

Local Anesthesia

Munir Gharaibeh, MD, PhD, MHPE

School of Medicine

The University of Jordan

February, 2019

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.

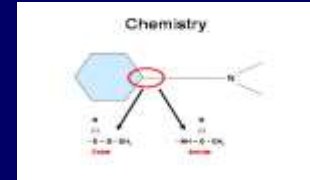
Reversible effect.

Low systemic toxicity.

Proper physical properties: Stability

Water solubility.

Chemistry of LA



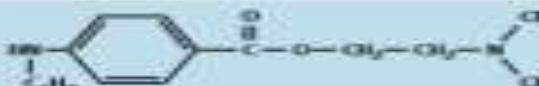
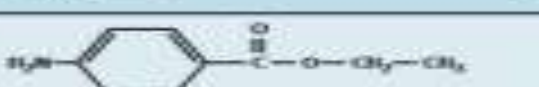
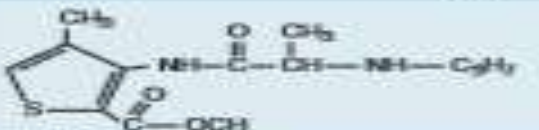
All LAs have three structural domains:

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.¹

	Structure	Potency (Procaine = 1)	Duration of Action
Esters			
Cocaine		2	Medium
Procaine (Novocain)		1	Short
Tetracaine (Pontocaine)		16	Long
Benzocaine		Surface use only	
Amides			
Lidocaine (Xylocaine)		4	Medium
Mepivacaine (Carbocaine, Isocaine)		2	Medium
Bupivacaine (Marcaine), Levobupivacaine (Chirocaine)		16	Long
Ropivacaine (Naropin)		16	Long
Articaine		18 ²	Medium

¹Other chemical types are available including ethers (pramoxine), ketones (glydine), and phenol derivatives (phenacaine).²Data not found.

