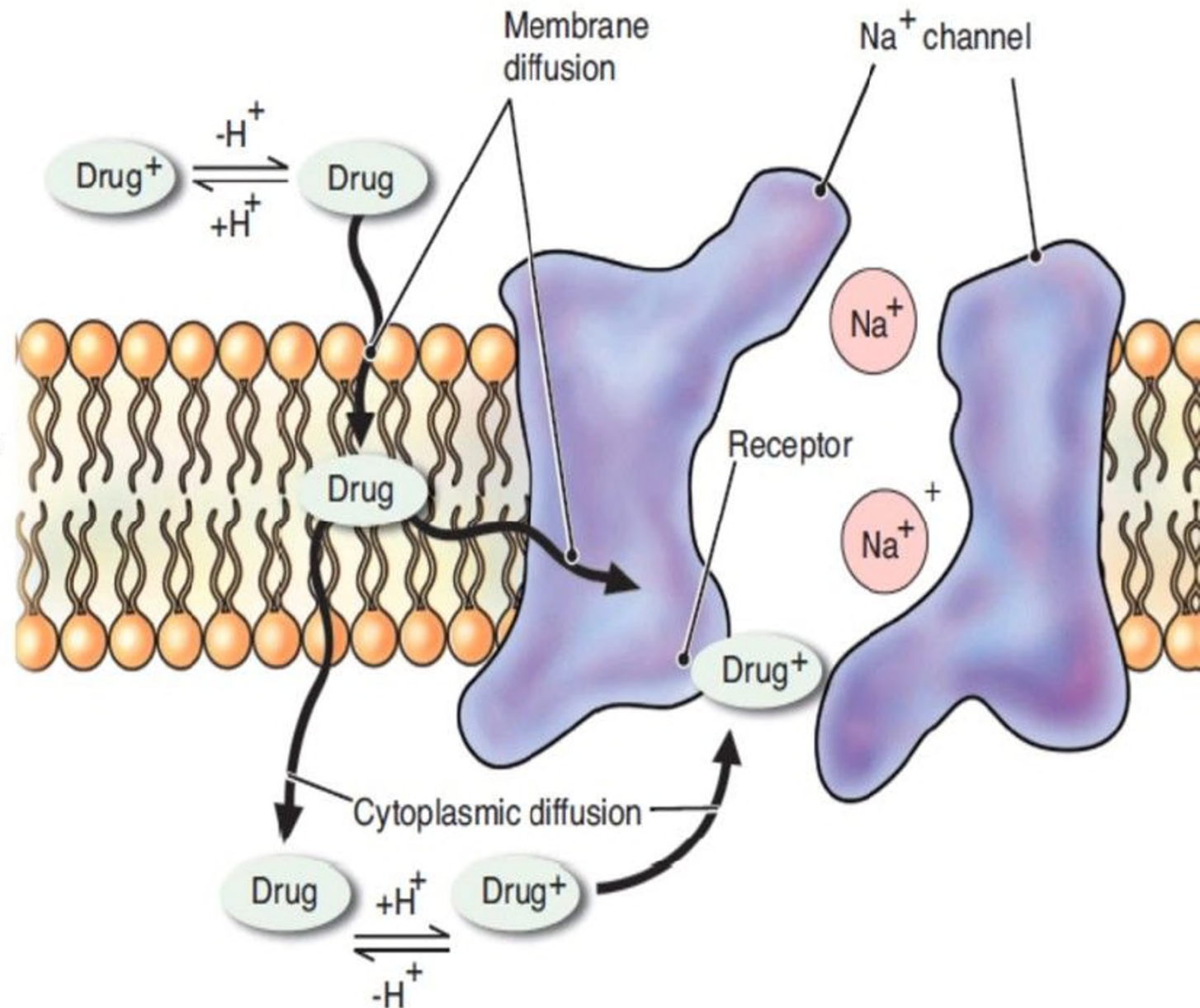


Anesthetics 4

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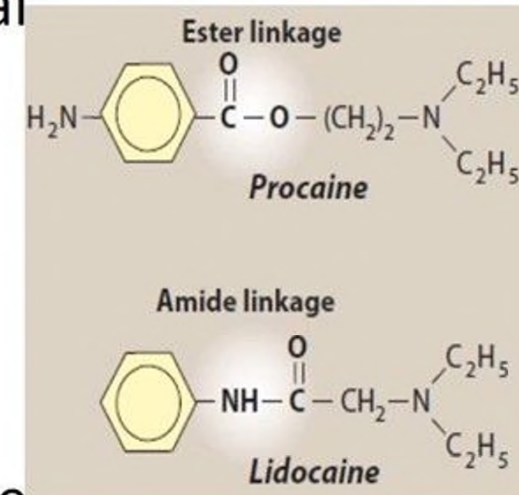
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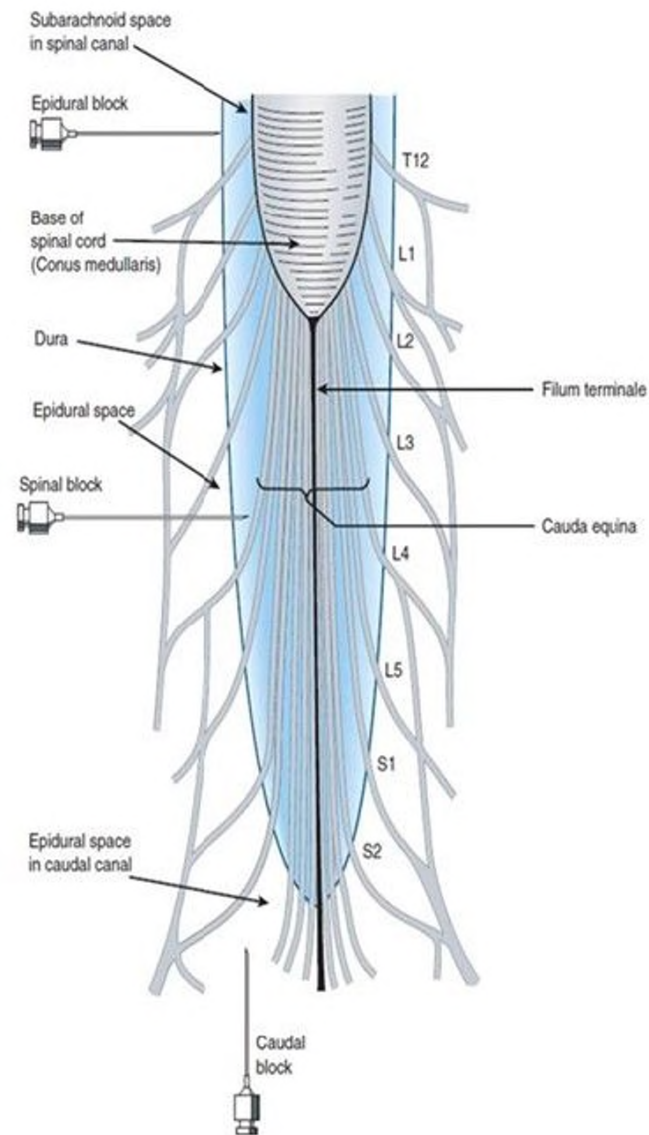


LOCAL ANESTHETICS

Local anesthetics provide a reversible regional loss of sensation. They reduce pain and thereby facilitate surgical procedures. Local anesthetics block nerve conduction of sensory impulses and in higher concentrations block motor impulses from the periphery to the CNS. Sodium ion channels are blocked to prevent the transient increase in permeability of the nerve membrane to Na^+ that is required for an action potential. When propagation of action potentials is prevented, sensation cannot be transmitted from the source of stimulation to the brain. *Cocaine* is a naturally occurring compound indigenous to the Andes Mountains, West Indies, and Java. It was the first anesthetic to be discovered and is the only naturally occurring local anesthetic; however, it is not used clinically because of its adverse effects and abuse potential. All other anesthetics are synthetically derived. Procaine, the first synthetic derivative of *cocaine*, was developed in 1904

