Local Anesthesia Notes

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Record notes are added in the red color

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Local Anesthesia

(to produce anesthesia in a certain part of the body)

Definition and Scope

History:

Nerve compression and refrigeration

Coca leaves used by the Incas (the first local anesthetic)

1860, Cocaine was isolated.

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

1903, Adrenaline added (because most of the local anesthetics produce vasodilation upon systemic absorption)

1905, Procaine then Lidocaine in 1943

Features of an Ideal LA

- Rapid onset of action.

- Not irritating.

- Sufficient duration of action for the duration of the procedure.

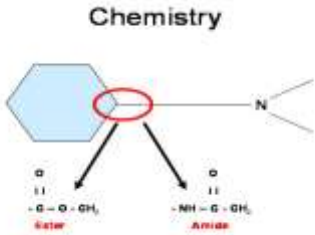
- Reversible effect.

- Low systemic toxicity.

- Proper physical properties: Stability

- Water solubility.

Chemistry of LA



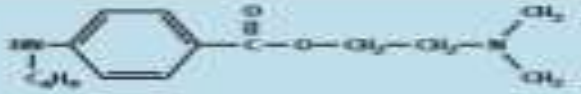
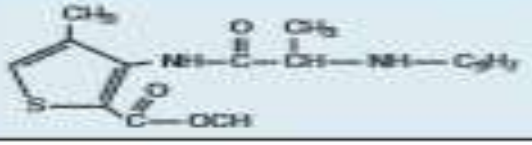
All LAs have three structural domains:

<u>Aromatic group</u> (benzene ring): influences the hydrophobicity of the drug.

<u>Amide or Ester linkage</u>: influences the duration of action and toxicity(allergy) of the drug(the dr. emphasized on this point), LAs are divided either amide or ester .

<u>Amine group</u>: 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)			Medium
Bupivacaine (Marcaine), Levobupivacaine (Chirocaine)		16	Long
Ropivacaine (Naropin)		16	Long
Articaine		8[2]	Medium

The first three have ester bonds

The rest contain amide bonds

[1] Other chemical types are available including ethers (pramoxine), ketones (dyclonine), and phenetidin derivatives (phenacaine).

[2] Data not found.

Mechanism of Action of LA

Blockade of voltage-gated sodium channels <u>from inside the channel</u>, must enter across the membrane (lipid soluble drugs).

-All of them have the same MOA.

