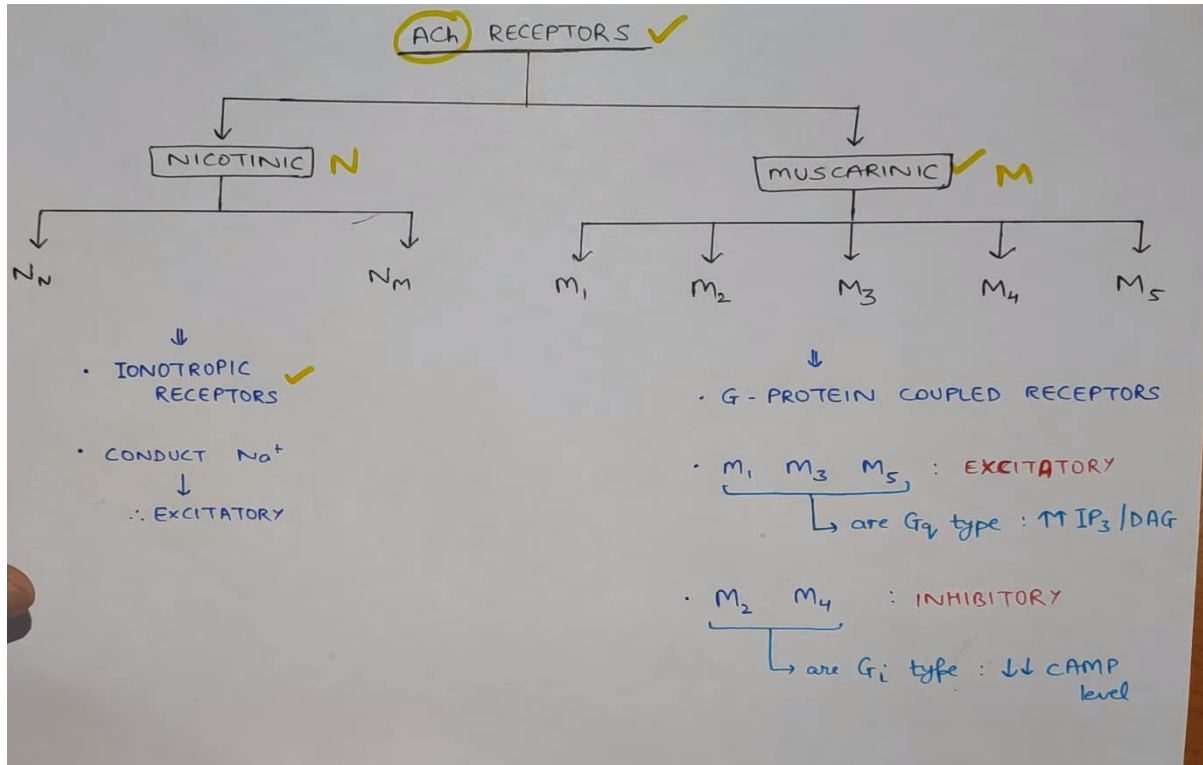


Parasympathomimetics



LOCATION

N₂ : NICOTINIC - NEURONAL

: POST-GANGLIONIC NEURONS OF

- PSNS (↑↑ ACh Release)
- SNS (↑↑ Norepi. & Dopamine Release)
- ADRENAL MEDULLA (↑↑ Epi. Release)

N_m : NICOTINIC - SKELETAL MUSCLES

: PART OF SOMATIC N.S.

