

Local anaesthetics (LAs)

- Local anaesthetics (LAs) 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.

Classification

I. Injectable anaesthetic

- *Low potency, short duration:*

Procaine; Chlorprocaine

- *Intermediate potency and duration:*

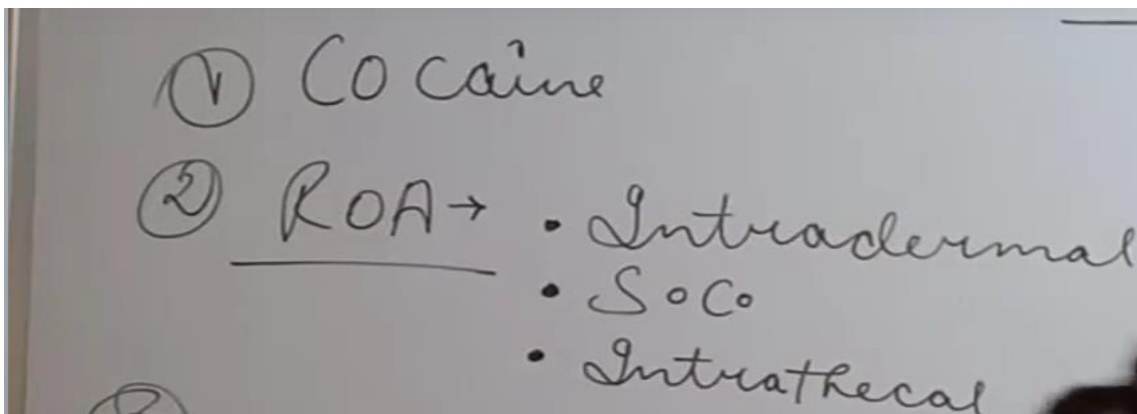
Lidocaine (Lignocaine); Prilocaine

- *High potency, long duration:*

Tetracaine (Amethocaine); Bupivacaine;

Ropivacaine;

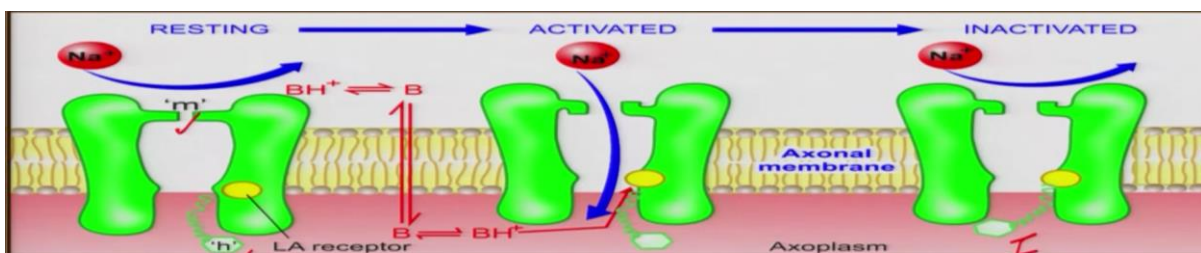
Dibucaine (Cinchocaine)



