Chapter-2
Pharmacology & Toxicology

D.Pharma 2nd Year Notes

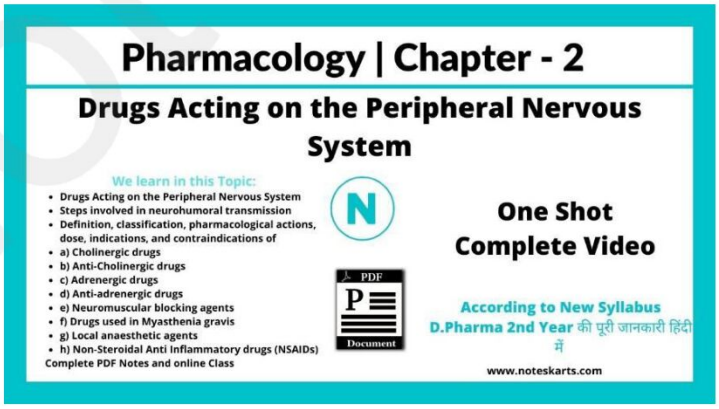
Chapter- 2

Drugs Acting on the Peripheral Nervous System

Steps involved in neurohumoral transmission

Definition, classification, pharmacological actions, dose, indications, and contraindications of

a) **Cholinergic drugs**
b) **Anti-Cholinergic drugs**
c) **Adrenergic drugs**
d) **Anti-adrenergic drugs**
e) **Neuromuscular blocking agents**
f) **Drugs used in Myasthenia gravis**
g) **Local anaesthetic agents**
h) **Non-Steroidal Anti Inflammatory drugs (NSAIDs)**



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Drugs Acting on the Peripheral Nervous System

- The peripheral nervous system consists of the nerves that branch out from the brain and spinal cord.
- These nerves form the communication network between the CNS and the body parts. The peripheral nervous system is further subdivided into the somatic nervous system and the autonomic nervous system.
- The somatic nervous system consists of nerves that go to the skin and muscles and is involved in conscious activities.
- The autonomic nervous system consists of nerves that connect the CNS to the visceral organs such as the heart, stomach, and intestines.

Neuro-Humoral Transmission:

- Neurohumoral transmission implies that nerves transmit their message across synapses and neuro-effector junctions by the release of humoral chemical) messengers.

Steps in neurohumoral transmission:

1. **Impulse conduction :**

- The resting membrane potential of a neuron is about -70 mV. This is because the axon's membrane allows a lot of potassium (K+) to pass through and there is a high concentration of K+ inside the cell, while it allows very little sodium (Na+) to pass through, and Na+ is actively pumped out of the neuron.
- When a neuron is stimulated or receives an electrical impulse, the membrane suddenly allows more Na+ to enter. This causes the inside of the neuron to become positive (about +20 mV), a process called depolarization.
- Then, K+ ions move out of the cell, making the inside negative again, which is called repolarization. During the refractory period, the Na+/K+ pump restores the normal distribution of these ions.
- The action potential (AP) that is generated causes local currents that open ion channels in the next part of the membrane (the next node of Ranvier in myelinated nerves), allowing the AP to move along the nerve without losing strength.

2. **Transmitter release:**

- The transmitter (excitory or inhibitory) is stored in prejunctional nerve endings within sympathetic vesicles. Nerve impulse promotes fusion of vesicular and neuronal membranes through Ca+2 entry which fluidizes membranes.
- All contents of the vesicle transmitter, enzymes and other proteins) are extruded (exocytosis) in the junctional cleft. The release process can be modulated by the transmitter itself and by other agents through activation of specific receptors located on the prejunctional membrane.

Example : Noradrenaline (NA) release is inhibited by NA (receptor), dopamine, adenosine, prostaglandins and enkephalins while isoprenaline (B2 receptor) and angiotensin AT1 receptor) increase NA release.

3. **Transmitter action on post junctional membrane:**

- The released transmitter combines with specific receptors on the post junctional membrane and depending on its nature induces an excitatory postsynaptic potential (EPSP) or an inhibitory postsynaptic potential (IPSP).

a) **EPSP:** Increase in permeability to all cations > Na^+ or $Ca2^+$ influx (through fast or slow channels) causes depolarization followed by K^+ efflux. These ionic movements are passive as the flow is down the concentration gradients.

b) **IPSP:** Increase in permeability to smaller ions, i.e. K^+ and Cl- (hydrated K^+ ion is smaller than hydrated Na^+ ion) only, so that K^+ moves out and Cl- moves in (in the direction of their concentration gradients) resulting in hyper-polarization.

4. **Post junctional activity:**

- A suprathreshold EPSP generates a propagated post junctional AP which results in nerve impulse (in neurone), contraction (in muscle) or secretion (in gland). An IPSP stabilizes the post junctional membrane and resists depolarizing stimuli.

5. **Termination of transmitter action :**

- Following its combination with the receptor, the transmitter is either locally degraded (e.g. ACh) or is taken back into the pre-junctional neurone by active uptake or diffuses away (e.g. NA,GABA).

