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Local Anesthetics and Peripheral Nerve Blocks in the Emergency Department

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Local anesthetics work by blocking the conduction of neural messages. Sodium is mostly an extracellular ion. Closed sodium channels located on the axoplasmic side of the nerve cell prevent its influx into the cell. In this resting state the electrical potential inside a nerve cell is negative in reference to the outside of the cell. This is the resting potential of the nerve cell. After mechanical, chemical, or electrical excitation the sodium channels open and allow sodium ions to move into the cell causing depolarization and propagation of the nerve impulse. In the inactive state, the sodium channels are susceptible to the action of local anesthetic molecules that bind to the channels, causing them to remain inactive and prevent subsequent depolarization [1]. Further conduction by the nerve is blocked until the local anesthetic is displaced from the neural membrane.

Structure of local anesthetics

Local anesthetics are weak bases that require the addition of a hydrochloride salt to be water soluble, facilitating their injection. They usually have an aromatic (hydrophobic) ring structure connected to a tertiary amine (hydrophilic) by an intermediate chain that includes an ester or amide linkage. The chemical composition of local anesthetics determines their potency, duration, and onset of action while the nature of the intermediate chain establishes the two classes of local anesthetics: esters and amides (Table 1).

Lipid solubility determines potency [2]. The more lipophilic a local anesthetic is, the more easily it penetrates the nerve cell membranes, resulting in more effective blockade of the neural signal. The plasma protein binding

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Table 1
Local anesthetics and their properties

Generic (Trade)	Potency	PKa	Duration	Maximum Dose (mg/kg)
AMIDES				
Bupivacaine (Marcaine)	4	8.1	4	3
Dibucaine (Nupercaine)	4	8.8	4	1
Etidocaine (Duranest)	4	7.7	4	4
Lidocaine (Xylocaine)	2	7.8	2	4.5 (7 with epinephrine)
Mepivacaine (Carbocaine)	2	7.6	2	4.5 (7 with epinephrine)
Prilocaine (Citanest)	2	7.8	2	8
Ropivacaine (Naropin)	4	8.1	4	3
ESTERS				
Chloroprocaine (Nesacaine)	1	9.0	1	12
Cocaine	2	8.7	2	3
Procaine	1	8.9	1	12
Tetracaine (Pontocaine)	4	8.2	3	3

Adapted from Morgan GE, Mikhail MS, Murray MJ, Larson CP. Local anesthetics. In: Morgan GE, Mikhail MS, Murray MJ, Larson CP (editors). Clinical Anesthesiology, 3rd edition. New York: Lange Medical Books; 2002. p. 233–41.

potential determines the duration of action of the local anesthetic molecule [3], presumably because the local anesthetic receptor is also a protein [4]. Those with more protein binding remain associated with the neural membrane for a longer period of time—making it unavailable for metabolism and clearance. For example, procaine is poorly protein bound, and its duration of neural blockade is relatively short. On the other hand, bupivacaine is highly protein bound, and consequently, has a long duration of action [1]. Last, pK_a determines the speed of onset of neural blockade. The pK_a is the pH at which equal percentages of the drug exist in the ionized and nonionized forms. Local anesthetics are weak bases. They therefore tend to become positively charged as the pH of the local milieu declines. Only the nonionized base is able to pass easily through the neural membrane. Local anesthetics with pK_a values closer to the physiologic pH produce higher concentrations of this nonionized base. This equates to a more rapid onset of action. This is why the local anesthetics are less effective in an acidic environment, and why alkalinization speeds onset of action and increases duration. Furthermore, epinephrine is unstable in alkaline environments. Commercially prepared solutions containing it are therefore made more acidic, further increasing the time of onset. Once inside the nerve cell, the nonionized base reaches equilibrium with its ionized form. It is this ionized form (cation) that actually binds to the receptor within the sodium channel and inactivates it.

Toxicity

All local anesthetics have a similar toxic profile predominantly affecting the central nervous and cardiovascular systems. Toxicity is related to the