The concept and chemistry of anesthesia ("an" meaning without + "esthesia" meaning sensation), now routinely welcomed by all but the most masochistic dental patients, is a relatively new phenomenon. Many of the agents currently in use were unknown only a generation ago.

Due to the amount of material, anesthetic agents are being presented in two chapters: local anesthesia and general anesthesia. As the names imply, the terms represent the extent of activity for the drugs used, in addition to the differences in their ADME characteristics.

By the completion of this section, you should be able to:

1. Describe the mechanism of action of local anesthetics
2. Differentiate between the major categories of local anesthetics (amides and esters) and discuss their distinguishing properties
3. Identify potential crossover allergies between local anesthetic agents and discuss their clinical significance
4. Differentiate between a drug allergy and a panic reaction
5. Understand the effect of physiological pH on the activity of injected local anesthetics
6. Discuss the effect of inflammation on the effectiveness of a local anesthetic
7. Describe the action of epinephrine when added to local anesthetics
8. Discuss the clinical significance of epinephrine entering the bloodstream when used as part of the local anesthetic.
9. Relate the consequences of using these agents in patients with certain drug allergies or pre-existing conditions.

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**Evolution of Local Anesthesia**

It took more than the development of the individual drugs to bring local anesthesia into clinical practice—it took the invention of a usable syringe. The combination of a hollow needle attached to a glass barrel was known for many years prior to Alexander Wood’s invention of 1853—his was the first to permit the injection of small, measured volumes.

Here is how local anesthetic therapy evolved after that:

1856: proposed use of coca leaves as an anesthetic by Samuel Percy
1860: cocaine isolated by Albert Niemann
1884: Carl Koller demonstrates analgesic properties of cocaine in the eye
1887-1892: addiction and death from cocaine use reported in over 25 publications
1900: Benzocaine isolated by A. Eihorn
1905: Procaine (Novacain) isolated
1930: Tetracaine (Pontocaine) isolated, the last of the ester class to be developed
1948: Lidocaine (Xylocaine) first used clinically
1957: Mepivacaine introduced
1960: Prilocaine developed
1965: Bupivicaine becomes the first single-compound long-acting amide anesthetic
1976: Articaine (Septacaine) first reaches dental practice
1996: Ropivacaine introduced
Introduction

Local anesthetics represent the most often used drugs in dental practice. Their obvious indication is to reduce the pain and discomfort that can occur during a dental procedure. Local anesthetics are useful, therefore, in

- single, uncomplicated extractions
- multiple extractions
- extractions of impacted teeth
- apical resections
- removal of cysts
- preparations of cavities

These agents act locally, meaning, their anesthetic effects are limited to a specific area, during which time the patient is generally conscious and able to communicate with the dentist and hygienist. The effect is obtained either by topical application or by localized injection.

There are five general routes for applying local anesthetics:

1. topical, by creams, patches, sprays, or lozenges
2. infiltration, by direct intradermal or subcutaneous injection into the tissue near the area of operation
3. nerve block, by injection near a bundle of nerves (a “sensory nerve trunk”), to induce anesthesia and relieve pain or spasms along several nerve pathways
4. spinal, by direct injection into the subarachnoid space cerebral spinal fluid (CSF) in the lumbar area, to induce anesthesia in the nerve roots of the body’s complete lower trunk. The density of the solution and the position of the patient affects the diffusion of the anesthetic
5. epidural, by injection into the epidural space of the spinal column, primarily for anesthesia for labor and delivery; takes a relatively large amount of anesthetic to diffuse across the localized area

The action of a properly used local anesthetic is reversible, with complete recovery of the affected tissues. For ease of use and prevention of infection, the agents need to be stable in solution and remain intact during sterilization. The agents need to penetrate tissues with ease, and should be metabolized and excreted with minimal effects on the hepatic or renal systems.
**Mechanism of Action of Local Anesthetics**

Nerves generate impulses by creating changes in membrane permeability. This change in permeability allows for a substantial inflow of sodium ions across the nerve membrane, which creates an action potential. The generated action potential then becomes part of the information relay along the nerve, allowing communication between the peripheral and central nervous systems.

Restricting the action potential can therefore block this communication, and if a long enough portion of the nerve can become involved, anesthesia will result.

