

# **Local Anesthesia**

**Munir Gharaibeh, MD, PhD, MHPE**

**School of Medicine**

**The University of Jordan**

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**[mgharaib@ju.edu.jo](mailto:mgharaib@ju.edu.jo)**

# Local Anesthesia

## Definition and Scope

### History:

Nerve compression and refrigeration.

Coca leaves used by the Incas.

1860, Cocaine was isolated.

1884, Cocaine was used in eye surgery and dentistry, and then in nerve blocks.

1903, Adrenaline added

1905, Procaine then Lidocaine in 1943

# Features of an Ideal LA

**Rapid onset.**

**Not irritating.**

**Sufficient duration of action.**

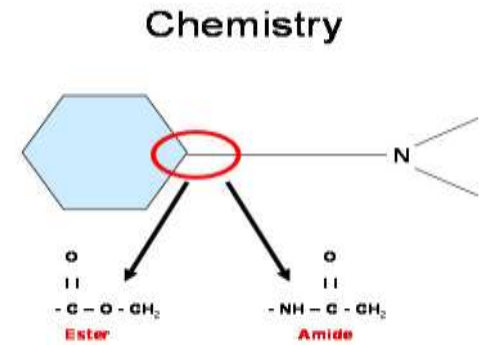
**Reversible effect.**

**Low systemic toxicity.**

**Proper physical properties: Stability**

**Water solubility.**

# Chemistry of LA



**All LAs have three structural domains:**

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

**Amide or Ester linkage**: influences the duration of action and toxicity (allergy) of the drug.

**Amine group**: influences the rate of onset and potency of the drug.

**TABLE 26-1 Structure and properties of some ester and amide local anesthetics.<sup>1</sup>**

	Structure	Potency (Procaine = 1)	Duration of Action
<b>Esters</b>			
Cocaine		2	Medium
Procaine (Novocain)		1	Short
Tetracaine (Pontocaine)		16	Long
Benzocaine		Surface use only	
<b>Amides</b>			
Lidocaine (Xylocaine)		4	Medium
Mepivacaine (Carbocaine, Isocaine)		2	Medium
Bupivacaine (Marcaine), Levobupivacaine (Chirocaine)		16	Long
Ropivacaine (Naropin)		16	Long
Articaine		16 <sup>2</sup>	Medium

<sup>1</sup>Other chemical types are available including ethers (pramoxine), ketones (glycoline), and phenol derivatives (phenacaine).

<sup>2</sup>Data not found.

# **Mechanism of Action of LA**

**Blockade of voltage-gated sodium channels from inside the channel.**

**LAs are dispensed as hydrochloride salts with an acidic pH of ~6, so they are more ionized and therefore water soluble for storage and injection.**

**When injected into the body, buffers raise the pH which increases the free base form.**

**They cross the nerve membrane in the non-ionized form (free base).**

**LAs block sodium channels in the ionized form (cation)**

# Importance of pKa

**Strongly Influences time of onset. ⑩**  
**s cross neuronal membrane in 'LA ⑩**  
**base form**

**The closer pKa is to physiologic pH ⑩**  
**the more drug will be in the ,(7.4)**  
**base form and thus will have a**  
**faster onset time.**





**RELATIONSHIP OF pKa TO PERCENT BASE FORM AND TIME FOR 50 PERCENT CONDUCTION BLOCK IN ISOLATED NERVE**

<b>Agent</b>	<b>pKa</b>	<b>% Base at pH 7.4</b>	<b>Onset (min)</b>
<b>Prilocaine</b>	<b>7.7</b>	<b>35</b>	<b>2-4</b>
<b>Lidocaine</b>	<b>7.7</b>	<b>35</b>	<b>2-4</b>
<b>Etidocaine</b>	<b>7.7</b>	<b>35</b>	<b>2-4</b>
<b>Bupivacaine</b>	<b>8.1</b>	<b>20</b>	<b>5-8</b>
<b>Tetracaine</b>	<b>8.6</b>	<b>5</b>	<b>10-15</b>
<b>Procaine</b>	<b>8.9</b>	<b>2</b>	<b>14-18</b>

# Tissue acidosis

Usually associated with sepsis ⑩ or infection near site of block.

pH<7.4 causes greater amount ⑩ of local anesthetic to be in the ionized form.

