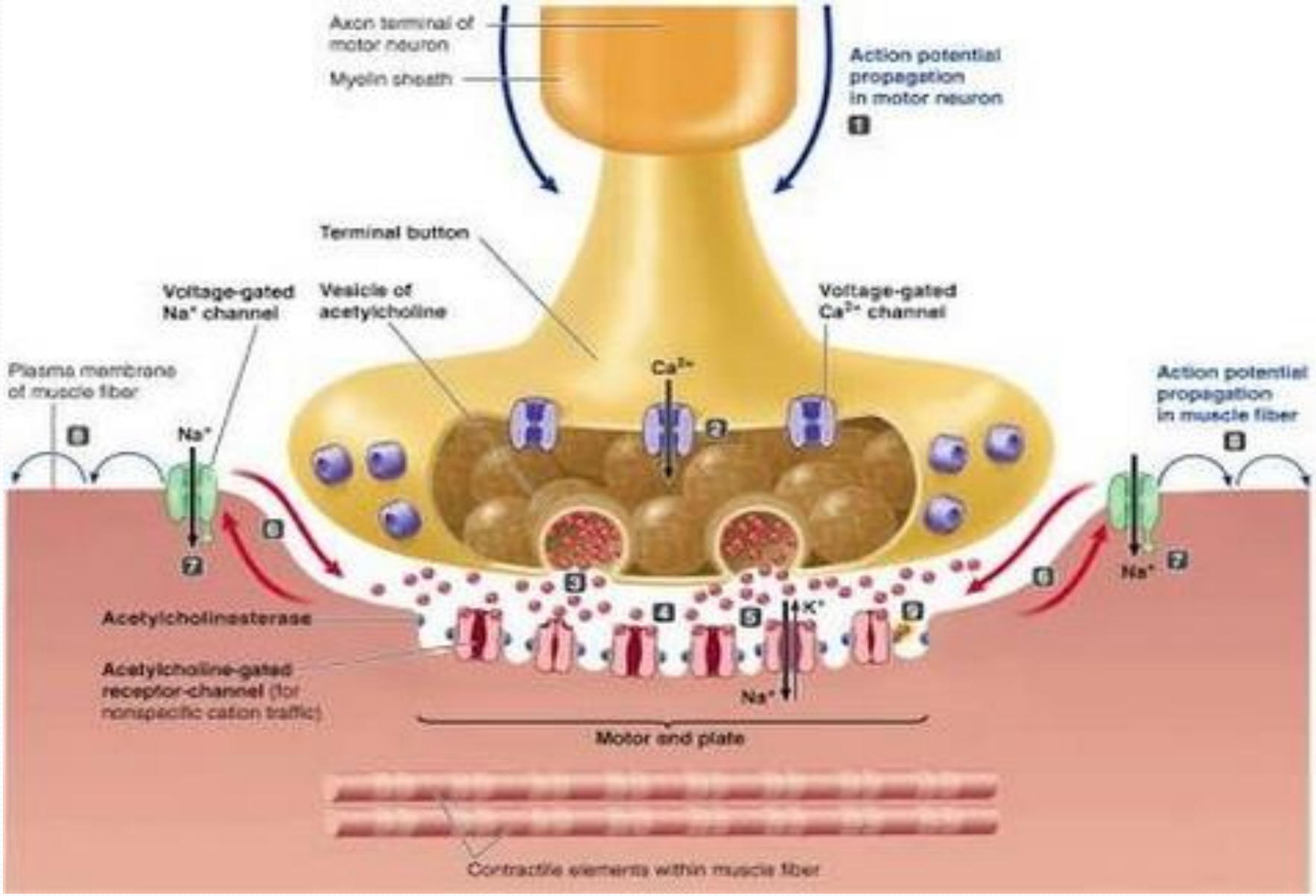