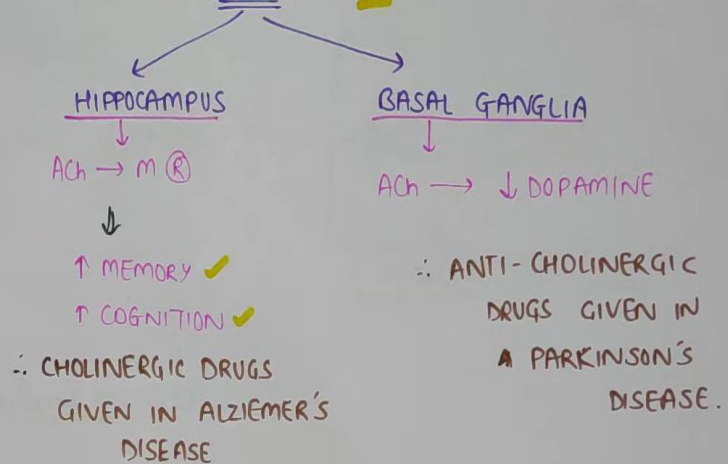
: function : MUSCLE CONTRACTION [Na⁺ entry → Depolarisation]

N_m ANTAGONISTS : k/a NON-DEPOLARIZING MUSCLE RELAXANTS

- CURARE
- CURIUM
- CHRONIUM

eg. d-Tubocurarine
Vecuronium etc.

MUSCARINIC (R) : ① All present on CNS (M₁ is PREDOMINANT)



2) Periphery :

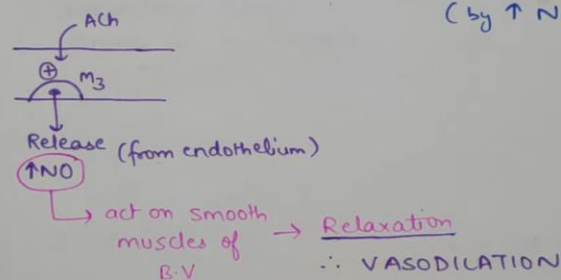
i) M_1 : $\checkmark$ STOMACH $\rightarrow$ $\uparrow$ HCl PRODUCTION
(G_q)

ii) M_2 : $\checkmark$ HEART $\rightarrow$ $\downarrow$ HEART RATE
(G_i)

iii) M_3 : Rest of Body
(G_q)

① GLANDS : $\uparrow$ SECRETION $\therefore$ $\uparrow$ SWEATING
 $\uparrow$ LACRIMATION
 $\uparrow$ SALIVATION
 $\uparrow$ PANCREATIC ENZYME SECRETION

② ENDOTHELIUM OF BLOOD VESSELS : VASODILATION
(by $\uparrow$ NO gas Release)



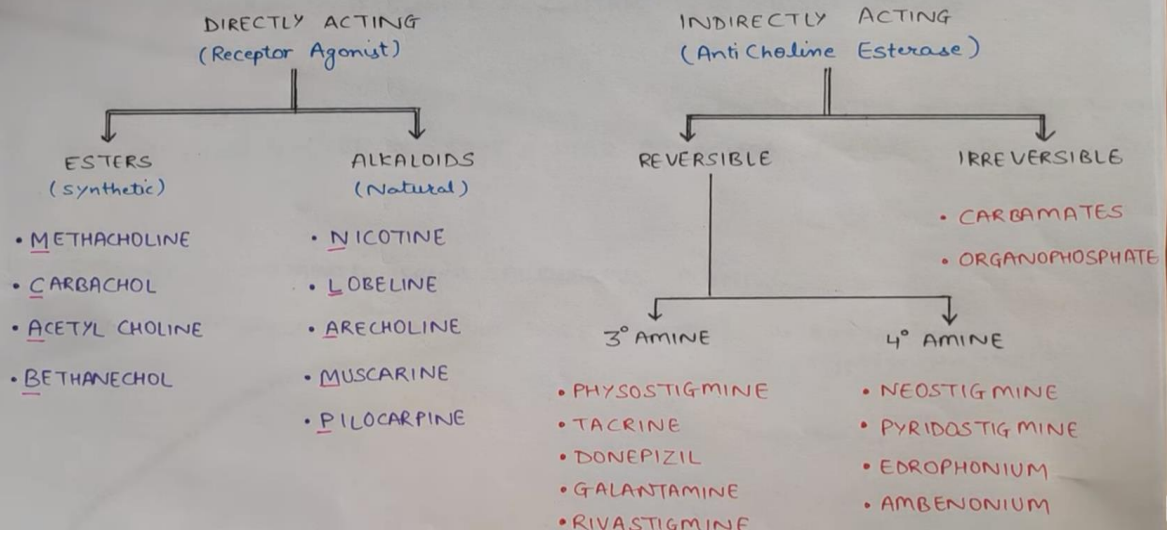
③ SMOOTH MUSCLES : $\uparrow$ CONTRACTION