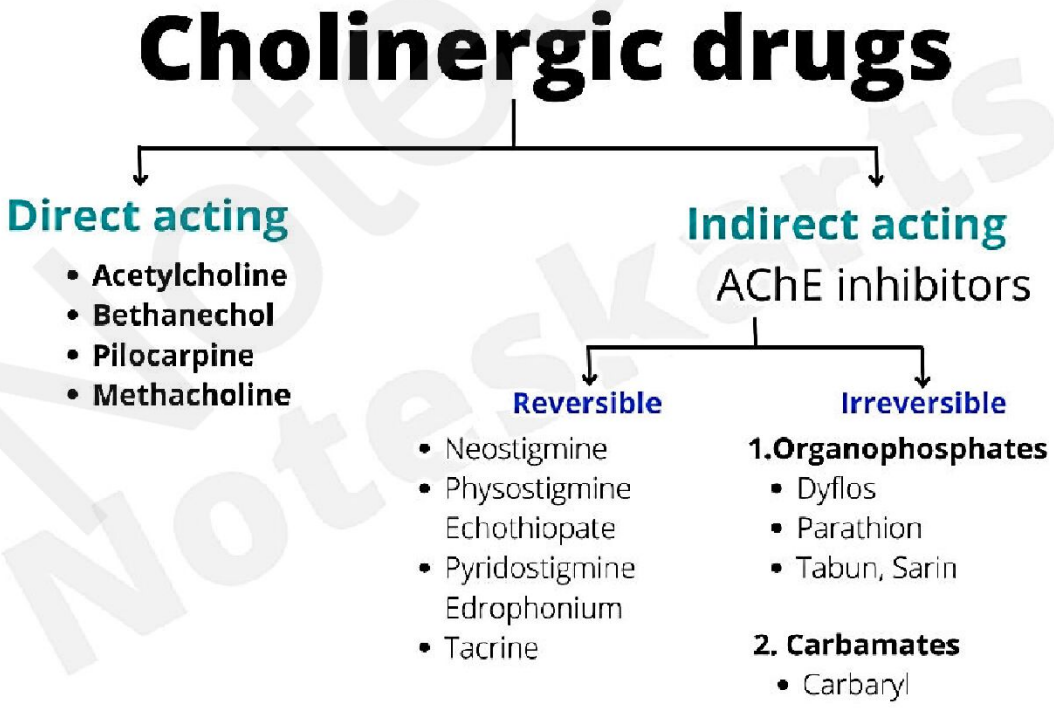
a) Cholinergic drugs:

- These are the drugs which produces actions similar to that of ACh, either by directly or indirectly interacting with cholinergic receptors or by increasing availability of Ach at these sites (anticholinesterases).

Or

- Cholinergic drugs, also known as cholinomimetics, are a type of autonomic nervous system drug that mimic the actions of acetylcholine (ACh), a neurotransmitter in the parasympathetic nervous system.
- ACh is released from nerve endings and binds to receptors on cell membranes in organs, tissues, and glands. Cholinergic drugs can be used to treat conditions and symptoms of the nervous system that maintain normal body function.
- They can also be used to block messages and reduce unwanted or harmful responses.

Classification Of Cholinergic Drugs:



Pharmacological actions of Cholinergic drugs:

A. Muscarinic actions:

a. Heart

- ACh hyperpolarizes the SA nodal cells and decreases their rate of diastolic depolarization. As a result, rate of impulse generation is reduced-bradycardia or even cardiac arrest may occur.
- At the A-V node and His-Purkinje fibres refractory period (RP) is increased and conduc tion is slowed: P-R interval increases and partial to complete A-V block may be produced.
- The force of atrial contraction is markedly reduced and RP of atrial fibres is abbreviated. Due to nonuniform vagal innervation, the intensity of effect on RP and conduction of different atrial fibres varies-inducing inhomogeneity and pre disposing to atrial fibrillation or flutter.
- Ventricular contractility is also decreased but the effect is not marked. The cardiac muscarinic receptors are of the M, subtype.

b. Smooth muscle

- Smooth muscle in most organs is contracted (mainly through M, recep tors). Tone and peristalsis in the gastrointestinal tract is increased and sphincters relax →abdominal cramps and evacuation of bowel.
- Peristalsis in ureter is increased.
- The detrusor muscle contracts while the bladder trigone and sphincter relaxes → voiding of bladder.
- Bronchial muscles constrict, asthmatics are highly sensitive → bronchospasm, dyspnoea, precipitation of an attack of bronchial asthma.

c. Glands

- Secretion from all parasympathe tically innervated glands is increased via M and some M, receptors: sweating, salivation, lacrimation, increased tracheobronchial and gastric secretion.
- The effect on pancreatic and intestinal glands is not marked. Secretion of milk and bile is not affected.

d. Eye

- Contraction of circular muscle of iris resulting in miosis.

- Contraction of ciliary muscle causing spasm of accommodation, increased aqueous outflow facility, reduction in intraocular tension (especially in glaucomatous patients).

B. Nicotinic actions

1. **Autonomic ganglia** Both sympathetic and parasympathetic ganglia are stimulated. This effect is manifested at higher doses. High dose of ACh given after atropine causes tachycardia and rise in BP due to stimulation of sympathetic ganglia and release of catecholamines.
2. **Skeletal muscles** Iontophoretic application of ACh to muscle endplate causes contraction of the fibre. Intraarterial injection of high dose can cause twitching and fasciculations, but I.V. injection is generally without any effect (due to rapid hydrolysis of ACh).
3. **CNS actions** ACh injected i.v. does not penetrate blood-brain barrier and no central effects are seen. However, direct injection into the brain produces arousal response followed by depression. Cholinergic drugs which enter brain produce complex behavioral and neurological effects.

Indications

- Indirect-acting cholinergic agonists are indicated for the following medical conditions:
- Treatment of myasthenia gravis, antidote for nondepolarizing neuromuscular junction blockers, increased survival after exposure to nerve gas
- Treatment of mild to moderate Alzheimer's disease.

Contraindications and Cautions

The following are contraindications and cautions for the use of indirect-acting cholinergic agonists:

- Allergy
- Bradycardia, intestinal/urinary tract obstruction.
- Pregnancy
- Asthma, coronary disease, peptic ulcer, arrhythmias, epilepsy, parkinsonism.
- Hepatic or renal dysfunction.