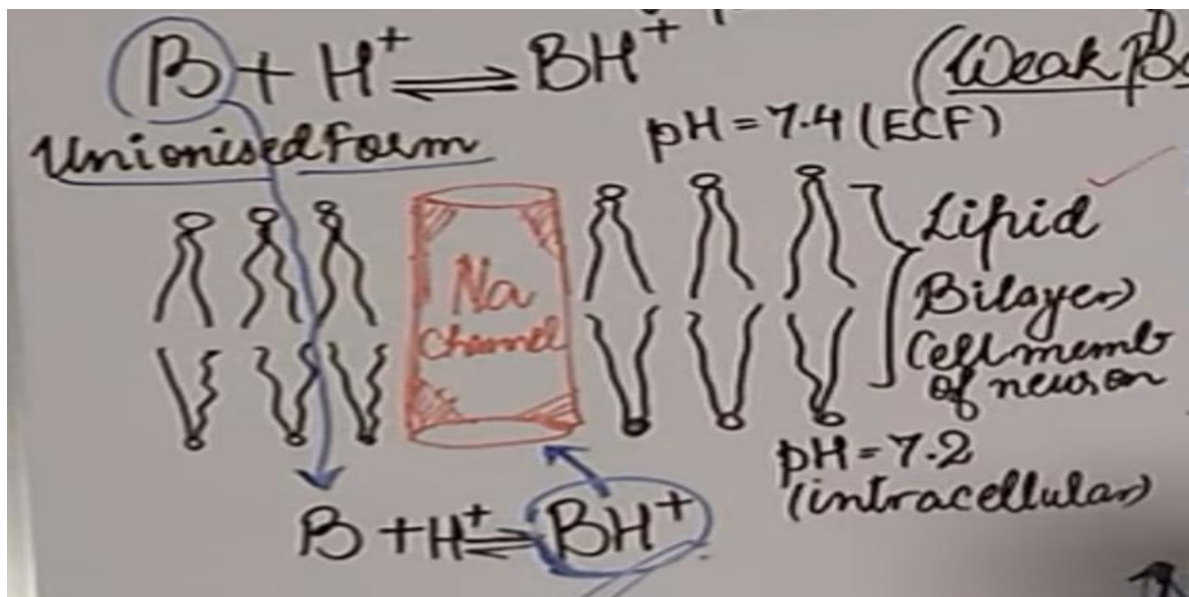
Mechanism of action

- The LAs block nerve conduction by decreasing the entry of Na^+ ions during upstroke of action potential (AP).
- As the concentration of the LA is increased, the rate of rise of AP and maximum depolarization **decreases** causing **slowing of conduction**.
- Finally, local depolarization fails to reach the threshold potential and conduction block ensues.

- The LAs interact with a receptor situated within the voltage sensitive Na^+ channel and **raise the threshold** of channel opening.
- Impulse conduction is interrupted when the Na^+ channels over a critical length of the fibre (2–3 nodes of Ranvier in case of myelinated fibres) are blocked.
- Potency of a LA generally corresponds to the lipid solubility of its base form (B), because it is this form which penetrates the axon.
- Blockade of conduction by LA is not due to hyperpolarization.
- The onset time of blockade is related primarily to the pKa of the LA.



- The Na^+ channel has an activation gate (make or 'm' gate) near its extracellular mouth and an inactivation gate (halt or 'h' gate) at the intracellular mouth. In the resting state the activation gate is closed.
- Threshold depolarization of the membrane opens the activation gate allowing Na^+ ions to flow in along the concentration gradient.



Bases) Local Anaesthetics (Unionised FORM)