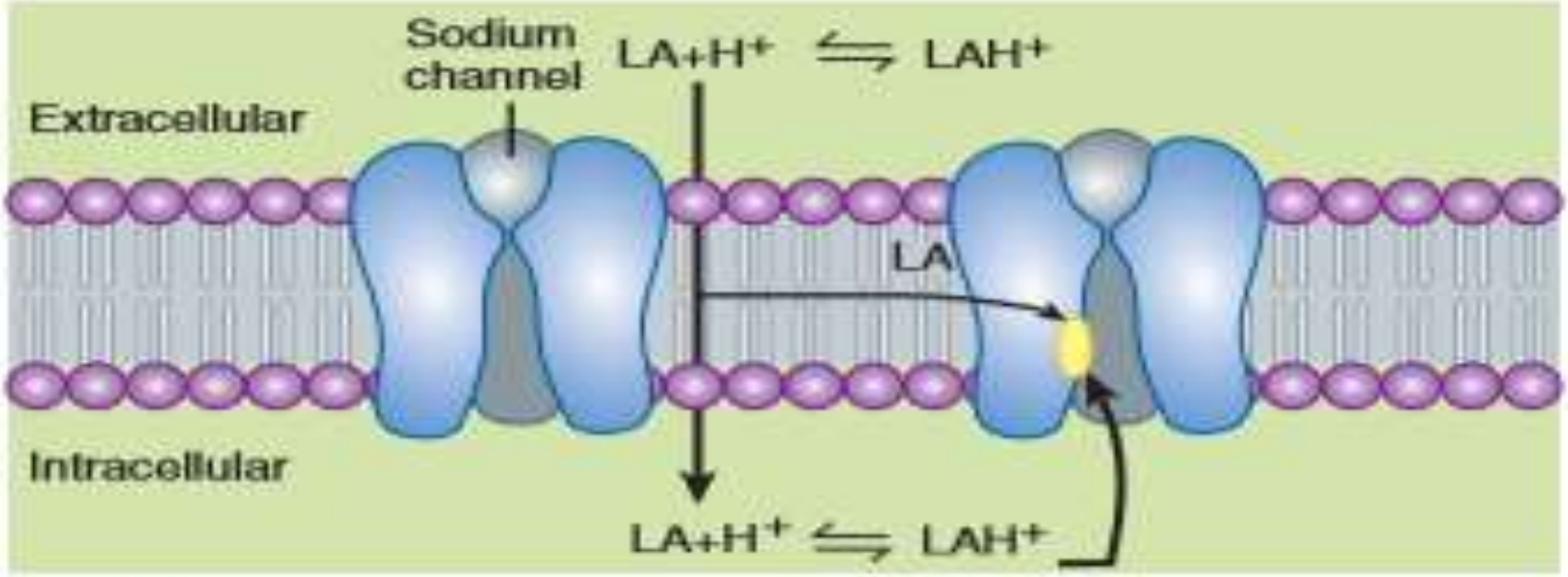
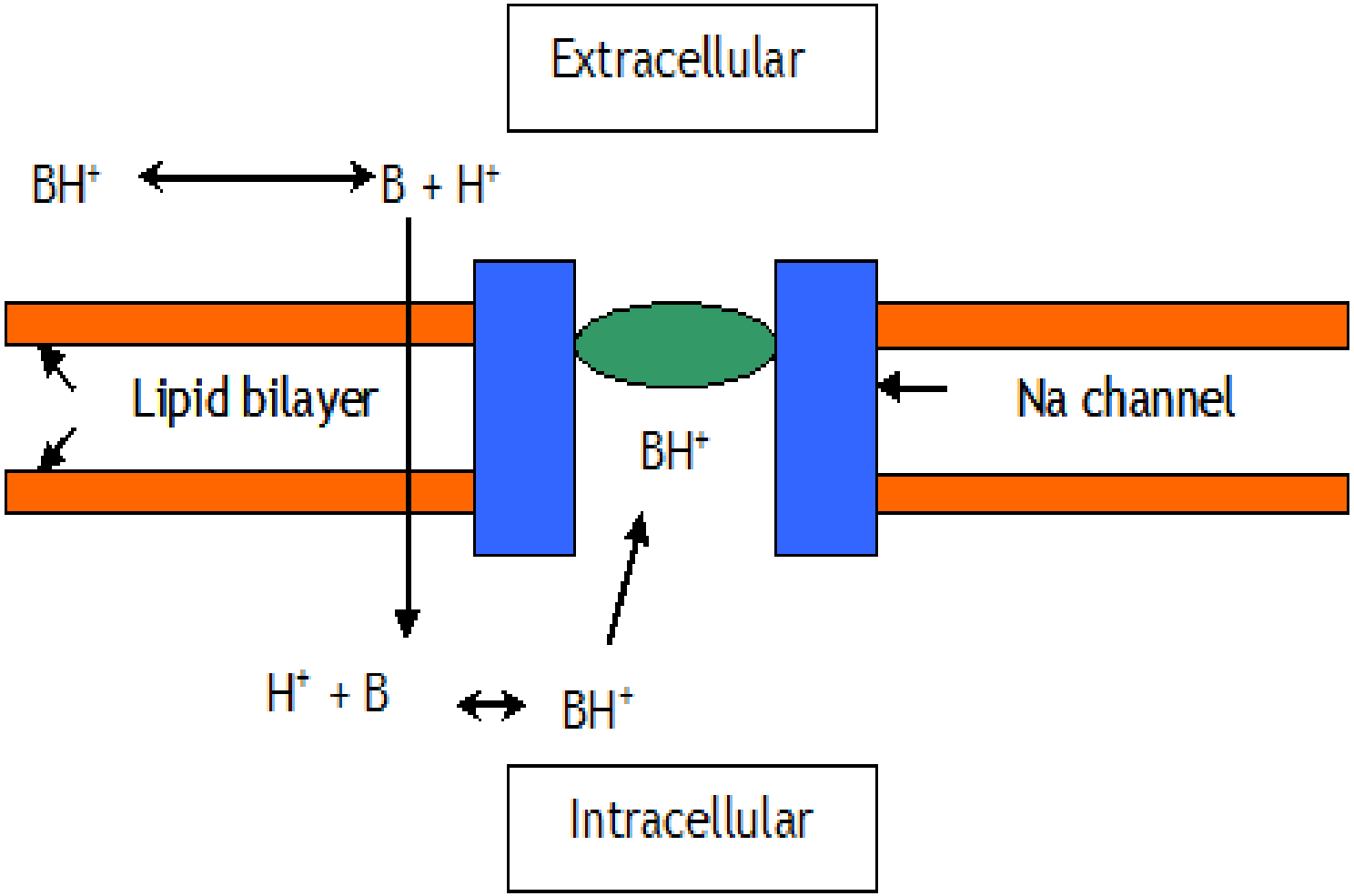