In the simplest of terms, local anesthetics bind to receptors near the sodium channel on the nerve membrane. As the amount of the local anesthetic accumulates, the sodium channels become obstructed. Impulses along the nerve are slowed, the strength and propagation of the action potential are diminished, and communication along the fiber is blocked.

Larger nerves require larger doses of the local anesthetic to achieve this effect.
The Effect of pH on Local Anesthetics

In the discussion of lipid solubility in chapter two, nonpolar drugs are shown noteworthy for their lack of an electrical charge. This uncharged form of a drug is more readily absorbed by tissues because it is lipophilic. If the same drug were to develop an electrical charge, its absorption would be diminished. One way to create this situation is by altering the pH of the environment where the drug appears.

The concept of pH is useful in determining whether an environment is acidic, basic, or neutral. Neutral pH has the numeric value of 7. Above a pH of 7, the environment is basic. Below 7, the environment is acidic. The body has a physiological pH of 7.4. This means the body, in general, is slightly basic.

Questions to Consider

The mechanism of action of local anesthetics is to

- block nerve synapses
- coagulate nerve protein reversibility
- persistently depolarizing the nerve membrane
- block nerve conduction by preventing nerve depolarization

Or, to put it in another way:

Local anesthetics produce their primary effects by

- inhibiting inflammation
- blocking nerve conduction
- constricting blood vessels
- depressing the reticuloactivating system (RAS)

Or, even this way:

Local anesthetics exert their action by

- interfering with the flow of potassium across neural membranes
- increased strength of action potential depolarization
- interfering with the flow of sodium across neural membranes
- altering the pH of the neural intracellular fluid

Comparison of acidic, basic, and physiologic pH

<table>
<thead>
<tr>
<th>Acidic</th>
<th>Neutral</th>
<th>Basic</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>7.0</td>
<td>7.4 (Physiologic)</td>
</tr>
</tbody>
</table>

Chemically, most local anesthetic agents are categorized as weak bases. This means that, once introduced and diluted at the injection site, they are in a weakly basic environment (physiological pH), and do not possess an effective electrical charge. Since there is no electrical charge, they have lipophilic activity and adequate tissue penetration.

If the physiological pH is altered, especially as it approaches 7 or below, the extracellular environment becomes relatively acidic. In these cases, drugs that are weak bases can develop a charge. When a drug develops an electrical charge, it is considered polarized, and as such, becomes less lipophilic. If it is less lipophilic, its relative tissue penetration is reduced.
An infection can cause an influx of histamine, bradykinins, and prostaglandins to the affected area. These components of the body’s inflammatory response can cause a localized drop in the extracellular pH.

An oral infection with the accompanying inflammation can, therefore, create a reduction in pH, which in turn can cause a local anesthetic to develop a charge, become polarized, and have diminished tissue penetration.

**Considerations with the Topical Application of Local Anesthetic Agents**

The discussions that follow center on injectable local anesthetic agents. However, as already mentioned, there are other methods for administering these drugs, most notably, topically. Some agents are available in patch form (Lidoderm, containing lidocaine) or as sprays (Americaine, containing benzocaine). There are some points to make regarding these methods of application.

Patches work best when applied to dry or dried areas, to soft tissues, and to regions that are not thickened by repeated use (non-calloused or “nonkeratinized” tissues).

Sprays have several limits to their use, since it is difficult to control the quantity of drug being administered, it is difficult to confine the effect of a drug to a small area, and perhaps most significantly, sufficient amounts could be inhaled to cause a toxic reaction (tracheal absorption of these drugs is nearly as efficient as by injection).

