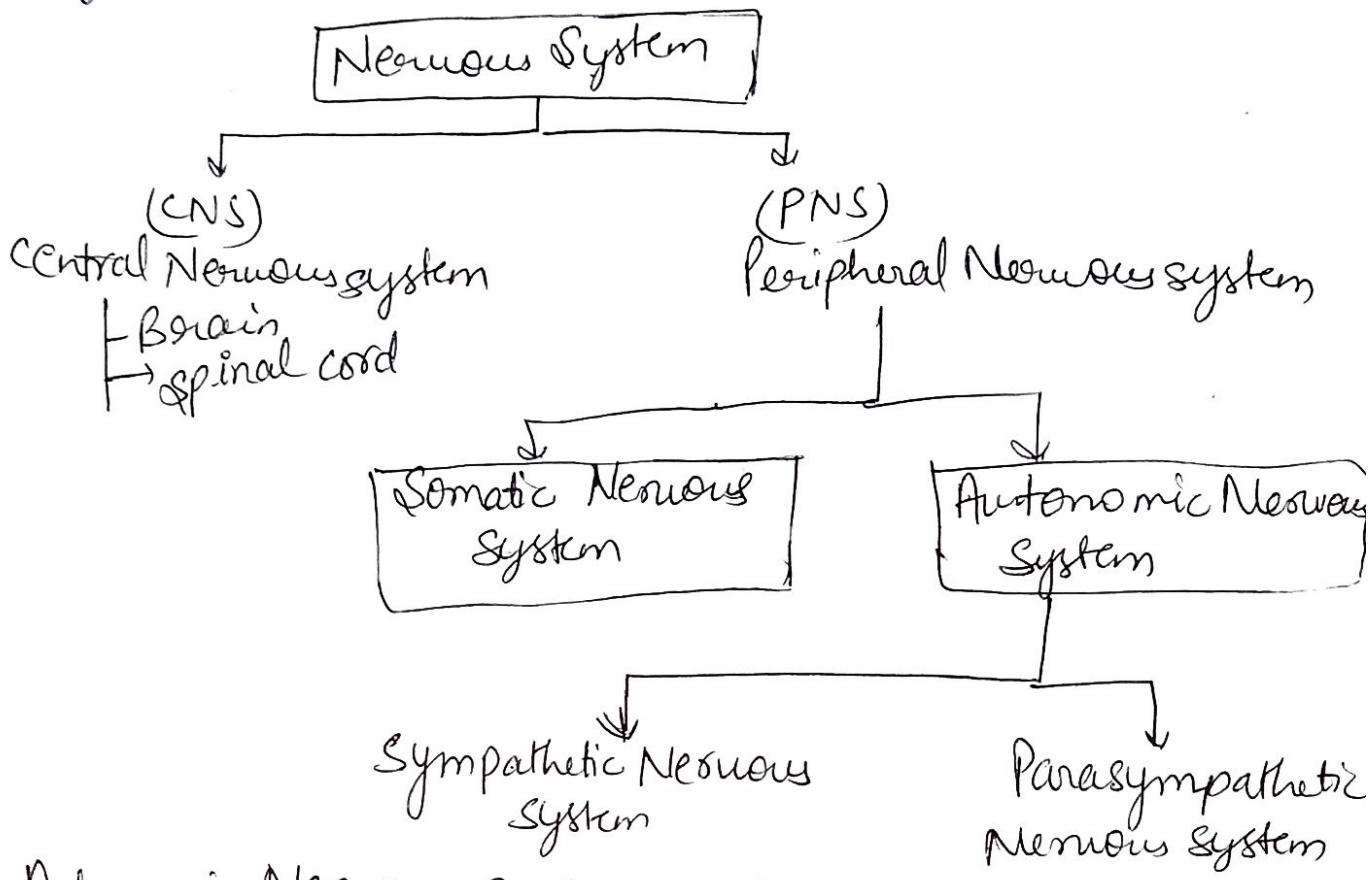
UNIT-III[rd]

Pharmacology of drugs Acting on peripheral Nervous System :-

* Nervous system :- It control & co-ordinate the human body and it gives the quick response to our body.



Autonomic Nervous System :- In this system, involuntary movement happened (which we can't control).

eg: Breathing, Digestion, Heart rate etc.

* Now, we have to study about the Action of that drugs which act on PNS.

(1) Sympathetic Nervous System :- Fight / Flight situation [Abnormal].

Activate in condition of three F 3F

Fear Fight Flight

Those system which Active in abnormal situation of body & maintain the body. Ex:- Tease heart Rate etc.

(2) Parasympathetic Nervous System:- In this, our body come back to normal conditions after any abnormal situation eg:- Normal heart Rate etc.

Both system are important to maintain the homeostasis and work of our body.

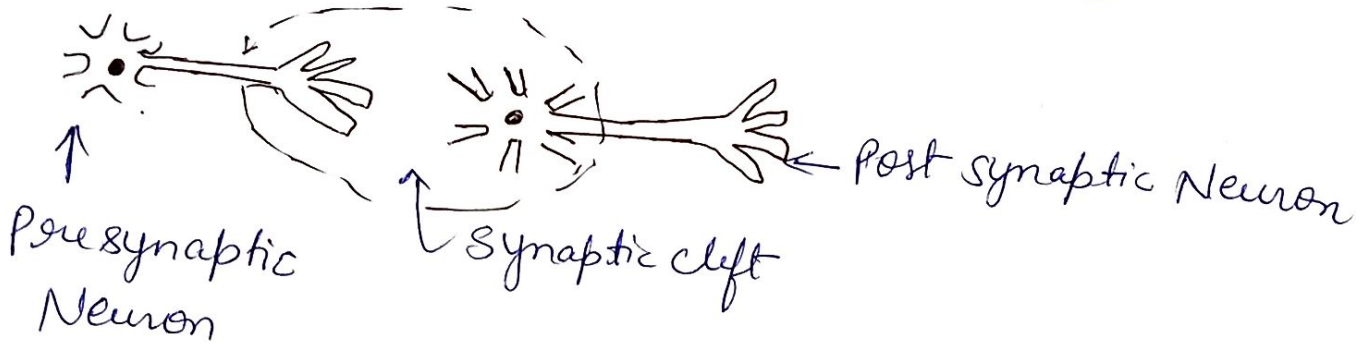
Diffrent b/w Symapathetic & Parasympathetic System:-

Symapathetic Ns	Parasympathetic NS
• Involved in the fight or flight response • prepare the body for any potential danger • Increase heartbeat muscles tense up. • pupil dilate • Saliva Secreation is inhibited	• Involved in maintaining homeostasis and also, promits the rest & digest response. • to bring the body to a state of calm. • Reduces heartbeat, muscle relaxes. • pupil contract • Saliva Secretion ↑eases digestion ↑ease.
Neurotransmitter release ↓ Adrenaline & Noradrenaline	Neurotransmitter Release ↓ Acetylcholine

Neurohumoral Transmission

Neurohumoral → Neuro → Nerve / Neuron
+
Humoral → Chemical messenger

It is the process of transfer of any message or signal from one neuron to another neuron with the help of any chemical messenger (Neurotransmitter, hormones).