- $\therefore$
- BRONCHO-CONSTRICTION
 - BLADDER CONTRACTION
 - INTESTINAL CONTRACTION
 - MIOSIS (Sphincter pupillae contraction)

Effect of ACh :

D	DIARRHOEA
U	URINATION
M	MIOSIS
B	BRADYCARDIA
B	BRONCHO CONSTRICTION
E	EMESIS
L	LACRIMATION
S	SWEATING

CHOLINERGIC DRUGS



BETHANECHOL : M_3 Agonist. : CONTRACT SMOOTH MUSCLES

: Function :- i) BLADDER = CONTRACT DETRUSSOR MUSCLE.

∴ USED AS A R_x FOR

NON-OBSTRUCTIVE URINARY RETENTION.
(e.g. POST OPERATIVE URINARY RETENTION)

ii) INTESTINE = USED AS R_x FOR PARALYTIC ILEUS
(MEGACOLON)

PILOCARPINE : OBTAINED FROM PILOCARPUS PLANT.

: EFFECTS - IN LOW DOSE = $M \oplus$ ie Bradycardia
Hypotension etc.

IN HIGH DOSE = $M \oplus$

$N \oplus$: Tachycardia

: USES = i) TOPICAL EYE DROPS (0.5-4%) - MYOTIC AGENT
(PILOCARPINE)

- DOC: OPEN-ANGLE GLAUCOMA
- ACUTE CONGESTIVE GLAUCOMA
- USED TO REVERSE THE PUPILLARY DILATION AFTER REFRACTION TESTING.
- USED ALTERNATIVELY WITH MYDRIATICS TO BREAK ADHESIONS B/W IRIS & LENS.

ii) TO INCREASE SALIVATION (SIALAGOGUE). - FOR R_x OF XEROSTOMIA.
(Dry Mouth)

: S/E = i) CONSTRICTION OF PUPIL $\therefore$ $\downarrow$ VISUAL ACUITY.
(PILOCARPINE)

- ii) CRYING $\therefore$ OF $\uparrow$ LACRIMATION & PUNCTAL STENOSIS OF NASO-LACRIMAL DUCT.
- iii) CILIARY SPASM LEADING TO PAIN & STINGING SENSATION.

ANTI-CHOLINESTRASES

ANTICHOLINESTRASES

→ INHIBIT THE ENZYME
ACETYL CHOLINE ESTERASE

→ NO HYDROLYSIS i.e.
NO METABOLISM OF
ACh.

3° AMINE
• LIPID SOLUBLE
• CROSS BBB
• CROSS CORNEA

4° AMINE
• WATER SOLUBLE
• X
• X

↓
ACh $\uparrow$ CHOLINERGIC
EFFECTS.

REVERSIBLE ANTI-CHOLINESTRASES :
(3° AMINES)

i) PHYSOSTIGMINE : Uses = a) GLAUCOMA - It reduces IOP By Producing Miosis.

b) ATROPINE POISONING - DOC: i/v PHYSOSTIGMINE

ii) DRUGS FOR ALZHEIMER'S DISEASE :

Neurodegeneration
of Cholinergic Neurons.

a) Centrally Acting Anti-Cholinesterases : ↑ ACh in BRAIN
↓
↑↑ COGNITION & MEMORY

DRUGS : • TACRINE : Banned
• DONEPILZIL : DOC : ORAL & LONGEST ACTING
• GALANTAMINE
• RIVASTIGMINE

b) MEMANTINE : NMDA Blocker
↳ Ⓡ of Glutamate

QUATERNARY AMINES :→

(i) NEOSTIGMINE : indirect action = INHIBITS CHOLINESTERASES ∴ ↑ ACh concentration at NMJ.

direct action = STIMULATES N_m RECEPTORS at NMJ.