Pilocarpine:

Definition: Pilocarpine is a cholinergic agonist that acts at the same site as the neurotransmitter acetylcholine (ACh). It increases the activity of ACh receptor sites throughout the body.

Pharmacological Actions: Pilocarpine stimulates muscarinic receptors, leading to effects such as increased salivation, sweating, and miosis (constriction of the pupils).

Dose: The dose varies depending on the condition being treated. For dry mouth due to Sjogren's syndrome, the usual dose is 5 mg three times a day.

Indications:

- Dry mouth caused by radiotherapy in head and neck cancer patients.
- Dry mouth in patients with Sjogren's syndrome.
- Glaucoma (to reduce intraocular pressure).

Contraindications:

- Hypersensitivity to pilocarpine.
- Uncontrolled asthma.
- Cardiovascular disease.

Adverse Effects: Sweating, salivation, nausea, and blurred vision.

Neostigmine:

- **Definition**: Neostigmine is an indirect-acting cholinergic agonist used for myasthenia gravis and to reverse neuromuscular junction blocker effects.
- **Pharmacological Actions**: Neostigmine inhibits acetylcholinesterase, leading to increased ACh availability at neuromuscular junctions.
- **Dose**: The dose varies based on the specific indication. For myasthenia gravis, the usual dose is 15-375 mcg/kg every 3-4 hours.
- **Indications**:
    - Myasthenia gravis (to improve muscle strength).
    - Reversal of neuromuscular blockade after surgery.
- **Contraindications**:
    - Hypersensitivity to neostigmine.

- Mechanical intestinal or urinary obstruction.

Tacrine:

- **Definition**: Tacrine is an indirect-acting cholinergic agonist used for Alzheimer's disease.
- **Pharmacological Actions**: Tacrine inhibits acetylcholinesterase, increasing ACh levels in the brain.
- **Dose**: The initial dose is 10 mg four times a day, gradually increasing to 40 mg/day.
- **Indications**: Alzheimer's disease (to improve cognitive function).
- **Contraindications**:
  - Hypersensitivity to tacrine.
  - Liver dysfunction.
- **Adverse Effects**: Nausea, vomiting, diarrhea, and hepatotoxicity.

b) Anti-Cholinergic drugs:

- The Anti-Cholinergic drugs is restricted to those which block actions of ACh on automatic effectors and in the CNS exerted through muscarinic receptors.

Classification of Anti-Cholinergic drugs:

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, Pipenzolate methyl bromide, Isopropamide, Glycopyrrolate.

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

(c) **Vasicoselective:** Oxybutynin, Flavoxate, Tolterodine.

(d) **Antiparkinsonian:** Trihexyphenidyl (Benzhexol), Procyclidine, Biperiden.

1. **Atropine**:
   - **Definition**: Atropine is a tropane alkaloid and anticholinergic medication.
   - **Pharmacological Actions**:
     - Inhibits parasympathetic nerve impulses.
     - Increases heart rate.
     - Reduces salivation and other secretions.
     - Causes pupil dilation (mydriasis).
     - Relaxes smooth muscles of the gastrointestinal and urinary tracts.

Dose:

- Typically given intravenously or by injection into a muscle.

- Dosage varies based on the specific indication.

- **Indications**:
  - Poisoning (nerve agents, pesticides).
  - Bradycardia.
  - Surgical procedures (to reduce saliva).
- **Contraindications**:
  - Hypersensitivity to atropine.
  - Glaucoma.
  - Urinary retention.
  - Cardiac arrhythmias.
  - Caution in elderly patients due to risk of overdose.

2. **Hyoscine (Scopolamine)**:
   - **Definition**: Hyoscine is an anticholinergic medication.
   - **Pharmacological Actions**:
     - Inhibits muscarinic acetylcholine receptors.
     - Reduces motion sickness by acting on the central nervous system.
     - Decreases salivation and gastrointestinal secretions.
     - Causes sedation and amnesia..
   - **Dose**:
     - Available as a patch (1.5 mg) applied behind the ear every 72 hours.
   - **Indications**:
     - Motion sickness.
     - Nausea.
   - **Contraindications**:

- Hypersensitivity to hyoscine.
- Caution in cognitive side effects.

3. **Procyclidine**:
   - **Definition**: Procyclidine is an anticholinergic medication.
   - **Pharmacological Actions**:
     - Blocks central and peripheral muscarinic receptors.
     - Reduces muscle stiffness and tremors.
     - Improves motor function in Parkinson's disease.
   - **Dose**:
     - Initially 5 mg daily, then adjusted based on response.
     - Maintenance dose: 5–15 mg daily in divided doses.
   - **Indications**:
     - Parkinson's disease.
     - Extrapyramidal symptoms due to antipsychotic drugs..
   - **Contraindications**:
     - Hypersensitivity to procyclidine.

4. **Oxybutynin**:
   - **Definition**: Oxybutynin is an anticholinergic medication.
   - **Pharmacological Actions**:
     - Blocks muscarinic receptors in the bladder.
     - Reduces bladder muscle spasms.
     - Increases bladder capacity.
   - **Dose**:
     - Oral tablets or syrup.
     - Dosage varies based on individual response.

- **Indications**:
  - Overactive bladder.
- **Contraindications**:
  - Hypersensitivity to oxybutynin.
  - Urinary retention.
  - Glaucoma.
  - Caution in elderly patients due to risk of adverse effects.