FIGURE 26–1 Schematic diagram depicting paths of local anesthetic (LA) to receptor sites. Extracellular anesthetic exists in equilibrium between charged and uncharged forms. The charged cation penetrates lipid membranes poorly; intracellular access is thus achieved by passage of the uncharged form. Intracellular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



Easier for storage and injection

BH+: ionized form, cation
H_2O soluble

B: unionized form, free
base lipid soluble

- **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

pKa is the PH at which 50% of the drug is ionized (water soluble, cant cross the membrane) and 50% is nonionized (the active form which can cross the membrane)

Strongly Influences time of onset.

LA's cross neuronal membrane in base form.

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

the lower the pKa, the greater the percentage of nonionized species at a given pH. Because the pKa of most local anesthetics is in the range of 7.7–8.9, the ionized form will constitute the larger percentage at physiologic pH.

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 or infection near site of block.

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

<u>Acidosis causes slow onset and poor quality of nerve block.</u>

The functional form of Local anesthetics is the non-ionized form because it's the form which crosses the membrane to block the NA channels from the inside

****that is why we want the Pka of the drug to be near the physiological PH of the body (more of the drug will be in the non-ionized form)**

Mechanism of Action of LA

Prevent increases in permeability of nerve membranes to Na+ ions

Slows rate of depolarization

Threshold potential is never reached

<u>Produce Differential Blockade of the nerves</u>:

C--B – A (C fibers are affected first then B and finally A)

When we give a LA the nerves/modalities which get blocked are in this order:

