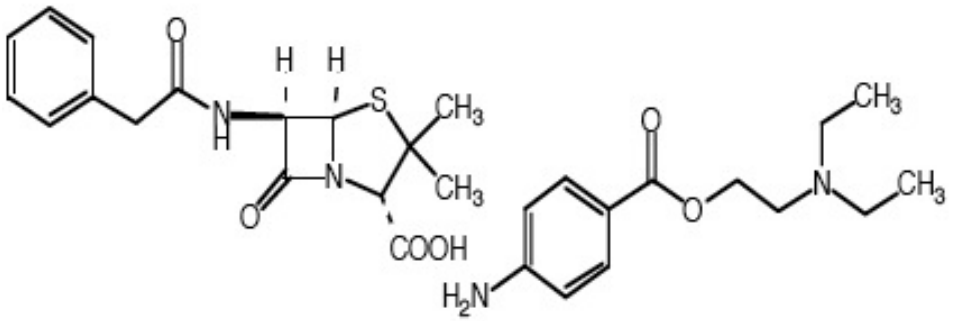
Local Anesthetics

• The first local anaesthetic was **Cocaine** (**leaves of E. Coca**) that was introduced into clinical practice by **Koller** in 1884 as an ophthalmic anaesthetic. Cocaine has powerful central stimulating side effects and induces dependence

• The first synthetic local anaesthetic was **Procaine** which introduced in 1905. It produce adverse effects like **local irritation and tissue damage in addition to systemic toxicity.** At present, it is only used as an amide (procainamide) for cardiac arrhythmias and in procaine penicillin for slow release of penicillin.

***E.* Coca**



procaine penicillin

Local Anesthetics

produce a transient and reversible loss of sensation in a restricted region of the body without loss of consciousness.

Common Uses of Local Anesthetics

Excision

Dermatology

Dentistry

Spinal Anesthesia

Local anesthetic mechanism of action

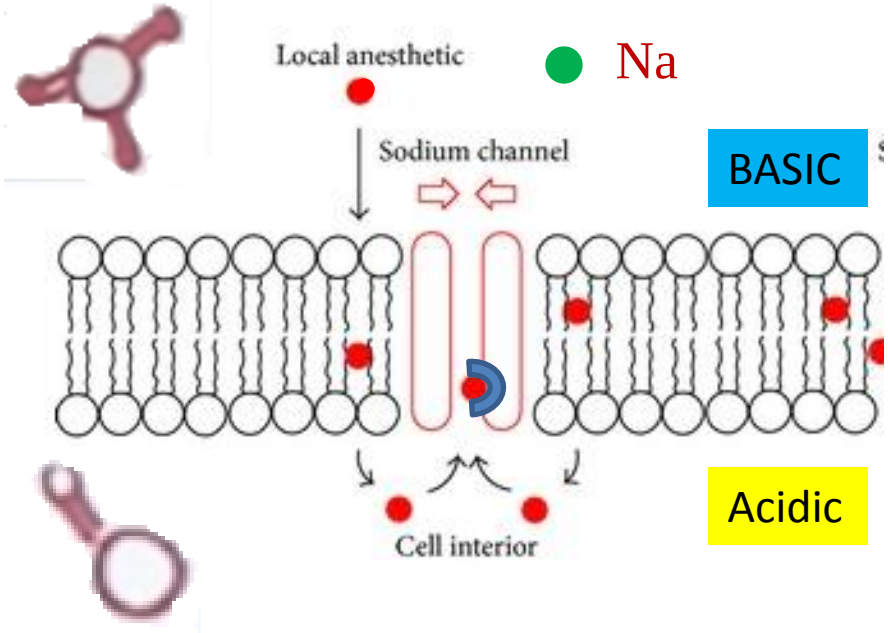
Un-Ionized form = can penetrate cell membrane (effective)

LA Weak base (pka 8-9)