Mechanism of Action of LA

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

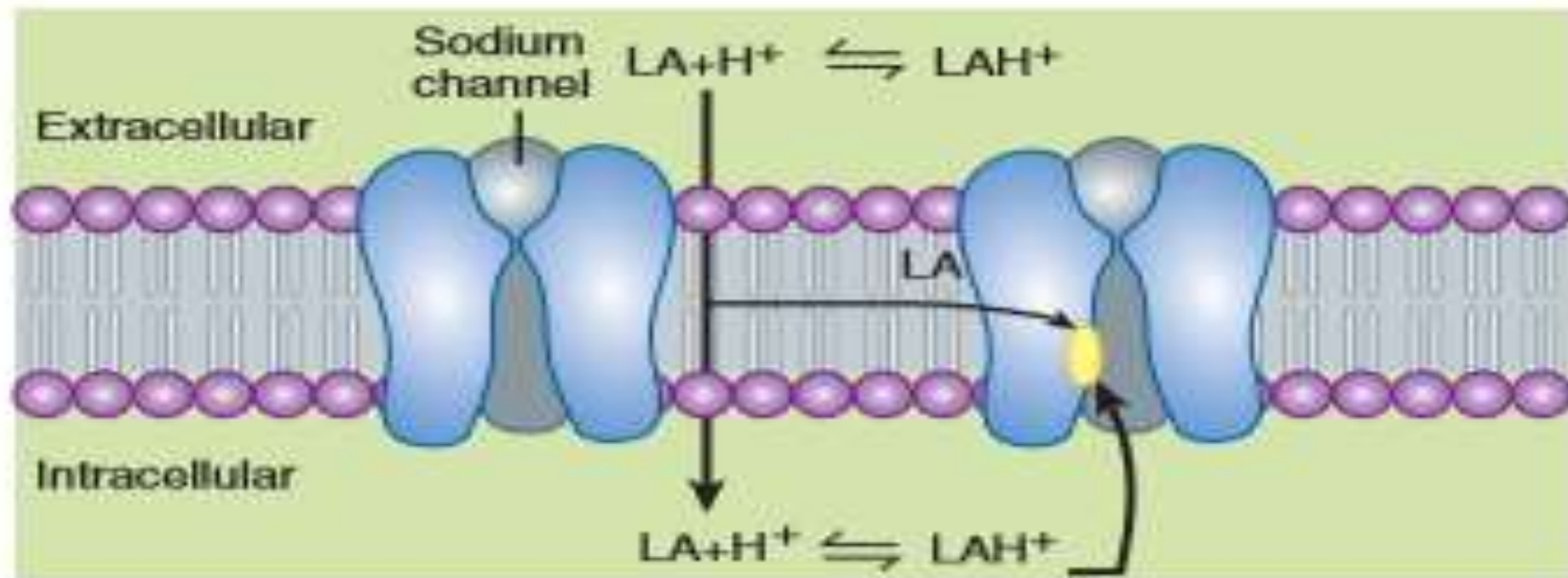
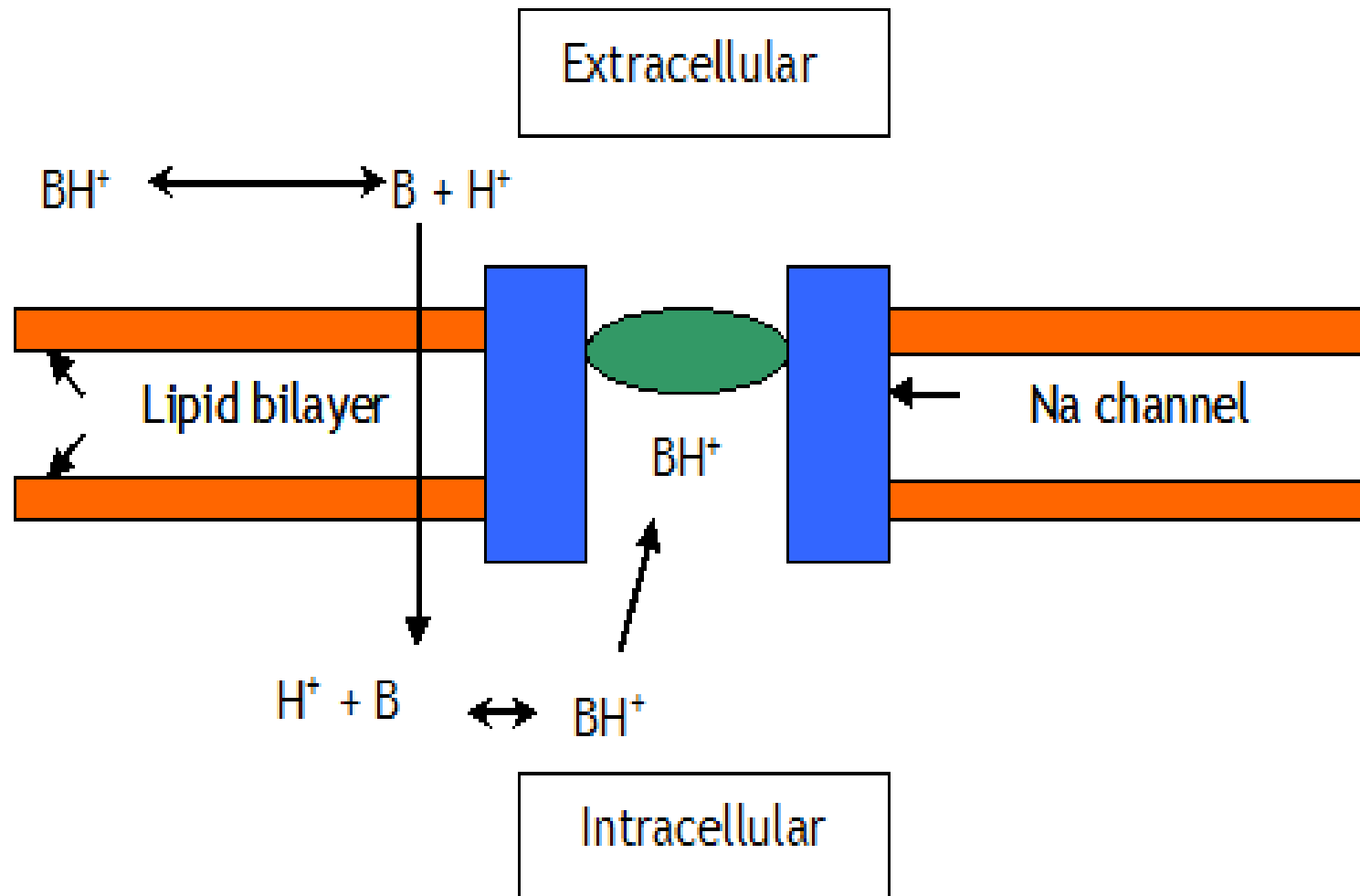


