**Dr.Hayder M. Alkuraishy**

A local anesthetic (LA) is a [drug](http://en.wikipedia.org/wiki/Medication) that causes reversible [local anesthesia](http://en.wikipedia.org/wiki/Local_anesthesia), generally for the aim of having a local analgesic effect, that is, inducing absence of [pain](http://en.wikipedia.org/wiki/Pain) sensation. Clinical local anesthetics belong to one of two classes: aminoamide and aminoester local anesthetics. Synthetic local anesthetics are structurally related to [cocaine](http://en.wikipedia.org/wiki/Cocaine). They differ from cocaine mainly in that they have no abuse potential and do not act on the [sympatho-adrenergic system](http://en.wikipedia.org/w/index.php?title=Sympathoadrenergic_system&action=edit&redlink=1), i.e. they do not produce [hypertension](http://en.wikipedia.org/wiki/Hypertension) or local [vasoconstriction](http://en.wikipedia.org/wiki/Vasoconstriction), with the exception of [Ropivacaine](http://en.wikipedia.org/wiki/Ropivacaine) and [Mepivacaine](http://en.wikipedia.org/wiki/Mepivacaine) that do produce weak vasoconstriction. Local anesthetics vary in their [pharmacological](http://en.wikipedia.org/wiki/Pharmacology) properties and they are used in various techniques of [local anesthesia](http://en.wikipedia.org/wiki/Local_anesthesia) such as:

* [Topical anesthesia](http://en.wikipedia.org/wiki/Topical_anesthetic) (surface)
* [Infiltration](http://en.wikipedia.org/wiki/Infiltration_%28medical%29)
* Plexus block
* [Epidural (extradural) block](http://en.wikipedia.org/wiki/Epidural)
* [Spinal anesthesia](http://en.wikipedia.org/wiki/Spinal_anaesthesia) (subarachnoid block)

The local anesthetic [lidocaine](http://en.wikipedia.org/wiki/Lidocaine) (lignocaine) is also used as a Class Ib [antiarrhythmic](http://en.wikipedia.org/wiki/Antiarrhythmic) drug.

## Mechanism of action

[Membrane](http://en.wikipedia.org/wiki/Plasma_membrane) stabilizing reversibly decreases the rate of depolarization and repolarization of excitable membranes. Though many other drugs also have membrane stabilizing properties, not all are used as local anesthetics ([propranolol](http://en.wikipedia.org/wiki/Propranolol), for example). Local anesthetic drugs act mainly by inhibiting [sodium](http://en.wikipedia.org/wiki/Sodium) influx through sodium-specific [ion channels](http://en.wikipedia.org/wiki/Ion_channel) in the [neuronal](http://en.wikipedia.org/wiki/Neuron) [cell membrane](http://en.wikipedia.org/wiki/Cell_membrane), in particular the so-called voltage-gated sodium channels. When the influx of sodium is interrupted, an [action potential](http://en.wikipedia.org/wiki/Action_potential) cannot arise and signal conduction is inhibited. The receptor site is thought to be located at the cytoplasmic (inner) portion of the sodium channel. Local anesthetic drugs bind more readily to sodium channels in an activated state, thus onset of neuronal blockade is faster in neurons that are rapidly firing. This is referred to as state dependent blockade.

Local anesthetics are weak [bases](http://en.wikipedia.org/wiki/Base_%28chemistry%29) and are usually formulated as the hydrochloride salt to render them water-soluble. At a pH equal to the protonated base's pKa, Acidosis such as caused by inflammation at a wound partly reduces the action of local anesthetics. This is partly because most of the anesthetic is ionized and therefore unable to cross the cell membrane to reach its cytoplasmic-facing site of action on the sodium channel.

All nerve fibers are sensitive to local anesthetics, but due to a combination of diameter and myelination, fibers have different sensitivities to local anesthetic blockade, termed "Differential Blockade." Type B fibers (sympathetic tone) are the most sensitive followed by Type C (Pain), Type A delta (temperature), Type A gamma (proprioception), Type A beta (sensory touch and pressure) and Type A alpha (motor). Although Type B fibers are thicker than Type C fibers, they are myelinated, and thus are blocked before the unmyelinated, thin C Fiber.