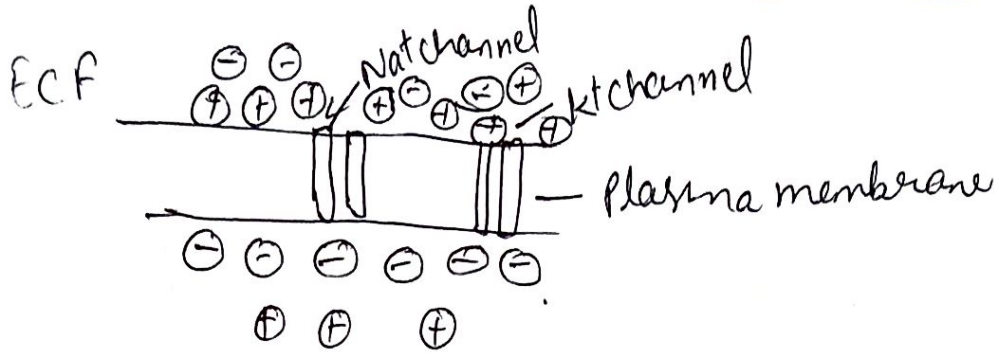
Neurohumoral transmission involves following steps:-

(i) Impulse Conductance
(ii) Transmitter release
(iii) Transmitter action on post junctional membrane.
(iv) Post junctional activity
(v) Termination of transmitter action.

(i) Impulse Conductance :- In this step firstly impulse is generated by the process of "Action potential"

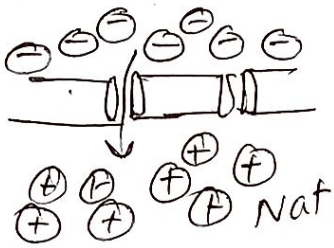
At Resting state [when nerve impulse is not transmitted from neuron]. Resting transmembrane potential is -70mV

Na^+ ion have lease concentration at outside and K^+ ion have high concentration at inside the cell.



Resting Membrane Potential (-70mV)

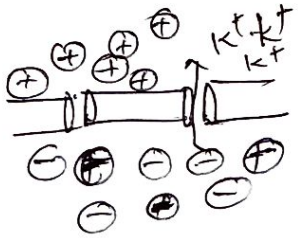
- Depolarisation :- When any kind of stimulus detected then it changes the Resting membrane potential to less potential (increases) If stimulus change resting potential (-70mV) to (-55mV) then it is called (threshold potential). In this potential open Nat ion channel. So Na+ ion enters inside the cell and (+ve) charge and (-ve) at outside the cell and it is called depolarisation.



Depolarisation.

Repolarisation :- Stimulus continuous increase the potential now when potential reach at (+20mV to +30mV) it open k^+ ion channel and move outside the cell. Ionic distribution is normalized during the refractory period by the Activation of Nat kt pump.

Actionpotential works 1000 times in one second.



Repolarisation

Resting Membrane Potential (−70mV)

↓ Stimulus

Threshold potential (−55)

↓

Na^+ channel open

↓

Influx of Na^+ ion

↓

Depolarisation

↓

K^+ channel open

↓

Efflux of K^+ ion

↓

Repolarisation

↑

Normalized

↑

Nerve impulse

(ii) Transmitter release :- Nerve impulse promotes fusion of vascular & axonal membrane, through Ca^{++} entry which fluidized membrane. This promotes exocytosic (transmitter release from vesicle) in Synaptic cleft.

(iii) Transmitter action on postjunction membrane :- The transmitter release and attached with specific receptor on postjunctional membrane and depending on nature it induce two types of Action.

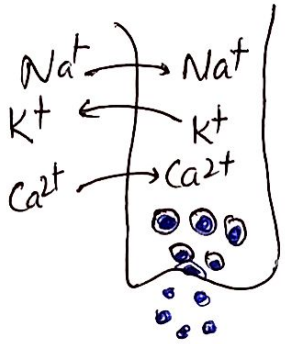
- EPSP [Excitatory Post-Synaptic potential]
  - ↓
  - Increase in permeability to all cation
  - → Na^+ or Ca^+ influx cause depolarisation followed by K^+ efflux.
- IPSP [Inhibitory post synaptic potential]
  - ↓
  - It inhibitory neurotransmitter act increase in permeability to smaller ion or animals.
  - K^+ & Cl^- moves in resulting (movement out) Hyperpolarisation.

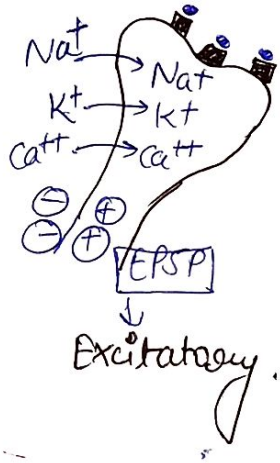
(iv) Nerve impulse, contraction in muscle, secretion in glands in depolarisation.

Resist depolarizing Stimuli.

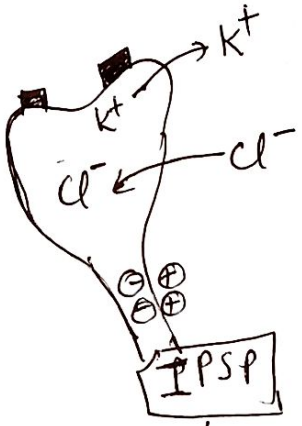
(v) Termination of transmitter Action:- Neurotransmitter is degraded locally or any other mechanism. It can also be degraded by enzymatic action.

eg:- Acetylcholine degraded by cholinesterase





Excitatory.



Inhibitory

Co-Transmission:- Peripheral and central nervous system release more than one active substance when stimulated.

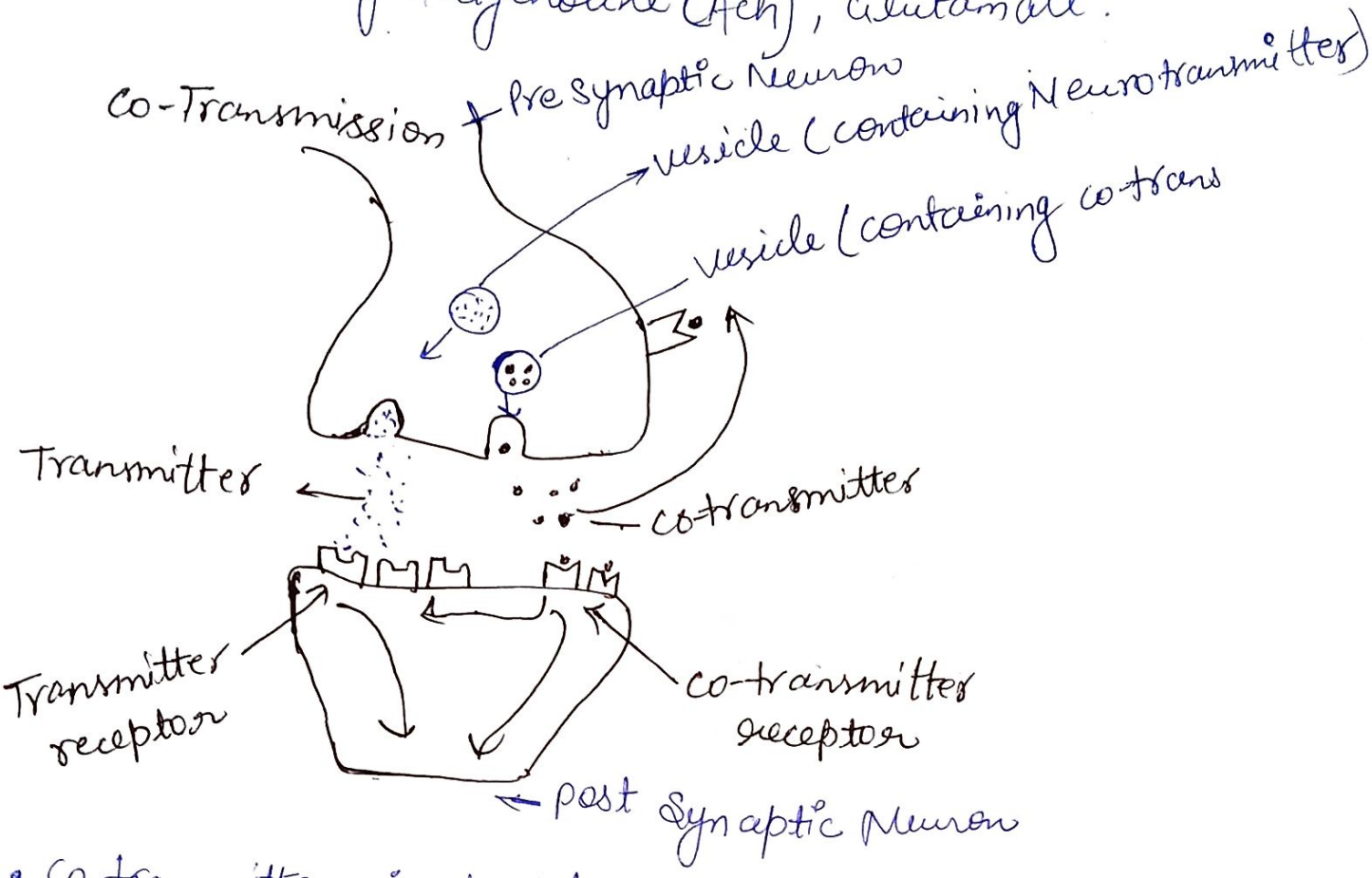
Definition:- Cotransmission is the release of several types of Neurotransmitter from a single nerve terminal.