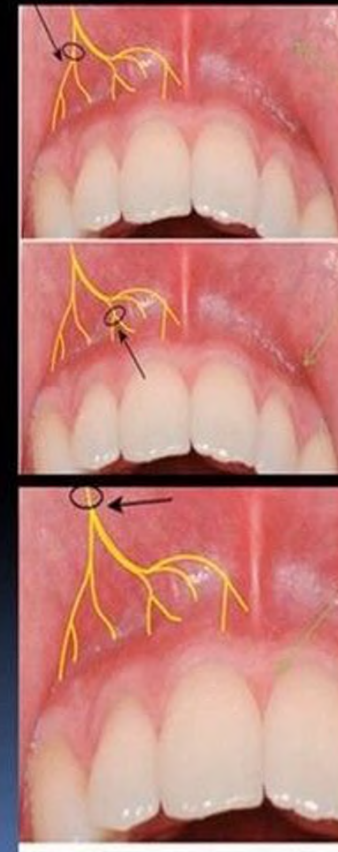
All local anesthetics have a similar chemical structure, The degree of lipid solubility of each anesthetic is an important property because the lipid solubility enables its diffusion through the highly lipophilic nerve membrane. The extent of an anesthetic's lipophilicity is directly related to its potency. All local anesthetics are weak bases that require the addition of hydrochloride salt in order to be water soluble and therefore injectable. Salt equilibrates between an ionized form and a nonionized form in aqueous solution. Equilibration is crucial because, although the ionized form is injectable, it is the nonionized base which has the lipophilic properties and is responsible for their diffusion into the nerve cell membrane. The duration of action of an anesthetic is determined by their protein-binding capacity to anesthetic receptors along the nerve cell membrane. The most widely used local anesthetics are *bupivacaine*, *lidocaine*, *mepivacaine*, *ropivacaine* and *tetracaine*.