Acidosis causes slow onset and ⑩ poor quality of nerve block.



# Mechanism of Action of LA

Prevent increases in permeability of nerve membranes to  $\text{Na}^+$  ions ⑩

Slows rate of depolarization ⑩

Threshold potential is never reached ⑩

Produce Differential Blockade of the nerves:

**C--B -- A**

Autonomic

Pain

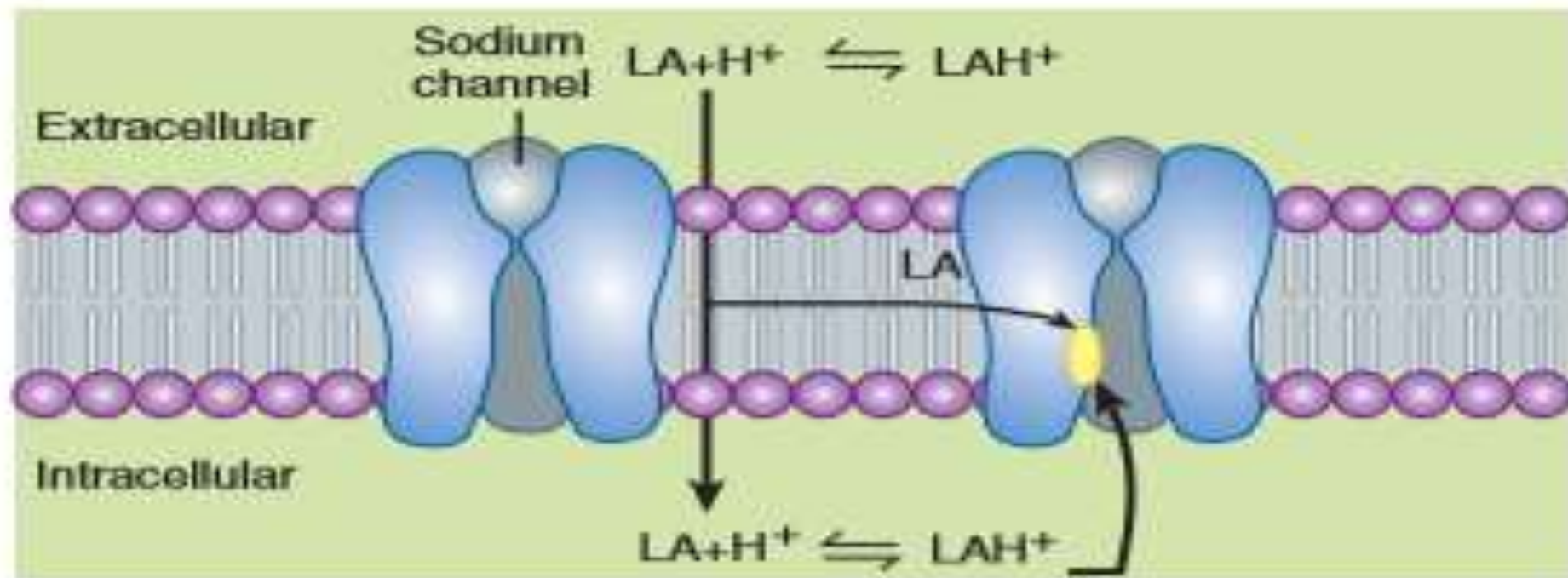
Cold

Warmth

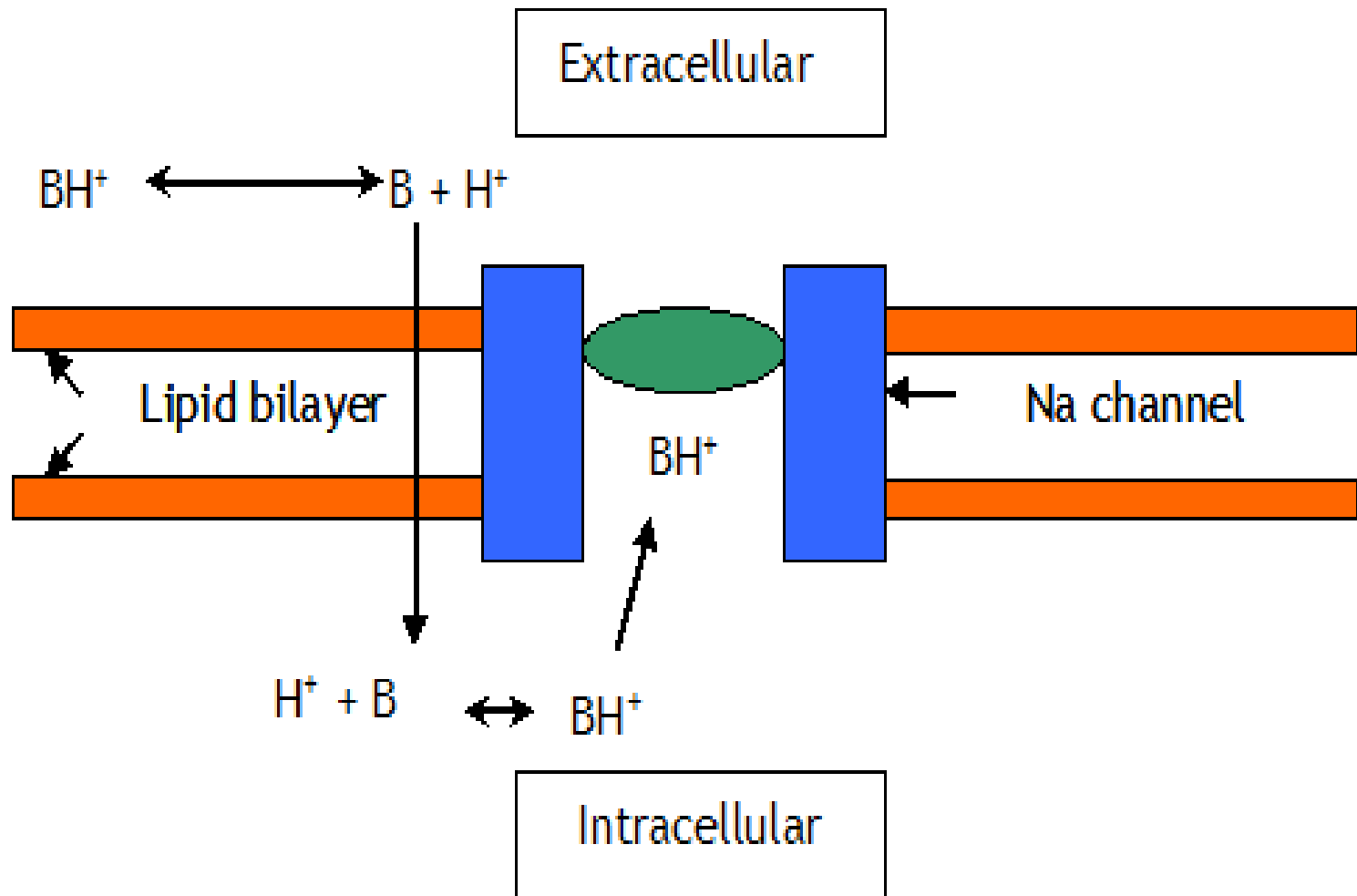
Touch

Pressure

Motor



**FIGURE 26-1** Schematic diagram depicting paths of local anesthetic (LA) to receptor sites. Extracellular anesthetic exists in equilibrium between charged and uncharged forms. The charged cation penetrates lipid membranes poorly; intracellular access is thus achieved by passage of the uncharged form. Intracellular re-equilibration results in formation of the more active charged species, which binds to the receptor at the inner vestibule of the sodium channel. Anesthetic may also gain access more directly by diffusing laterally within the membrane (hydrophobic pathway).



