Local Anesthetics
Chemistry

All L A are weak bases. Have three structural domains:

1. **Aromatic group:**
   influences the hydrophobicity of the drug.

2. **Amide or Ester linkage:**
   influences the duration of action and toxicity of the drug.

3. **Amine group:**
   influences the rate of onset and potency of the drug.
Esters:
cocaine, procaine, tetracaine, & chloroprocaine
Hydrolyzed in plasma by pseudo-cholinesterase.
One of the by-products of metabolism is paraaminobenzoic acid (PABA), the common cause of allergic reactions seen with these agents

Amides:
Lidocaine, mepivicaine, prilocaine, bupivacaine, and etidocaine.
metabolized in the liver.
True allergic reactions rare (especially with lidocaine)
Mechanism of Action

Blockade of voltage-gated sodium channels.

1) slow rate of depolarization
2) reduce height of action potential
3) reduce rate of rise of action potential
4) slow axonal conduction
5) ultimately prevent propagation of action potential
6) do not alter resting membrane potential
7) increase threshold potential
Factors affecting local anesthetic action

Effect of pH
Charged form binds to receptor site, uncharged form penetrates membrane.
Lower pH solution, (more acidic) shifts equilibrium toward the ionized form, delaying the onset action. Inflammation increases the acidity of the medium. This leads to lesser penetration into the nerves and, therefore, lesser activity.

Effect of lipophilicity
Highly lipophilic LAs penetrate the nerve membrane more easily. More lipophilic agents are more potent as local anesthetics.

Effect of vasodilator activity
Greater vasodilator activity = decreased potency and decreased duration of action.
Order of sensory function block

Small nerve fibers are more susceptible than large fibers; however, the type of fiber degree of myelination, fiber length and frequency-dependence are also important in determining susceptibility

1. pain
2. cold
3. warmth
4. touch
5. deep pressure
6. motor

Recovery in reverse order
• **TOXICITIES OF LOCAL ANESTHETICS**

• **Hypersensitivity**.
  Usually with esters due to PABA.

• **CNS Toxicities.**
  CNS excitement (Tremors and convulsions).
  Higher amounts, can cause CNS depression characterized by respiratory depression and respiratory arrest.

• **Cardiovascular Toxicities**.
  **Cardiac Effects:** Decreased excitability, conductivity, and contractility.
  **Vascular Effects:** vasodilation (except cocaine which is vasoconstrictive), hypotension.

These may ultimately result in both cardiac and respiratory arrest.
Routes of Administration of LA.

Surface Anesthesia.
Application of LA to skin.
Relieve itching, burning, & surface pain (minor sunburns).

Topical Block.
Applying LA to mucous membrane to block the nerve terminals in the mucosa.
Used during examination procedures involving the respiratory tract.
The anesthetic agent is rapidly absorbed into the bloodstream.
The topical block easily anesthetizes the surface of the cornea (of the eye) and the oral mucosa.
**Infiltration:**
the injection of LA directly into tissue without taking into consideration the course of nerves. The LA used most frequently for infiltration anes. are:
1- lidocaine
2- procaine
3- bupivacaine
When used without EP, greater amounts could be given.

**Nerve Block .**
A LA is injected around a nerve that leads to the operative site. Most LAs
Spinal Anesthesia. In use since 1898. LA is injected into the subarachnoid space. **Lidocaine, Tetracaine**

**Lumbar Epidural:** LA is injected into the peridural space. **Lidocaine, Bupivacaine**

**Caudal.** Procedure is easy in pediatric population. Calcification of sacrococcygeal ligament may make technique difficult or impossible in older adults.
Intravenous Extremity Block

Lidocaine, Tetracaine.
Vasoconstrictors

Decrease the rate of vascular absorption which allows more anesthetic to reach the nerve membrane and improves the depth of anesthesia.

50% prolongation of action and 30% reduction in blood levels.

1:200,000 epinephrine is the best vasoconstrictor.
Ester Local Anesthetics

Cocaine
Used in eye surgery and dentistry in 1884. Current clinical use is largely restricted to **topical anesthesia for ear, nose, and throat** procedures, where its intense vasoconstriction can serve to reduce bleeding.
Cardiototoxic and euophoric.

**Procaine (1905)**
Not effective topically.
Used for infiltration, nerve block, and spinal anesthesia.
It has a slow onset and short (1hour) duration.
Chloroprocaine.
Greater potency and less toxicity than procaine. Has short half-life so commonly used in obstetrics. No residual effects on the neonate.

Benzocaine
Usually for topical use.

Tetracaine
Long acting, highly potent, used in spinal & topical anesthesia.
More potent and more toxic than procaine and cocaine.
Has 5-minute onset and 2 to 3 hours of action.
Amide Local Anesthetics

Lidocaine (*Xylocaine*) (1943)

The most commonly used local anesthetic for all types of local anesthesia and as an antiarrhythmic agent.

Has a medium action & more intense & more prolonged duration of action than procaine.

The reference standard against which most anesthetics are compared.
Bupivacaine

Long action, 24 hours; an advantage for postoperative analgesia.

Its use for *epidural anesthesia in obstetrics* it relieves the pain of labor at concentrations of 0.125% while permitting some motor activity of abdominal muscles to aid in expelling the fetus.

Approved for *spinal anesthesia* and it is *4 times* more potent and more toxic than mepivacaine and lidocaine.
Levobupivacaine
S- enantiomer of bupivacaine.
Has long action.
Less CNS and cardiac toxicity than bupivacaine.
It also is slightly more motor sparing than is bupivacaine.

Ropivacaine
Duration similar bupivacaine, but slightly less potent.
Advantage over bupivacaine is its less cardiotoxicity.

Etidocaine
Chemically similar to lidocaine,
Has a more prolonged action.
Used for regional blocks, including epidural anesthesia.

exhibits a preference for motor rather than sensory block; therefore, its use in obstetrics is limited
Mepivacaine

Longer acting than lidocaine and has a more rapid onset of action (3–5 minutes).

**Topical application is not effective.**

has a tendency toward vasoconstriction rather than vasodilation which has made it a popular choice for major peripheral blocks.

Slowly metabolized by the fetus, making it a poor choice for epidural anesthesia.

When used for spinal anesthesia, mepivacaine has a slightly lower incidence of Transient neurologic symptoms than lidocaine (e.g. pain in the lower extremities).
Prilocaine
Onset slightly longer & duration same as lidocaine. 40% less toxic than lidocaine, so especially suitable for regional anesthetic techniques. metabolized by the liver to orthotoluidine, when accumulates, can cause methemoglobin. As a spinal anesthetic, prilocaine's duration of action is slightly longer than that of lidocaine, and it carries a low risk of TNS.

Ropivacaine
Reduced cardiotoxicity, so widespread use for high-volume peripheral blocks. Popular choice for epidural infusions for control of labor and postoperative pain.
TOPICAL AGENTS

EMLA

EMLA (Eutectic Mixture of Local Anesthetics). containing 2.5% of lidocaine and 2.5% prilocaine, permits anesthetic penetration of the keratinized layer of skin, producing localized numbness. Commonly used in pediatrics to anesthetize the skin prior to venipuncture for intravenous catheter placement.

No significant local or systemic toxicity.
TAC
A topical mixture of anesthetics frequently used in pediatric emergency departments for repair of minor lacerations.
The usual mixture is:
Tetracaine 0.5%, Adrenaline 1:2,000, and Cocaine 11.8%.
Because of potential complications (seizures), lower concentrations of cocaine and epinephrine in a tetracaine 1% solution have been suggested (TAC III)