

Local anaesthesia

- Local anaesthetics block the initiation and spread of action potentials in nerve fibres by preventing the voltage-dependent increase in Na^+ conductance.
- They do this in two ways :
 - (1) By acting non-specifically to stabilise the membrane.
 - (2) by specifically plugging Na^+ channels. The latter mechanism is the most important for most local anaesthesia.
- Most are used with adrenaline to prolong duration of action by constricting blood vessels.

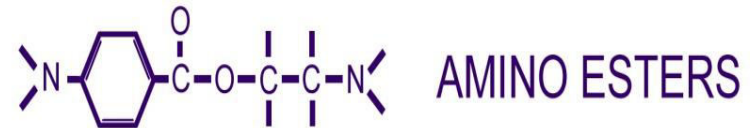
Chemistry

Chemical structure of local anesthetics

All local anesthetics contain **structural components:**

- an aromatic ring (usually substituted)
- a connecting group which is either an ester (e.g., novocain) or an amide (e.g. lidocaine)
- an ionizable amino group

Aromatic lipophilic portion - Intermediate chain - Amine hydrophilic portion



Lipid solubility:

determines, **potency, plasma protein binding and duration of action** of local anesthetics

| | Lipid solubility | Relative potency | Plasma protein binding (%) | Duration (minutes) |
|-------------------|-------------------------|-------------------------|-----------------------------------|---------------------------|
| procaine | 1 | 1 | 6 | 60-90 |
| lidocaine | 4 | 2 | 65 | 90-200 |
| tetracaine | 80 | 8 | 80 | 180-600 |

weak bases

– proportion of free base ($R-NH_2$) and salt ($R-NH_3^+$) forms depends on **pH** and **pK** of amino group

$$pH = pK + \log \frac{[base]}{[salt]}$$

(Henderson-Hasselbalch equation)

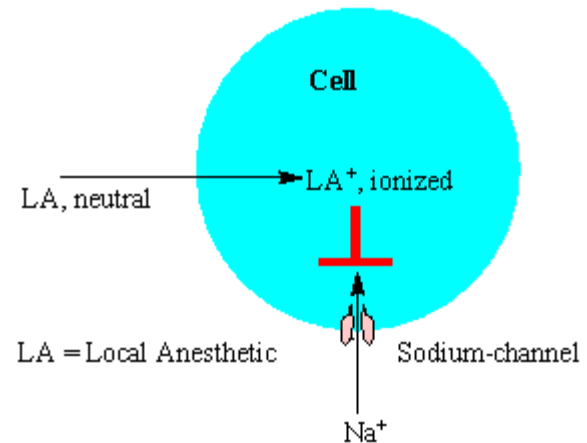
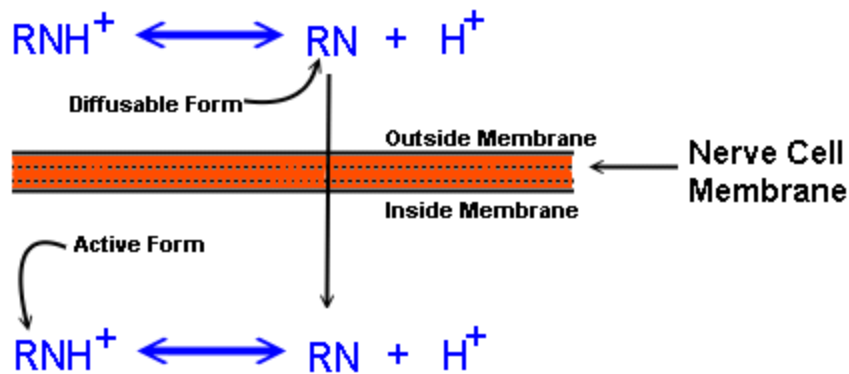
Example: Calculate the proportions of free base and salt forms of tetracaine ($pK = 8.5$) at $pH (7.5)$.

$$7.5 = 8.5 + \log \frac{[base]}{[salt]}$$

$$\log \frac{[base]}{[salt]} = -1$$

$$\frac{[base]}{[salt]} = 10^{-1} = \frac{1}{10}$$

local anesthetic enters nerve fibre as neutral free base and the cationic form blocks conduction by interacting at inner surface of the Na^+ channel



inflammation → reduced susceptibility to anesthesia
(lowered local pH increases proportion of anesthetic in charged form that cannot permeate nerve membrane)

