LOCAL ANAESTHETICS

- 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.

- Pharmacokinetics:

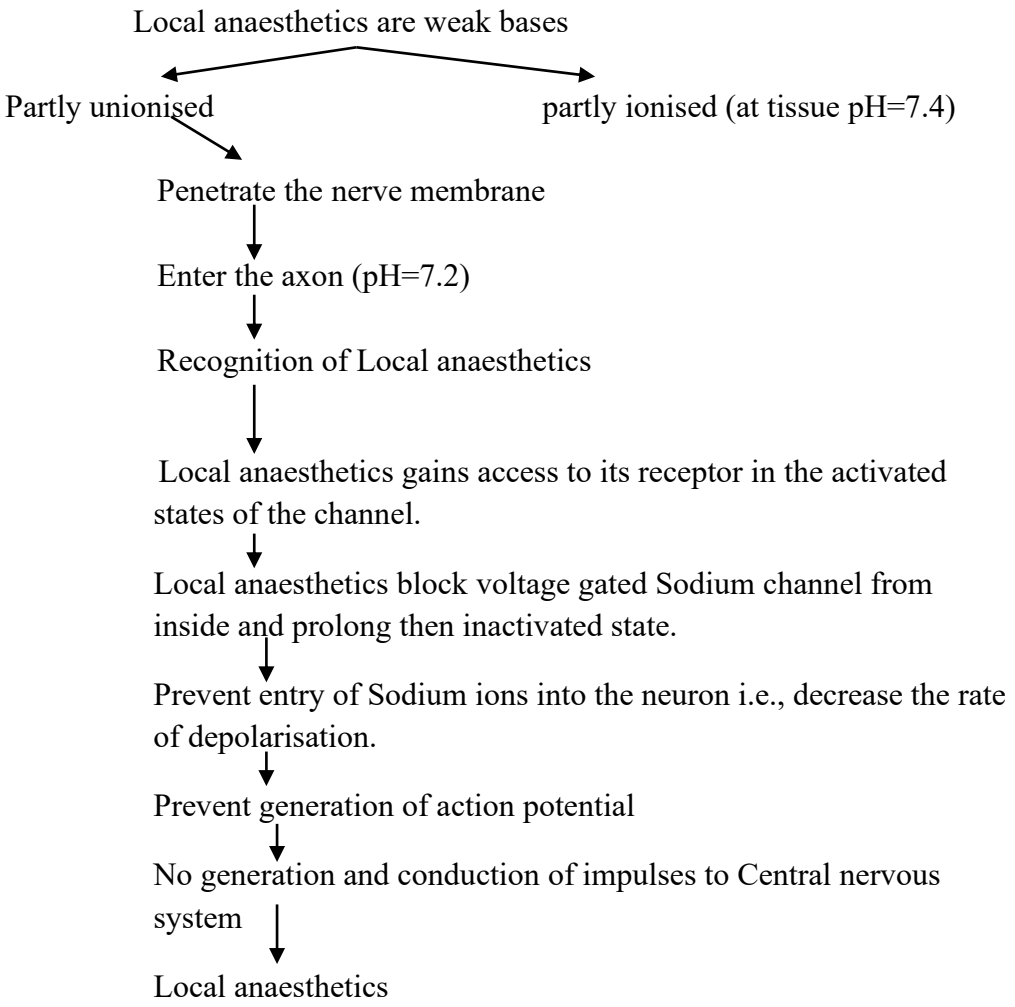
    i. Most of the ester linked Local anaesthetics are rapidly metabolised by plasma cholinesterase, whereas amide-linked drugs are metabolised in liver.
    ii. Local anaesthetics (procaine, lignocaine) are too effective orally because of high first pass metabolism.
    iii. In liver disease, metabolism of lignocaine may be impaired. Hence, dose must be reduced accordingly.

- Pharmacological Action:

    - Local action:
        i. Local anaesthetics have minimal local irritant action and it blocks sensory nerve trunk, neuromuscular junction, ganglionic synapse and receptors.
        ii. They reduce the release of acetylcholine from motor-nerve endings.
        iii. The order of blockade is Pain→Temperature sense →Touch →Deep→Pressure sense.
    - Systemic actions:
        i. Central nervous system: Local anaesthetics produce stimulation which is followed by depression.
        ii. Cardiovascular structure:
            - Local anaesthetics are cardiac depressants i.e. they block sodium channels.
            - At high doses, they decrease automaticity, excitability, contractility, conductivity and prolong refractory period.
        iii. Blood vessels: they produce hypotension due to vasodilatation.

- Mechanism of Action:

i. Local anaesthetics act by blocking sodium (Na) channel blockade.
ii. Sodium channel exist in resting, active and inactived states. The channels have to recover from the inactive state before they can be opened in response to an impulse.
iii. Local anaesthetics receptors are located in the Sodium channel of axonal membrane.
iv. Action of Local anaesthetics is pH dependent and the penetrability of Local anaesthetics is increased at Alkaline pH (i.e., when the unionised form is more). At low pH, ionisation of drug occurs resulting in decreased permeability.
v. Thus, in 'unionised form' Local anaesthetics easily penetrates into the nerve sheath and the axon membrane. Within the axoplasm, the molecules become ionised and block the voltage gated channels.



- Adverse effects:

    i. Central Nervous system:
        - They produce a sequence of stimulantion followed by depression.
        - The early symptoms includes: numbness, dizziness, blurred vision.
        - The later symptoms include: excitation, restlessness, agitation, muscle twitching.

    ii. Cardiovascular system: effects are bradycardia, hypertension, cadiac arrhythmias.

    iii. Injections are painful and may delay the wound healing.

- Adrenaline:

    - Advantages:
        - Prolong duration of action of Local anaesthetics.
        - Reduces the systemic toxicity of Local anaesthetics (due to reduced rate of absorption and metabolism of Local anaesthetics).
        - Provides a bloodless field for surgery.

    - Disadvantages:
        - Intense vasospasm and ischemia in tissue with end arteries may cause gangrene of that part. (Ex: - finger, toes, penis, ear lobules).
        - Absorption of adrenaline can cause systemic toxicity – tachycardia, palpitation, rise of blood pressure.
        - May delay wound healing by reducing blood flow to the affected area?

- Uses of Local anaesthetics:

    i. Used as nerve blockage in tooth extraction by giving nerve block.

    ii. Used in surface anaesthetic, epidermal anaesthetic and in spinal anaesthesia.

    iii. Used as anti-arrhythmic agent.

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Ester Local anaesthetics	Amide Local anaesthetics
Short acting	Intermediate acting
Has poor tissue permeability hence no surface anaesthetic effect	Has good tissue permeability
Has slow onset of action	Has rapid onset of action
Allergic reaction are common	Allergic reactions are rare