Unionized can penetrate cell membrane

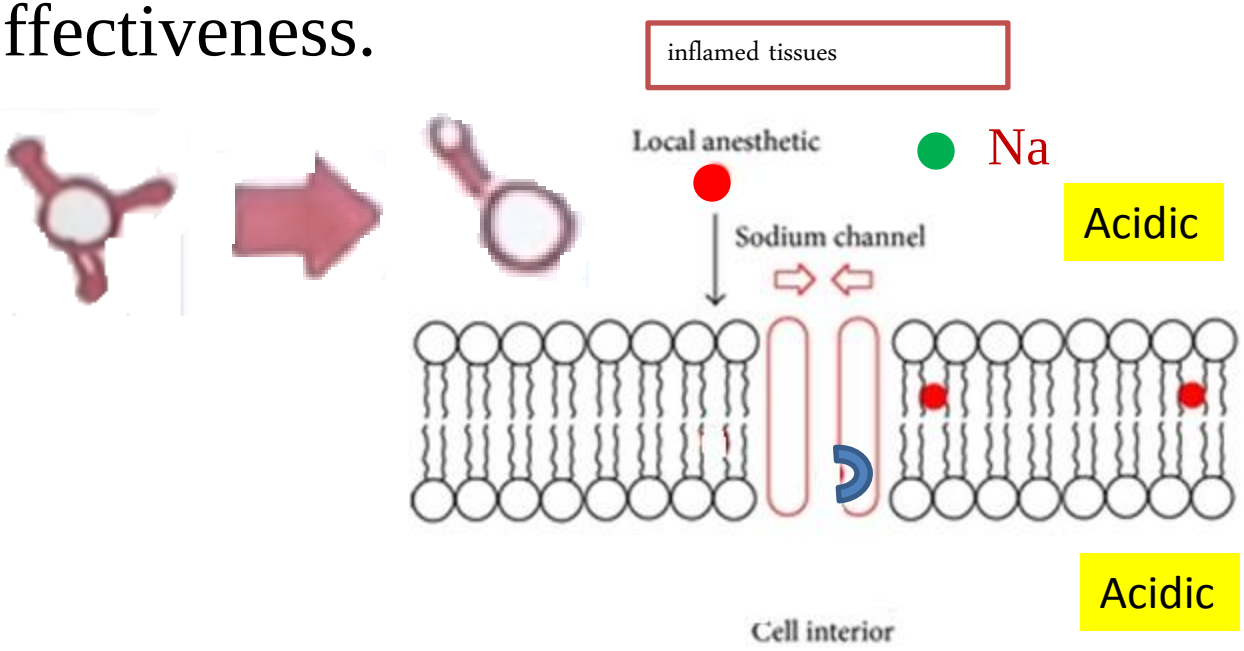
Weak base

ionized form in acidic media



Local anaesthetic in inflamed tissues

Reduced pH ,as in inflamed tissues, increases the prevalence of the **ionized form**, which reduces diffusion into nerves and thereby reduces local anaesthetic effectiveness.



Local Anesthetics
Chemistry and Toxicity

- **Esters**

Procaine, Cocaine, Benzocaine, Tetracaine

are metabolized by **plasma and tissue esterases**

- (Slow & Rapid metabolizers **Genetic poly morphism**)
- short acting & may cause allergic reaction
- **antagonize** the action of **sulfonamides** due to degradation of PABA.