Co-Transmitter :- It is a chemical substance that is release along with primary neurotransmitter.

Examples:- Primary Neurotransmitter → Ach, NA

Co-transmitter are → Purines – ATP, Adenosine
Nitric oxide
Prostaglandings (PG)

* On Release of Acetycholine (Ach), Glutamate.



• Co-transmitter is stored with primary transmitter vesicles or in different (separate) vesicle.

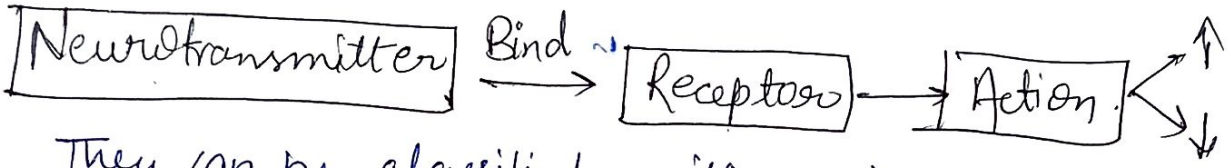
Function – (i) enhance or regulate presynaptic release of primary Neurotransmitter.

(ii) Modulate post-synaptic sensitivity of primary neurotransmitter.

(iii) Serve as a alternate to primary neurotransmitter.

Classification of Neurotransmitters :-

- **Neurotransmitter :-** These are chemical messenger that transmit signal from a neuron to a target cell across a synapse. These are stored into synaptic vesicles in pre-synaptic neurons.



They can be classified as either excitatory or inhibitory.

Excitatory :- Activate receptor on post synaptic membrane and enhance the effect of the action potential (↑ eas Activity).

Inhibitory :- Decrease the Activity of transmitter or receptor (decrease the effect of the Action potential).

Some neurotransmitter show both type of activity.

Excitatory :- Acetycholine, Adrenaline, Dopamine etc.

Inhibitory :- GABA, Serotonine

Both - Acetycholine, Nor-adrenaline, Dopamine.

Acetycholine (learning) :- Involved in thought, learning and memory. It Activate muscle contraction in the body and is also associated with attention & awakening.

Adrenaline (Fight or flight) :- released by the adrenal gland but some neurons may secrete it as a neurotransmitter. It is produced in stressful situation, ↑ease heart Rate & blood flow.

Nor-adrenaline:- (concentration):- It improve attentio & responding actions in the brain. ↑easing blood vessels

Dopamine [Pleasure]:- Feeling of pleasure also addiction movement & motivational.

Serotonin [mood]:- contributes to well beings & happiness Help sleep cycle & digestive system regulation.

GABA [calming]:- Calm firing nerves in the CNS.
High level — Improve focus
low level — cause anxiety.

Histamine → Released by mast cells. Involved in local Immune responses.

Glutamate (memory):- Involved in learning & memory.

Drug Acting on Autonomic Nervous System:-

These all are those drugs which act on Autonomic Nervous system & produce effect on it.

- Adrenergic drug [sympathomimetics] } Sympathetic Nervous System
- Antiadrenergic drugs [sympatholytics] }
- Cholinergic drugs [Parasympathomimetics] } Parasympathetic Nervous System
- Anti-cholinergic drugs [Parasympatholytics] }

CHOLINERGIC SYSTEM

Also known as Parasympathomimetics system.

Parasympathomimetics — [Parasympatho – Parasympathetic Nervous system.
Mimetic (mimic) → copy the Action.

These drugs bind with cholinergic receptors [muscarinic + Nicotinic] + drugs give their Action.

When the Neurotransmitter of parasympathetic Nervous system (Acetylcholine) in body is less as per demand then we use drugs externally which act as a cholinergic Neurotransmitter. ie. Parasympathomimetics.

eg:- Acetylcholine, carbachol, physostigmine etc.

Synthesis storage + Release of Acetylcholine:-

Basically cholinergic neurotransmitter Acetylcholine is synthesised inside the parasympathetic Neuron.

Acetylcholine is synthesized locally in the cholinergic Nerve endings by the following pathway -

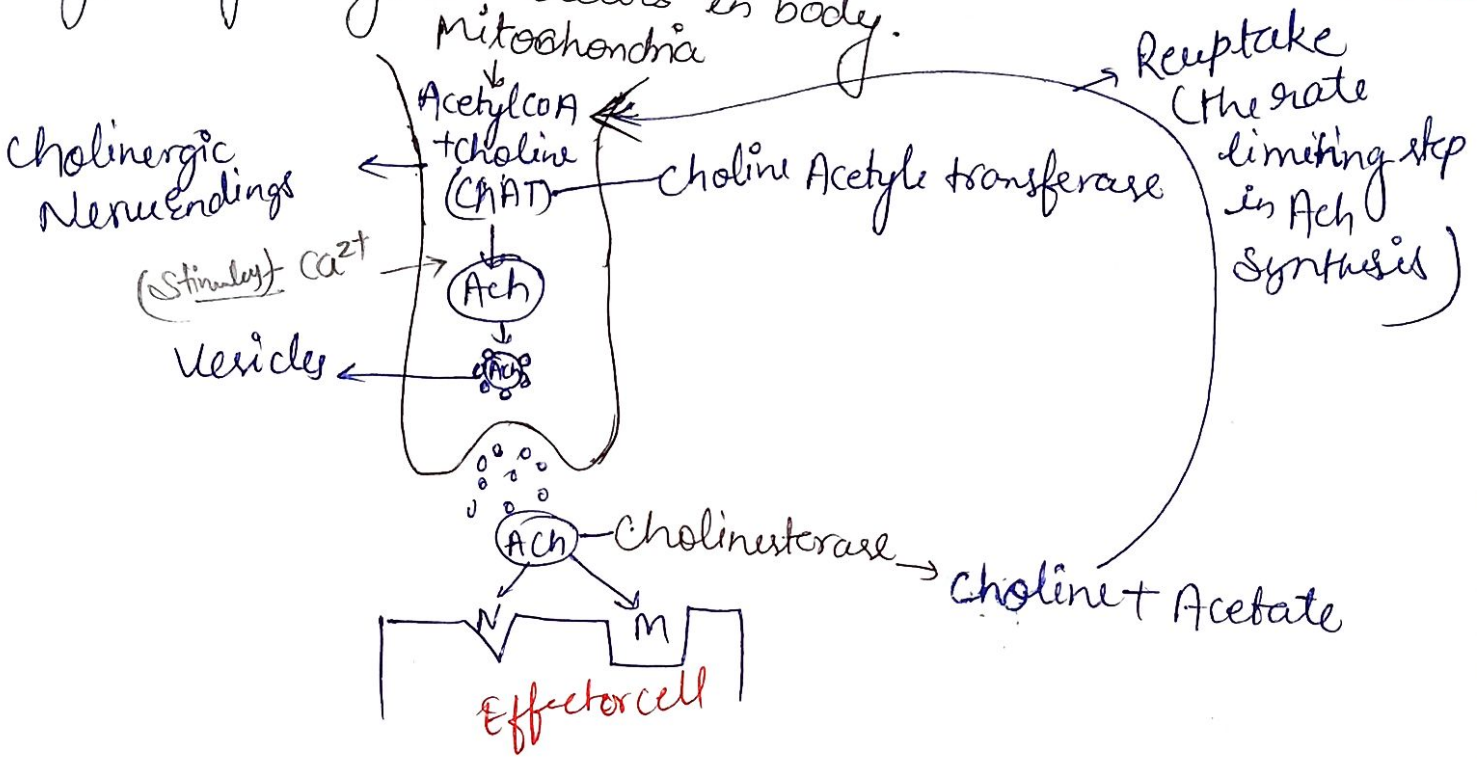
Ach (Acetylcholine) is the principle neurotransmitter in the choline.