Autonomic

Pain

Cold

Warmth

Touch

Pressure

Motor

Classification of Nerve fibers

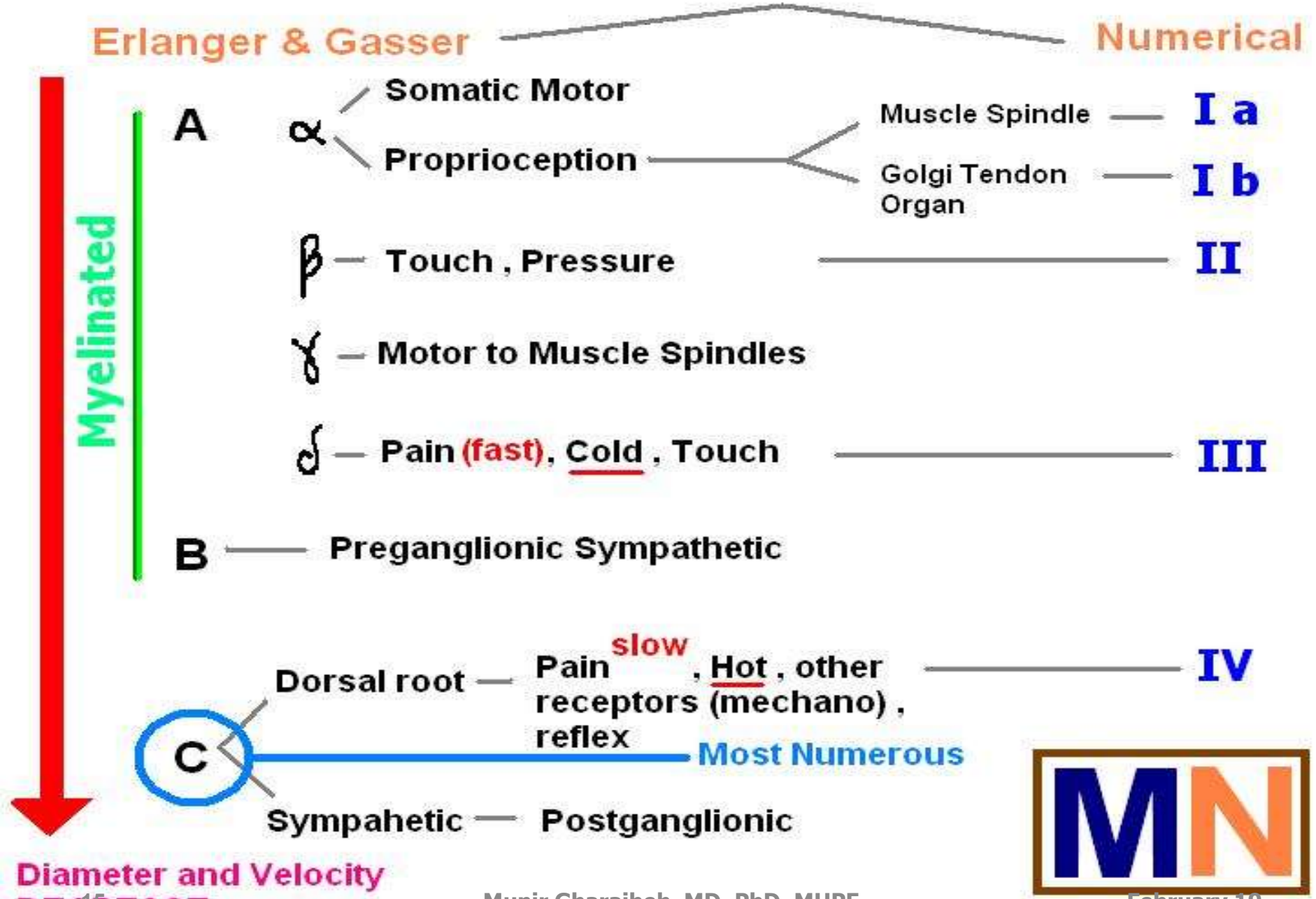


TABLE 26–3 Relative size and susceptibility of different types of nerve fibers to local anesthetics.

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: (used for giving birth) Lidocaine, Bupivacaine

