

Local Anesthetics

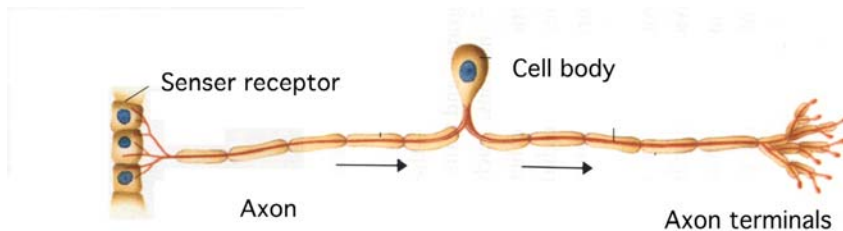
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Local anesthetics are drugs used to prevent or relieve pain in specific regions of the body without loss of consciousness

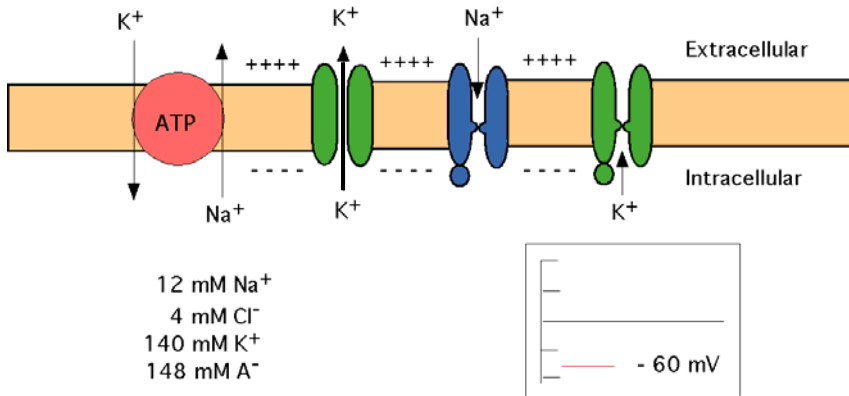
Local anesthetics block pain sensation by blocking nerve conduction

Mechanisms of neural transmission

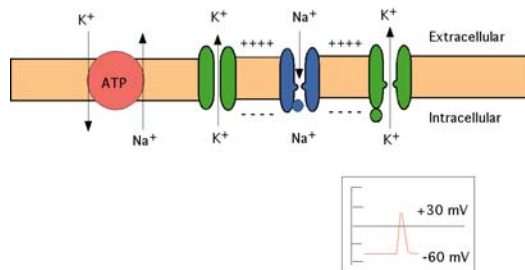
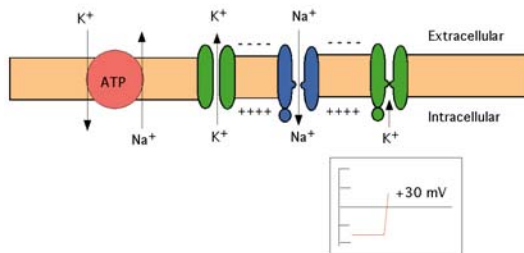