∴ MUSCLE POWER IN PATIENTS WITH MYASTHENIA GRAVIS.

(ii) PYRIDOSTIGMINE : same features like Neostigmine.

: LONGER ACTING.

(iii) EDROPHONIUM : RAPID ONSET & SHORT ACTING (8-10 minutes)

Uses - a) DIAGNOSIS OF MYASTHENIA GRAVIS [TENSILON TEST]

b) DIFFERENTIATE B/W MYASTHENIC CRISIS & CHOLINERGIC CRISIS.

USES OF REVERSIBLE ANTICHOLINESTRASES :

- I. GLAUCOMA - as MIOTICS.
 - II. MYASTHENIA GRAVIS
 - III. CURARE POISONING & REVERSAL OF NON-DEPOLARIZING
MUSCLE RELAXANTS.
 - IV. ATROPINE POISONING.
 - V. POSTOPERATIVE URINARY RETENTION & PARALYTIC ILEUS
 - VI. SNAKE BITE POISONING :
(COBRA) venom $\rightarrow$ Blocks N_M (R) $\rightarrow$ SKELETAL MUSCLE
PARALYSIS
&
RESPIRATORY
PARALYSIS
- Rx: ANTIVENOM
+
NEOSTIGMINE

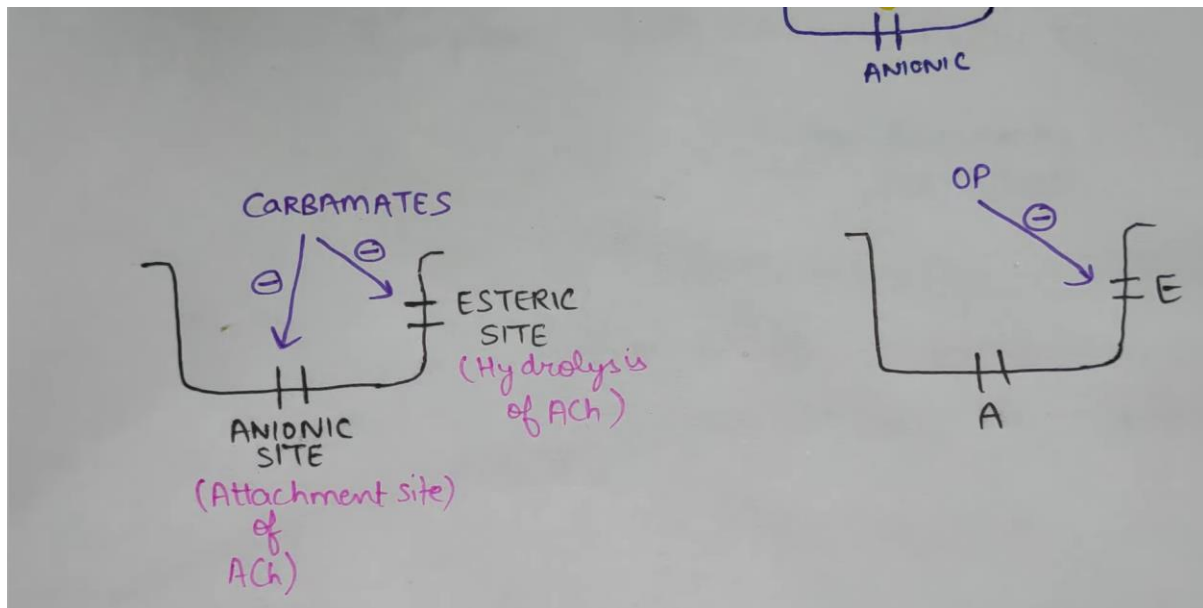
IRREVERSIBLE ANTI-CHOLINESTRASES

CARBAMATES

- CARBARYL
- ALDICARB
- PROPOXUR

ORGANOPHOSPHATES

- MALATHION
- PARATHION
- CHLORPYRIFOS
- NERVE GASES : TABUN
SARIN
SOMAN



OP POISONING :- MOST DANGEROUS

- OP are highly lipid soluble drugs $\therefore$ absorb from any body surface.
- OP undergoes ageing

Ageing

Signs & Symptoms : i) MUSCARINIC EFFECTS -

- PROFUSE SWEATING, SALIVATION, LACRIMATION, BRONCHOSPASM, VOMITING, MIOSIS, BRADYCARDIA, HYPOTENSION, ABDOMINAL CRAMPS etc.