The effect of pH also has a distinct effect on the activity of topically applied local anesthetic agents. Absorption across a mucous membrane is hampered due to the poor buffering nature of the tissue, meaning the mucosal environment can possess a pH of as low as 5.5. In such relatively acidic surroundings, topically applied agents will develop a polarized charge, hampering their effective absorption. This explains why effective concentrations of topical agents are higher than those of their injectable counterparts (a good example being lidocaine, which is effective as a 1% injection, but which can be in concentrations of

---

**Question to Consider**

An infection in an area can prevent the accumulation of effective concentrations of local anesthetic solution because of

- **a. low tissue pH**
- **b. excessive dilution with tissue fluids**
- **c. the intense stimulation of pain due to the infection**
- **d. rapid absorption of the solution into the systemic circulation**

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**EMLA cream**

*EMLA topical cream (eutectic mixture of local anesthetics)*

A combination of lidocaine, 25mg/ml and prilocaine, 25mg/ml

Where many aspects of pain therapy focus on the grand scale of intractable, severe affliction, there remains a distinct need for brief, localized analgesia for the multitude of comparatively minor assaults that cause discomfort in the course of medical therapy. Fear of needles or dermatological incisions often enhance the level of perceived pain by the patient. For this reason, local anesthetics have been long employed in the dental field. Of these local anesthetics, two, namely lidocaine and prilocaine, have demonstrated topical effectiveness in providing temporary anesthesia and pain relief for incidental procedures involving needles and for many dermatological operations.

EMLA, or “eutectic mixture of local anesthetics,” represents a combination of two amide-type local anesthetics: lidocaine in 2.5% concentration with prilocaine in a 2.5% concentration. Approximately one hour prior to the appropriate procedure, a small amount of the cream should be applied directly to the skin. The cream is then generally covered with a patch such as Tegaderm, and left covered for 30 to 60 minutes. After the patch is removed, the cream can remain in place without the anesthetic effect diminishing for up to three hours.

As more and more procedures become performed in an outpatient or office setting, the availability of local anesthetics such as EMLA will become increasingly important.
5-10% in topical gels or solutions).

**Toxicity and Challenges in the Use of Local Anesthetics**

When correctly used, local anesthetics are very safe. Children, through resistance and fear of needles, and the elderly, when confused, may present challenges for administration.

Allergies to specific agents may emerge with local anesthetics, as is possible with any drug. Allergies predominate among those local anesthetics of the *ester* classification (to be discussed). In addition, multiple dose vials containing preservatives known as *methylparabens* may pose problems for patients sensitive to the preserving agent (methylparabens do not appear in recently-formulated, *single use* dental cartridges). Antioxidants known as *sulfites* may also represent difficulties. Sulfites such as *sodium bisulfite* or *sodium metasulfite* are added to prevent the breakdown of vasoconstrictive drugs that are added to local anesthetics. Patients suffering from asthma are more prone to allergies of this nature.

It is important to perform a careful patient history to check for specific drug allergies. For example, most patients equate local anesthesia with a single, antiquated drug known as *Novocain* (generic name *procaine*). If a patient who states an allergy to “Novocain” does not appear to have had his first dental visit prior to 1950, chances are that he is unaware of the specific nature of his drug allergy, and that means further investigation is needed.

*Also, it is important to appreciate that some patients may confuse panic reactions with allergies.* If a patient describes his allergy as “palpitations,” “cold perspiration,” or even “fainting,” chances are that the “allergy” is actually a panic reaction.

The best way to prevent a toxic reaction from the administration of a local anesthetic is to:

- be thorough with the patient history
- aspirate the syringe (draw back on the plunger) once the needle is in place before injecting the local anesthetic – if, when drawing back, you introduce blood into the syringe, chances are that you have struck a blood vessel and are, therefore, at increased risk of injecting the anesthetic into the blood supply
- use the least amount necessary – frequent exposure of unnecessary quantities of any drug can potentially produce drug sensitivities or allergies
- inject slowly (approximately 1ml per minute)
- avoid repeated injections into the same area – if a vasoconstrictor such as epinephrine is present, repeated injections will decrease blood flow. Edema and tissue damage can occur at that point, causing delays in healing
- give the anesthetic agent sufficient time to work before beginning the dental procedure
- avoid injections into inflamed or infected areas

**Question to Consider**

A patient states "I'm allergic to Novocain." When questioned further, he describes his experience as "shortness of breath, palpitations, cold perspiration and fainting for a few moments." From this information the dental hygienist should suspect that the patient is

- a drug addict
- *apprehensive about receiving dental care*
- likely to experience anaphylactic shock if injected with Novocaine
- suffering from an undiagnosed systemic disturbance and should be referred to a physician for consultation
The Use of Vasoconstrictors in Local Anesthesia

With the exception of cocaine, local anesthetics cause a transient vasodilation following application or injection. Vasodilation causes an increased perfusion of blood to the injected area, with two possible results:

(1) the drug being carried away, and therefore becoming less effective, and
(2) the anesthetic agent reaching the cardiac muscle with the potential for undesired myocardial effects.