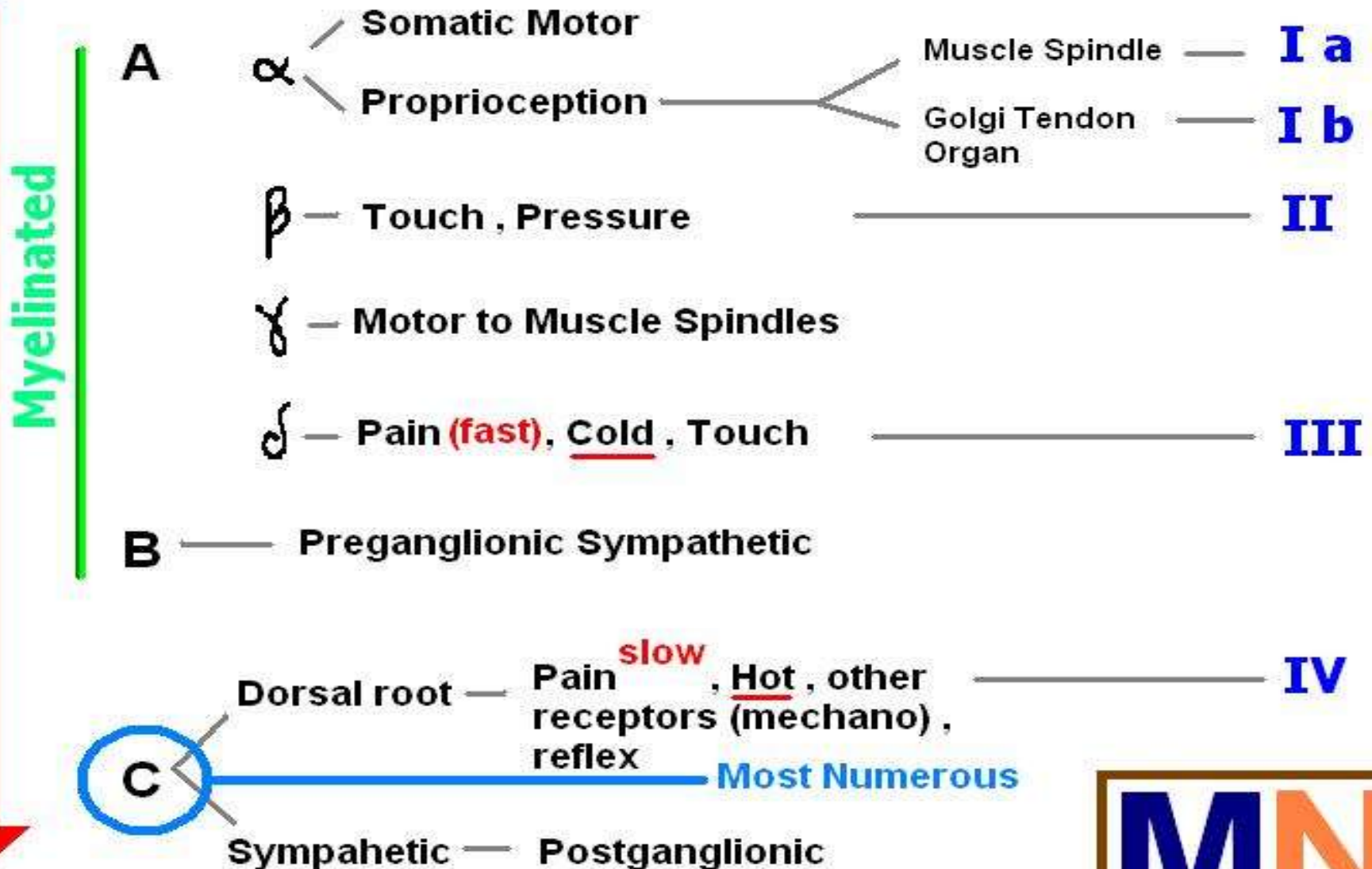
$BH^+$ : ionized form, cation  
 $H_2O$  soluble