- **Amides**

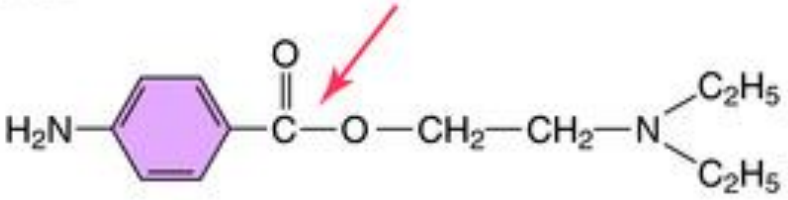
Lidocaine , Bupivacaine, Mepivacaine

are metabolized by **liver amidases** so **(Liver state is very important)**

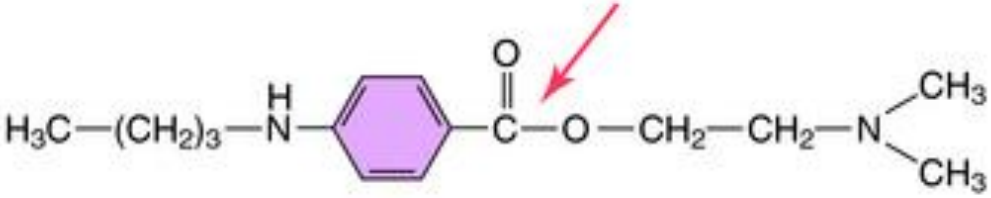
- long acting & less allergic reaction

Local Anesthetics

Esters

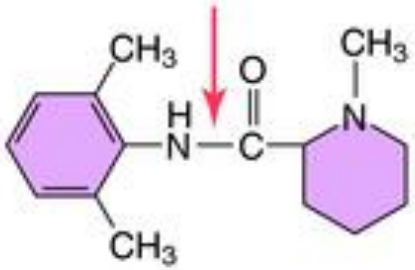


Procaine

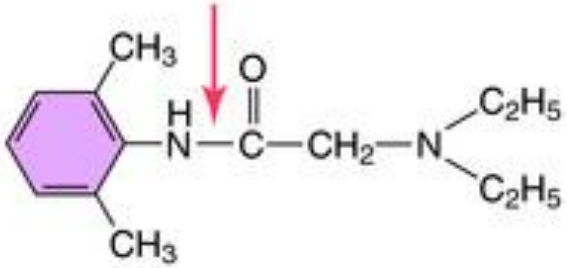


Tetracaine

Amides



Mepivacaine



Lidocaine

Local Anesthetics

- **Absorption**
  - **Co administration with α_1 agonists (Adrenaline);**
    - Decrease LA diffusion into the systemic circulation >> decrease toxicity
    - Prolong LA effects.

Local Anesthetics

- **Side effects ;**
- **Neurotoxicity:** **All LAs** if absorbed in systemic circulation can cause CNS toxicity manifests as excitation (**seizure**) followed by depression. Initial excitation is due to inhibition of inhibitory neurons.

- **Cardiotoxicty:** The primary site of action is the myocardium, decreases in electrical excitability, conduction rate, and force of contraction.

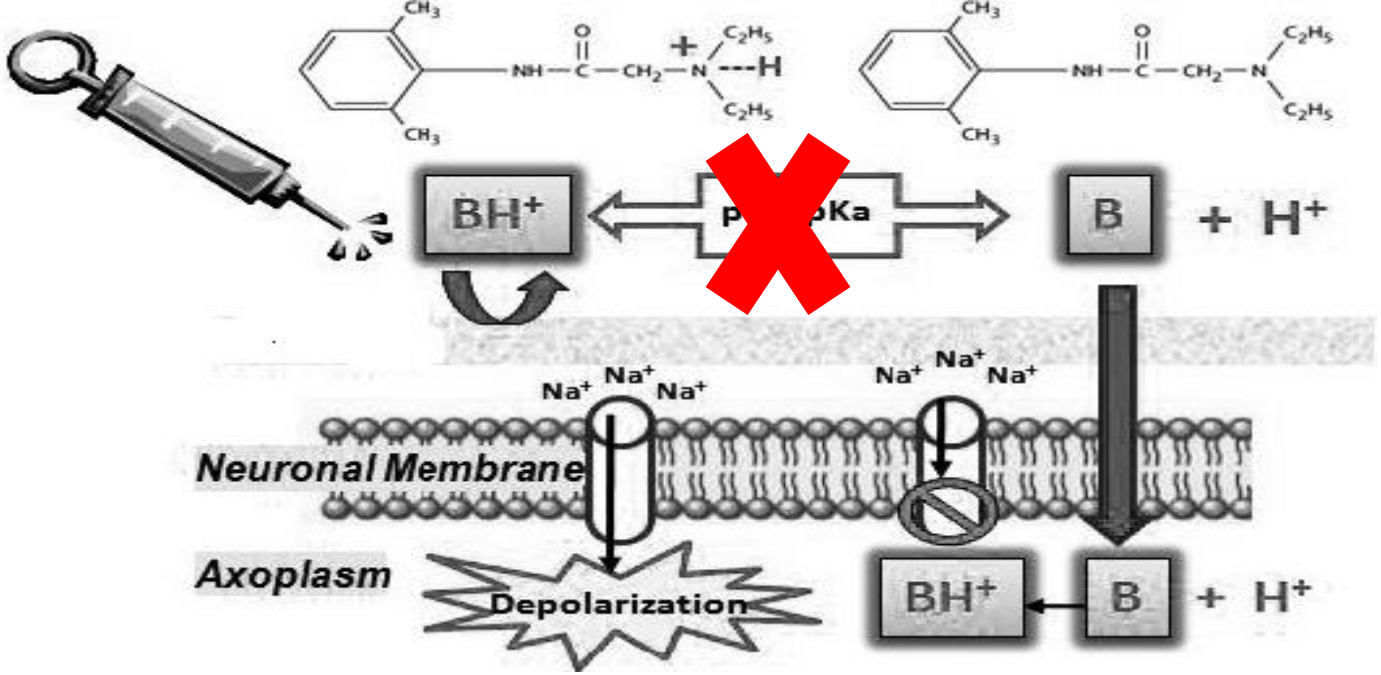
  All LAs decrease BP except cocaine (increases).