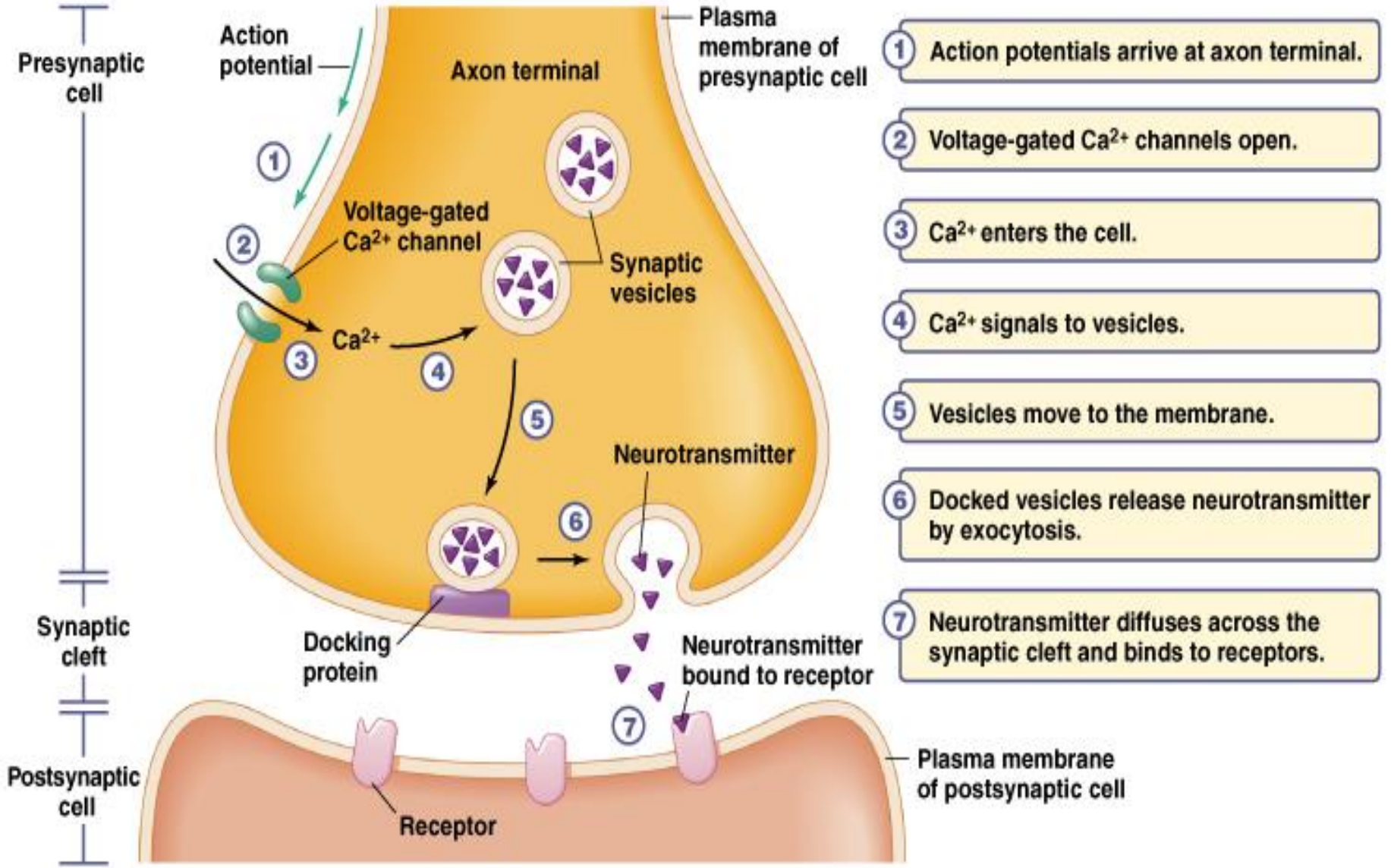
Neuromuscular junction