B: unionized form, free  
base lipid soluble

# Classification of Nerve fibers

Erlanger & Gasser

Numerical



Diameter and Velocity  
DECREASE

**TABLE 26-3** Relative size and susceptibility of different types of nerve fibers to local anesthetics.

Fiber Type	Function	Diameter ( $\mu\text{m}$ )	Myelination	Conduction Velocity (m/s)	Sensitivity to Block
<b>Type A</b>					
Alpha	Proprioception, motor	12-20	Heavy	70-120	+
Beta	Touch, pressure	5-12	Heavy	30-70	++
Gamma	Muscle spindles	3-6	Heavy	15-30	++
Delta	Pain, temperature	2-5	Heavy	5-25	+++
<b>Type B</b>	Preganglionic autonomic	< 3	Light	3-15	++++
<b>Type C</b>					
Dorsal root	Pain	0.4-1.2	None	0.5-2.3	++++
Sympathetic	Postganglionic	0.3-1.3	None	0.7-2.3	++++

# Routes of Administration of LA

**Topical or Surface:** Lidocaine and Tetracaine.

**Infiltration:** Most LAs

**Regional Block:**

**Nerve Block:** most LAs

**Spinal(Subarachnoid):** Lidocaine,  
Tetracaine

**Lumbar Epidural:** Lidocaine, Bupivacaine

**Caudal.**

**Intravenous Extremity Block(Bier Block):**  
Lidocaine, Tetracaine.



1884

William Stewart Halsted, uses anesthetics to (among other things) develop the Dental Nerve Block injections in use today

His other contributions include:



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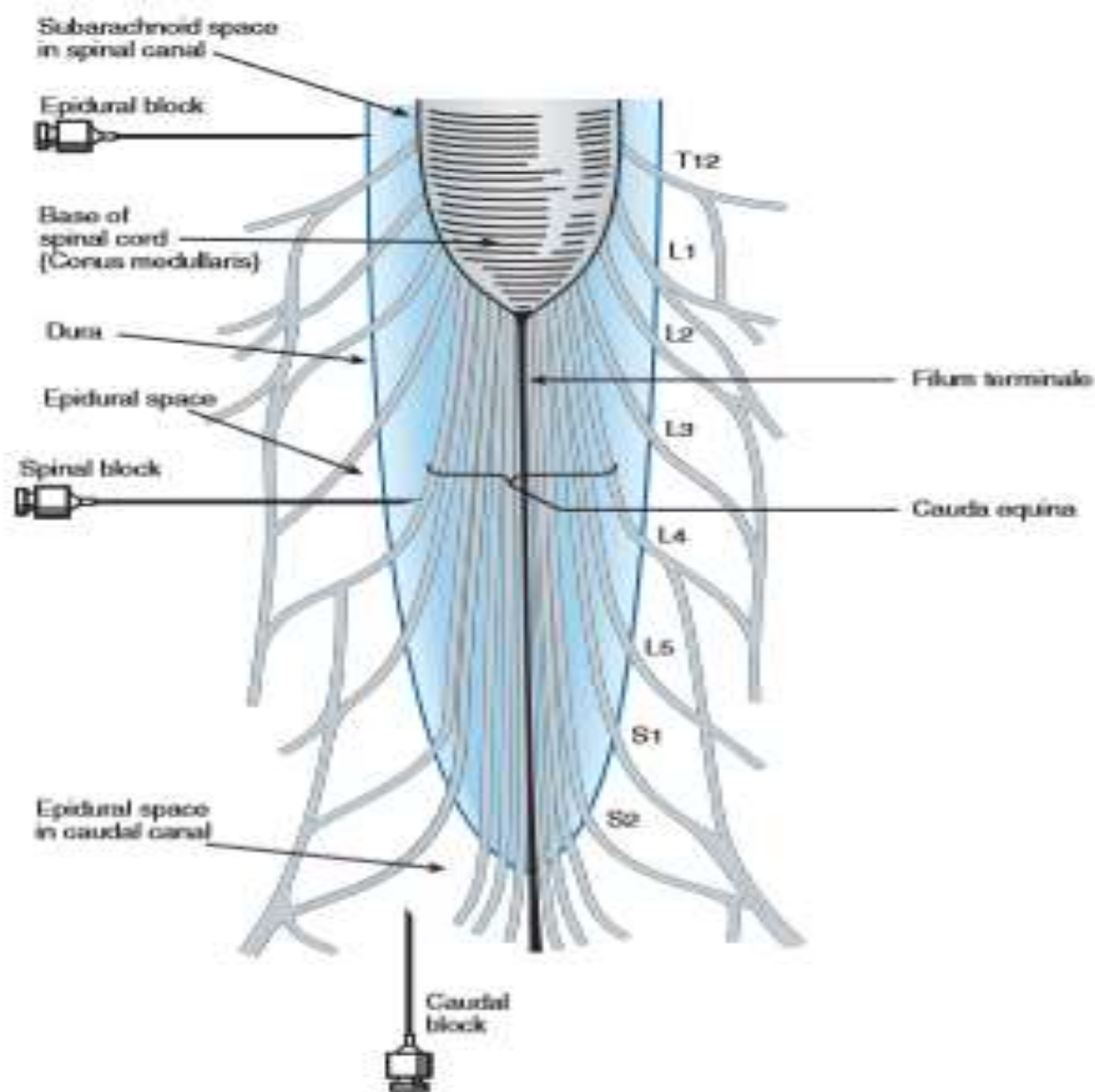