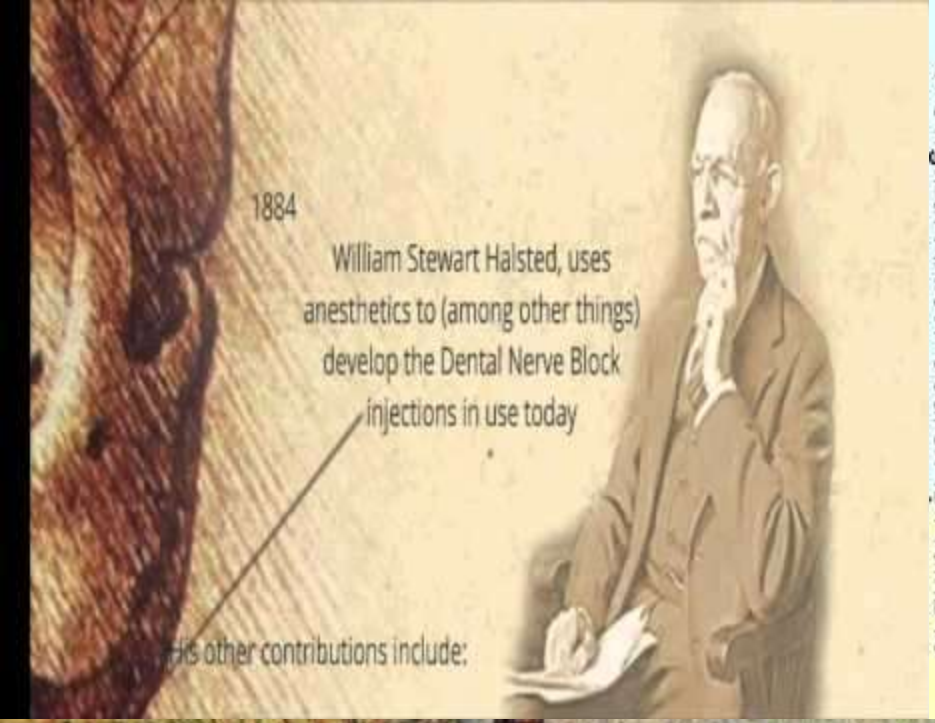
- Caudal.

Intravenous Extremity Block(Bier Block):

Lidocaine, Tetracaine

(squeeze the area to prevent the venous return, usually used for limbs).

Lidocaine is used by all routs of administration


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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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.