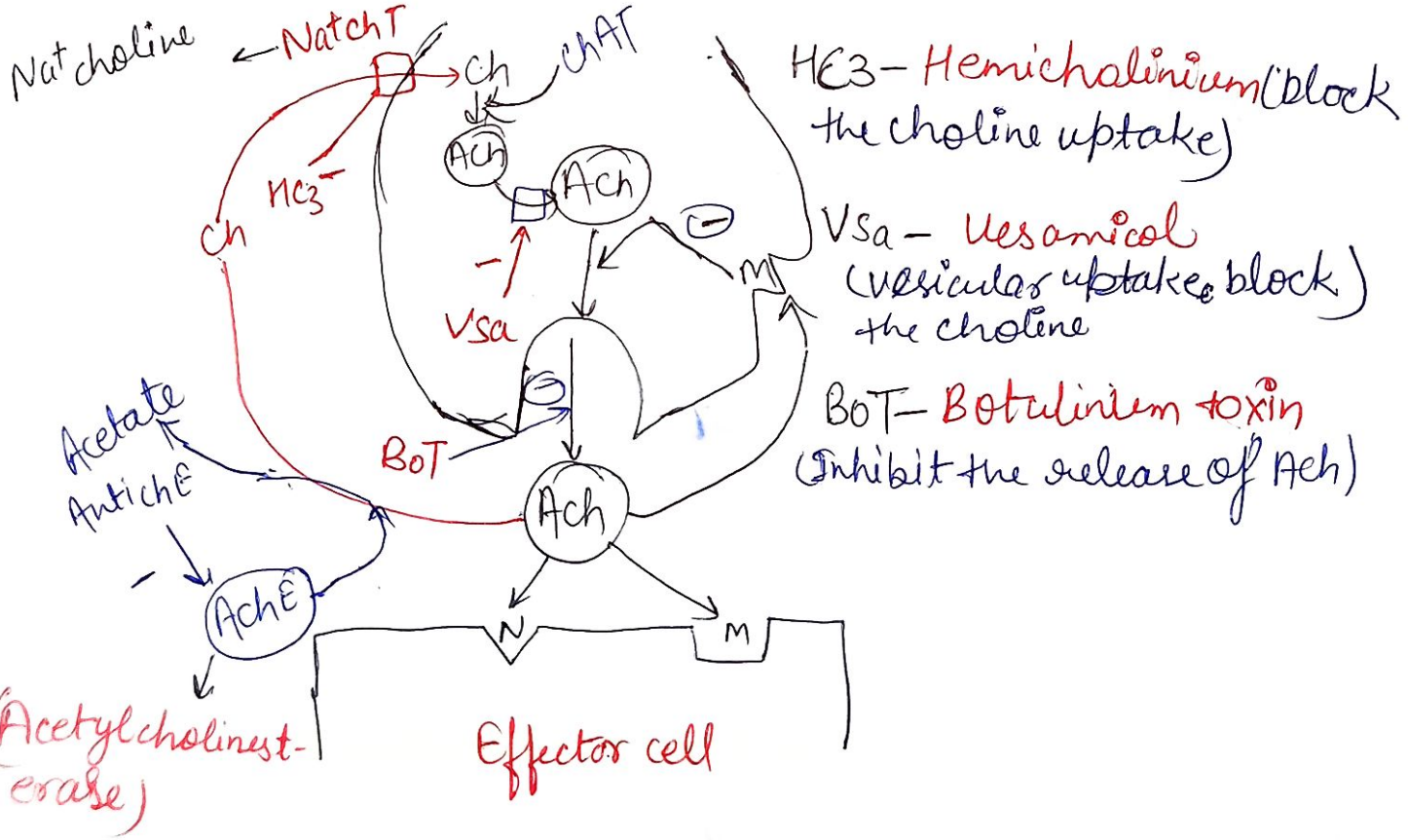
Acetylcholine is synthesized locally in cholinergic Nerve ending. Acetylcholine is quaternary ammonium compounds + is rapidly hydrolysed by cholinesterase's hence No therapeutic application.

ATP + Acetate + CoEn-A
↓ Acetate activating reaction
Acetyl coEnA + choline
↓ choline acetyl transferase
Acetylcholine + CoEn-A

Acetylcholine → cholinesterase → Choline + Acetate

Acetylcholinesterase - AchE or true cholinesterase) and (Butyeylcholinesterase - BUChE or pseudocholinesterase types of enzymes occurs in body.





HC3 - Hemicholinium (block the choline uptake)

Vsa - Vesamicol (vesicular uptake block) the choline

BoT - Botulinium toxin (Inhibit the release of Ach)

Anticholinesterases:- Tease concentration of Ach (Inhibiting the Ach metabolism)

Cholinergic Receptors:- Those receptors in which the Acetylcholine is bind they are called cholinergic receptors. Cholinergic receptors are two types -

(1) Nicotinic Receptor
(2) Muscarinic Receptor

(1) Nicotinic Receptor:- When the Acetylcholine is bind with this receptor then they produce the similar effect like nicotine. so this receptor is called Nicotinic receptor. On the basis of Nature & Action Nicotinic receptor of two types - (Ionotropic Receptor) - Nat

(i) Nm - (Neuromuscular Junction)
(ii) NN - (Neuronal ganglia)

(i) Nm Receptor:- Basically present in the all neuromuscular junction of body. When Acetylcholine is bind with the Nm receptor then they act as the contraction & relaxation of muscle.

(ii) NN Receptor:- Basically present on autonomic neuronal ganglia and when the Acetylcholine is bind with the NN receptor they control the release of Neurotransmitter. These are also called Neuronal Nicotinic receptor.

(2) Muscarinic Receptor :- These receptors are selectively stimulated by muscarine & blocked by atropine. They are located primarily on Autonomic effector cells in heart, blood vessels, eye, smooth muscles & glands of gastrointestinal, respiratory & urinary tracts, sweats glands etc.

The Nature of muscarinic receptor is GPCR. They have seven protein helix structure. Muscarinic receptor is of five type.

