Unit-3

Pharmacology-I

B.Pharma 4st Sem Notes

UNIT- III

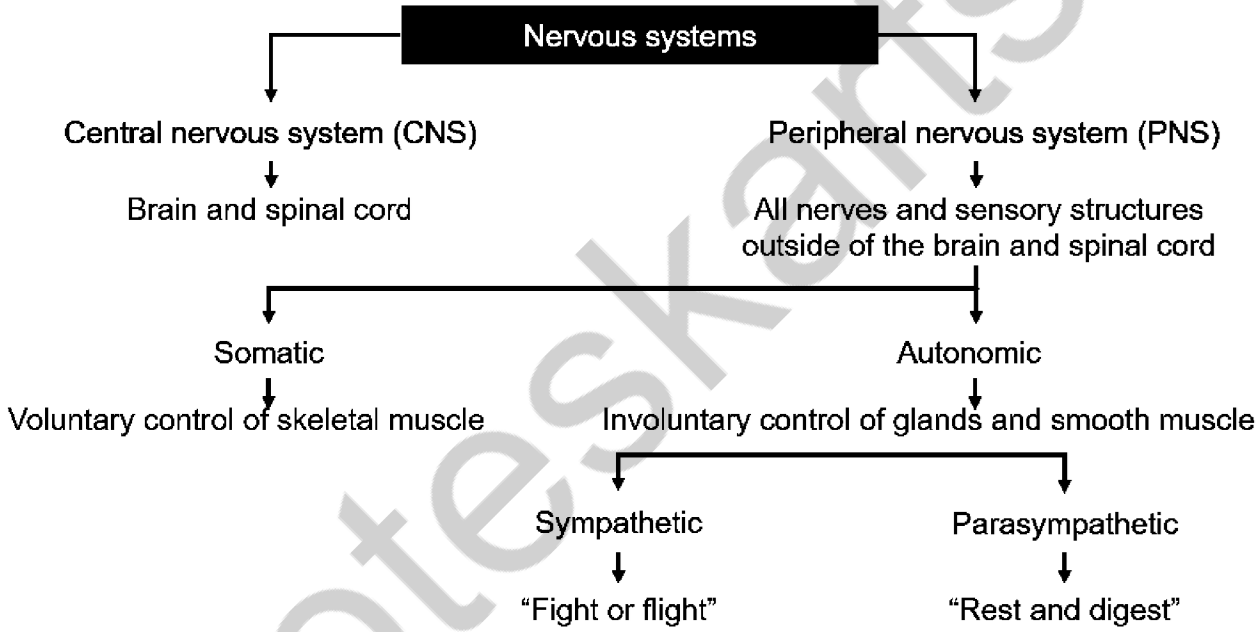
- **Pharmacology of drugs acting on peripheral nervous system**
  - Organization and function of ANS.
  - Neurohumoral transmission,co-transmission and classification of neurotransmitters.
  - Parasympathomimetics, Parasympatholytics, Sympathomimetics, sympatholytics.
  - Neuromuscular blocking agents and skeletal muscle relaxants (peripheral).
  - Local anesthetic agents.
  - Drugs used in myasthenia gravis and glaucoma

Nervous system:

- The nervous system is a complex network of nerves and cells that carry messages to and from the brain and spinal cord to various parts of the body.
- The proper functioning of these nerves ensures that each organ system, such as the cardiovascular, gastrointestinal, and immune systems, can adequately communicate with one another.

The nervous system can be divided into two main parts:

- Central Nervous System (CNS):
- Peripheral Nervous System (PNS):



1. Sympathetic Nervous System:

- In this types of ANA the ganglionic junction is present away to the organ.
- The Sympathetic nervous system is best known for its role in responding to dangerous or stressful situations.
- In these situations, your sympathetic nervous system activates to speed up your heart rate, deliver more blood to areas of your body that need more oxygen or other responses to help your get out of danger.

2. Parasympathetic Nervous System:

- The parasympathetic nervous system predominates in quiet "rest and digest" conditions while the sympathetic nervous system drives the "fight or flight" response in stressful situations.
- The main purpose of the PNS is to conserve energy to be used later and to regulate bodily functions like digestion and urination.