The effect on the heart muscle is a valid consideration since one of the prototype drugs in these discussions, lidocaine, has a use in medical emergencies in the treatment for life-threatening ventricular arrhythmia.

In order to maintain effective concentrations of local anesthetics at the injection site, vasoconstrictive drugs are often added to the solution. The primary additive is epinephrine, already discussed for its sympathomimetic (or adrenergic) properties (see Chapter 5).

The addition of epinephrine not only minimizes the vasodilation caused by the local anesthetic agent, but causes vasoconstriction of the blood vessels in the area surrounding the injection. The vasoconstriction decreases perfusion of blood to the region, and the local anesthetic is not carried away.

Questions to Consider:
The action of epinephrine when combined with a local anesthetic is to
a. increase the amount of local anesthetic needed for effect
b. increase vasodilation to the immediate area
c. enhance circulation and wash the anesthetic from the site of action more quickly
d. increase the duration of anesthesia

When a local anesthetic containing epinephrine is mistakenly injected into a blood vessel, the patient could demonstrate
a. watery saliva – this would be a cholinergic or parasympathetic action
b. bradycardia – this is another cholinergic action
c. an elevation in blood pressure

Patients with diabetes are predisposed to problems with capillary circulation. The addition of epinephrine can cause further vasoconstriction to capillaries already compromised by the disease process. Patients with diabetes may experience an increase in tissue damage as a result.

The amount of epinephrine added to a local anesthetic is expressed in terms of dilution, i.e., “1:100,000” or “1:200,000.” As discussed in Chapter 5, these numbers represent the number of grams per milliliter volume. A 1:100,000 dilution of epinephrine is, therefore, 1 gram of epinephrine in 100,000 milliliters of solution.

Another vasoconstrictor, levonordefrin, is occasionally used. As the name implies, it is another chemical cousin to norepinephrine. The most common dilution for levonordefrin is 1:20,000.

Question to Consider:
The effective use and application of a topical anesthetic solution is dependent on
a. a review of the patient's history (to determine true allergies)
b. an explanation of the procedure to the patient (to reduce fear and apprehension)
c. a generous application to a large surface (not a good idea, since it can result in sensitization to the local anesthetic)
d. application to a surface that is dried with a gauze sponge or cotton roll (dry, non-keratinized tissue has greater absorption)
e. performance of clinical services immediately after application (all things take time, even local anesthesia)
Specific Local Anesthetic Agents – the Esters and the Amides

Based on similarities in their chemical structures, there are two primary classes of local anesthetic drugs—“esters” and the “amides.”

The ester classification is the older of the two, representing the earliest examples of local anesthetic agents (it is here where the well-known but long outmoded Novocaine appears). A patient having an allergy to one of the ester-type anesthetics will probably have a cross-over allergy to other esters.

The amides, however, have a far lower potential for allergic reactions in general and cross-over allergies in particular.

In addition, there have been no documented cross-over allergies between the ester and the amide classes of local anesthesia.

Categories of Local Anesthetic Agents

<table>
<thead>
<tr>
<th>Esters</th>
<th>Generic and (brand names)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzocaine (Solarcaine, Americaine)</td>
<td>topical</td>
<td></td>
</tr>
<tr>
<td>Chloroprocaine (Nesacaine)</td>
<td></td>
<td></td>
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<tr>
<td>Cocaine</td>
<td></td>
<td></td>
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<tr>
<td>Procaine (Novocain)</td>
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<td></td>
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<tr>
<td>Propoxycaine (Ravocaine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tetracaine (Pontocaine)</td>
<td>topical</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Amides</th>
<th>Generic and (brand names)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Articaine (Septocaine, Septanest)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bupivicaine (Marcaine, Sensorcaine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Etiodocaine (Duranest)*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Levobupivicaine (Chirocaine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lidocaine (Xylocaine, Nervocaine, Dilocaine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mepivicaine (Carbocaine, Polocaine, Isocaine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prilocaine (Citanest)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prilocaine with lidocaine (Oraquix)</td>
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</tbody>
</table>

*Note: etidocaine (Duranest) is used primarily for central nerve block or lumbar procedures

Sidebar Discussion – How Much Epinephrine and Lidocaine are Actually Present?