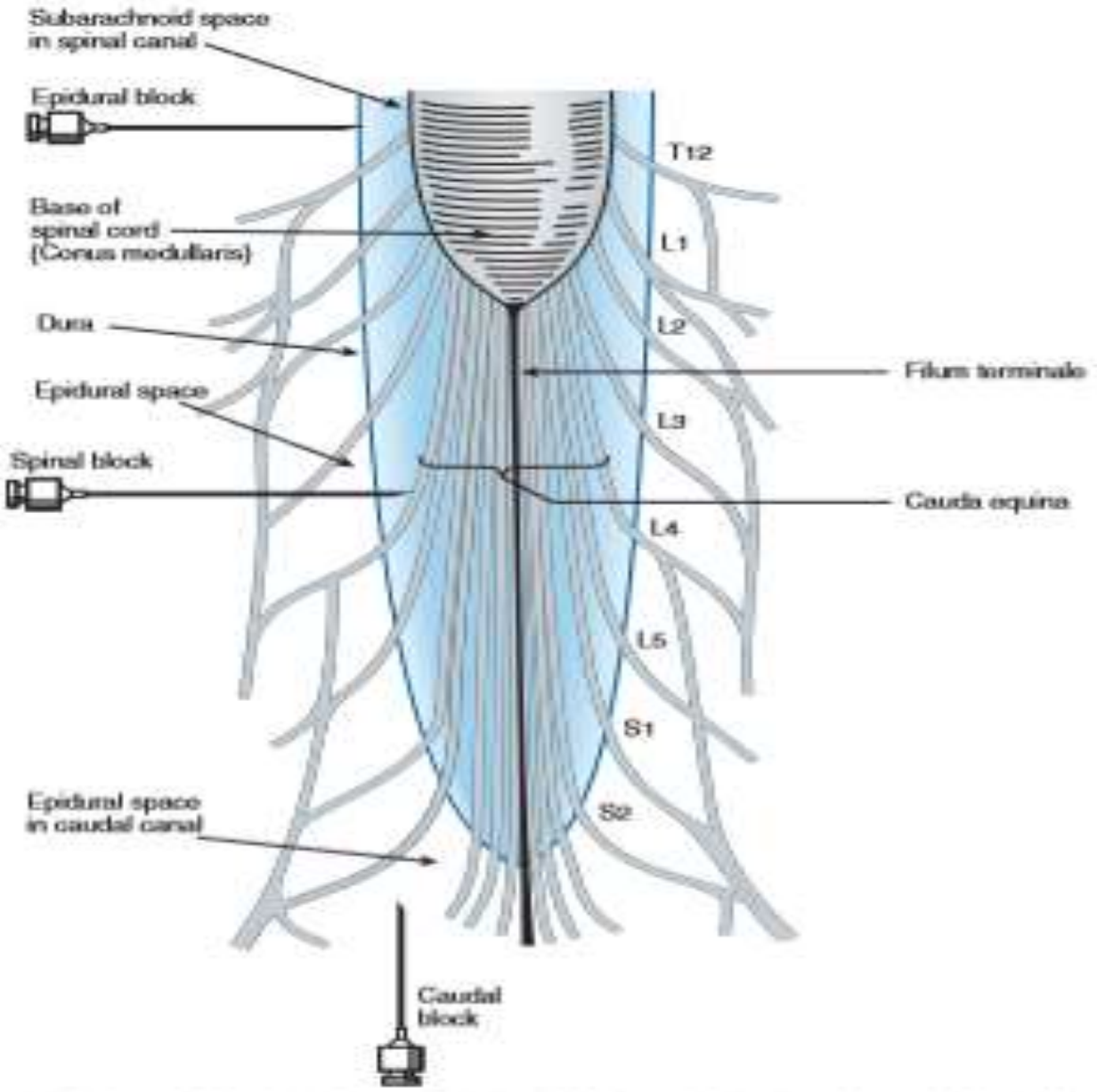


FIGURE 26–4 Schematic diagram of the typical sites of injection of local anesthetics in and around the spinal canal. When local anesthetics are injected extradurally, it is referred to as an epidural block. A caudal block is a specific type of epidural block in which a needle is inserted into the caudal 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 (added to the LAs) (50% prolongation of action and 30% reduction in blood levels, toxicity level).

Physicochemical Properties.

- The pH of the tissue.

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 (exception) .

Metabolism of LAs

AMIDES are metabolized by microsomal enzymes primarily in the liver (not by hydrolysis).

Slow process, more likely to cause systemic toxicity than esters

Hepatic disease decreases rate of metabolism, increases duration of action

Congestive heart failure decreases liver blood flow and can also slow metabolism

So esters cause Allergy while amides cause toxicity and esters get metabolized by cleavage while amides are 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 C.O.

- Cocaine causes constriction (inhibits norepinephrine reuptake), 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 (These effects are happened due to the cross of BBB and not through the nerves themselves):

- only at high doses
- Can cross BBB due to small size.
- Usually cause CNS stimulation (Stimulation happens at lower doses (by inhibiting the inhibitory mechanisms),while inhibition happens at higher doses).
- 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 (cardiac stimulation) and euphoric.

Procaine:

Short acting, used for infiltration and dental anesthesia

Benzocaine:

Usually for topical use usually in dermatology.

Chloroprocaine.

Tetracaine:

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

Amide Local Anesthetics

Lidocaine (xylocaine) (1944):

Given usually with vasoconstrictor (Adrenaline), but this preparation is contraindicated in cardiac arrythmia patients.

Most commonly used,

All routs, Rapid onset, Most intense, Medium duration.

Used for all procedures

Bupivacaine:

In obstetrics and postoperative anesthesia.

Long duration(24hrs).

Cardiotoxic.