FIGURE 26-1 Schematic diagram depicting paths of local anesthetic (LA) to receptor sites. Extracellular anesthetic exists in equilibrium between charged and uncharged forms. The charged cation penetrates lipid membranes poorly; intracellular access is thus achieved by passage of the uncharged form. Intracellular 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

LAs are **dispensed** as hydrochloride ⑩ 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 ⑩ raise the pH which increases the free base form.

They **cross** the nerve membrane in the ⑩ non-ionized form (free base).

LAs block sodium channels in the ⑩ ionized form (cation)



Importance of pKa

Strongly Influences time of **onset**. ⑩

LA's cross neuronal membrane in ⑩
base form.

The closer pKa is to physiologic pH ⑩
(7.4), the more drug will be in the
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

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

Tissue acidosis

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

$\text{pH} < 7.4$ 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 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

Classification of Nerve fibers

Erlanger & Gasser

Numerical

Myelinated

A

α Somatic Motor

α Proprioception

Muscle Spindle

I a

Golgi Tendon Organ

I b

β Touch, Pressure

II

γ Motor to Muscle Spindles

δ Pain (fast), Cold, Touch

III

B Preganglionic Sympathetic

Dorsal root Pain ^{slow}, Hot, other receptors (mechano), reflex

IV

C

Sympathetic Postganglionic

Most Numerous



Diameter and Velocity
DECREASE

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

Fiber Type	Function	Diameter (μm)	Myelination	Conduction Velocity (m/s)	Sensitivity to Block
Type A					
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	+++
Type B	Preganglionic autonomic	< 3	Light	3-15	++++
Type C					
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:



@ Original Artist / Search ID: rdin245



Rights Available from CartoonStock.com

An illustration of a young girl in a red dress and white apron, and a young boy in a yellow shirt and brown hat, building a small wooden house with sticks and bricks in a yard. A house and trees are in the background.

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.