In clinical emergency uses of epinephrine, effective therapeutic doses are 0.5-1.0mg.

The standard volume in a cartridge of a local anesthetic is 1.8ml.

If epinephrine is present in that cartridge at one of the standard dilutions of 1:200,000, there would be only 0.009mg of epinephrine present. Even at the dilution of 1:100,000, the total amount in the cartridge would be 0.018mg.

It is unlikely, therefore, that enough epinephrine would enter the bloodstream even with a direct intravenous infusion to cause a clinical effect on heart rate or blood pressure. However, care should still be taken with patients who have:

- uncontrolled hypertension
- hyperthyroidism
- a history of angina pectoris
- a history of heart attack or stroke
- using antidepressants known as MAO (mono-amine oxidase) inhibitors

In the case of lidocaine, the usual emergency doses for ventricular arrhythmia is 50-100mg as an intravenous infusion.

A 1% solution of lidocaine represents a dilution of 1 gram (1000mg) in 100ml. A 1.8ml dental cartridge would, therefore, contain 18mg of lidocaine. A 2% solution would contain 36mg in the same volume. These quantities of lidocaine approach clinically effective levels. If a cartridge were to be completely injected into a vein, the patient could experience changes in heart rate or rhythm.
Specific Local Anesthetics – The Esters

With the exception of cocaine, the local anesthetics of the ester class are all derivatives of para-aminobenzoic acid (PABA). The ester linkage is primarily hydrolyzed by plasma cholinesterases before going through further metabolism by the liver. The esters are excreted by the kidneys, nearly all as metabolites.

Historically, the esters represent the first collection of local anesthetic agents. As noted, they are more prone to cause allergic reactions among patients. Since they are derivatives of PABA, ester-type anesthetics can interfere with the antibacterial effects of the sulfonamide class of antibiotics (see Chapter 10, Antibiotic Therapies). Today, their infrequent use explains their unavailability in dental cartridge format. When used, anesthetics in the ester class are generally called upon for infiltration, nerve block, or for spinal anesthesia.

**Procaine (Novocain) and Chloroprocaine (Nesacaine)**

*Procaine (Novocain)* can trace its popularity from its appearance in 1905 until the mid-1950s. In fact, the popular subconscious grew to equate “Novocain” as synonymous with any “local anesthesia” (especially if they were raised on a strong diet of Three Stooges films). Again, this re-emphasizes the importance of obtaining a careful and accurate drug allergy history if a patient claims an allergy to “Novocain.”

*Chloroprocaine (Nesacaine)* is an alternative product to procaine, available in a 2% solution. It, too, has an extremely short half-life in the body.

Both procaine and chloroprocaine have half-lives of under a minute. The effect of the plasma cholinesterases is obviously powerful. However, some patients have a genetically-driven deficiency of the enzyme cholinesterase. These patients will experience a much longer drug half-life, and with that, an increase in duration of anesthesia. In addition, concurrent use of drugs that inhibit the effect of cholinesterase may increase the potential for toxic reactions.

*Procaine* and *chloroprocaine* are the least toxic of the ester-based anesthetics, and are not effective topically. Both are used for infiltration and nerve-block local anesthesia.

**Propoxycaine**

Propoxycaine is very potent, but also potentially very toxic. It is rarely, if ever, used today, and then only in combination with procaine and the vasoconstrictor levonordefrin.

**Tetracaine (Pontocaine)**

Tetracaine, at concentrations of 2%, is useful as a potent topical anesthetic agent. It is very toxic if administered as an injection. Care must also be taken to avoid applying tetracaine to abraded tissues. Tetracaine has a longer duration of action than either procaine or chloroprocaine.

**Benzocaine (Solarcaine, Americaine, and many others)**

Benzocaine is available in ointments, powders, and sprays. It is used only in topical forms. It may also be listed in product ingredients as "ethyaminobenzoate."