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An advertisement for 'COCAINE TOOTHACHE DROPS'. The top part of the ad shows a young girl in a red dress and white apron standing next to a boy in a yellow shirt and hat who is kneeling and building a wooden structure. The background shows a house and trees. The text below the illustration reads:

**COCAINE**  
**TOOTHACHE DROPS**  
Instantaneous Cure!  
PRICE 15 CENTS.  
Prepared by the  
**LLOYD MANUFACTURING CO.**  
219 HUDSON AVE., ALBANY, N. Y.  
For sale by all Druggists.  
(Registered March 1885.) See other side.





**FIGURE 26-4** Schematic diagram of the typical sites of injection of local anesthetics in and around the spinal canal. When local anesthetics are injected extradurally, it is referred to as an epidural block. A caudal block is a specific type of epidural block in which a needle is inserted into the caudal canal via the sacral hiatus. Injections around peripheral nerves are known as perineural blocks (eg, paravertebral block). Finally, injection into cerebrospinal fluid in the subarachnoid (intrathecal) space is referred to as a spinal block.

# Pharmacokinetics of LA

## Absorption and Distribution:

**Dose.**

**Site of injection.**

**Drug Tissue Binding.**

**Vascularity (local blood flow).**

**The use of vasoconstrictors( 50% prolongation of action and 30% reduction in blood levels).**

**Physicochemical Properties.**

**pH.**

# Metabolism of LAs

**AMIDES** are metabolized by <sup>10</sup> microsomal enzymes primarily in the **LIVER**

**Slow process, more likely to cause <sup>10</sup> systemic toxicity than esters**

**Hepatic disease decreases rate of <sup>10</sup> metabolism, increases duration of action**

**CHF decreases liver blood flow and <sup>10</sup> can also slow metabolism**

## Metabolism of LAs

**ESTERS** undergo hydrolysis in the plasma by pseudocholinesterase enzyme.

Metabolites are inactive, but may be structurally similar to PABA.

Allergy is more common with esters.

Cocaine is an ester that is metabolized in the liver.

# **Systemic Effects of LA**

## **Cardiac Effects:**

**Decreased excitability, conductivity, and contractility.**

## **Vascular Effects:**

**Usually vasodilation which will reduce venous return and consequently cardiac output. Cocaine causes constriction, so there is no need for a vasoconstrictor.**

## **Hypersensitivity Reactions:**

**Usually with esters, due to PABA.**

**Might also be due to the preservatives.**

**Can cause allergic dermatitis or asthma.**

# Systemic Effects of LA

## Central Effects:

Can cross BBB due to small size.

Usually cause CNS stimulation.

CNS depression occurs with high doses.

## Neuromuscular & Ganglia:

Can decrease ACh release.

## Local Irritation.

# Ester Local Anesthetics

## Cocaine:

Medium potency, medium duration of action, mainly in ophthalmology, also topical, cardiotoxic and euphoric.

## Procaine:

Short acting, used for infiltration and dental anesthesia

## Benzocaine:

Usually for topical use.

## Chloroprocaine.

## Tetracaine:

Long acting, highly potent, used in spinal and topical anesthesia.