Local Anesthetics

Tachyphylaxis

* Local anaesthetics are weak bases and marketed as hydrochloride salts (pH 4 to 6) for **reasons of solubility and stability**

* After injection, the salts are buffered in the tissue to physiological pH, thereby providing sufficient free base for diffusion through axonal membranes.



However, repeated injections deplete the local available buffer. The ensuing acidosis **increases the extracellular cationic** form, which diffuses poorly into axons.

Call tachyphylaxis, especially in areas of limited buffer reserve, such as the cerebrospinal fluid. Therefore, an agent with a long duration of action like bupivacaine is preferred in this condition to **avoid repeating the dose**.

Local anesthetic administration

- **Topical** [**Lignocaine** is the commonly used agent for topical anesthesia of mucous membranes].

  [**Oxethazaine** (mucaine) can be used to provide symptomatic relief in gastritis (it remains unionized in the acidic pH of stomach]

- **Infiltration** [injected s.c. in the area of operation site for blocking the sensory nerve endings used in minor surgeries like excisions, suturing. **Adrenaline** can be added to the LA to prolong its duration of action and to prevent systemic side effects].

- **Nerve block** [Injection of local anesthetic into or about individual peripheral nerves or nerve plexuses produces even greater areas of anesthesia ; dangerous , skills, e.g. Pudendal n. in episiotomy].

- **Epidural** **Mainly used for controlling postoperative pain** ; injecting local anesthetic into the epidural space ; lignocaine 1-2% with adrenaline, require high skill . e.g. Low concentration—0.25%, of bupivacaine, often with 2 µg/mL of fentanyl added, frequently are used to provide analgesia during labor

- **Intravenous regional Block (Bier's Block)** indicated for any procedure on the **arm below the elbow or leg below the knee that will be completed within 40-60 minutes.** An intravenous cannula is inserted in a distal vein in the limb scheduled for surgery. The tourniquet is then applied to the upper arm or thigh.
- The drug of choice for IVRA is **prilocaine**

- **Spinal nerve block** [injection of local anesthetic into the CSF in the lumbar space.]