Different between Sympathetic and Parasympathetic System

Feature	Sympathetic Nervous System	Parasympathetic Nervous System
Division	Part of the autonomic nervous system	Part of the autonomic nervous system
Activation	Activated during "fight or flight" responses	Activated during "rest and digest" responses
Effects on Organs	- Increases heart rate and blood pressure	- Decreases heart rate and blood pressure
	Eye:- Dilates pupils	- Constricts pupils
	Digestion: - Inhibits digestion and peristalsis (movement of intestines)	- Stimulates digestion and peristalsis
	Liver:- Stimulates release of glucose from the liver	- Stimulates storage of glucose in the liver
	Urinary System:- Inhibits urinary bladder contraction	- Stimulates urinary bladder contraction
Neurotransmitter Release	Releases neurotransmitter norepinephrine (noradrenaline)	Releases neurotransmitter acetylcholine
Origin of Fibers	Preganglionic fibers originate from thoracic and lumbar	Preganglionic fibers originate from cranial nerves (e.g., vagus)
	regions of the spinal cord, and postganglionic fibers	and sacral regions of the spinal cord, and postganglionic fibers
	extend to ganglia near the spinal cord	extend to ganglia near or within target organs

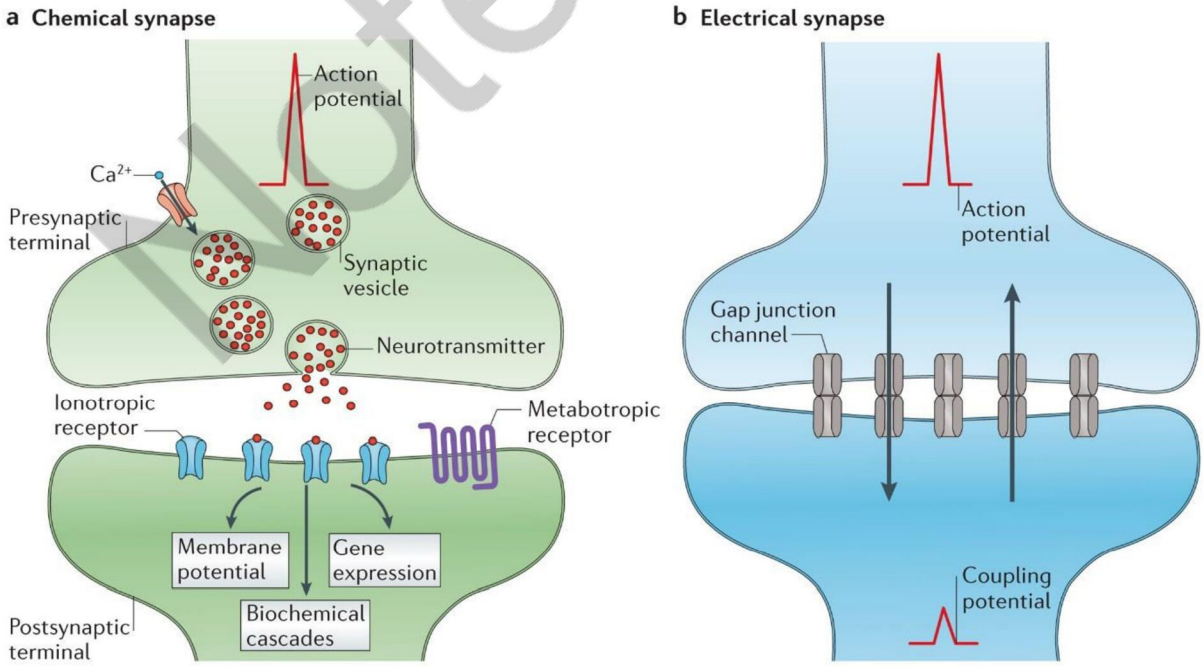
Neurohumoral transmission:

- Neuroendocrine transmission refers to the process by which neurons communicate with target cells through the release of both neurotransmitters and hormones.
- While neurotransmitters act locally at synapses, hormones are released into the bloodstream and travel to distant target cells.
- This process involves several steps, i.e. biosynthesis, storage, release, receptor interaction and inactivation of the transmitter.