It should be noted here that excessive use of either benzocaine (a popular ingredient in sunburn and OTC-oral lesion creams and ointments) or tetracaine can sensitize patients not only to these agents, but to all ester class anesthetic agents.
**Cocaine – Uses, Abuses, and Sigmund Freud**

Despite its greater notoriety as a drug of abuse, cocaine is an excellent topical local anesthetic and can be legally prescribed. It is considered a controlled substance, and resides in DEA Category II (“C-II”), along with morphine, methylphenidate (Ritalin), and dextroamphetamine (Dexedrine).

Cocaine stimulates the sympathetic nervous system, explaining its unique ability among anesthetic agents to induce vasoconstriction.

Chemically, cocaine is an alkaloid, derived from the coca plant (*Erythroxylon coca*). In its rare use as a local anesthetic, cocaine causes topical anesthesia within one minute of application, with a possible duration of action of up to two hours. Unmetabolized cocaine does appear in the urine. While solutions are available ranging in concentration from 2% to 10%, a strength of 4% is rarely exceeded. Sympathetic symptoms of restlessness, hypertension, and rapid breathing can escalate to cardiac arrhythmia, hyperpyrexia (elevated body temperature), seizures, and respiratory arrest.

Cocaine addiction is associated with dopamine accumulation. Dopamine is an important neurotransmitter in those parts of the brain controlling pleasure responses. At most neural synapses, salvage mechanisms reabsorb unused dopamine. Cocaine blocks the uptake of excess dopamine, increasing the effects on the pleasure center neurons.

National Institute for Drug Abuse conservatively estimates that 35-40 million Americans have tried cocaine in one form or another. In South America, native Indians ingest the unprocessed coca leaf, obtaining the equivalent of 400mg of cocaine in 50 grams of leaves. Ironically, this generally malnourished population may actually derive some benefit from chewing the leaves—the same 50 grams of leaves contain high doses of vitamin C, B1, and riboflavin, helping prevent scurvy in regions where fresh fruit and vegetables are in short supply. The highly addictive form of cocaine, known as *crack*, is purified alkaloidal cocaine, a concentration that is widely abused and potentially lethal.

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**Why all this talk about cocaine?**

Granted, this is a rather lengthy discussion of a drug that has limited use in the dental field. However, cocaine holds a unique place in being the first local anesthetic. We owe much of this early knowledge to Dr. Sigmund Freud, the “father of psychiatry.” Freud was interested in the specific effects of cocaine that alleviated hunger (addiction was not a big concern in the 1880s, but workers taking lunch breaks were) and set his assistant, Carl Köller, to work on the investigation. Köller placed some cocaine on his tongue and experienced numbness and loss of taste. He and an associate then applied solutions of cocaine to *their eyes* and discovered that no sensation could be felt when *their corneas were touched by a pinhead*. Cocaine soon became the local anesthetic of choice for the removal of cataracts and in other types of eye surgery.
Specific Local Anesthetics – The Amides

Anesthetics in the amide class of local anesthetics are derivatives of the dye aniline. These agents are metabolized in the liver and are excreted by the kidneys.

The prototype agent in this category is lidocaine.

Lidocaine (Xylocaine)

Introduced in the 1940s, lidocaine is perhaps the most frequently used local anesthetic. It is well absorbed by mucous membranes and is available in several dosage forms, including:

- sterile injection, 1%, 1.5%, and 2%, with or without epinephrine
- topical ointment, 5%
- topical jelly, 2%
- topical oral spray, 10%
- viscous solution 2%
- topical patches