Amide Local Anesthetics

Ropivacaine

Etidocaine

Mepivacaine

These are not for memorization

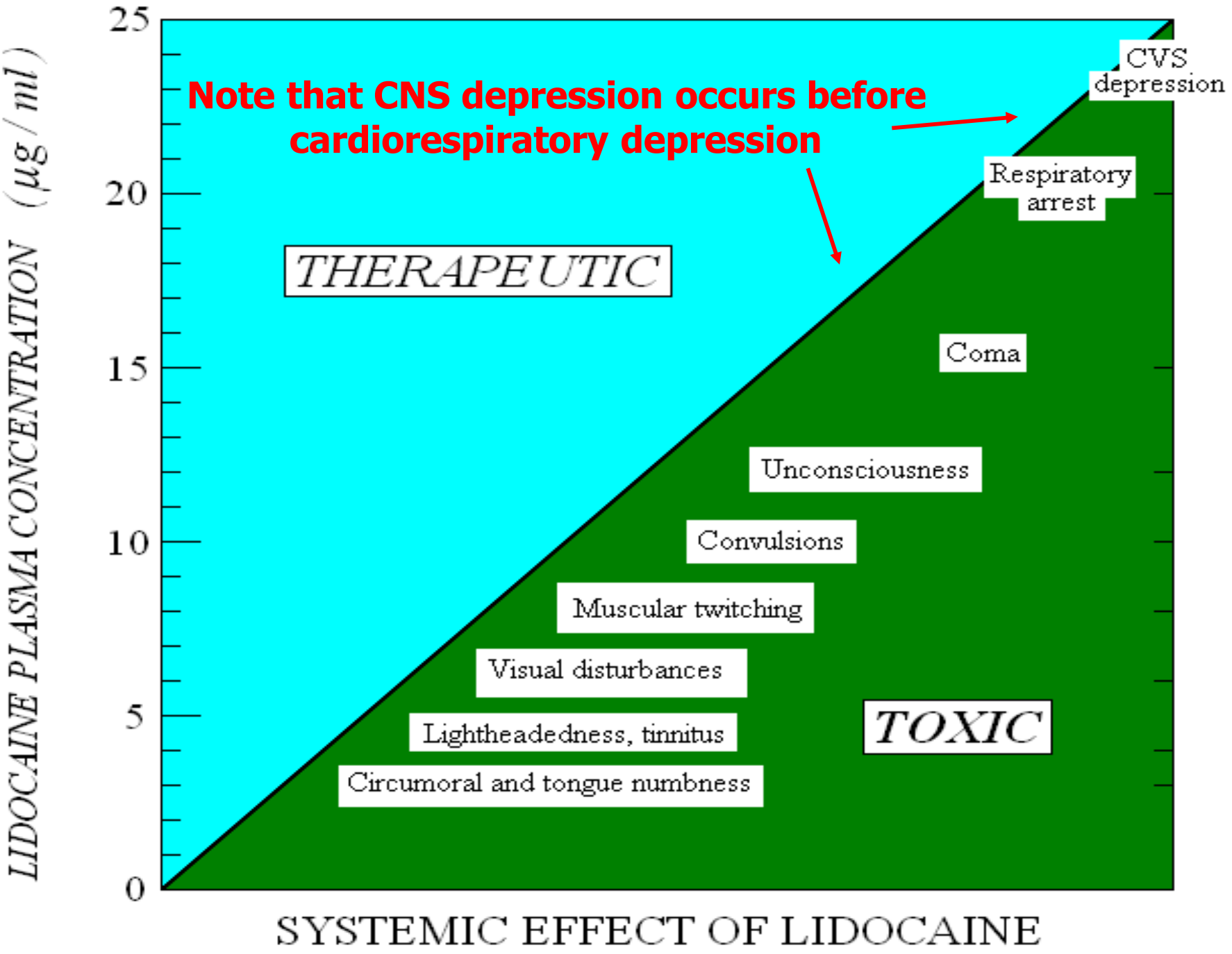
Prilocaine:

Has some vasoconstrictor effect, no need to add epinephrine.