There are two main types of neurotransmission:

1. **Chemical transmission**: This is the most common type of neurotransmission. It involves the release of neurotransmitters from the presynaptic neuron into the synaptic cleft, the small gap between the presynaptic and postsynaptic neurons. The neurotransmitters then bind to receptors on the postsynaptic neuron, causing a change in its membrane potential and transmitting the signal.

2. **Electrical transmission**: In certain cases, neurons communicate through direct electrical connections called gap junctions. This type of transmission allows for very rapid communication between neurons, but it is less common than chemical transmission.

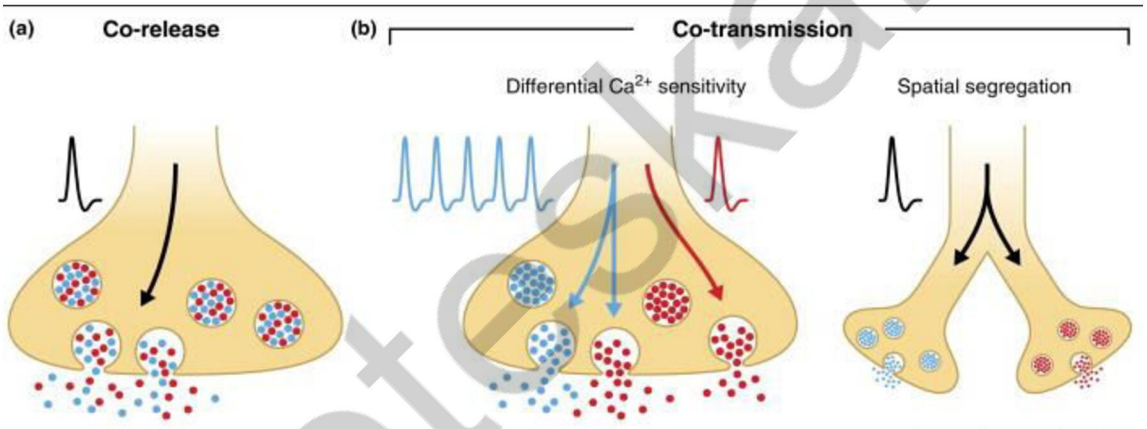


Co-transmission:

- **Co-transmission** refers to the release of multiple neurotransmitters from a single neuron.
- Neurons can contain and release more than one type of neurotransmitter, and this phenomenon allows for more complex signaling and modulation of neural circuits.
- Co-transmission can involve different neurotransmitters being released from separate vesicles within the same neuron or being released from the same vesicle.

It's important to distinguish between co-release and co-transmission:

- **Co-release:** Multiple transmitters are packaged within the same vesicle and released together.
- **Co-transmission:** Transmitters reside in separate vesicles and are released independently, although triggered by the same neuronal activity.



Classification of neurotransmitters:

- Neurotransmitters are chemical messengers that play crucial roles in communication within the nervous system.
- They transmit signals across synapses, the junctions between neurons, allowing for the transmission of information between nerve cells and other cells such as muscle or gland cells.

They can be classified as either excitatory or Inhibitory.

1. Excitatory neurotransmitters:

- Acetylcholine
- Adrenaline
- Nor. Adrenaline

- Dopamine
- Glutamate

2. Inhibitory neurotransmitters:

- GABA
- Serotonine

3. Both:

- Acetylcholine
- Dopamine
- Nor-adrenaline

1. Excitatory neurotransmitters:

Acetylcholine (ACh):

- **Function:** Neuromuscular transmission, memory, and learning.

Adrenaline (Epinephrine):

- **Function:** Fight-or-flight response, increased heart rate and blood pressure.

Noradrenaline (Norepinephrine):

- **Function:** Alertness, attention, mood regulation, and blood pressure control.

Dopamine:

- **Function:** Reward, motivation, movement, and learning.

Glutamate:

- **Function:** Major excitatory neurotransmitter, involved in learning, memory, and thinking.