Resting membrane potential

150 mM Na⁺
 120 mM Cl⁻
 4 mM K⁺
 34 mM A⁻

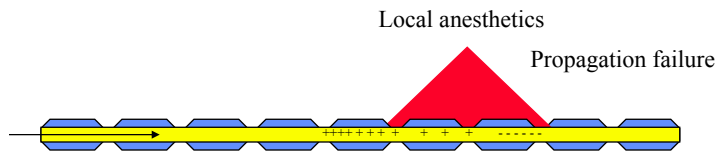


Action potential

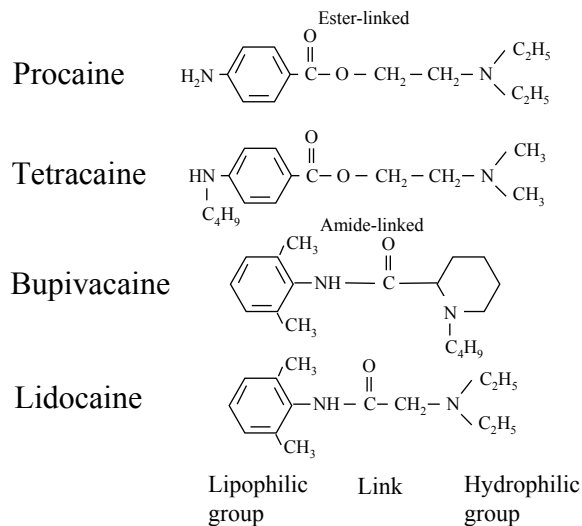


Mechanism of action

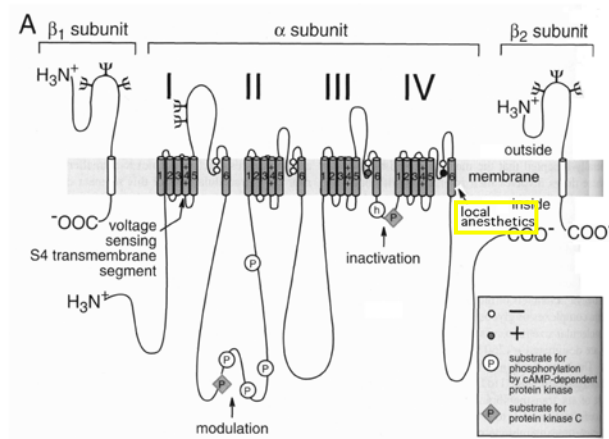
Local anesthetics reversibly bind to the voltage-gated Na⁺ channel, block Na⁺ influx, and thus block action potential and nerve conduction.



Structure of local anesthetics



Voltage-gated Na⁺ channel



Local anesthetics preferably block small nerve fibers

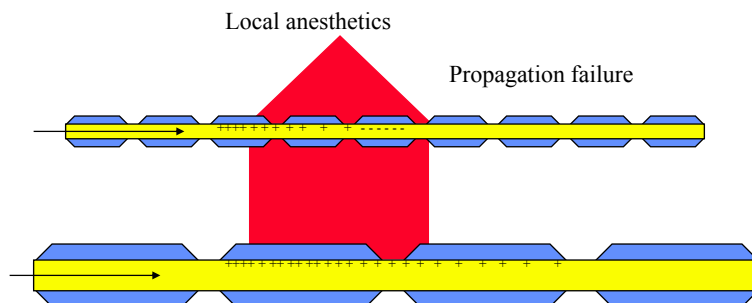
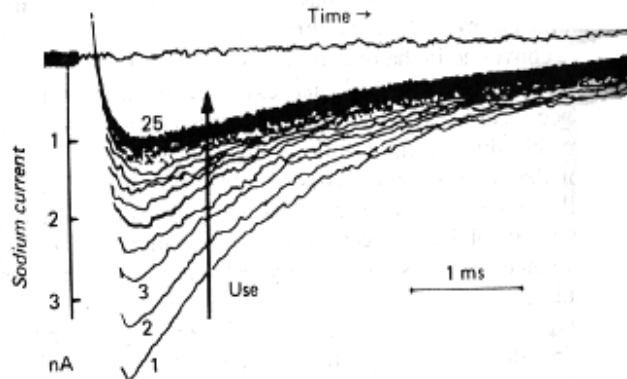


Table 2. Relative size and susceptibility to block of types of nerve fibers.

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	12–30	+++
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	++++

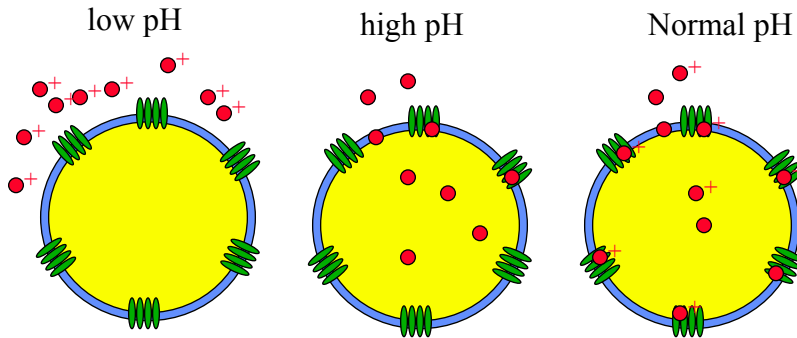
Nerves with higher firing frequency and more positive membrane potential are more sensitive to local anesthetic block

Use-dependent block by local anesthetics



In nerve bundles, fibers that are located circumferentially are affected first by local anesthetics

Effectiveness of local anesthetics are affected by pH of the application site



Metabolism of local anesthetics

- Most ester-linked local anesthetics are quickly hydrolyzed by enzymes in blood.
- Amide-linked local anesthetics can be widely distributed via the circulation and are hydrolyzed in the liver.
- Water-soluble metabolites are excreted in the urine.