5. **Cyclopentolate**:
   - **Definition**: Cyclopentolate is an anticholinergic medication.
   - **Pharmacological Actions**:
     - Blocks muscarinic receptors in the eye.
     - Causes pupil dilation (mydriasis).
     - Paralyzes the ciliary muscle (cycloplegia).
   - **Dose**:
     - Eye drops (1% concentration).
     - Titrate as necessary/tolerated.
   - **Indications**:
     - Eye examinations (pupil dilation).
   - **Contraindications**:
     - Hypersensitivity to cyclopentolate.
     - Angle-closure glaucoma.
6. **Tolterodine**:
   - **Definition**: Tolterodine is an anticholinergic medication.
   - **Pharmacological Actions**:
     - Blocks muscarinic receptors in the bladder.
     - Reduces bladder muscle contractions.
     - Increases bladder capacity.

- **Dose**:
  - Oral tablets.
  - Dosage varies based on individual response.
- **Indications**:
  - Overactive bladder with symptoms of urinary frequency, urgency, or urge incontinence.
- **Contraindications**:
  - Hypersensitivity to tolterodine.
  - Urinary retention.
  - Gastric retention.
  - Caution in patients with reduced liver function.

c) Adrenergic drugs:

- Adrenergic drugs are medications that stimulate certain nerves in your body.
- They do this either by mimicking the action of the chemical messengers epinephrine and norepinephrine or by stimulating their release.
- These drugs are used in many life-threatening conditions, including cardiac arrest, shock, asthma attack, or allergic reaction.

Classification Of Adrenergic Drugs:

1. **Direct sympathomimetics:** They act directly as agonists on α and/or β adrenoceptors— Adr, NA, Isoprenaline (Iso), Phenylephrine, Methoxamine, Xylometazoline, Salbutamol and many others.

   Eg: Epinephrine or Norepinephrine

2. **Indirect sympathomimetics:** They act on adrenergic neurone to release NA, which then acts on the adrenoceptors— **Eg:** Tyramine, Amphetamine.

3. **Mixed action sympathomimetics:** They act directly as well as indirectly— **Eg:** ephedrine, dopamine, mephentermine.

Pharmacological Action:

α actions	*β actions*
1. Constriction of arterioles and veins → rise inBP (α_1 + α_2)	Dilatation of arterioles and veins → fall in BP (β_2)
2. Heart—little action, arrhythmia at high dose (α_1)	Cardiac stimulation (β_1), ↑ rate, force and conduction velocity
3. —	Bronchodilatation (β_2)
4. Contraction of radial muscles of iris → mydriasis (α_1), decreased aqueous secretion	No effect on iris, slight relaxation of ciliary muscle, Enhanced aqueous secretion
5. Intestinal relaxation, contraction of sphincters	Intestinal relaxation (β_2)
6. Bladder trigone—contraction (α_1)	Detrusor—relaxation (β_2)
7. Uterus—contraction (α_1)	Relaxation (β_2)
8. Splenic capsule—contraction (α_1)	Relaxation (β_2) (slight)
9. Neuromuscular transmission facilitated, ↑ ACh release	Active state—prolonged in fast contracting muscle, abbreviated in slow contracting muscle; tremors (β_2)
10. Insulin secretion inhibited (α_2) (dominant)	Augmented insulin (mild) and glucagon secretion (β_2)
11. Liver—glycogenolysis (α in some species)	Liver—glycogenolysis (β_2) → hyperglycaemia Muscle—glycogenolysis (β_2) → hyperlactacidaemia Fat—lipolysis (β_1 + β_2 + β_3) → increased blood FFA, calorigenesis
12. —	Renin release from kidney (β_1)
13. Male sex organs—ejaculation (α_1)	—
14. Salivary gland—K^+ and water secretion (α_1)	Ptylin secretion
15. —	ADH secretion from posterior pituitary (β_1)
16. Nictitating membrane—contraction (in animals)	—

Salbutamol

Salbutamol is a beta-2 adrenergic receptor agonist used to treat asthma, bronchitis, COPD, as well as prevent exercise induced bronchospasms.

Mechanism of action:

- Salbutamol stimulate β2 adrenergic receptors which are predominant receptors in bronchial
- smooth muscle (β2-receptors are present in human heart in a concentration between 10% and 50%).
- Stimulation of β2 receptors leads to the activation of enzyme adenyl cyclase that form cyclic AMP (adenosine-mono-phosphate) from ATP (adenosine-tri-phosphate).

Dose

- The usual dose of oral salbutamol is 2 to 4 mg three times a day in adult and 1 to 2 mg three times a day in children.

Adverse effect / Indication:

- The most common adverse reactions associated with use of salbutamol inhalation aerosol are palpitations (occurring in less than 10% of patients, anxiety (less than 10%), tremors (less than 15% of patients) and increased blood pressure (approximately 5%), occasionally resulting in hypertension.
- The most common adverse reactions to salbutamol tablets or syrup are tremors (occurring in 10-20% of patients) and anxiety (9- 20%).

Contraindication:

- Salbutamol and Pregnancy
- Caution when used during pregnancy.
- Either studies in animals have revealed adverse effects on the foetus (teratogenic or embryocidal or other) and there are no controlled studies in women or studies in women and animals are not available.
- Drugs should be given only if the potential benefit justifies the potential risk to the foetus.

d) Anti-adrenergic drugs:

- These are drugs which antagonize the receptor action of adrenaline and related drugs.
- They are competitive antagonists at α or β or both α and β adrenergic receptors and differ in important ways from the "adrenergic neurone blocking agents", which act by interfering with the release of adrenergic transmitter on nerve stimulation.

Classification of Antiadrenergic Drugs:

I. **Nonequilibrium type**

(i) β-Haloalkylamines— Phenoxybenzamine.