Block the Voltage Gated Na^+ channels

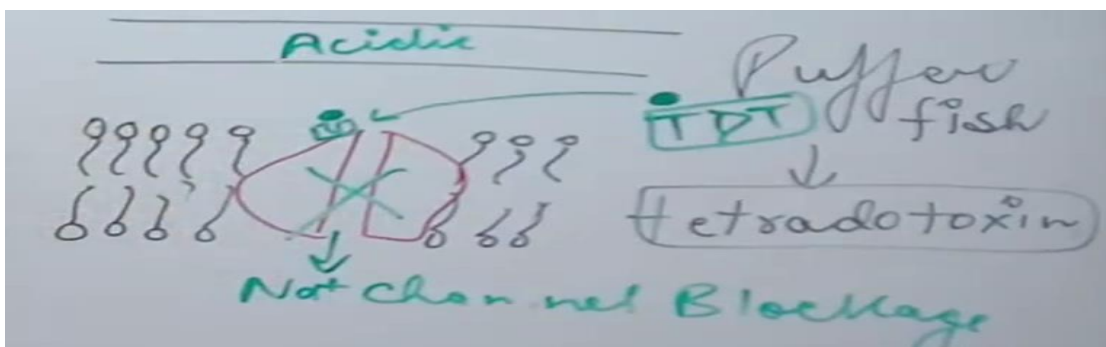
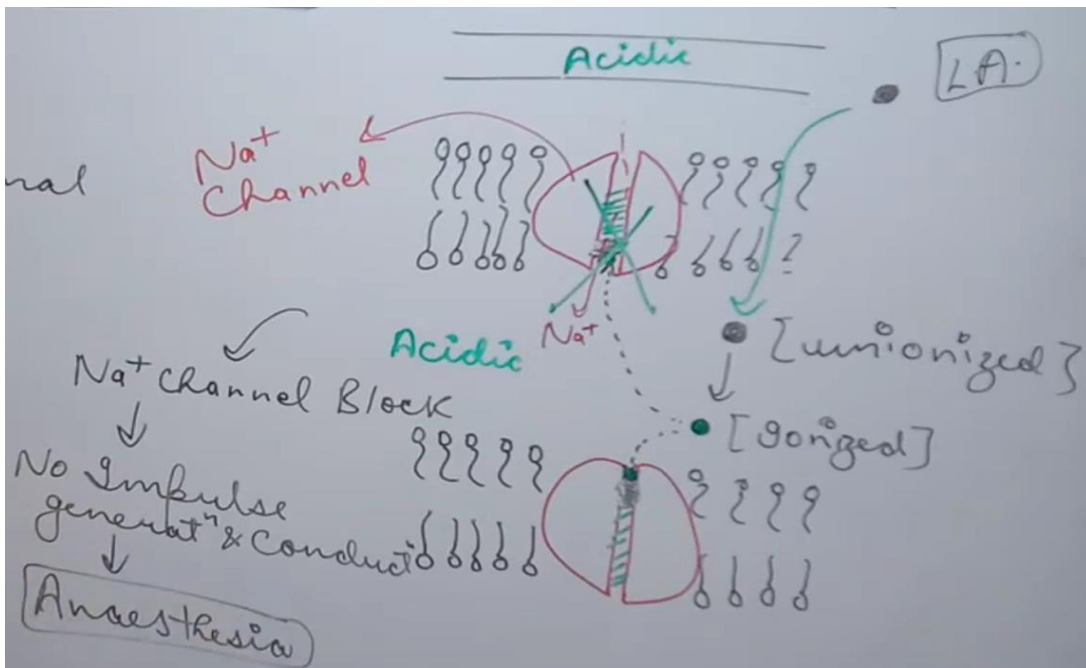
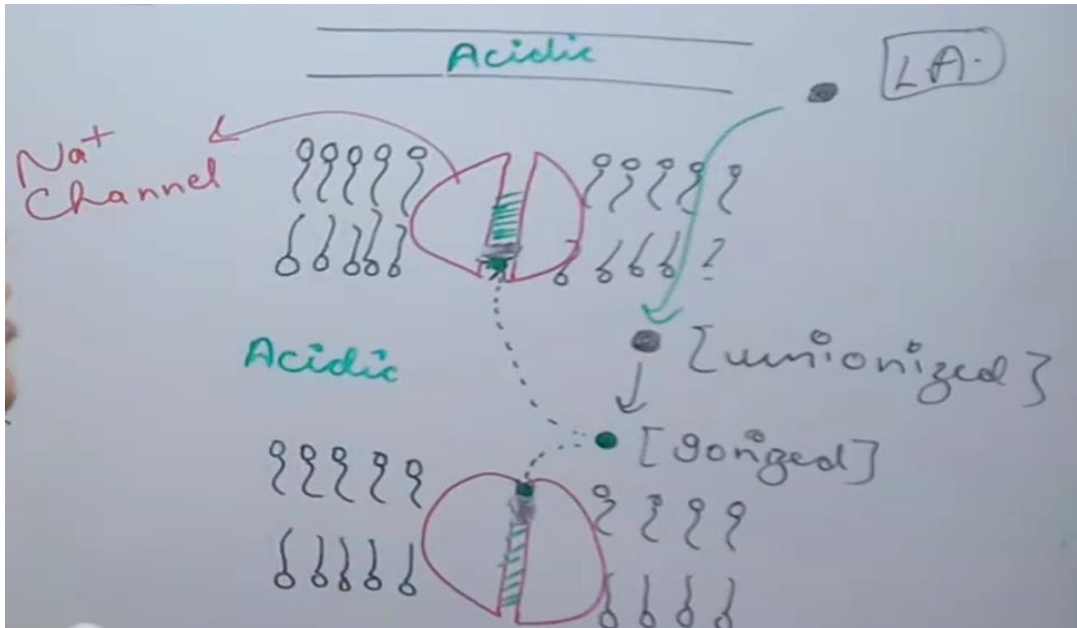
No entry of Na^+ ions into Cell

No depolarisation

No generation of Action Potential

No generation of Impulse to CNS

conduction ↓ NO ESTHESIA



Side Effect →

Dizziness, Headache }
Confusion, CNS depression }
Myocardial activity ↓