2. Inhibitory neurotransmitters:

GABA (Gamma-Aminobutyric Acid):

- **Function:** Major inhibitory neurotransmitter in the central nervous system, promoting calmness and relaxation.

Serotonin:

- **Function:** Involved in mood regulation, sleep, appetite, and learning.

3. Both:

Acetylcholine (ACh):

- Function: Plays a vital role in memory, learning, and neuromuscular transmission (movement).

Dopamine:

- **Function:** Associated with reward, motivation, movement, and reinforcement of pleasurable activities.

Noradrenaline (Norepinephrine):

- Function: Involved in alertness, attention, mood regulation, and blood pressure control.

Parasympathomimetics, Parasympatholytics, Sympathomimetics, sympatholytics.

1. Parasympathomimetics:

- **Function:** Mimic the effects of the parasympathetic nervous system (PSNS).
- **Mechanism:** Act by:
    - Directly stimulating **muscarinic and nicotinic receptors**, the cellular targets of the neurotransmitter acetylcholine (ACh), which is the primary neurotransmitter of the PSNS.
    - Inhibiting the enzyme **acetylcholinesterase**, which breaks down ACh, allowing it to linger and exert a prolonged effect.
- **Effects:** Generally promote a state of **rest and relaxation**. Examples include:
    - Slower heart rate
    - Increased gut motility
    - Constricted pupils

2. Parasympatholytics:

- **Function:** Block the actions of the parasympathetic nervous system.
- **Mechanism:** Primarily target **muscarinic receptors**, preventing ACh from binding and exerting its effects.
- **Effects:** Opposite of parasympathomimetics, they induce a state of **increased alertness and arousal**. Examples include:
    - Increased heart rate
    - Dilation of pupils

- Decreased gut motility

3. Sympathomimetics:

- **Function:** Mimic the effects of the sympathetic nervous system (SNS).
- **Mechanism:** Act by:
  - Directly stimulating **adrenergic receptors**, the cellular targets of the neurotransmitters norepinephrine and epinephrine (adrenaline).
  - Increasing the release of these neurotransmitters from nerve terminals.
- **Effects:** Prepare the body for **action and energy expenditure**. Examples include:
  - Increased heart rate and blood pressure
  - Bronchodilation (opening of airways)
  - Increased blood sugar levels

4. Sympatholytics:

- **Function:** Block the actions of the sympathetic nervous system.
- **Mechanism:** Primarily target **adrenergic receptors**, preventing norepinephrine and epinephrine from binding and exerting their effects.
- **Effects:** Counteract the "fight-or-flight" response, promoting a state of **calmness and reduced activity**. Examples include:
  - Lower heart rate and blood pressure
  - Bronchoconstriction (narrowing of airways)

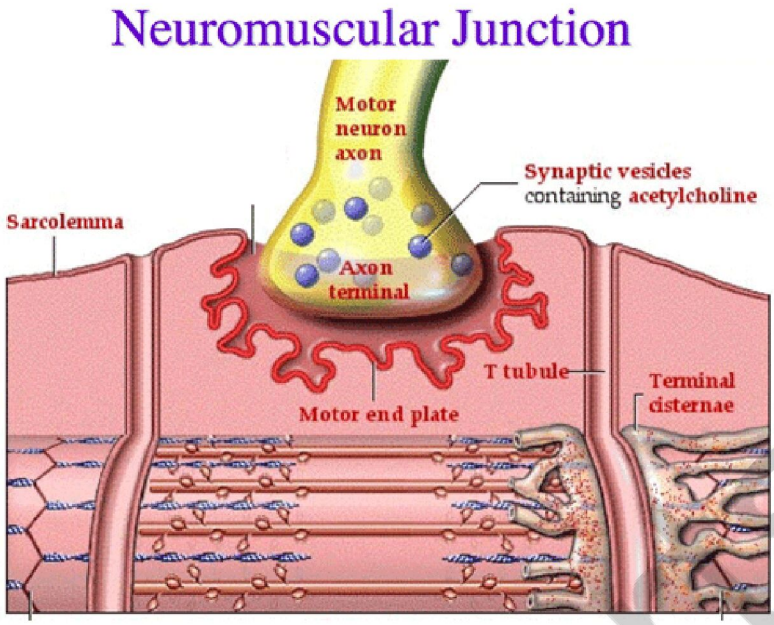
Neuromuscular blocking agents and skeletal muscle relaxants (peripheral).