II. **Equilibrium type (competitive)**

A. **Nonselective**

(a) Ergot alkaloids— Ergotamine, Ergotoxine
(b) Hydrogenated ergot alkaloids— Dihydroergotamine (DHE), Dihydroergotoxine
(c) Imidazoline— Phentolamine
(d) Miscellaneous– Chlorpromazine

B. **α1 selective:** Prazosin, Terazosin, Doxazosin, Alfuzosin, Tamsulosin

C. **α2 selective**: Yohimbine

Phenoxybenzamine

- Phenoxybenzamine is used to treat episodes of high blood pressure and sweating related to pheochromocytoma.

Dose:

- 20–60 mg/day oral; 1 mg/kg by slow i.v. infusion over 1 hour; used primarily in pheochromocytoma, occasionally in secondary shock and peripheral vascular disease.
- FENOXENE 10 mg cap, 50 mg/ml inj. BIOPHENOX 50 mg in 1 ml inj.

Indication:

- Phenoxybenzamine is indicated for the control of episodes of hypertension and sweating that occur with a disease called pheochromocytoma.

- If tachycardia is excessive, it may be necessary to use a beta- blocking agent concomitantly.

Contraindication:

- Nasal congestion
- Dizziness
- Upset stomach
- Sexual dysfunction (difficulty ejaculating)
- Dizziness

Dihydroergotamine

Definition: Dihydroergotamine is an ergot alkaloid derivative used primarily for the treatment of migraine headaches.

Pharmacological Actions:

- Acts as a vasoconstrictor by stimulating alpha-adrenergic and serotonin (5-HT1) receptors.
- Reduces neurogenic inflammation associated with migraines.
- Alters pain perception through central nervous system effects.

Dose:

- For migraine:
  - Nasal spray: 1 spray (0.5 mg) in each nostril, may repeat after 15 minutes if needed, not exceeding 4 sprays (2 mg) in a 24-hour period or 8 sprays (4 mg) per week.
  - Injection: 1 mg IV/IM/SC, may repeat every hour as needed, up to a total dose of 3 mg in 24 hours or 6 mg per week.

Indications:

- Acute treatment of migraine headaches with or without aura.
- Cluster headaches.

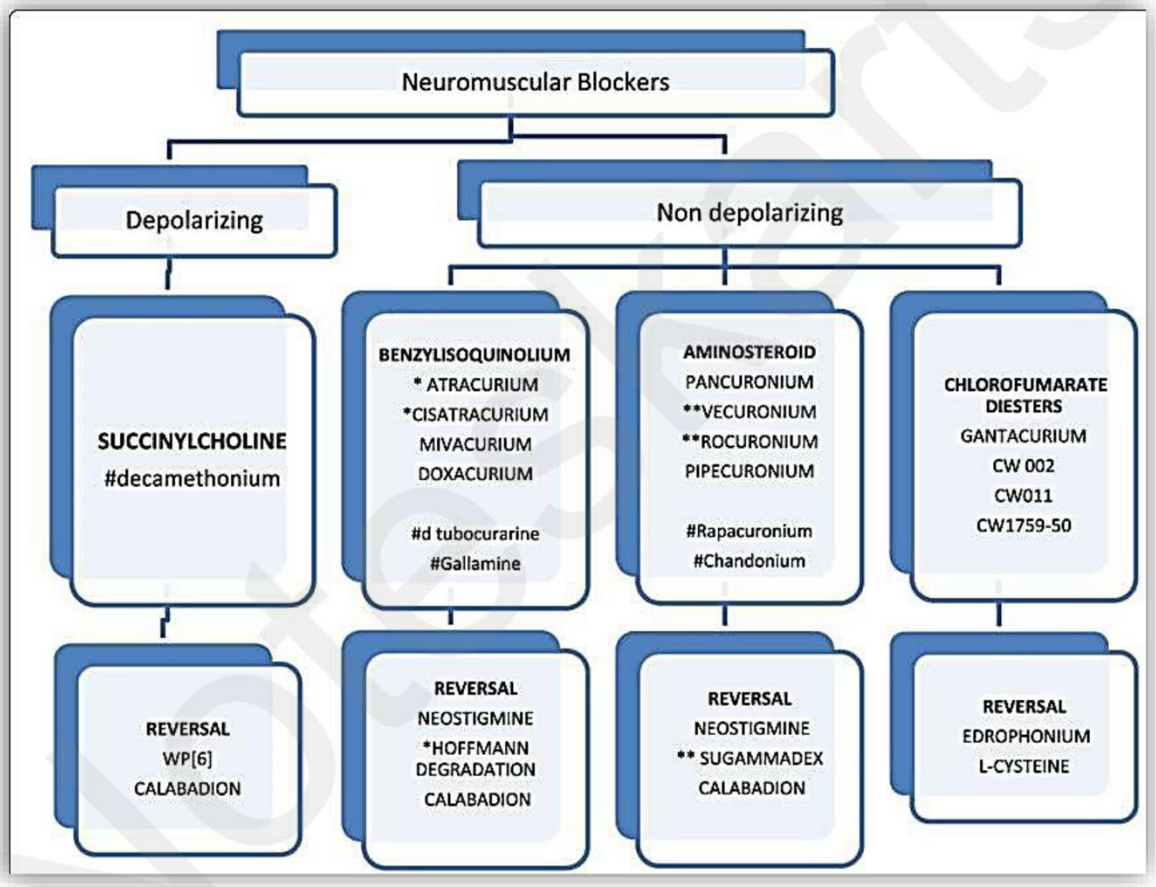
Contraindications:

- Uncontrolled hypertension.
- Coronary artery disease, peripheral vascular disease,
- Severe hepatic or renal impairment.
- Pregnancy and breastfeeding.

e) Neuromuscular blocking agents

- Neuromuscular blocking agents are potent muscle relaxants typically only used during surgery to prevent muscle movement.
- They are structurally related to acetylcholine (the main neurotransmitter in the body) and they cause muscle relaxation by binding to acetylcholine receptors postsynaptically (which prevents acetylcholine from binding).
- This blocks neuromuscular transmission and causes paralysis of the muscle.