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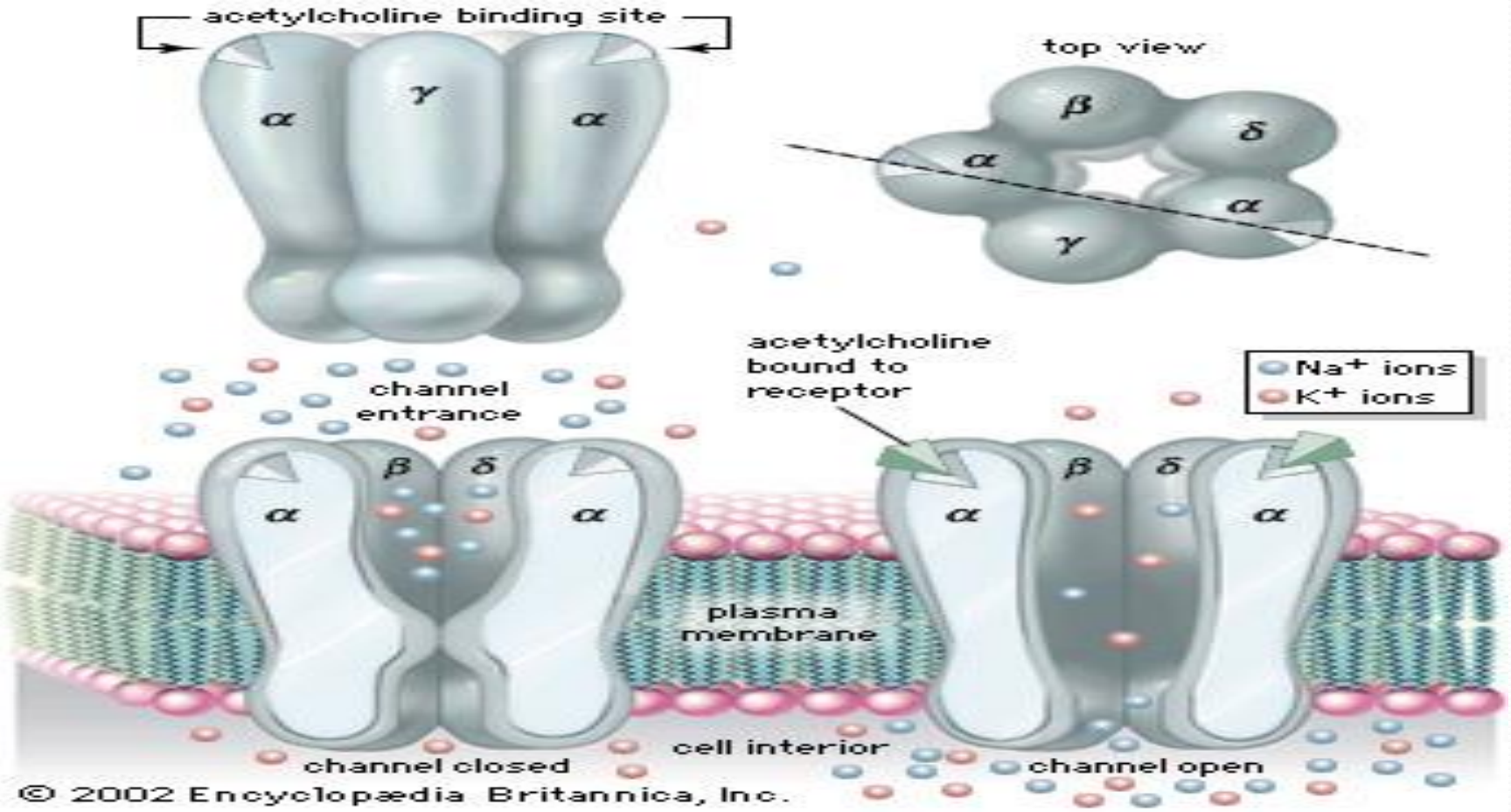
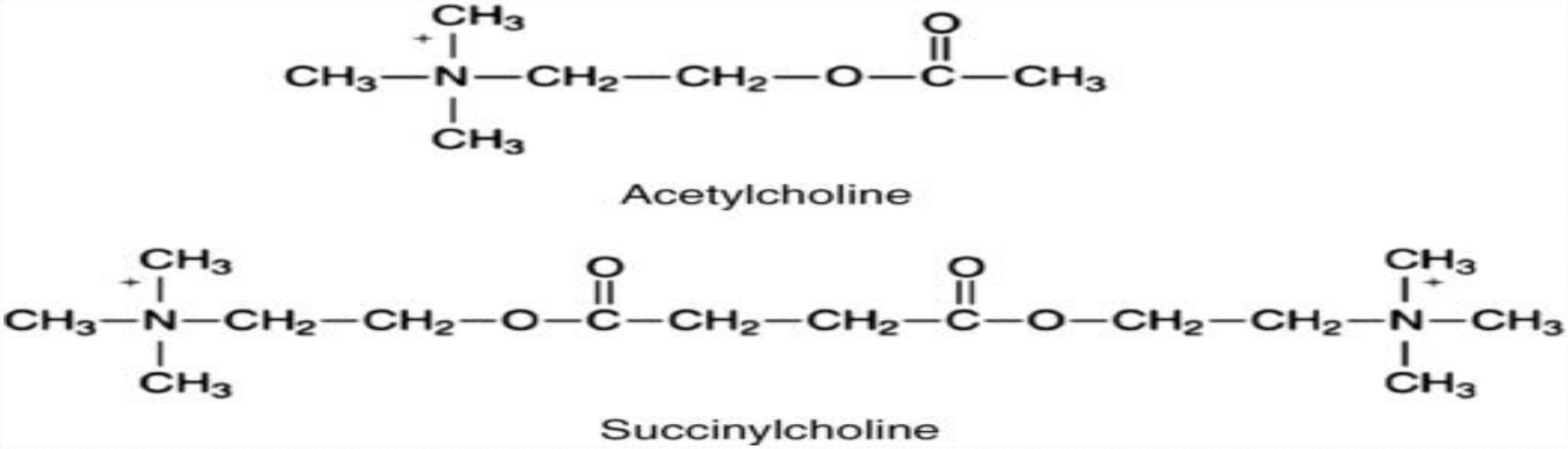
The structure of AChR receptors consists of five protein subunits: two α subunits and single β, δ, ε.