Neuromuscular blocking agents:

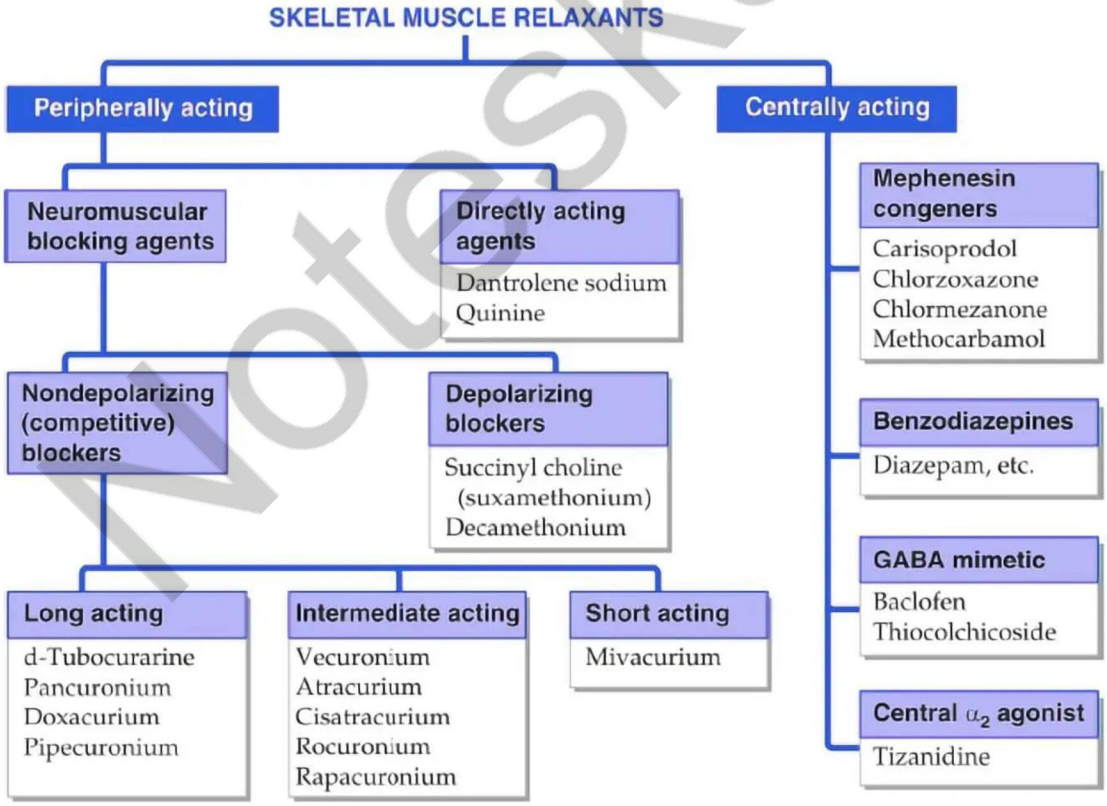
- These are those agents which are used to block the neuromuscular junction and inhibit the contraction of muscle and cause relaxation of muscles.
- They are also known as Skeletal muscle relaxants.

Neuromuscular Junction:

- The neuromuscular junction (NMJ) is a synaptic connection between the terminal end of a motor nerve and a muscle (skeletal/ smooth/ cardiac).
- It is the site for the transmission of action potential from nerve to the muscle. It is also a site for many diseases and a site of action for many pharmacological drugs.



Classification of Skeletal muscle relaxants (peripheral).



A. Non-depolarizing Blockers:

- Non-depolarizing blockers are a type of neuromuscular blocking agent (NMBA) that act on the neuromuscular junction (NMJ) to induce muscle relaxation.