Functional consequences of Na⁺ channel blockade by local anesthetics:

- **nerves**: decrease or abolition of conduction
- **vascular smooth muscle**: vasodilatation
- **heart**: decreased excitability (reduced pacemaker activity, prolongation of effective refractory period)
- **central nervous system**: increased excitability, followed by generalized depression

vasoconstrictor

Adrenaline is the conventional vasoconstrictor included in commercial local anesthetic preparations

The concentration of adrenaline in these preparations can vary and is expressed as grams/ml (e.g. 1:100,000 = 1 gram/100,000 ml)

Clinical Applications

nerve block: injected locally to produce **regional anesthesia** (e.g., dental and other minor surgical procedures)

- Local anesthesia is injected subcutaneously around sensory nerve endings. Useful in minor surgery.
- **Infiltration anesthesia** can produce with **0.25–0.5% aqueous solution of lidocaine or procaine** (usually with co-administration of adrenaline).

Topical Agents

- Local anesthesia is applied directly to mucous membranes such as those of the conjunctiva, nose, throat, or urethra.
- Agents of choice is Tetracaine, Lidocaine and Proparacaine.
- Onset of anaesthesia takes about 20 seconds and duration of action is about 8 minutes.
- **high concentrations (2–5%).**

Injection Agents

- Intravenous Regional Anaesthesia

Local anesthesia injected intravenously distal to a pressure cuff to arrest blood flow.

Remains effective until the circulation is restored.
Used for limb surgery. Mainly Lidocaine (Lignocaine) and Prilocaine.