Effect of vasoconstriction on local anesthetics

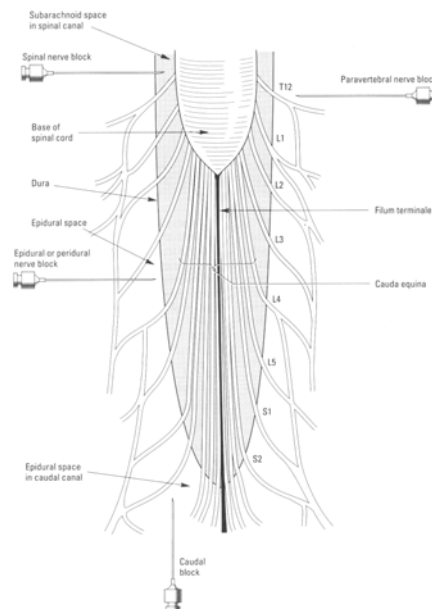
Local anesthetics are removed from depot site mainly by absorption into blood.

Addition of vasoconstrictor drugs such as epinephrine reduces absorption of local anesthetics, thus prolonging anesthetic effect and reducing systemic toxicity.

Epinephrine is included in many local anesthetic preparations. *Know your patient's health status!*

Examples of local anesthetic use:

- Infiltration
- Topical anesthesia
- Field block
- Nerve block
- Intravenous regional block
- Spinal nerve block
- Epidural nerve block



Toxicity and side effects

- **Central nervous system**
Stimulatory effects: restlessness, tremor, convulsion.
Suppression at high dosage may lead to respiratory failure.
- **Peripheral nervous system**
Inhibition of transmission at neuromuscular junctions and ganglionic synapse.
- **Smooth muscles**
Depress contractions of intestinal, vascular and bronchial smooth muscles.

Toxicity and side effects

- **Cardiovascular system:**
Decreases the electrical excitability, conduction rate and force of contraction in myocardium.
Causes dilation of blood vessels.
Cocaine may cause vasoconstriction, hypertension and cardiac arrhythmias.
Bupivacaine may cause cardiovascular collapse and ventricular tachycardia.
- **Allergic reactions**

Ester Linked Local Anesthetics

- 2 Chloroprocaine
- Procaine
- Tetracaine
- Cocaine

Ester Linked Local Anesthetics (cont.)

- Hydrolysed by Plasma Pseudocholinesterase
- Patients with Atypical Plasma Cholinesterase.
- Allergic reactions
- Formation of PABA.

Cocaine

- Used to provide topical anesthesia of the Upper Respiratory tract.
- Vasoconstrictive properties

Procaine

- Low potency
- Slow onset
- Short duration of action
- Infiltration Anesthesia and Diagnostic Nerve Blocks.

2-Chloroprocaine

- Breakdown in the Plasma less than a minute.
- Low potential for Systemic Toxicity.

2-Chloroprocaine (cont.)

- Prolonged Sensory and Motor Blockade associated with the use of Sodium Metabisulfite
- No reports of neurotoxicity with EDTA as the preservative.
- Muscular pain

2-Chloroprocaine (cont.)

- Newer preparation
- 3% 2-Chloroprocaine is the Local anesthetic of choice for PNB for surgical anesthesia of short duration with minimal postoperative pain
- Duration (1.5-2 hours)

Tetracaine

- Longest acting amino ester
- Rarely used

Amide-Linked Local Anesthetic

- Lidocaine
- Mepivacaine
- Prilocaine
- Etidocaine
- Bupivacaine
- Ropivacaine
- Levobupivacaine

Amide-Linked Local Anesthetic

- Amide-linked Local Anesthetics are metabolized by the liver

Lidocaine

- Lidocaine can be used for:
 - Epidural blockade 2%
 - Bier blocks
 - Avoid for spinals
 - Intermediate duration

Mepivacaine

- Intermediate duration local anesthetic
- Anesthetic of choice for Peripheral Nerve Blockade for intraoperative Anesthesia for surgery that lasts 3-6 hours

Prilocaine

- Intermediate Duration
- Causes Methemoglobinemia at an 8mg/kg dose.
- Not frequently used.

Etidocaine

- Profound Motor Blockade that outlasts Sensory Blockade
- Not used

Bupivacaine

- Long acting agent
- Most commonly used local anesthetic
 - Spinal
 - Epidural
 - Peripheral Nerve Blockade

Bupivacaine (cont.)

- Cardiotoxicity
 - Most cardiotoxic (severe ventricular arrhythmias and myocardial depression)
 - Difficult to treat
 - Acidosis, Hypercarbia and Hypoxemia

Ropivacaine

- Enantiomere of 1-propyl-2',6'piperidylidene that has less toxicity than Bupivacaine
- Local anesthetic of choice for PNB for surgeries that last long

Levobupivacaine

- Enantiomere of Bupivacaine
- Excellent less toxic alternative to bupivacaine