- Unlike depolarizing blockers, they **do not directly trigger muscle contraction**.
- They work by **competitively inhibiting the binding of acetylcholine (ACh)**, the natural neurotransmitter responsible for muscle activation, to the nicotinic acetylcholine receptors (nAChRs) on the postsynaptic membrane of the muscle fiber.

Mechanism of Action:

1. **ACh release:** An action potential travels down the motor neuron, leading to the release of ACh from the presynaptic terminal.
2. **Competition for binding:** ACh and the non-depolarizing blocker compete for binding sites on the nAChRs.
3. **Blocked ACh binding:** The blocker molecule occupies the binding site, preventing ACh from effectively activating the receptor.

Pharmacological Action:

1. Skeletal Muscles:
   - Induced flaccid paralysis
   - Paralysis according to this order:- Muscles of face →eye → finger → limb → neck
   - Recovery occurs in reverse order.
2. Histamine Release:
   - d-TC has a greater tendency to liberate histamine from most cells
3. Cardiovascular system:
   - d-TC produce hypotension due to histamine release.
   - Calamine cause tachycardia

Adverse Effect:

- Hypoxia
- Respiratory Paralysis
- Hypotension
- Constipation

B. Depolarizing blockers:

- Depolarizing blockers are a type of neuromuscular blocking agent (NMBA) that act on the neuromuscular junction (NMJ) to induce muscle relaxation.
- non-depolarizing blockers, they **directly trigger muscle contraction** but with a **prolonged blocking effect** leading to paralysis.

Mechanism of Action:

- The mechanism of action of depolarizing blockers involves mimicking the action of acetylcholine (ACh) at the neuromuscular junction.

- Specifically, succinylcholine binds to nicotinic cholinergic receptors on the motor endplate, initiating depolarization of the muscle cell membrane.
- This depolarization initially causes muscle fasciculations due to the sustained activation of the receptors. However, succinylcholine is resistant to degradation by acetylcholinesterase, the enzyme responsible for metabolizing ACh.
- As a result, succinylcholine remains bound to the receptors for an extended period, leading to sustained depolarization and subsequent muscle paralysis.

Pharmacological Action:

- Muscle twitching
- Muscle soreness

Adverse effect:

- Muscle rigidity
- prolonged apnoea
- Nausea and Vomiting

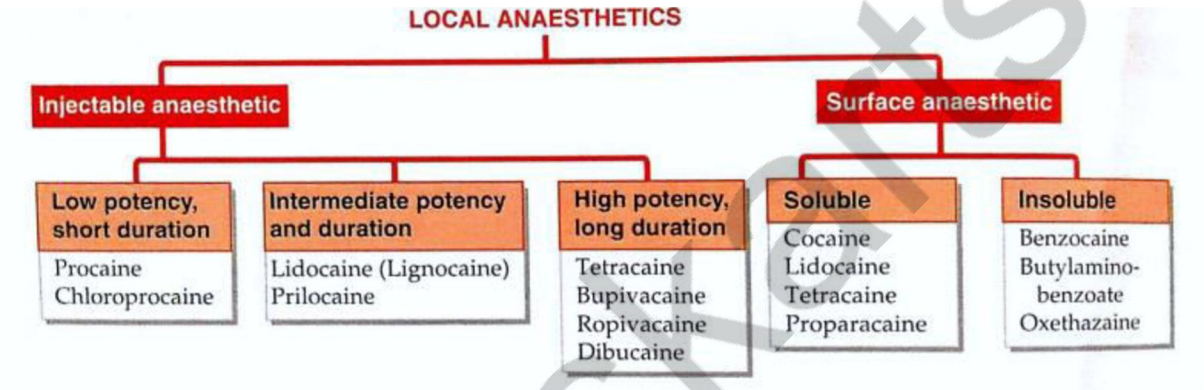
Local anesthetic agents:

- 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

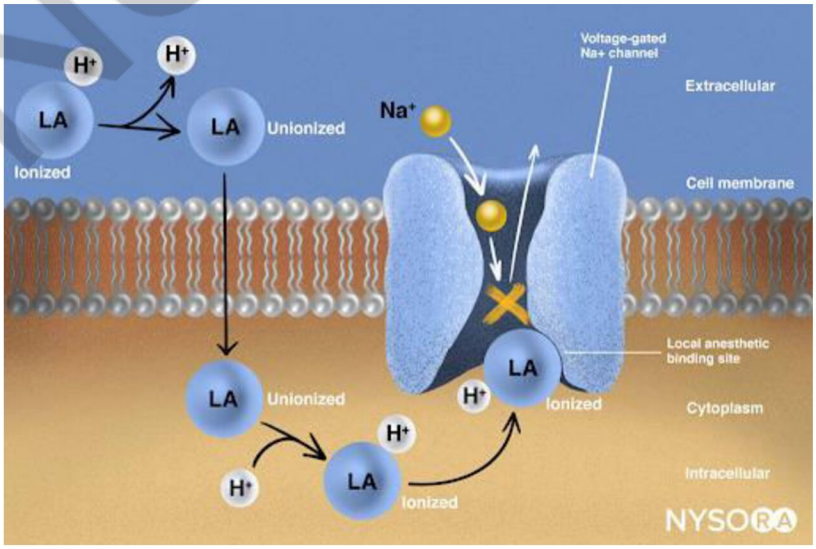
- Local Anesthetic are those drugs which blocks the neuronal condition at local particular area. And it is helpful for miner surgery.

Classification of Local Anesthetic agents:



Mechanism of action of local anesthetics.

- Local anesthetics work by binding to the α subunit of the voltage-gated Na+ channels, thus preventing the generation and conduction of nerve impulses.
- Subsequently, Na+ ions cannot flow into the cell, thereby halting the transmission of the advancing wave of depolarization down the length of the nerve. The fraction of local anesthetic molecules are in the ionized form. Local anesthetic molecules change from ionized to unionized in a fraction of a second.



Some important drugs (Exam Point of View):

Cocaine:

- **Definition:** A highly addictive and illegal stimulant drug derived from the coca plant. **It is important to note that cocaine is a dangerous and illegal substance with no legitimate medical use.**
- **Misuse:** Cocaine is a powerful stimulant that disrupts the central nervous system, producing intense feelings of pleasure followed by a crash. It is highly addictive and can lead to severe health problems, including:
    - Increased heart rate, blood pressure, and body temperature
    - Chest pain, heart attack, stroke
    - Seizures, coma, and death
    - Respiratory failure
    - Damage to the heart, lungs, liver, and kidneys
    - Mental health problems, including psychosis and depression

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

Uses of Local Anesthesia:

- 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.

Adverse Effects:

- Asthma
- Muscle Twitching
- Hypotension
- Redness of Skin

Drugs used in myasthenia gravis

Myasthenia Gravis

- 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.
- It is an auto-immune disorder in which our immune system produce antibioties that block or destroy muscle's receptor.
- Break down in communication between nerves and muscles.

Mechanism of action of Myasthenia Gravis

- It is an auto-immune disorder. In this disorder our immune system produce antibodies to block/ destroy the Nicotinic receptor.
- Because according to immune system these receptor are harmful for body. So these receptor and block them.
- Now due to blockage of receptor acetycholine (Ach) does not bind on receptor.
- Due to this there are loss of communication between nerves (Ach) and muscle.
- Which further decrese the contraction of muscles.
- Also muscle become weak and fatigue. These antibodies also destroy or kill the receptor. Due to this there are also decrease in the no. of receptors.

Drugs 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.

3. Immunosuppressant:

- Use these drugs to suppress the immune system to decrees the formation of antibodies.

Eg. Cyclosparine A, Methotrexate, Azathioprine, etc.