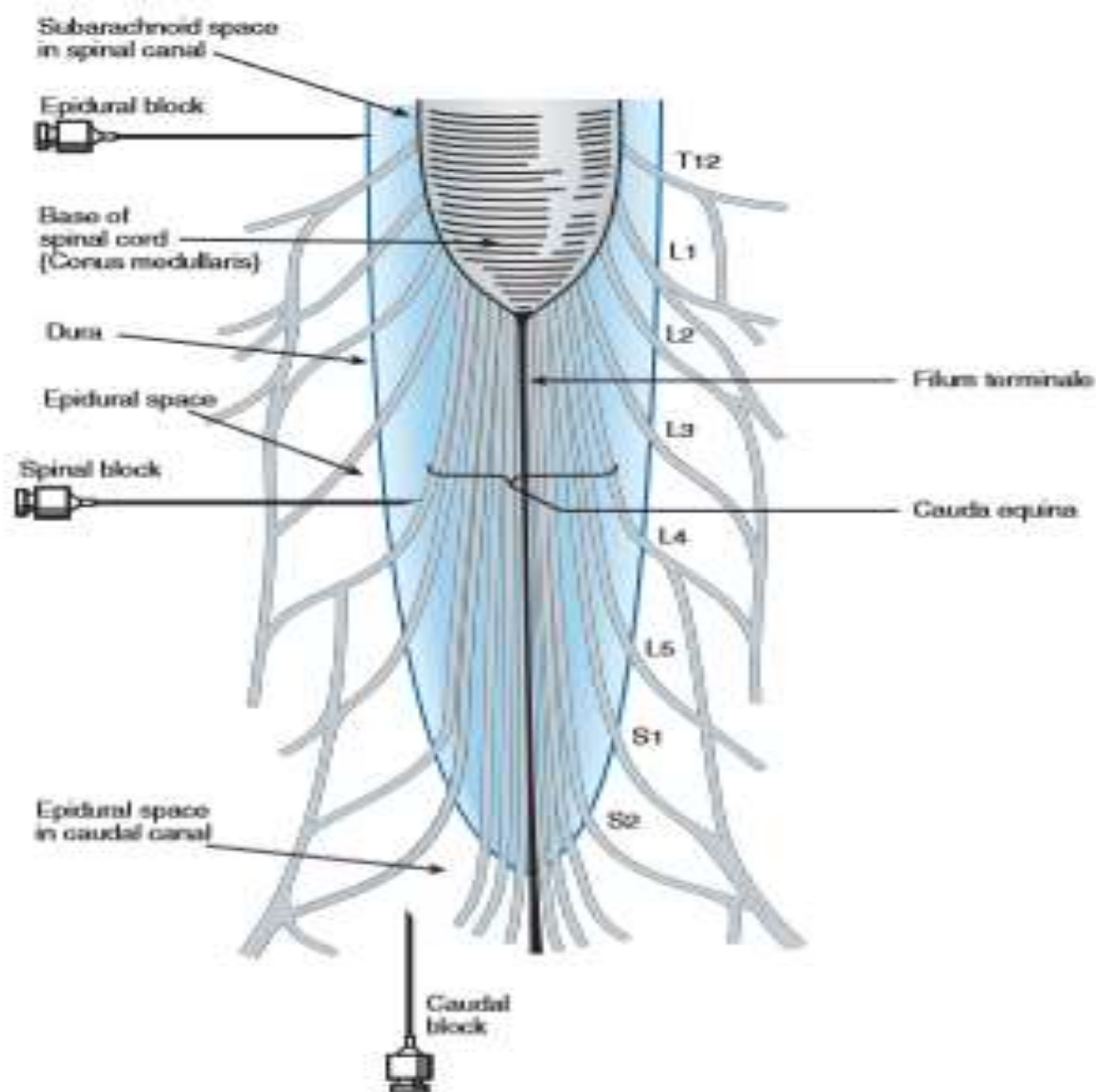


FIGURE 26-4 Schematic diagram of the typical sites of injection of local anesthetics in and around the spinal canal. When local anesthetics are injected extradurally, it is referred to as an epidural block. A caudal block is a specific type of epidural block in which a needle is inserted into the caudal 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

ESTERS undergo hydrolysis in the plasma by pseudocholinesterase enzyme. ⑩

Metabolites are inactive, but may be structurally similar to PABA. ⑩

Allergy is more common with esters. ⑩

Cocaine is an ester that is metabolized in the liver. ⑩



Metabolism of LAs

AMIDES are metabolized by ⑩ microsomal enzymes primarily in the liver.

Slow process, more likely to cause ⑩ **systemic** toxicity than esters

Hepatic disease decreases rate of ⑩ metabolism, increases duration of action

CHF decreases liver blood flow and ⑩ can also slow metabolism

Systemic Effects of LA

Cardiac Effects:

Decreased excitability, conductivity, and contractility.