Only the two α subunits are capable of binding ACH molecules.



- ACH is rapidly hydrolyzed into acetate and choline by acetylcholinesterase .
- Also this enzyme called true cholinestrease

- Neuromuscler blocking agents are divided into two classes ; depolarizing and nondepolarizing .
- By the mechanism of action , reversal of block .
- All neuromuscler blocking agent are quaternary ammonium compound



- Mechanism for depolarizing and nondepolarizing ???

- Reversal for dep and non-dep....

SUCCINYLCHOLINE ::::::::::::::::

- The onset of action 30-60 s , duration of action less than 10 min
- Metabolized by pseudocholinestrease into succinylmonocholine
- Low pseudocholinestrease level -→ prolongation

Pregnancy , liver disease , renal failure , genetics ???

- dose 1-1.5 mg/kg
- Stored under refrigeration 2-8 c

Side effects

- CVS effects are found most common in children , bradycardia following administration first dose and 2nd in adult
- Fasciculation
- Hyperkalemia
- Muscle pain
- Intragastric pressure elevation and increase lower esophageal sphincter tone
- Intraocular pressure elevation
- Masster muscle rigidity
- Malignant hyperthermia
- ICP ELEVATION

NON-DEPOLARIZING MUSCLE RELAXANT

- Chemically they are either benzylisoquinolines(B) or steroidal compound (S) ,(B)tends to release histamine , (S) TEND TO BE VAGOLYTIC
- The more potent one is the longer its speed of onset.
- In general the diaphragm , jaw , larynx , fascial muscles respond to and recover from muscle relaxation sooner than the thumb , but glottic musculature is quite resistant to blockade
- Water soluble .

Atracurium ::

- Benzylisoquinoline structure
- Metabolism by nonspecific estrease (ester hydrolysis) , or by hofman elimination (nonenzymatic chemical breakdown)-----→ laudanosine
- Dose 0.5 mg/kg onset of action 30- 60 s for intubation .
- Stored at room temp
- Side effect :

1. Hypotension and tachycardia
2. Bronchospasm
3. laudanosine toxicity
4. Allergic reaction

Cisatracurium

- Is a stereoisomer of atracurium that is four times more potent .
- Hofmann elimination --→ laudanosine
- Dose 0.1 – 0.15 mg/kg
- Stored under refrigeration
- Side effects not significant

Mivacurium

- Metabolized by pseudocholinestrease
- Side effects histamine release

- Other muscle relaxant doxacurium

Pancuronium

- Steroidal compound
- Metabolized by the liver and exerted renaly
- Dose 0.08-0.12
- Side effect

1. Hypertension and tachycardia (vagal blockade and sympathetic stimulation
2. Arrhythmias
3. Allergic reaction (bromide hypersensitivity)

- Pipecuronium : more potent but lack cvs side effects
- Vecuronium
- Rocuronium : rapid onset

Cholinestrease Inhibitors

- Acetylcholine is hydrolyzed by acetylcholinesterase into acetate and choline
- Two types of receptors for acetylcholine : nicotinic receptors and muscarinic receptors .
- Cholinestrease inhibtors cause increase acetylcholine which acts on several organ ; cvs , pulmonary , GI

NEOSTIGMINE

- Lipid insoluble , so can't cross BBB .
- Dose 0.04 mg / kg
- It is reported that It can cross the placenta and cause fetal bradycardia
- Side effects bradycardia , nausea , vomiting , fecal incontinence
- It is used to treat mystenia graves
- Pyridostigmine ; slower onset and less potent
- Edrophonium : less potent but the most rapid onset of action and shortest duration .
- Physostigmine ; lipid soluble so can cross BBB

ANTICHOLINERGIC DRUGS

- Ester linkage for an aromatic acid with organic base .
- Competitively blocks acetylcholine receptors (muscarinic receptors)

A. cardiovascular : blockade of MU receptors in SA node resulting in tachycardia , this effect is useful in reversing bradycardia due to vagal reflexes : eg , baroreceptor reflex , perperitoneal stimulation , oculocardiac reflex .
B. Respirtory : inhibit the secretions of the respirtory mucosa and relaxation of bronchial smooth muscle
C. Gastrointestinal ; reduce GI secretion
D. Ophthalmic ; mydrasis
E. Genitourinary ; urinary retention
F. Thermoregulation : inhibition of sweat gland rise temp

Atropine

- Dose 0.4 – 0.06 mg / kg
- Cross BBB

- SCOPOLAMINE
- GLYCOPYROLATE : can't cross BBB