Classification:



Dose:

Table 1. Pharmacokinetics of Neuromuscular Blockers

Agent	Dosing	Time to Peak (min)	Duration of Action (min)	Metabolism	Side Effects
			NONDEPOLARIZING		
Aminosteroids					
Pancuronium	0.05-0.1 mg/kg bolus; 0.8-1.7 mcg/kg/min infusion	2-3	60-100	Renal	Tachycardia, hypotension, and increased cardiac output
Vecuronium	0.08-0.1 mg/kg bolus; 0.8-1.7 mcg/kg/min infusion	3-4	20-45 (prolonged as active metabolite builds up)	Hepatic via hydrolysis, then bile; metabolites excreted renally	Hemodynamic instability
Rocuronium	0.6-1 mg/kg bolus; 8-12 mcg g/kg/min infusion; RSI: 1-1.2 mg/kg bolus	1-2	20-35 for bolus dose; 60-80 for RSI dose	Hepatic; no active metabolites	NA
Benzylisoquinoliniums					
Atracurium	0.4-0.5 mg/kg bolus; 5-20 mcg g/kg/min infusion	3-4	20-35	Hoffmann reaction	Seizures associated with neurotoxic metabolite (laudanosine), hypotension (histamine release)
Cisatracurium	0.1-0.2 mg/kg bolus; 3 mcg g/kg/min initial infusion; 1-2 mcg g/kg/min maintenance infusion	2-3	30-60	Hoffmann reaction	Bronchospasm
			DEPOLARIZING		
Succinylcholine	1 mg/kg bolus; infusions rarely used	<1	5-10	Plasma cholinesterase	Bradycardia, malignant hyperthermia, and hyperkalemia

f) Drugs used in Myasthenia gravis:

Myasthenia Gravis:

- Myasthenia gravis (MG) is a chronic autoimmune disorder in which antibodies destroy the communication between nerves and muscle, resulting in weakness of the skeletal muscles.
- Myasthenia gravis affects the voluntary muscles of the body, especially those that control the eyes, mouth, throat and limbs.
- It is an autoimmune disorder affecting about 1 in 10,000 population, due to development of antibodies directed to the nicotinic receptors (NR) at the muscle endplate.
- The number of free Nm cholinoceptors may be reduced to 1/3 of normal or less and structural damage to the neuromuscular junction.

Symptoms:

Symptoms of myasthenia gravis may include:

- Muscle weakness in your arms, hands, fingers, legs and neck.
- Fatigue.
- Droopy eyelids (ptosis).
- Blurry or double vision.
- Limited facial expressions.

Drug Used In Myasthenia Gravis:

1. Cholinesterase Inhibitors:

- **Pyridostigmine:**
- This is the most commonly used cholinesterase inhibitor. It works by inhibiting the breakdown of acetylcholine, thereby increasing its availability at the neuromuscular junction and improving muscle strength.
- Pyridostigmine is usually administered orally and may be adjusted based on individual response and tolerance.

2. Neostigmine:

- Neostigmine is a cholinesterase inhibitor, prescribed for Myasthenia Gravis.
- It inhibits the chemicals, which brings non-communication between the nervous and the muscular system. Neostigmine enhances the muscular movements in case of Myasthenia Gravis condition.

Dose: 0.5-2.5mg I.M./S.C. 15-30 mg orally

Indications:

- Muscle relaxant - reversal of non depolarising Muscle relaxant.
- Myasthenia gravis

Contraindications:

- Contraindications of neostigmine include hypersensitivity to neostigmine and peritonitis or mechanical obstruction of the intestinal or urinary tract.

3. Immunosuppressant:

- Use these drugs to suppress the immune system to decrees the formation of antibodies.
- Eg. Cyclosparine A, Methotrexate, Azathioprine, etc.

4. Plasmapheresis: (Plasma exchange)

- The plasma of the blood is exchange with substitute plasma, So Antibodies remove from body and immune system does not attack the body's own tissue.

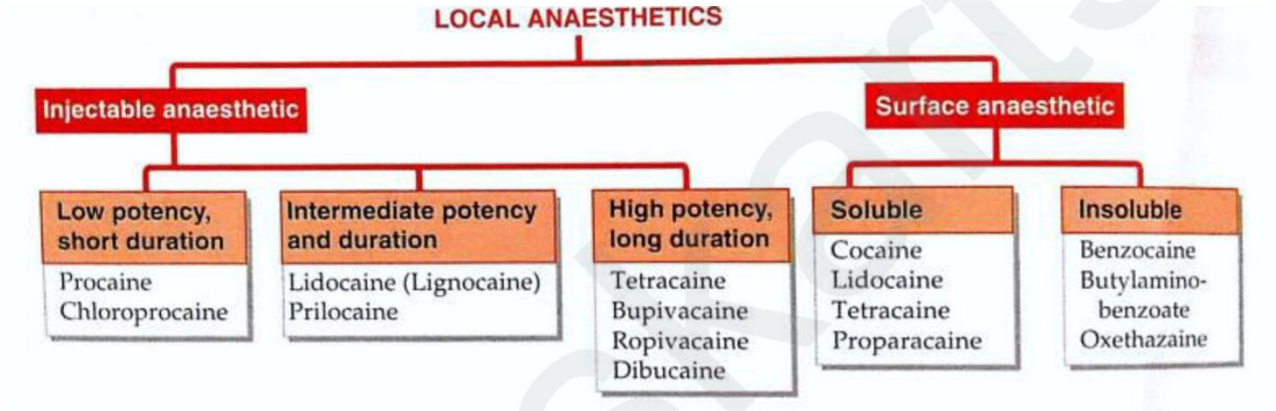
g) Local Anaesthetic agents

- Local anaesthetics are drugs which upon topical application or local injection cause reversible loss of sensory perception, especially of pain, in a restricted area of the body.