## Local anesthetics in clinical use

The names of each locally clinical anesthetic have the suffix "-caine". In general Amides have two "i"'s in their nomenclature while the Esters have only one.

Most ester local anesthetics are metabolized by [pseudocholinesterases](http://en.wikipedia.org/wiki/Pseudocholinesterase), while amide local anesthetics are metabolized in the liver. This can be a factor in choosing an agent in patients with liver failure.

### Esters

* [Procaine](http://en.wikipedia.org/wiki/Procaine)
* [Benzocaine](http://en.wikipedia.org/wiki/Benzocaine)
* [Chloroprocaine](http://en.wikipedia.org/wiki/Chloroprocaine)
* [Cocaine](http://en.wikipedia.org/wiki/Cocaine)
* [Cyclomethycaine](http://en.wikipedia.org/wiki/Cyclomethycaine)
* [Propoxycaine](http://en.wikipedia.org/wiki/Propoxycaine)
* [Procaine](http://en.wikipedia.org/wiki/Procaine)/[Novocaine](http://en.wikipedia.org/wiki/Novocaine)
* [Proparacaine](http://en.wikipedia.org/wiki/Proparacaine)
* [Tetracaine](http://en.wikipedia.org/wiki/Tetracaine)/[Amethocaine](http://en.wikipedia.org/wiki/Amethocaine)

### Amides

* [Lidocaine](http://en.wikipedia.org/wiki/Lidocaine)
* [Articaine](http://en.wikipedia.org/wiki/Articaine)
* [Bupivacaine](http://en.wikipedia.org/wiki/Bupivacaine)
* [Cinchocaine](http://en.wikipedia.org/wiki/Cinchocaine)/[Dibucaine](http://en.wikipedia.org/wiki/Dibucaine)
* [Etidocaine](http://en.wikipedia.org/wiki/Etidocaine)
* [Levobupivacaine](http://en.wikipedia.org/wiki/Levobupivacaine)
* [Lidocaine](http://en.wikipedia.org/wiki/Lidocaine)/[Lignocaine](http://en.wikipedia.org/wiki/Lignocaine)
* [Mepivacaine](http://en.wikipedia.org/wiki/Mepivacaine)

## Specific uses

### Acute pain

* Labor pain (epidural anesthesia)
* Postoperative pain (peripheral nerve blocks, epidural anesthesia)
* Trauma (peripheral nerve blocks, intravenous regional anesthesia, epidural anesthesia)

### Chronic pain

Local anesthetics can be applied repeatedly or continuously for prolonged periods to relieve chronic pain, usually in combination with medication such as [opioids](http://en.wikipedia.org/wiki/Opioid), [NSAIDs](http://en.wikipedia.org/wiki/NSAID), and [anticonvulsants](http://en.wikipedia.org/wiki/Anticonvulsant).