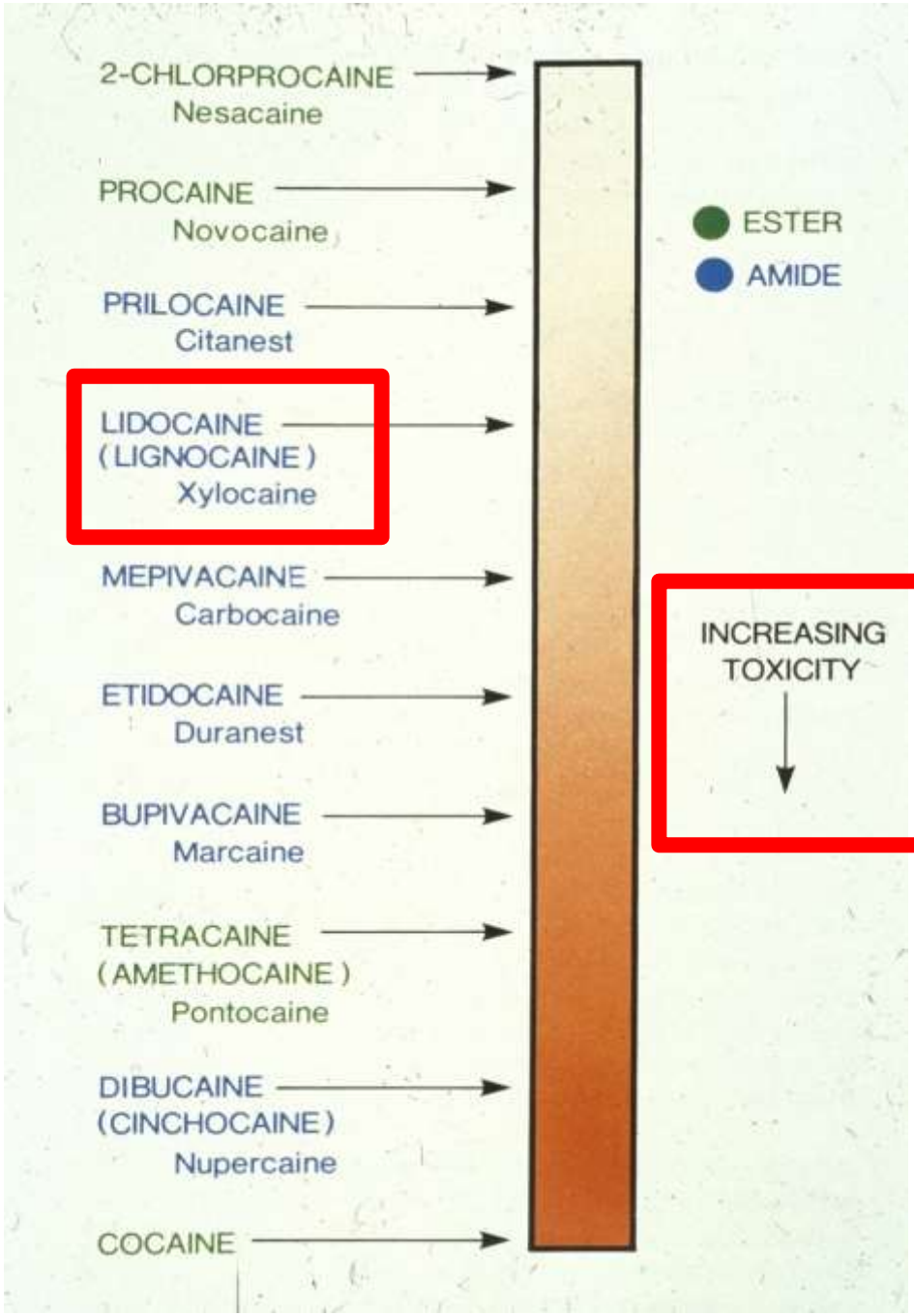
The dr. said we only need to know that cocaine and Procaine are esters and that lidocaine and Bupivacaine are amides

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.


LIDOCAINE PLASMA CONCENTRATION (μg / ml)
25
20
15
10
5
0
Note that CNS depression occurs before cardiorespiratory depression
THERAPEUTIC
TOXIC
CVS depression
Respiratory arrest
Coma
Unconsciousness
Convulsions
Muscular twitching
Visual disturbances
Lightheadedness, tinnitus
Circumoral and tongue numbness
SYSTEMIC EFFECT OF LIDOCAINE

Located in the first third with the safe drugs



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, in these cases EMLA is used instead of infiltration.

TAC:

Tetracaine + Adrenaline + Cocaine.

For repair of minor lacerations.