Vascular Effects:

Usually vasodilation which will reduce venous return and consequently C.O.

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).
Cardiotoxic.**

Amide Local Anesthetics

Ropivacaine

Etidocaine

Mepivacaine

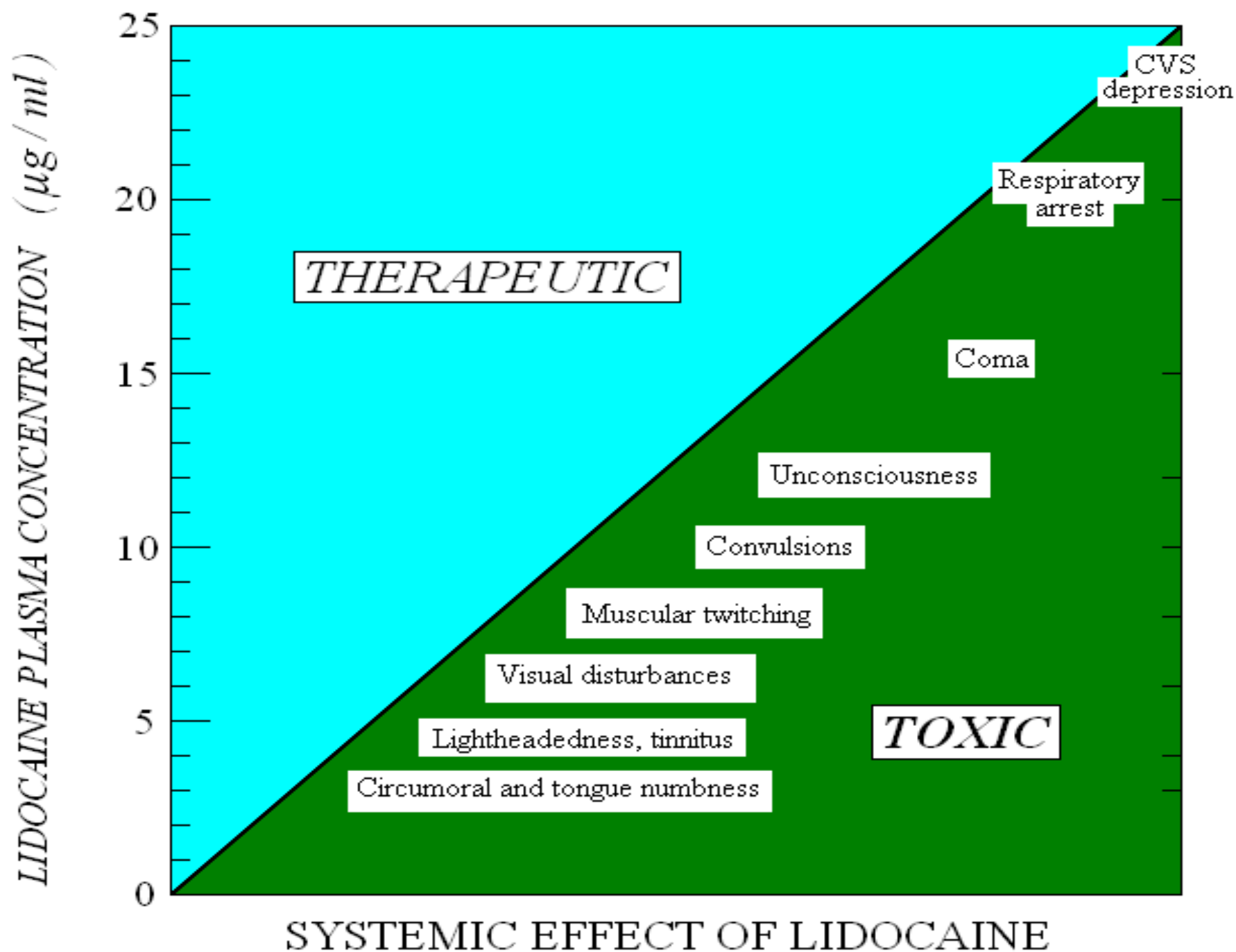
Prilocaine:

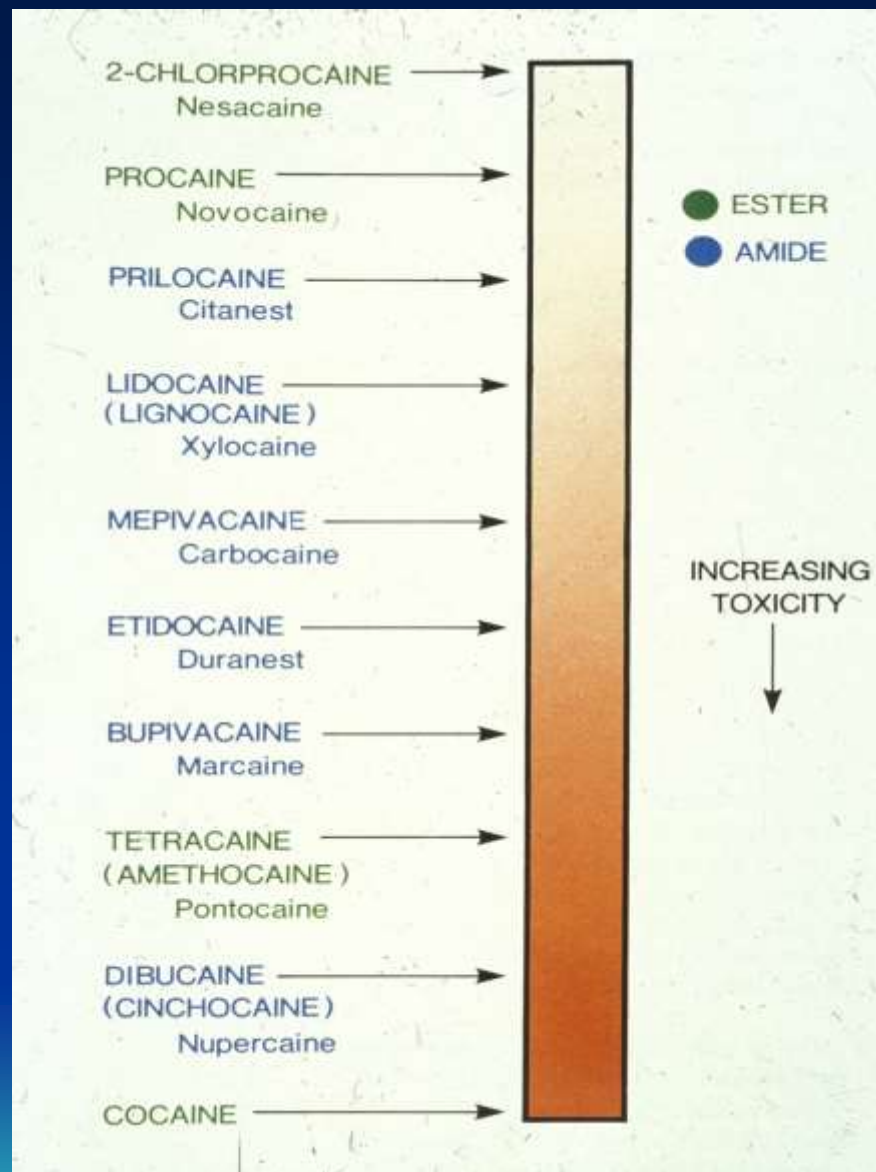
**Has some vasoconstrictor effect, no
need to add epinephrine.**

LA's Toxicity

Most toxic reactions are a direct ⑩ 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.