Red BRONCHIAL SECRETION

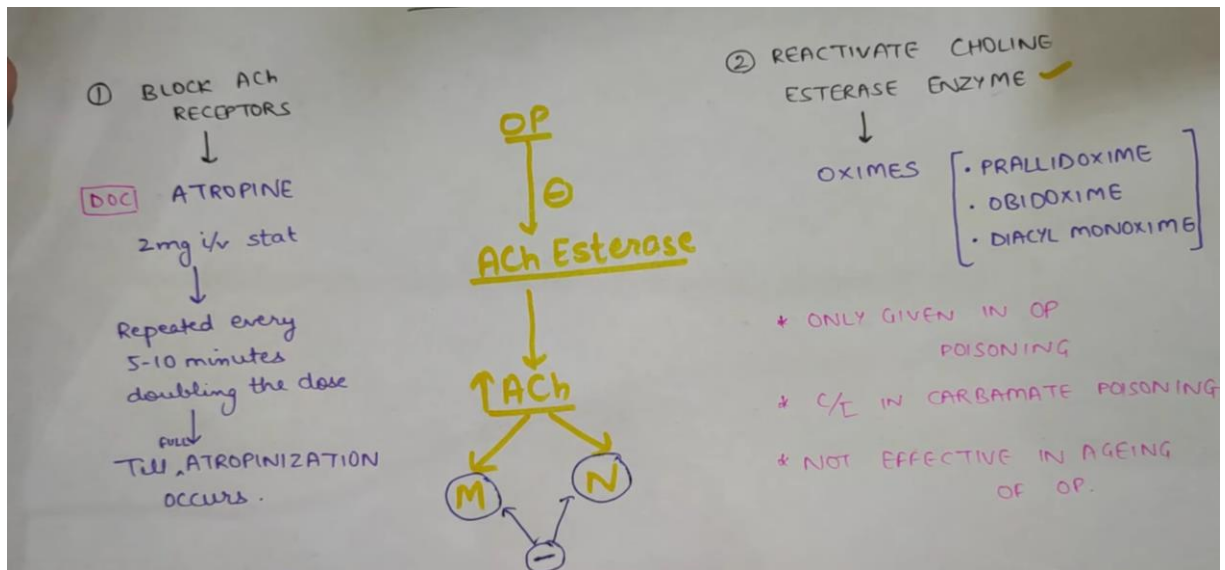
ii) NICOTINIC EFFECTS - MUSCLE WEAKNESS & PARALYSIS DUE TO PROLONGED DEPOLARIZATION.

iii) CENTRAL EFFECTS - HEADACHE, CONFUSION, CONVULSIONS, COMA & DEATH d/t RESPIRATORY FAILURE MAINLY.

Diagnosis : i) HISTORY OF EXPOSURE ✓
ii) CHARACTERISTIC SIGNS & SYMPTOMS ✓
iii) ESTIMATING CHOLINESTERASE ACTIVITY IN BLOOD IS DECREASED.

Treatment : General Measures : i) Remove contaminated clothes ; wash skin with soap & water
ii) Gastric lavage till returning fluid is clear.
iii) Airway should be maintained.
iv) Artificial Respiration is given, if necessary.
v) Diazepam should be used cautiously by slow i.v. injection to control convulsions.

Specific Treatment of OP poisoning



ATROPINIZATION:

- Mydriasis ✓
- Tachycardia ✓
- Constipation ✓
- **DRYNESS OF BRONCHIAL SECRETION** ✓

OXIMES: BIND TO ANIONIC SITE OF AChE enzyme & REMOVES OP FROM ESTERIC SITE. ✓