(i) M_1 - Stomach, Brain → HCl secretion ↑ ease
(ii) M_2 - Heart
(iii) M_3 - Bronchus, GIT, Bladder, Glands, Eye
(iv) M_4
(v) M_5

(Metabotropic Receptor)

Characteristics of Important Subtypes of Muscarinic receptor :-

	M_1	M_2	M_3
Location & function Subserved	Autonomic ganglia: Depolarization Gastric Hist. release acid glands: secretion CNS: Learning, memory motor functions	SA Node - Hyperpolarisation rate of impulse generation AV node & velocity of conduction.	Visceral smooth muscle contraction Iris - constriction of Pupil Ciliary Muscle :- contraction.
Nature	G_q - protein coupled	G_i / G_o - Protein coupled	G_q - protein coupled
Transducer Mechanism	IP_3 / DAG - ↑ cytosolic Ca^{2+}	K^+ channel opening ↓ cAMP	IP_3 / DAG - ↑ cytosolic Ca^{2+}
Agonists	MCN-343A, oxotremorine	Methacholine	Bethanechol
Antagonists	Pirenzepine, Telenzepine	Methoctramine, Tripitramine	Solifenacin Darifenacin.

Pharmacological Action of Acetylcholine :-

On the basis of Action pharmacological action of Acetylcholine is divided into two category

(i) Muscarinic Actions
(ii) Nicotinic Actions

(i) Muscarinic Actions

- **Action on eye :-** The cholinergic drug when bind with eye then it constrict the pupil and it causes miosis.
  Contraction of ciliary muscle → spasm of Accomodation, Increased outflow facility, reduction in intraocular tension (especially in glaucomatous patients).

- **Action on glands :-** Secretion from all parasympathetically innervated glands is increased via M_3 & some M_2 receptors :- sweating, salivation, lacrimation, increased tracheobronchial & gastric secretion.

- **Smooth muscle :-** Smooth muscle in most organs is contracted (mainly through M_3 receptors).
  Bronchial muscles constrict, asthmatics are highly sensitive → Bronchospasm, dyspnoea, precipitation of an attack of bronchial asthma.

- **Action on heart :-** M_2 receptor it cause inhibitory Action. The force are conduction & rythm of heart is decrease The Rate of pumping is also decrease (Bradycardia) BP level due to vasodilation.

- Action on blood vessels:- All Blood vessels are dilated through only few (skin of face, neck, salivary glands). Falls in BP and Flushing, especially in the blush area occurs. Muscarinic (M_3) receptors are present on vascular endothelial cells: vasodilation is primarily mediated through the release of an endothelium dependent relaxing factor (EDRF) which is nitric oxide (NO). The PLC - IP_3/DAG pathway (phospholipase C - Inositol trisphosphate/diacylglycerol - cat↑eas depolarisation.

- Action of GIT:- Acetylcholine acts on GIT excitatory Action. It ↑ease the Gastric acid secreation & peristalsis movement in the Intestine

(ii) Nicotinic Actions:-

- Autonomic ganglia:- Both Sympathetic & Parasympathetic ganglia are stimulated. High dose of Ach given after atropine cause tachycardia & rise in BP due to Stimulation of sympathetic ganglia.

- Skeletal Muscle:- Iontophoretic application of Ach to muscle endplate causes contraction of the fibre.

- CNS Actions:- ACh injected i.v. does not penetrate blood-Brain barrier & No central effects are seen.

Cholinergic Agonists

Choline esters
- Acetylcholine
- Methacholine
- Carbachol
- Bethanechol

Alkaloids
- Muscarine
- Pilocarpine
- Arecoline

Cholinergic Drug (Cholinomimetic, Parasympathomimetic)

Bethanechol:- Used in postoperative / postpartum nonobstructive urinary retention, neurogenic bladder to promote urination. By making the concentrations of the urinary bladder muscle strong in order to initiate urination and help empty the bladder.

Side effect:- Involentary urination, flushing & sweating. Fall in BP, Bronchospasm.

Cholinomimetic alkaloids:-

(i) Pilocarpine :- It is obtained from the leaves of *Pilocarpus microphyllus*. Pilocarpine causes marked sweating, salivation & lease in other secretions. Small dose generally cause fall in BP (muscarinic), But higher dose in rise BP (tachycardia). Applied to the eye, it penetrate cornea & promptly causes miosis, ciliary muscle contraction. Used only in the eye as 0.5 – 4% drops.

Mushroom poisoning:- At least 3 types of mushroom poison is known as. Muscarine type (Early mushroom poisoning):- Muscarinic actions appear within an hour of eating the mushroom.

Hallucinogenic type:- Due to muscimol & other isoxazole compounds which are present in A. muscaria & Amanita) These compounds activate amino receptors & Block muscarinic receptors in the brain.

- Phallodin type (late mushroom poisoning):- It is due to peptide toxins found in Amanita phalloides & other species. Inhibit RNA & protein Synthesis.

Anticholinesterases:-

Anticholinesterases (Anti ChEs) are agents which inhibit ChE, protect Ach from hydrolysis- produce cholinergic effects. On the Basis of their complex formation Anticholinesterases drugs are two types:-

Reversible

Carbamates
Physostigmine (Eserine)
Neostigmine
Pyridostigmine
Edrophonium
Rivastigmine, Donepezil
Galantamine

Acridine
Tacrine

Irreversible

Organophosphate

Dyflox (DEP)

Echothiophate

Malathion

Diazinon

Tabun, Sarin, Soman

Carbamates

Carbaryl

Propoxur

Physostigmine :- It is rapidly absorbed from g.i.t and parenteral sites. Short Acting time drug.

Neostigmine & Congeners :- These are poorly absorbed orally, oral dose is 20-30 times higher than parenteral dose. use - Glucoma, Myasthenia gravis.

Dyflox (DEP) :- It is Diisopropyl-fluoro-phosphate (DEP) a very potent & long-Acting anti-CHE it is now obsolete as a miotic.

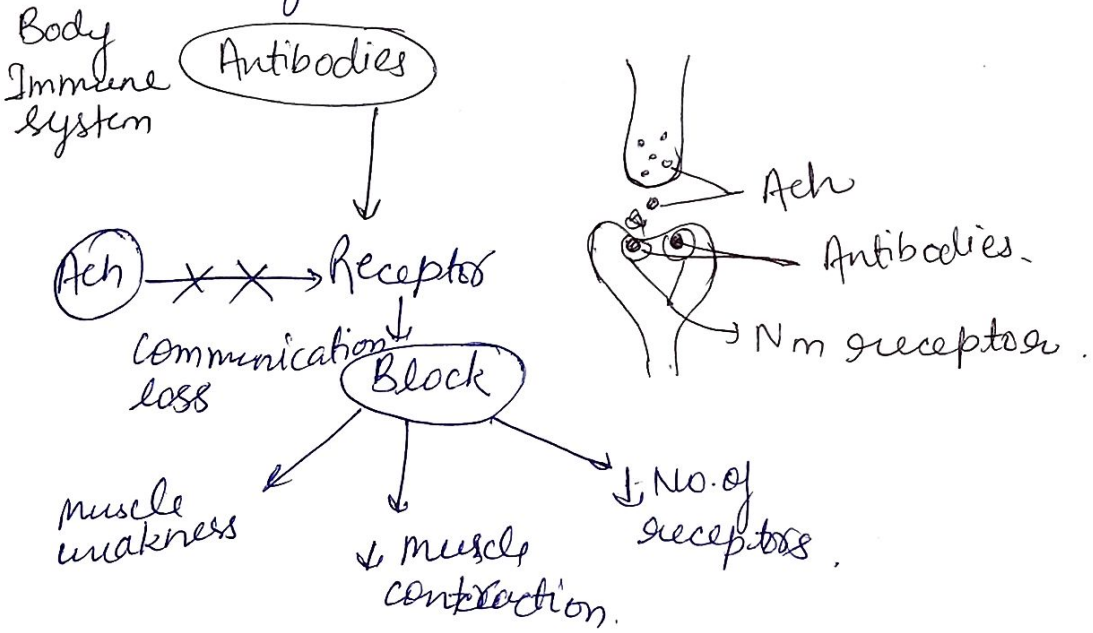
Drugs used in Myasthenia gravis :-

Myasthenia Gravis :- A weakness & rapid fatigue of muscle. It is an auto immune disorder, in which our immune system produce Antibodies that block or destroy muscle receptor. Breakdown in communication b/w nerves & muscles.