Or

- Local Anesthetic are those drugs which blocks the neuronal condition at local particular area. And it is helpful for miner surgery.

Classification of Local Anesthetic agents:



Procaine:

- A medication used as a **local anesthetic** to numb a specific area of the body. It was one of the first synthetic substitutes for cocaine.

Medical Uses:

- Procaine has been used in various medical procedures, including:
- Dental anesthesia (less common today due to better alternatives)
- Infiltration anesthesia for minor surgeries
- Spinal anesthesia (limited use due to potential allergic reactions)

Adverse Effects: Procaine can cause side effects, including:

- Allergic reactions (rare)
- Dizziness
- Headache
- Nausea and vomiting
- Nervous system problems (in high doses)

Lidocaine:

- A widely used medication that acts as a **local anesthetic** to numb a specific area of the body. It is considered a safer and more effective alternative to procaine.

Medical Uses:

Lidocaine is commonly used in various medical procedures, including:

Dental anesthesia

- Topical anesthetic for minor skin procedures (e.g., stitches, injections)
- Treatment of certain heart rhythm problems

Adverse Effects: Lidocaine can cause side effects, including:

- Dizziness
- Lightheadedness
- Drowsiness
- Numbness or tingling at the injection site
- Seizures (in high doses)

Benzocaine:

- A medication used as a **topical anesthetic** to numb the surface of the skin or mucous membranes for temporary pain relief.

Medical Uses: Benzocaine is found in various over-the-counter products, including:

- Lozenges for sore throat relief
- Teething creams for infants (use with caution and as directed by a healthcare professional)
- Topical ointments for minor skin irritations (e.g., sunburn, insect bites)

Adverse Effects: Benzocaine can cause side effects, including:

- Allergic reactions (skin rash, itching, swelling)
- Methemoglobinemia (a serious condition in which the blood's ability to carry oxygen is impaired) in rare cases, especially with overuse

Dose:

Comparative features of commonly used local anaesthetics

Drug	Surface anaesthesia	Nerve block					Cardio-toxicity
		Relative potency	Conc. used (%)	Max. dose	Onset	Duration (Min)	
Lidocaine	+	1	0.5–2.0	300 mg	Fast	60–120	+
Bupivacaine	–	4–5	0.25–0.5	150 mg	Interm.	120–360	+++
Ropivacaine	–	3–4	0.25–0.75	200 mg	Slow	120–300	++

Indications:

- Local anesthesia is given to reduce the stress associated with surgery, and to provide pain relief after surgery.
- More commonly, it is used for pain caused by hemorrhoids, fissures, insect bites, and minor burns.
- It is applied topically for these conditions. It is also indicated for vaginal, rectal and otological examinations, cystoscopy, and catheterization.

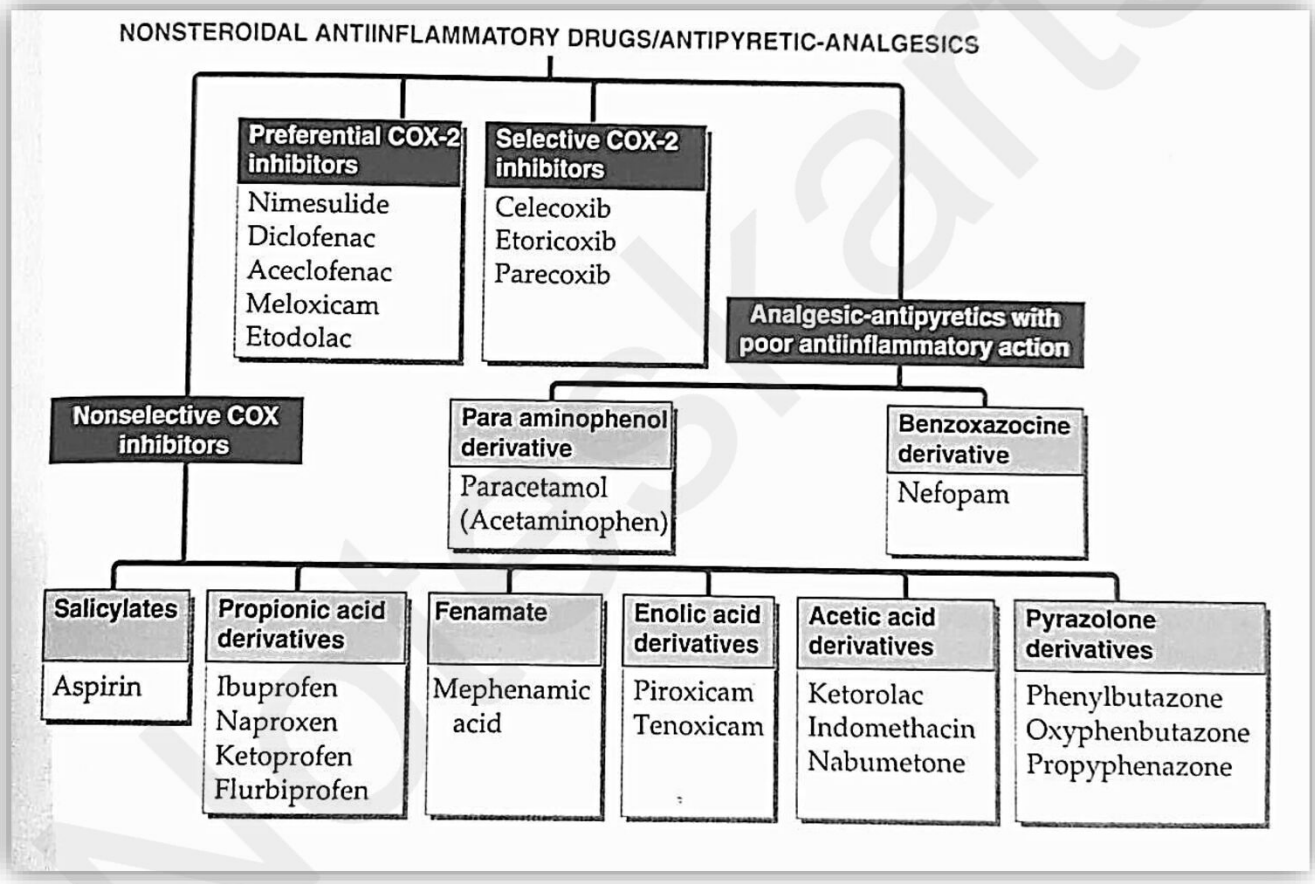
Contraindications:

- Convulsions, tremors, dizziness, blurred vision, nervousness, nausea
- Cardiovascular collapse and cardiac arrest may also occur in some cases
- Paralysis of the injected area.

h) Non-steroidal anti-inflammatory drugs (NSAIDs)

- The nonsteroidal anti-inflammatory drugs (NSAIDs) and antipyretic analgesics are a class of drugs that have analgesic, antipyretic and anti-inflammatory actions in different measures. In contrast to morphine they do not depress CNS.
- They are also called nonnar cotic, nonopioid or aspirin-like analgesics.

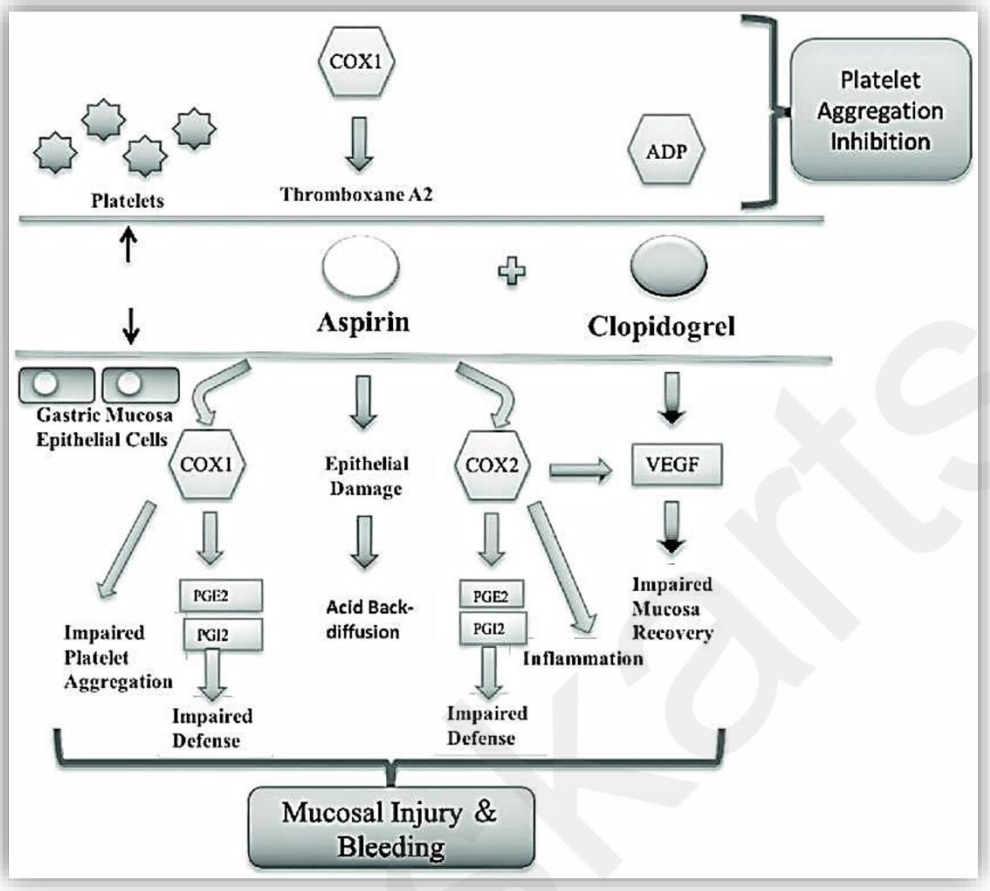
Classification:



Aspirin

- Aspirin is acetylsalicylic acid. It is rapidly converted in the body to salicylic acid which is responsible for most of the action.
- It used to treat pain, fever, inflammation, migraines, and reducing the risk of major adverse cardiovascular events.

Pharmacological Action:



Indication:

Used in Pain, fever, and inflammation cold, neck and back pain, dysmenorrhea, headache, tooth pain, sprains, fractures, myositis, neuralgia, synovitis, arthritis, bursitis, burns, and various injuries.

Contraindication:

- Sensitive Persons
- Children with viral diseases
- Peptic ulcer disease and bleeding disorders
- Chronic liver diseases
- Diabetes, CHF and juvenile Rh. Arthritis
- G-6-PD deficient persons
- Stop prior to surgery, near term pregnancy, breast feeding mothers etc.