Spinal & Epidural

- Spinal Anaesthesia

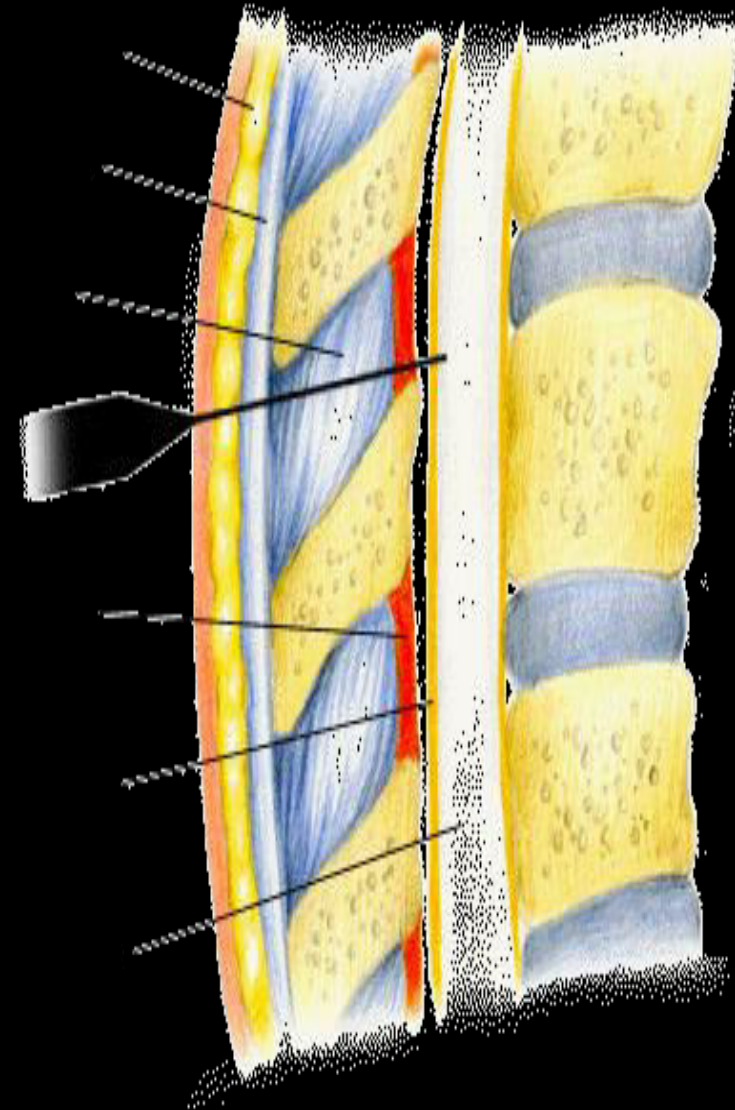
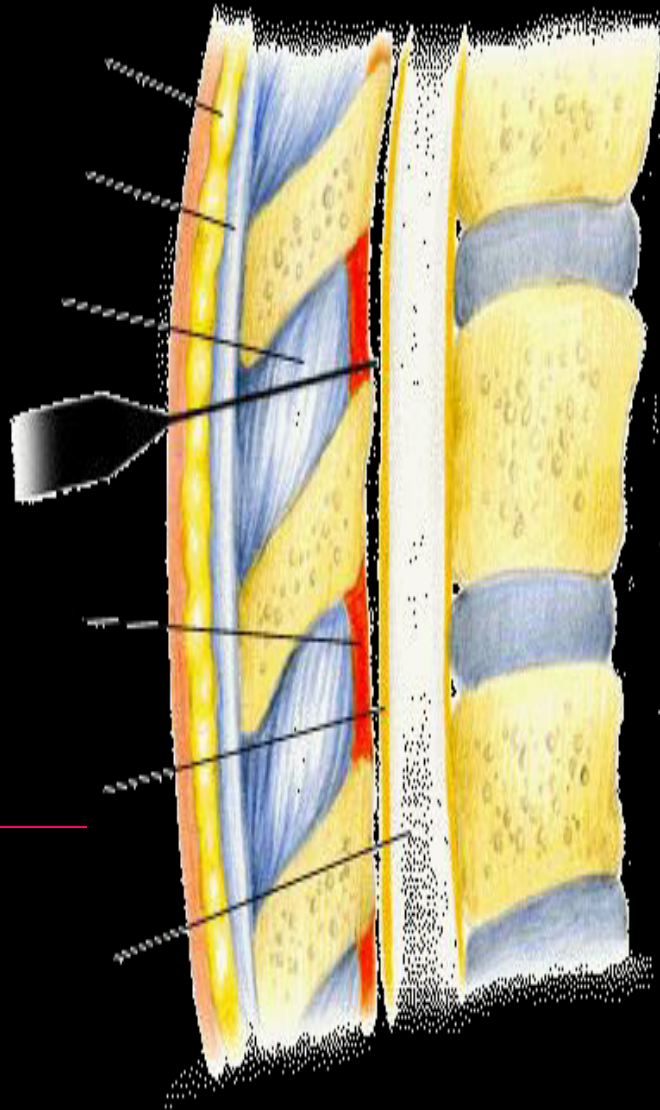
Local anaesthesia injected intrathecally into the CSF of the subarachnoid space to act on spinal roots and spinal cord.

Used for surgery to abdomen, pelvis or leg when general anaesthesia not appropriate. Mainly Lidocaine and Tetracaine.

- Epidural anesthesia (injection of the Local anesthesia to the spinal column but outside the dura mater), used in obstetrics.

Epidural

Spinal



Conclusion

| Anesthetic | pKa | Onset | Duration (with Epinephrine) in minutes | Max Dose (with Epinephrine) |
|--------------------|------------|---------------|---|--|
| Procaine | 9.1 | Slow | 45 - 90 | 8mg/kg – 10mg/kg |
| Lidocaine | 7.9 | Rapid | 120 - 240 | 4.5mg/kg – 7mg/kg |
| Bupivacaine | 8.1 | Slow | 4 hours – 8 hours | 2.5mg/kg – 3mg/kg |
| Prilocaine | 7.9 | Medium | 90 - 360 | 5mg/kg – 7.5mg/kg |
| Articaine | 7.8 | Rapid | 140 - 270 | 4.0mg/kg – 7mg/kg |

- Length of time from induction until the reversal process is complete.
- **Short-acting:**
 - Local anesthetic agent lasts less than 30 minutes.
- **Intermediate-acting:**
 - Local anesthetic agent lasts about 60 minutes.
- **Long-acting:**
 - Local anesthetic agent lasts longer than 90 minutes.