Symptoms :- • weakness in the arms & leg muscles
• Difficulties with speech & chewing
• Fatigue, shortness of breath

Mechanism :- when myasthenia gravis not occured & body behave normal & contraction & relaxation happened normally in muscles.

In this disorder, our immune system produce antibodies to block / destroy the Nicotinic receptor. So, these Ab binds with these receptor & block them. Now due to blockage of receptor (Ach) does not bind on receptor. decrease the contraction of muscles. also Antibodies destroy or kill the receptor.



Treatment :- Drugs used (i) Anticholinesterase :- use these drug to treat myasthenia gravis.

Anticholinesterase drugs → Inhibit → Cholinesterase Enzyme

eg :- Pyridostigmine, Neostigmine etc.

(ii) Immunosuppressant :- Use these drugs to suppress the Immune system to decrease the formation of Antibodies.

eg :- Cyclosporine A, cyclophosphamide etc.

Drugs Used in Glaucoma :-

- Glaucoma :- A group of eye condition that can cause blindness (loss of vision).

In this, the nerve connecting the eye to the brain (optic nerves) is damaged due to high eye pressure (intra ocular pressure). Intra ocular pressure is more than ↑ 21 mmHg.

Two main cause/reason – (i) Increase production of aqueous humor

(ii) ↓ drainage of aqueous humor.

loss of vision ← optic Nerve damage ← eye pain ← I.O.P ↑ Increase.

Symptoms :-
- Eye pain
- Redness of the eye
- vision loss, blurred vision.

Risk factor :- ↑ Increased pressure in the eye.
High blood Pressure
Excessive use of steroids.

Diagnosis :- Dilated eye examination.

Types of Glaucoma – (i) Open Angle glaucoma
(ii) Closed angle glaucoma.

(i) Also known as chronic glaucoma.
Symptoms – gradual vision loss.

(ii) Also known as acute glaucoma.

Treatment :- (i) α-agonist - ↓ I.O.P by ↑easing uveoscleral outflow.

eg: Dipivefrine, Brimonidine etc.

↓ drainage of aq. humor.

(ii) β-Blocker - ↓ I.O.P by decreasing the formation of aq. humor.

eg :- Timolol etc.

(iii) Prostaglandin (P.G) analogues - same as α-agonist

↓ I.O.P by ↑ uveoscleral outflow.

eg: Latanoprost etc.

(iv) Carbonic Anhydrase inhibitors - used orally

↓ aqueous formation by ↓ bicarbonate ion in ciliary epithelium.

eg: Acetazolamide etc.

(v) Miotics :- ↓ I.O.P Increasing the ciliary muscle tone.

eg: Pilocarpine (4-6 hrs)

Anticholinergic Drugs

(Muscarinic receptor Antagonists, Atropinic, Parasympatholytic)

Parasympatholytic → lytics
- lytics → lysis (breakdown) → oppose the effect
- Parasympathetic Nervous System

The Term 'anticholinergic drugs is restricted to those which block actions of ACh on autonomic effectors and in the CNS exerted through muscarinic receptors.

* Classification of drug;

Pharmacological Actions of Parasympatholytics (Atropine):-

(1) CNS :- Atropine has an overall CNS stimulant Action. It can cross the (Blood Brain Barrier) so it can produce their effect CNS. It cause respiratory depression. Cause drowsiness & sedative effects.

(ii) CVS :- It is due to blockade of M_2 receptors on the SA node through which vagal tone decrease HR (Heart Rate). Tease the heart Rate (Tachycardia) Tease the conduction from SA node.

(iii) Eye :- The autonomic control of iris muscles and the action of mydriatics as well as miotics. (dilate the pupil in eye).

(iv) Smooth muscles :- All visceral smooth muscles that receive parasympathetic motor innervation are relaxed by atropine (M_3 blockade). Contractions of stomach & intestine are reduced. (constipation may occurs spasm may be relieved. Atropine causes Bronchodilation and reduced airway resistance. (treatment of Asthma).

(v) Glands :- Atropine markedly decreases sweat, salivary, tracheobronchial & lacrimal secretion (M_3 blockade). Skin & eyes become dry, talking and swallowing may be difficult.

(vi) Body temperature :- Rise in body temperature occurs at higher doses. Sweating is decreases.

(vii) GIT :- Decreases the Gastric Acid secretion so it is used in the treatment of peptic ulcer.

(viii) Uterus :- Constriction Teased.

(ix) Local Anaesthetic :- Atropine has a mild anaesthetic action on the cornea.

Atropine is a natural alkaloids which is obtained from the atropa belladona plant. Atropin inhibit the binding of Ach in the muscarinic receptor.

Atropine $\xrightarrow{\text{Bind}}$ Muscarinic receptor then block the Action of Ach drug.

Pharmacokinetics of Atropine :-

Atropine are rapidly absorbed from g.i.t. applied to eyes they Freely penetrate cornea. About 50% of atropine is metabolized in liver & rest is excreted unchanged in urine. It has a t1/2 of 3-4 hours.

Therapeutic uses :-
- mydriasis
- Anti parkinsonism agent
- Motion sickness
- Peptic ulcer
- Bronchial Asthma
- Preanaesthetic Medication.

Adverse effect :- May cause - glaucoma in some patients
Tachycardia.

Interactions :- 1) Absorption of most drugs is slowed because atropine delays gastric emptying.
2) Antacids interfere with absorption of Anticholinergics.

Sympathomimetics / Adrenergic drug :-

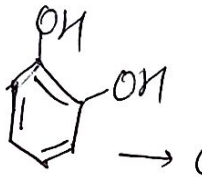
Sympatho → Sympathetic Nervous System

mimetics → mimic [copy the Action].

These are those chemical Agents or drugs which copy the Action of Sympathetic nervous System.
These drugs bind with adrenergic receptors [α & β] & give their Action.

eg:- Adrenaline [epinephrine]
Nor-adrenaline [Nor-epinephrine]

A catecholamine (CA) is a monoamine neurotransmitter an organic compound that has catechol (Benzene with two OH group side next to each other) and a side-chain amine.



→ catechol

Catecholamines are derived from the Amino acid tyrosine, which is derived from dietary source as well as synthesis from phenylalanine.