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.

Identify which technique is which?



A. Infiltration

B. Field Block

C. Nerve Block

Delivery techniques of local anesthetics

Various delivery techniques broaden the clinical applicability of local anesthetics. These techniques include topical administration, infiltration, perineural, and neuraxial (spinal, epidural, or caudal) blocks. Small, unmyelinated nerve fibers for pain, temperature, and autonomic activity are most sensitive. These are as follows.

1. **Regional anesthesia:** It makes a specific part of the body numb to relieve pain or allow surgical procedures to be done. Local anesthetics are safer than general or systemic anesthetics; therefore, they are preferred whenever possible.
2. **Surface anesthesia:** It is used during ocular tonometry, intubation, and endoscopic procedures. *Tetracaine* 2% and *lidocaine* 2% to 4% are used. The anesthetic effect is superficial and does not last long.
3. **Infiltration anesthesia:** The local anesthetic is injected directly into the skin or deeper structures to carry out incision, excision, hydrocoele, herniorraphy, incision and drainage of an abscess, etc. *Lignocaine* and *bupivacaine* are generally used for infiltration anesthesia.

4. Field block: The local anesthetic is injected subcutaneously proximal to the site where anesthesia is desired. All nerves distal to the site of injection are blocked. *Lidocaine* (1% to 2%) is used for intermediate duration of anesthesia in dental extraction, operation on forearms, legs, herniorrhaphy, etc.

5. Nerve block: The local anesthetic is injected around a nerve plexus or a nerve trunk. This results in a large area of anesthesia. Thus even with a small amount of drug, a large area of anesthesia can be produced. *Lidocaine* is most commonly used apart from *bupivacaine*. Intercostal, sciatic, brachial plexus, facial, and phrenic are commonly performed nerve blocks.

6. Spinal anesthesia: A single dose of the local anesthetic is injected into the subarachnoid space in the lower end of the spinal cord (lumbar region). The site of action is nerve roots, resulting in loss of pain sensation and paralysis of the lower abdomen and hind limbs. *Lidocaine*, *bupivacaine*, and *tetracaine* are most commonly used for spinal anesthesia. The duration of anesthesia depends on the concentration and the drug used. Spinal anesthesia is associated with various complications such as respiratory paralysis, hypotension, headache, nausea, vomiting, bradycardia, and septic meningitis. It is used during operations on lower limbs, pelvis, lower abdomen, etc.

Actions

All local anesthetics cause vasodilation, which leads to a rapid diffusion away from the site of action and short duration when these drugs are administered alone. By adding the vasoconstrictor *epinephrine*, the rate of local anesthetic absorption and diffusion is decreased. This minimizes systemic toxicity and increases the duration of action. However, *epinephrine* should not be coadministered for nerve block in extremities such as fingers and toes as vasoconstriction of end arteries may lead to ischemia and necrosis. It should be used with caution in patients with thyrotoxicosis or cardiovascular disease and in labor. Hepatic function does not affect the duration of action of local anesthesia because that is determined by redistribution rather than biotransformation. Some local anesthetics have other therapeutic uses (for example, *lidocaine* is an IV antiarrhythmic).

pKa & pKb have convenient values to memorize than that of Ka & Kb.

pKa is defined as " Log of reciprocal of K_a

OR

Negative log of K_a .



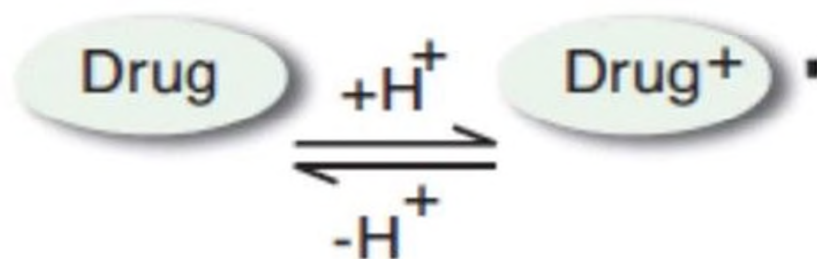
$$pK_a = \log \frac{1}{K_a}$$

OR

$$pK_a = -\log K_a$$

Larger the pK_a value $\rightarrow$ lower the $K_a \rightarrow$ weaker will be the acid