### Surgery

* [Dentistry](http://en.wikipedia.org/wiki/Dentistry) (surface anesthesia, infiltration anesthesia or intraligamentary anesthesia during restorative operations or extractions, regional nerve blocks during extractions and surgeries.)
* [Podiatry](http://en.wikipedia.org/wiki/Podiatry) (Cutaneous, nail avulsions, matricectomy and various other podiatric procedures)
* Eye surgery (surface anesthesia with [topical anesthetics](http://en.wikipedia.org/wiki/Topical_anesthetic), [retrobulbar block](http://en.wikipedia.org/wiki/Retrobulbar_block))
* ENT operations, head and neck surgery (infiltration anesthesia, field blocks, peripheral nerve blocks, [plexus anesthesia](http://en.wikipedia.org/w/index.php?title=Plexus_anesthesia&action=edit&redlink=1))
* Shoulder and arm surgery (plexus anesthesia, [intravenous regional anesthesia](http://en.wikipedia.org/wiki/Intravenous_regional_anesthesia))
* Heart and lung surgery ([epidural anesthesia](http://en.wikipedia.org/wiki/Epidural_anesthesia) combined with [general anesthesia](http://en.wikipedia.org/wiki/General_anesthesia))
* Abdominal surgery ([epidural](http://en.wikipedia.org/wiki/Epidural_anesthesia)/[spinal anesthesia](http://en.wikipedia.org/wiki/Spinal_anesthesia), often combined with general anesthesia)
* Gynecological, obstetrical and urological operations ([spinal](http://en.wikipedia.org/wiki/Spinal_anesthesia)/[epidural anesthesia](http://en.wikipedia.org/wiki/Epidural_anesthesia))
* Bone and joint surgery of the pelvis, hip and leg ([spinal](http://en.wikipedia.org/wiki/Spinal_anesthesia)/[epidural anesthesia](http://en.wikipedia.org/wiki/Epidural_anesthesia), [peripheral nerve blocks](http://en.wikipedia.org/wiki/Peripheral_nerve_blocks), [intravenous regional anesthesia](http://en.wikipedia.org/wiki/Intravenous_regional_anesthesia))
* Surgery of skin and peripheral blood vessels ([topical anesthesia](http://en.wikipedia.org/wiki/Topical_anesthesia), field blocks, [peripheral nerve blocks](http://en.wikipedia.org/wiki/Peripheral_nerve_block), spinal/epidural anesthesia)

### Other uses

Topical anesthesia, in the form of [lidocaine/prilocaine](http://en.wikipedia.org/wiki/Lidocaine/prilocaine) (EMLA) is most commonly used to enable relatively painless [venipuncture](http://en.wikipedia.org/wiki/Venipuncture) ([blood](http://en.wikipedia.org/wiki/Blood) collection) and placement of [intravenous cannulae](http://en.wikipedia.org/w/index.php?title=Intravenous_cannula&action=edit&redlink=1). It may also be suitable for other kinds of punctures such as [ascites](http://en.wikipedia.org/wiki/Ascites) drainage and [amniocentesis](http://en.wikipedia.org/wiki/Amniocentesis). Surface anesthesia also facilitates some [endoscopic](http://en.wikipedia.org/wiki/Endoscopy) procedures such as [bronchoscopy](http://en.wikipedia.org/wiki/Bronchoscopy) (visualization of the lower airways) or [cystoscopy](http://en.wikipedia.org/wiki/Cystoscopy) (visualization of the inner surface of the bladder).

## Local Undesired effects

1. neurotoxicity
2. excessive fluid pressure in a confined space
3. severing of nerve fibers
4. injection-site [hematoma](http://en.wikipedia.org/wiki/Hematoma)
5. Injection-site infection

### General adverse effects

#### Central nervous system

At lower concentrations, cause selective depression of inhibitory neurons results in cerebral excitation, which may lead to generalized [convulsions](http://en.wikipedia.org/wiki/Convulsion). A profound depression of brain functions occurs at higher concentrations which may lead to [coma](http://en.wikipedia.org/wiki/Coma), [respiratory arrest](http://en.wikipedia.org/wiki/Respiratory_arrest) and death. Such tissue concentrations may be due to very high plasma levels after intravenous injection of a large dose. Another possibility is direct exposure of the central nervous system through the CSF, i.e., overdose in [spinal anesthesia](http://en.wikipedia.org/wiki/Spinal_anesthesia) or accidental injection into the [subarachnoid space](http://en.wikipedia.org/wiki/Subarachnoid_space) in [epidural anesthesia](http://en.wikipedia.org/wiki/Epidural_anesthesia).

#### Cardiovascular system

The conductive system of the heart is quite sensitive to the action of local anesthetic causing bradycardia.

#### Hypersensitivity/allergy

Adverse reactions to local anesthetics (especially the esters) are not uncommon, but true [allergy](http://en.wikipedia.org/wiki/Allergy) is very rare. Allergic reactions to the esters are usually due to sensitivity to their metabolite, [para-aminobenzoic acid](http://en.wikipedia.org/wiki/Para-aminobenzoic_acid) (PABA), and does not result in cross-allergy to amides. Therefore, amides can be used as alternatives in those patients. Non-allergic reactions may resemble allergy in their manifestations.