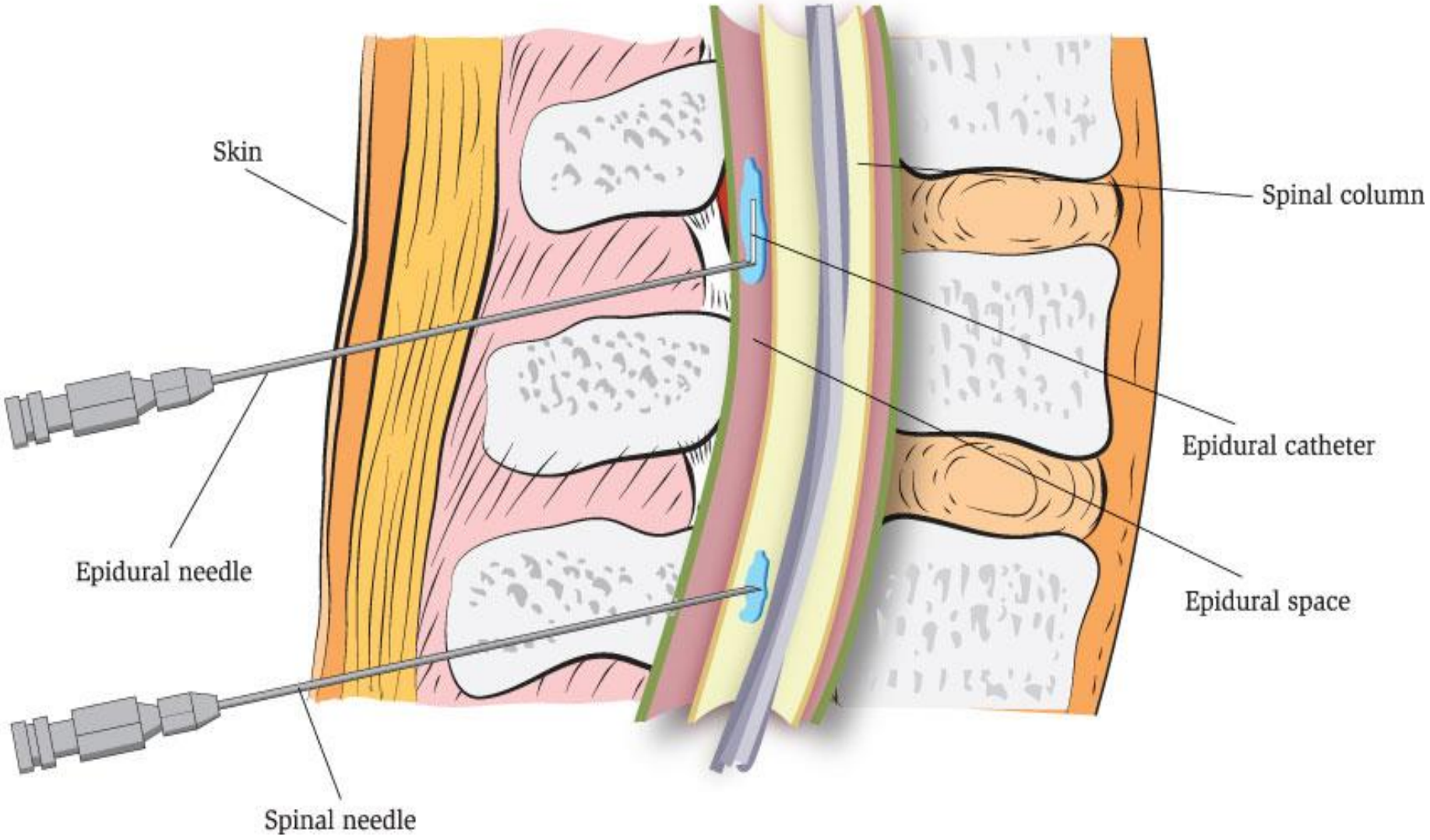
Drugs used for Spinal Anaesthesia

- Lignocaine – 5% in 7.5% dextrose
- Bupivacaine – 0.5% in 8% dextrose

Indications

- Orthopaedic surgery of lower limbs and pelvis.
- Surgery of lower abdomen (all pelvic and perineal surgeries, hernia, hydrocele, appendix)
- Gynaecological and obstestrics surgeries (hysterectomy, cervical surgeries, tubectomy, tuboplasty, caesarean section).

s/e : headache (CSF leakage), hypotension


Skin
Spinal column
Epidural catheter
Epidural needle
Epidural space
Spinal needle

Special remarks

- **All LAs are vasodilators except cocaine** (act as sympathomimetic due to inhibition of nor-adrenaline reuptake) which is a vasoconstrictor.
- **Chlorprocaine** is the **shortest acting** local anaesthetic and is **contra-indicated in spinal anaesthesia** (It may cause paraplegia due to the presence of sodium metabisulphite as preservative, which is neurotoxic).
- **Lignocaine** is the most commonly used LA and is the drug of choice for ventricular tachycardia.