Drug	pKa	% Base Form at pH 7.4	Onset of Action (min)
Mepivacaine	7.7	33	2-4
Articaine	7.8	29	2-4
Lidocaine	7.9	25	2-4
Prilocaine	7.9	25	2-4
Bupivacaine	8.1	17	5-8



Onset, potency, and duration of action

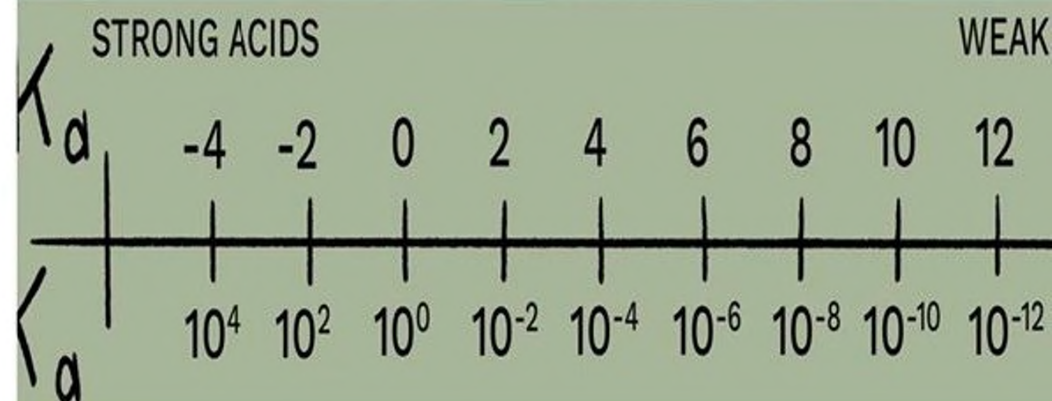
The onset of action of local anesthetics is influenced by several factors including tissue pH, nerve morphology, concentration, pKa, and lipid solubility of the drug. Of these, the pKa is most important. Local anesthetics with a lower pKa have a quicker onset, since more drug exists in the unionized form at physiologic pH, thereby allowing penetration of the nerve cell membrane. Once at the nerve membrane, the ionized form interacts with the protein receptor of the Na⁺ channel to inhibit its function and achieve local anesthesia. The pH may drop in infected sites, causing onset to be delayed or even prevented. Potency and duration of these agents depend mainly on lipid solubility, with higher solubility correlating with increased potency and duration of action.

What Is pK_a in Chemistry?

The pK_a value is the negative base-10 logarithm of the acid dissociation constant (K_a) of a solution.

$$pK_a = -\log_{10} K_a$$

The smaller the value of pK_a, the stronger the acid.



Metabolism

Biotransformation of amides occurs primarily in the liver. *Prilocaine*, a dental anesthetic, is also metabolized in the plasma and kidney, and one of its metabolites may lead to methemoglobinemia. Esters are biotransformed by plasma cholinesterase (pseudocholinesterase). Patients with pseudocholinesterase deficiency may metabolize ester local anesthetics more slowly. At normal doses, this has little clinical effect. Reduced hepatic function predisposes patients to toxic effects, but should not significantly increase the duration of action of local anesthetics.

Allergic reactions

Patient reports of allergic reactions to local anesthetics are fairly common, but often times reported “allergies” are actually side effects from the coadministered *epinephrine*.

Local anesthetic systemic toxicity

Treatment for LAST may include seizure suppression, airway management, and cardiopulmonary support. Administering a 20% lipid emulsion infusion (lipid rescue therapy) is a valuable asset.

CHARACTERISTIC	ESTERS • Benzocaine • Chloroprocaine • Cocaine • Procaine • Tetracaine	AMIDES • Bupivacaine • Lidocaine • Mepivacaine • Prilocaine • Ropivacaine
Metabolism	Rapid by plasma cholinesterase	Slow, hepatic
Systemic toxicity	Less likely	More likely
Allergic reaction	Possible- PABA derivatives form	Very rare
Stability in solution	Breaks down in ampules (heat, sun)	Very stable chemically
Onset of action	Slow as a general rule	Moderate to fast
pK _a 's	Higher than physiologic pH (8.5–8.9)	Close to physiologic pH (7.6–8.1)

DRUG	POTENCY	ONSET	DURATION
<i>Bupivacaine</i>	High	Slow	Long
<i>Chloroprocaine</i>	Low	Rapid	Short
<i>Lidocaine</i>	Low	Rapid	Intermediate
<i>Mepivacaine</i>	Low	Moderate	Intermediate
<i>Procaine</i>	Low	Rapid	Short
<i>Ropivacaine</i>	High	Moderate	Long
<i>Tetracaine</i>	High	Slow	Long (spinal)