#### Methemoglobinemia

The systemic toxicity of [prilocaine](http://en.wikipedia.org/wiki/Prilocaine) is comparatively low, however its metabolite, o-toluidine, is known to cause [methemoglobinemia](http://en.wikipedia.org/wiki/Methemoglobinemia). As methemoglobinemia reduces the amount of [hemoglobin](http://en.wikipedia.org/wiki/Hemoglobin) that is available for oxygen transport, this side effect is potentially life-threatening. Therefore dose limits for prilocaine should be strictly observed. Prilocaine is not recommended for use in labor pains or infants.

 Local anesthetics mixed with other local anesthetics include

* [Lidocaine/prilocaine](http://en.wikipedia.org/wiki/Lidocaine/prilocaine) (EMLA)
* Lidocaine/tetracaine (Rapydan)

[**Local anesthetics and vasoconstrictors**](http://en.wikipedia.org/wiki/Local_anesthetics_and_vasoconstrictor)

 [Vasoconstrictors](http://en.wikipedia.org/wiki/Vasoconstrictor) increase the duration of local anesthesia by constricting the blood vessels, thereby safely concentrating the anesthetic agent for an extended duration, as well as reducing [hemorrhage](http://en.wikipedia.org/wiki/Hemorrhage). Examples include:

* [Prilocaine](http://en.wikipedia.org/wiki/Prilocaine) hydrochloride and [epinephrine](http://en.wikipedia.org/wiki/Epinephrine)
* [Lidocaine](http://en.wikipedia.org/wiki/Lidocaine), [bupivacaine](http://en.wikipedia.org/wiki/Bupivacaine), and [epinephrine](http://en.wikipedia.org/wiki/Epinephrine) (recommended final concentrations of 0.5%, 0.25% and 1:200, respectively)

## Naturally derived local anesthetics

* [Saxitoxin](http://en.wikipedia.org/wiki/Saxitoxin)
* [Neosaxitoxin](http://en.wikipedia.org/wiki/Neosaxitoxin)
* [Tetrodotoxin](http://en.wikipedia.org/wiki/Tetrodotoxin)
* [Menthol](http://en.wikipedia.org/wiki/Menthol)
* [Eugenol](http://en.wikipedia.org/wiki/Eugenol)

Naturally occurring local anesthetics not derived from cocaine are usually [neurotoxins](http://en.wikipedia.org/wiki/Neurotoxin), and have the suffix -toxin in their names.  Unlike cocaine produced local anesthetics which are [intracellular](http://en.wikipedia.org/wiki/Intracellular) in effect, saxitoxin, neosaxitoxin & tetrodotoxin bind to the [extracellular](http://en.wikipedia.org/wiki/Extracellular) side of sodium channels.

**Lidocaine** alters signal conduction in neurons by blocking the fast voltage-gated Na+ channels in the neuronal cell membrane responsible for signal propagation. With sufficient blockage, the membrane of the postsynaptic neuron will not depolarize and will thus fail to transmit an action potential. This creates the anesthetic effect by not merely preventing pain signals from propagating to the brain, but by stopping them before they begin. The same principle applies for this drug's actions in the heart. Blocking sodium channels in the conduction system, as well as the muscle cells of the heart, raise the depolarization threshold, making the heart less likely to initiate or conduct early action potentials that may cause an arrhythmia.

## Medical uses

### Local anasthetic

### Heart arrhythmia

* Antitussive

**Note:** Relative insensitivity to lidocaine is genetic. In hypokalemic sensory overstimulation, relative insensitivity to lidocaine has been described in people who also have attention deficit hyperactivity disorder. In dental anesthesia, a relative insensitivity to lidocaine can occur for anatomical reasons due to unexpected positions of nerves. Some people with Ehlers-Danlos syndrome are insensitive to lidocaine.

### Contraindications of LA:

* Heart block
* Severe sinoatrial block
* Bradycardia
* Porphyria
* Prior use of amiodarone hydrochloride
* Pseudocholinesterase deficiency
* Elderly patients