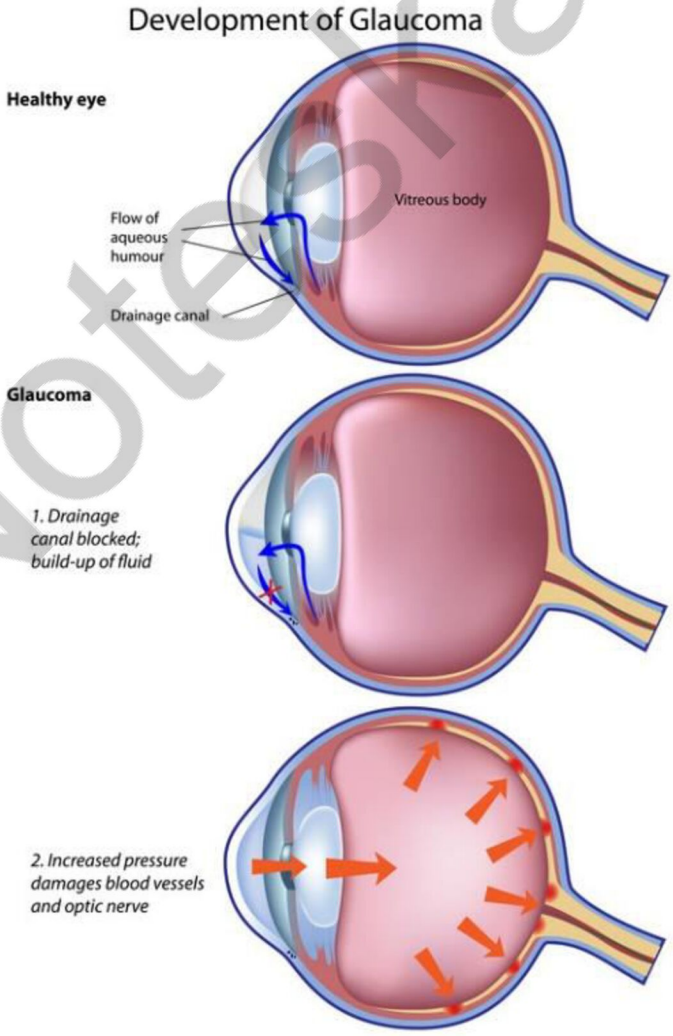
4. Plasmapheresis: (Plasma exchange)

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.

Drugs used in glaucoma:

Glaucoma: (Vision loss and blindness)

- Glaucoma are eye conditions associated with damage of the optic nerve (which connects the eye to the brain) and the nerve fibres from the retina (the light-sensitive nerve tissue that lines the back of the eye). Glaucoma often affects both eyes, usually to varying degrees.
- The optic nerve sends visual information from your eye to your brain and is vital for good vision. Damage to the optic nerve is often related to high pressure in your eye.
- But glaucoma can happen even with normal eye pressure.
- Glaucoma can occur at any age but is more common in older adults. It is one of the leading causes of blindness for people over the age of 60.



Symptoms:

- Eye Pain
- Redness of the Eye
- Vision loss, Blurred Vision

Types of Glaucoma:

1. Open Angle Glaucoma
2. Close angle Glaucoma

1. Open Angle Glaucoma:

- It is also known as chronic and wide angle glaucoma.

Symptoms:

- Gradual Vision loss.
- Optic nerve damage
- Most common type of glaucoma.

2. Close angle Glaucoma

- It is also known as acute and narrow angle glaucoma.

Drug used in Glaucoma:

1) Atropine-

- Naturally obtain from Atropa belladonna
- It is competitive antagonists of all five muscarinc receptor
- It gives temporary relief from bradycardia
- Antidote for cholinesterase poisoning
- Poisoning from mashrum containing muscarine

2) Scopolamine-

- It is belladonna alkaloids
- Well absorb through skin
- Crosses BBB
- It prevent motion sickness and nausea associated with the use of opioid analgesics

3) Tropicamide-

- Short acting antimuscarinic drug
- Applied as eye drops prior to retinal exam
- They produce mydriasis by inhibiting the contraction of the iris spincter muscles

- They are sometimes co-administered with phenylephrine 4) Ipratropium bromide-
- It is quaternary analog of atropine
- Used to prevent bronchospasm assosiated with COPD and asthma. 16

5) Glycopyrrolate-

- It is quaternary analog of atropine.
- Used as preoperative medication to reduce salivary and respiratory secretion
- In combination with neostigmine to reserve the effect of non- depolarizing skeletal muscle relaxant at the end of surgery