Catecholamine are two types such as-

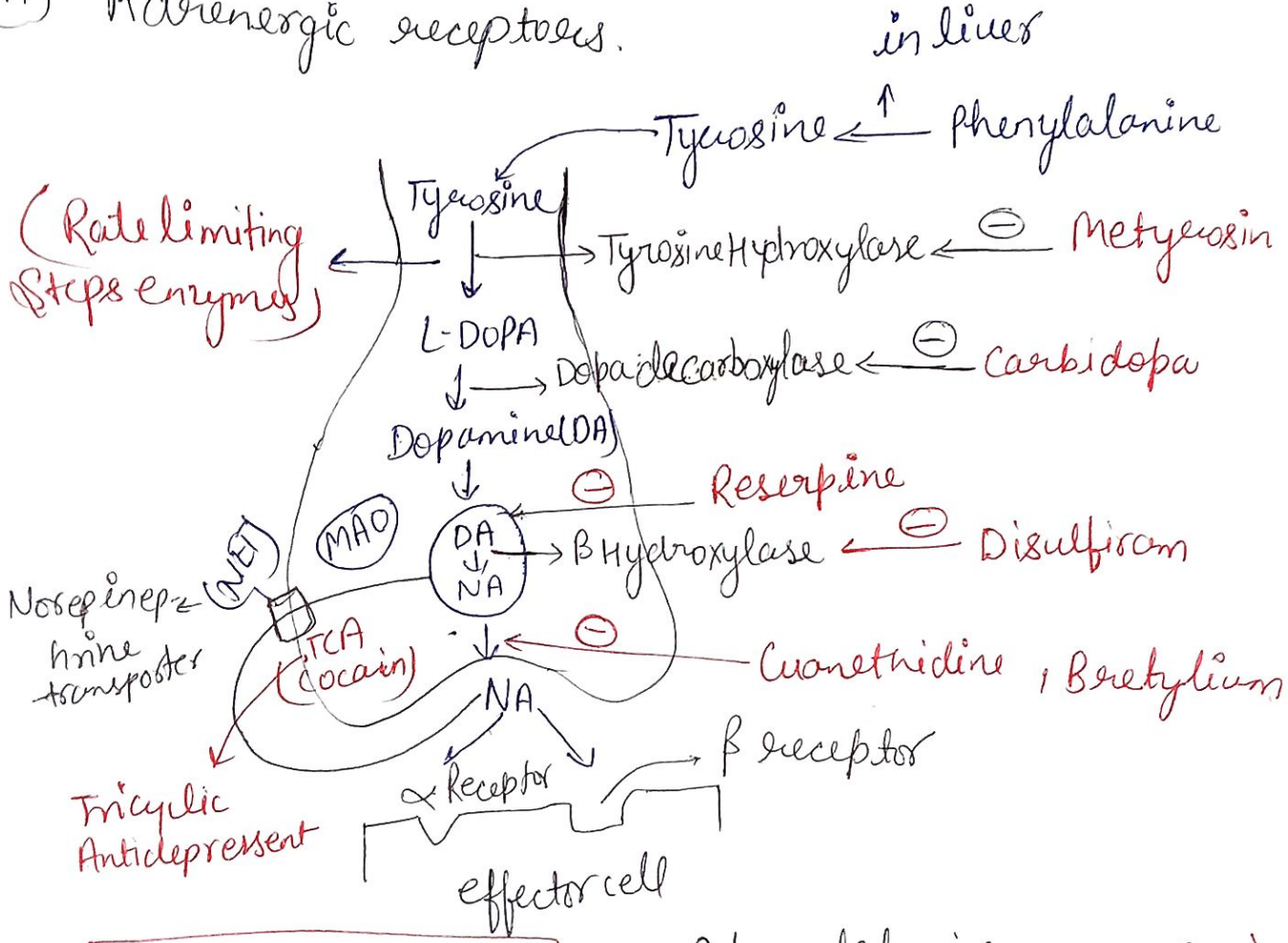
(i) Endogeneous catecholamines – (AND) → Dopamine.
Adrenaline
Noradrenaline

(ii) Exogeneous catecholamines – (ID) → Dobutamine.
Isoprenaline

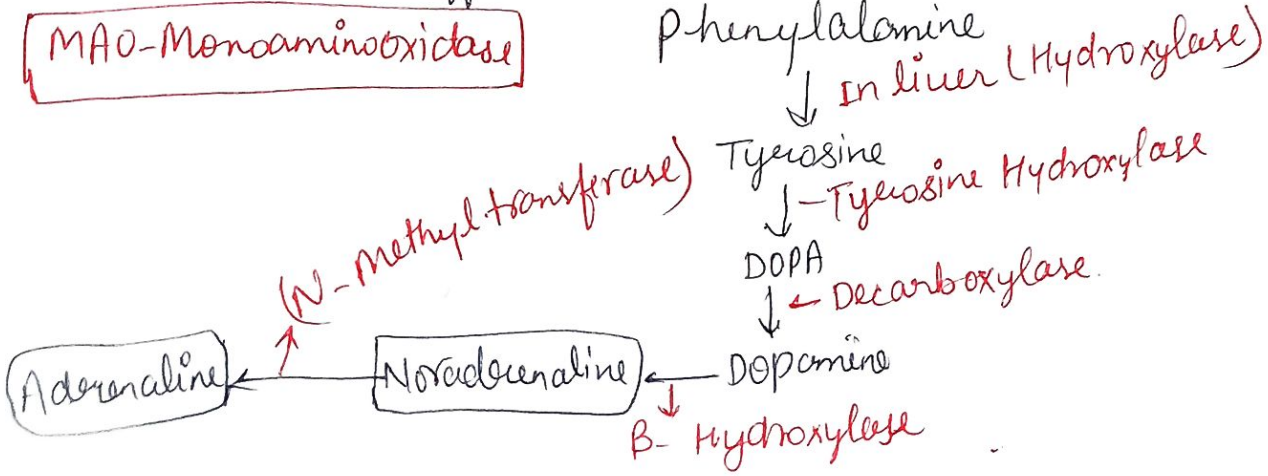
(iii) Non-catecholamine – TEAS → Salbutamol
Tyramine
Ephedrine
Amphetamine

Synthesis, Storage & Release of catecholamines :-

i) Synthesis of CAs
ii) Storage of CAs
iii) Release of CAs
iv) uptake of Catecholamines.
v) Metabolism of CAs
vi) Adrenergic receptors.



MAO-Monoaminooxidase



Adrenergic Receptors

- **α-Adrenergic Receptor**
  - α_1 (G_q) → Post Synaptic present → phospholipase Activation
  - α_2 (G_i) (autoreceptor) → Presynaptic present → (cAMP) decrease.
    - Blood
    - Liver
    - Glands — Secretion ↓
    - Eye
- **β-Adrenergic Receptor** (Gs)
  - β_1 → Heart
  - β_2 → Lungs
    - GIT
    - Uterus
    - Liver
    - Skeletal Muscle
    - Blood vessels
  - β_3 → Adipose Tissue
    - Coronary vessels
    - Urinary bladder

α_1 – ↑ IP_3/DAG → Ca^{++} → Contraction.

Adrenaline – α_1, α_2, β_1, β_2 and weak β_3 Action

Noradrenaline – α_1, α_2 ↑ β_1 agonist

Isoprenaline – β_1, β_2 ↑ β_3 Agonist

Dobutamide – β_1 agonist

Pharmacological Action:- (Active)

(i) **Eye:-** mydriasis dilates on Stimulation
ciliary vasodilation by stimulation of β_2 receptor
- ↓ secretion of aqueous humor

(ii) **Prosthetic Urethra** - less outflow of urine on Stimulation.

β_1:-

(iii) **Heart:-** HR on Stimulation (Tachycardia)

(iv) JG cells - Release renin (BP) on Stimulation.

β_2 :

(v) Bronchess :- Bronchodilation on stimulation.

(vi) GIT - Constipation.

(vii) Bladder - Relax

(viii) Uterus :- Relaxation

(ix) Skeletal Muscle and coronary artery blood vessels - Vasodilation

(x) liver :- Glucose production (glycogenolysis) (glycogen - glucose)

~~Skeletal Muscle~~

β_3 :- Adipose tissue :- Lipolysis.

Direct Sympathomimetics :- They act directly as agonist on α and β receptor.

Indirect Sympathomimetics :- They Act on adrenergic Neurons to release NA and Metabolism decreases.

Mixed Sympathomimetics :- They Act directly as well as indirectly.