# Amide Local Anesthetics

## Lidocaine(1944):

**Most commonly used,  
All routes  
Rapid onset,  
Most intense,  
Medium duration.**

## Bupivacaine:

**In obstetrics and postoperative anesthesia.  
Long duration(24hrs).**

# Amide Local Anesthetics

**Ropivacaine**

**Etidocaine**

**Mepivacaine**

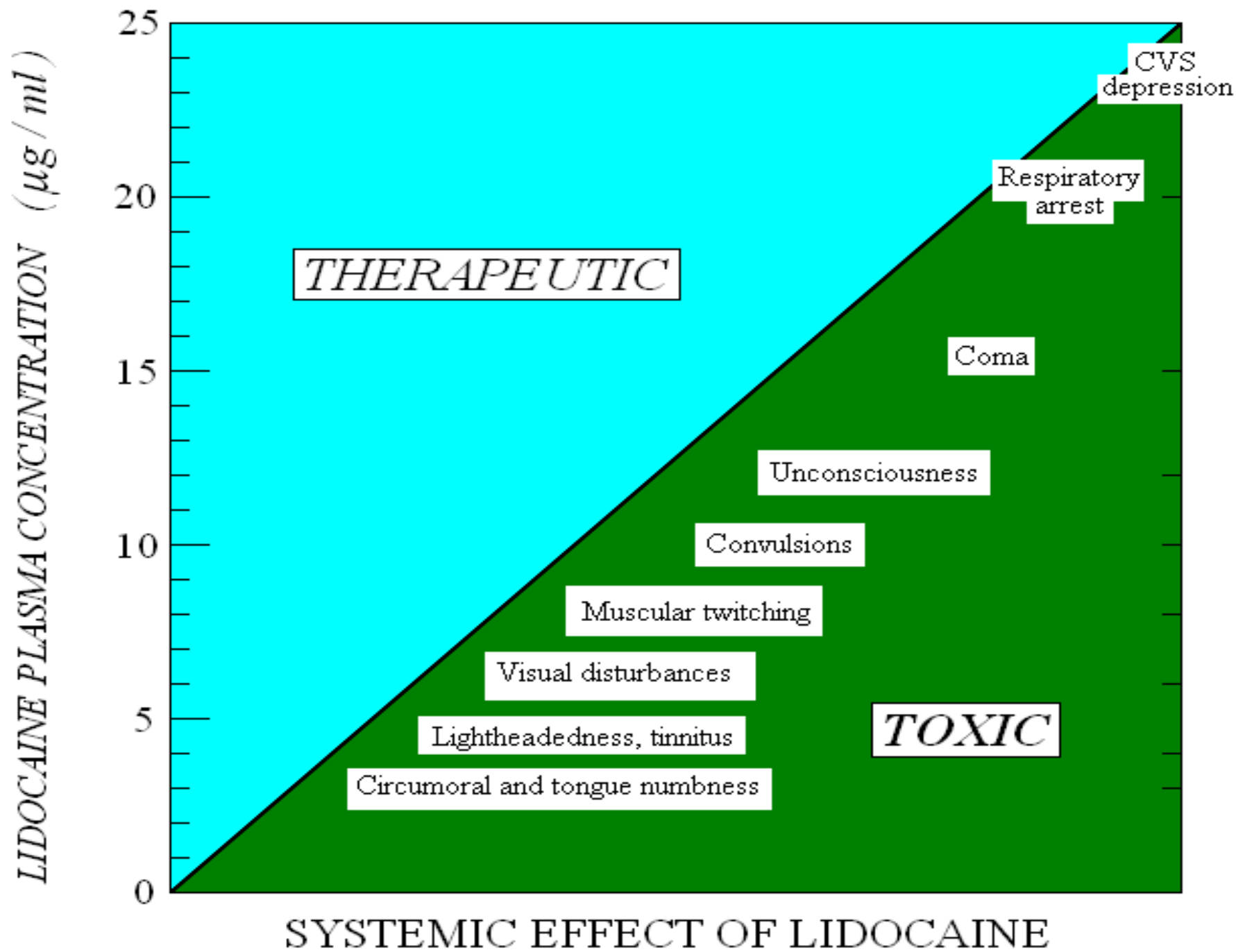
**Prilocaine:**

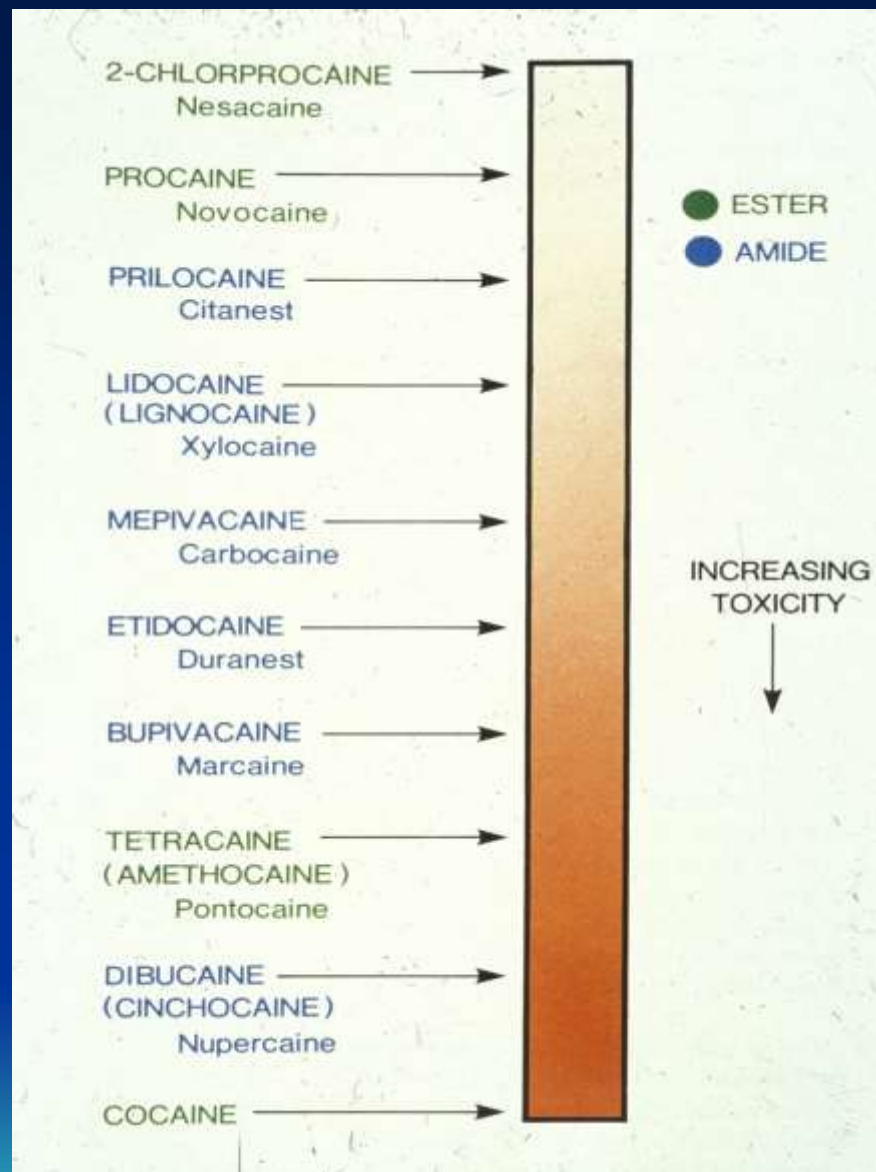
**Has some vasoconstrictor effect, no need to add epinephrine.**

# LA's Toxicity

**Most toxic reactions are a direct result of placement of the local anesthetic in the wrong place, e.g. intraneural, intrathecal or intravenous.**







# Topical Agents

## EMLA:

*“Eutectic Mixture of Local Anesthetics”:*

Mixture of lidocaine and prilocaine.

Patch or cream.

For children to reduce the pain of venipuncture, arterial cannulation, lumbar puncture, dental procedures, and skin graft donor site.

## TAC:

Tetracaine + Adrenaline + Cocaine.

For repair of minor lacerations.