Classification based on Therapeutic uses :-

AB CDE FG

A - Anaphylactic Shock

B - Bronchial Asthma

C - Cardiac resuscitation

D - Duration of Anaesthesia

E - Epistaxis (Control) (Nose bleeding)

F

G - Glaucoma

Adverse effect & Contraindications :-

- Transient restlessness, headache, palpitation, Anxiety tremor occurs after S.C / im. injection of Adrenaline
- Adrenaline is contraindicated Hypertensive, hyperthyroid & Angina patient.
- Adrenaline should not be given during anesthesia with halothane (risk of arrhythmias) not patient receiving B Blocker
- Marked rise in BP leading to cerebral hemorrhage, ventricular tachycardia, Angina, (CVS) problems - not given

Antiadrenergic Drugs (Sympatholytic):-

Sympatho → Sympathetic Nervous System

lytic (lysis) → oppose (Breakdown)

These are drugs which inhibit the effects of sympathomimetic drugs by blocking the receptor.

It is also known as - Anti adrenergic drugs
Adrenergic antagonist
Adrenergic blocker

β, α - Adrenergic Blocking drugs inhibit adrenergic responses mediated through the α adrenergic receptors. and also mediated through the β adrenergic receptors,

Pharmacological Actions :-

- α_1 Blockers :- Vasodilation and ↓B.P.
- α_2 Blockers :- Stimulates release of Nor-adrenaline ↓ Tachycardia.

Non-Selective

α-Blockers — produce Hypotension, tachycardia ↑eased cardiac output.

β_1 Blockers — decrease heart rate.

β_2 Blockers — Cause Bronchoconstriction

β_3 Blockers — Block lipolysis & glycogenolysis.

Therapeutic Uses :-

(i) α Blockers
- Hypertension
- Congestive Heart failure
- Peripheral vascular disease

(ii) β-Blockers
- Angina pectoris
- Mycocardial infarction
- Cardiac arythmias.
- Glaucoma.

Neuromuscular Blocking Agents :-

These are those agents or drugs which are used to Block the Neuromuscular Junction (NMJ) and inhibit the contraction of muscle and cause relaxation of muscles. They are also known as Skeletal muscle relaxant.

Uses:- Generally used for relaxation of muscle during operation.

- Impetuous symptoms such as muscle spasm, pain etc.
- Used as a alternate of anaesthetic.
- Used to curare — hunting Animals.

Mechanism of Action :-

Tubocurarine and other non-depolarizing blockers have quaternary compounds with two positively charged nitrogen. So, they have affinity to bind (Nm Nicotinic receptor) but have no intrinsic activity.

- Ach and these blockers fight for one place (receptor) and finally these blockers bind with receptor in place of Ach. So, Ach not bind with receptor → Nat channel not open → Depolarisation not occur. Therefore, the motor nerve impulse cannot transmit & contraction is stopped (prevent) Finally, Skeletal muscle relaxation occurs.

(i) **Non-depolarizing blockers :-** The first neuromuscular blocking drug was found- curare use by south American hunter to paralyse the Animals.
Used — d-tubocurarine (d-Tc)

Pharmacological Action –

(i) Skeletal muscle :- Induced flaccid paralysis.
Paralyse acc to this order - muscle of face → eye → finger → limb → neck.

(ii) Histamine release :- d-Tc has a greater tendency to liberate Histamine from mast cells.

(iii) Cardiovascular system :- d-Tc (d-Tubocurarine) produce hypotension due to histamine release.

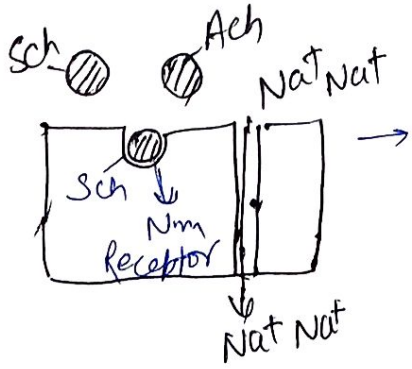
(iv) Respiratory ganglia :- Bronchospasm

(v) Autonomic Ganglia :- Overcome or reverse by use of Neostigmine and Pyridostigmine which ↑ease the availability of Ach (↑ease concentration) by inhibiting Acetylcholinesterase (enzyme).

Adverse effect :- Respiratory paralysis, Hypoxia, Hypotension, constipation.

(ii) Depolarizing blockers :- These are Non-competitive antagonist. Succinylcholine does not hydrolyzed by Acetylcholinesterase.

Mechanism :-



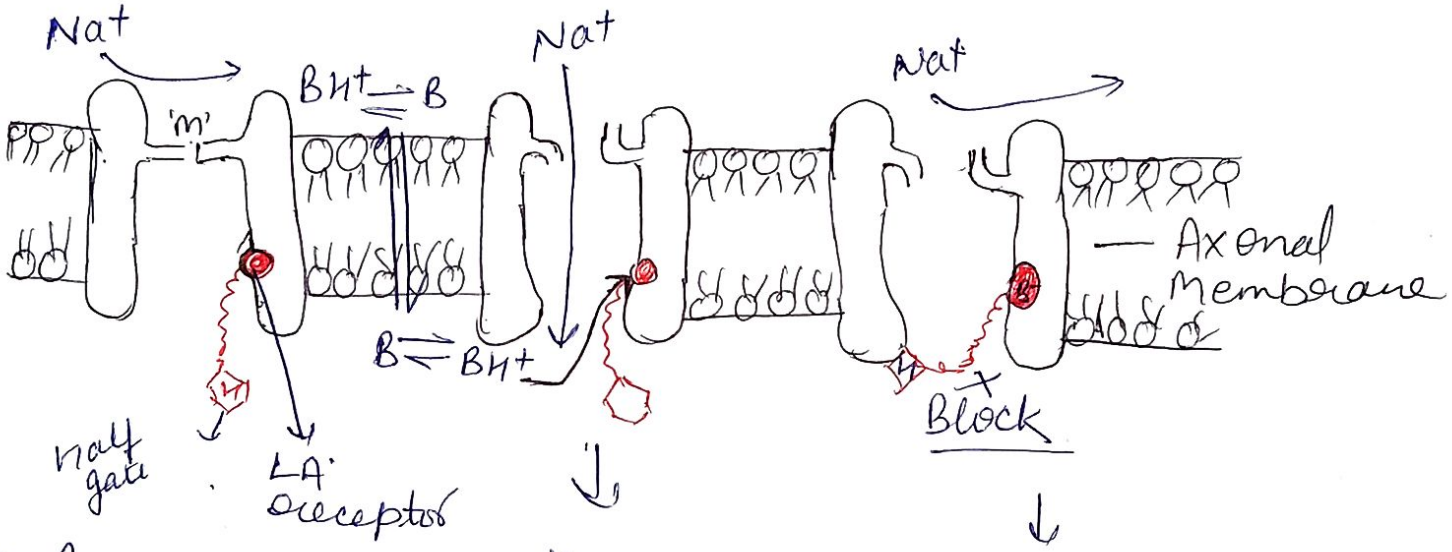
→ Continuous depolarisation
↓
Receptor desensitization
↓
also Na⁺ channel blocks
↓
Repolarisation fatigue
↓
Relaxed

Pharmacological Action :- • Muscle twitching - small muscle contraction.
• Muscle soreness (pain), Apnoea (Muscle & tissue in the throat relax (total blockage of airway that last for 10secs).

Local Anaesthetics :-

Anaesthetic → Those drugs which reduce sensation which further reduce pain. Reversible loss of sensation. (Sensation back after some time / work).
Eg :- Procaine, Lidocaine etc.

Mechanism :-



(i) Resting
(ii) Activated (Depolarisation occurs)
(iii) Inactivated Depolarisation stop → loss of sensation ↓ Reversibly

Uses :- Loss of sensation (reduce pain)
Nerve Block (Block voltage gated Na+ channel)

Adverse effects :- Hypotension, Redness of skin, Asthma etc.