<table>
<thead>
<tr>
<th>Ester Local Anesthetic</th>
<th>Concentrations Available</th>
<th>Application</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzocaine (Solarcaine, Americaine)</td>
<td>up to 20%</td>
<td>topical</td>
<td>topical only: various, generally extended</td>
</tr>
<tr>
<td>Chloroprocaine (Nesacaine)</td>
<td>1-2%</td>
<td>injection</td>
<td>P: 6-10 minutes/ S: 30-45 minutes</td>
</tr>
<tr>
<td>Cocaine</td>
<td>varies, maximum of 4%</td>
<td>topical</td>
<td>topical only: up to 2 hours</td>
</tr>
<tr>
<td>Propoxycaine/Procaine</td>
<td>0.4%/2%</td>
<td>injection</td>
<td>Pupal: 30-60 minutes/ S: 2-3 hours</td>
</tr>
<tr>
<td>Tetracaine (Pontocaine)</td>
<td>2%</td>
<td>topical</td>
<td>topical only: 45 minutes</td>
</tr>
</tbody>
</table>
In surgery and dental practice, lidocaine is used for topical anesthesia, infiltration, and nerve block. Its ability to cause vasodilation after injection is countered with the aforementioned addition of epinephrine, in concentrations of 1:100,000 or 1:200,000.

Patients may experience some sedation, shivering, and positional headaches following exposure to lidocaine.

Using a 2% solution, for infiltration and nerve block, the expectation for local anesthesia can break down as follows:

- Pulpal anesthesia: 5-10 minutes
- Soft tissue anesthesia: 1-2 hours

Adding epinephrine to the solution yields the following expectations:

- Pulpal anesthesia: 60-90 minutes
- Soft tissue: 2-4 hours

There are several alternatives to lidocaine, all of them members of the amide class of local anesthetics:

**Articaine (Septocaine, Septanest)**

Introduced in Europe in the 1970s and in the United States only in the past few years, articaine is one of the newest of the amide class. It is approximately 1.5 times as potent as lidocaine, with similar vasodilating properties. The manufacturers specifically warn against intravenous or intravascular injection due to the likelihood for pronounced cardiac effects.

Articaine is available in solutions of 4%, or with epinephrine dilutions of 1:100,000 or 1:200,000. Its use is nearly exclusively in dental practice, for infiltration and nerve block anesthesia. A unique contraindication to the use of articaine is an allergy to sulfa drugs. In addition, articaine solutions use sulfites as a preservative. Sulfites have been known to cause bronchospasm in susceptible patients with asthma.

Anesthesia following infiltration is within one to three minutes, with a duration of effect from 45 to 75 minutes per cartridge.

Use in children under four years of age is not recommended, and the maximum dose is 7mg/kg of patient body weight.

**Bupivacaine (Marcaine)**

Structurally, bupivacaine is similar to mepivacaine (Carbocaine, see below). With its extended duration of action, its 0.5% solution is useful for dental procedures requiring anesthesia for longer than 90 minutes. This effect can reduce the need for post-operative analgesic use.

The extended duration of effect can contribute to some problems, however. Tissue laceration is more likely, especially among children or patients who have mental impairments. The laceration potential is increased with the addition of epinephrine.

**Etidocaine (Duranest)**

For central nerve block or lumbar procedures
Mepivacaine (Carbocaine)
Mepivacaine, available since 1960, is equal to lidocaine in potency, but is not effective when
applied topically. Vasodilation and sedation with mepivacaine are minimal.
The 3% solution of mepivacaine delivers the following duration of anesthesia:

- pulpal anesthesia: 20-40 minutes
- soft tissue anesthesia: 2-3 hours

The vasoconstrictor Levonordefrin (Neo-Cobefrin) is mixed with mepivacaine as an
alternative to epinephrine, at a dilution of 1:20,000.

Prilocaine (Citanest, Citanest Forte)
Prilocaine is more rapidly metabolized than others in the amide class, and as a result, is
generally considered less toxic. This allows for higher concentrations to be used.
Rarely, a blood condition known as methemoglobinemia may develop with prilocaine, but
this usually involves a genetic predisposition or the concurrent administration of substantial doses of
acetaminophen.
Prilocaine is available in 4% solutions, alone or mixed with epinephrine in a dilution of
1:200,000.

Ropivacaine (Naropin)
Ropivacaine is a relatively new amide agent and is used primarily for epidural blocks. It is
not used in routine dental practice.

<table>
<thead>
<tr>
<th>Amide Type for Injection</th>
<th>Concentrations Available</th>
<th>Duration (Pulpal and Soft tissue)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Articaine (Septocaine, Septanest)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>with epinephrine 1:200,000</td>
<td>4%</td>
<td>P: 45-60 minutes / S: 2-5 hours</td>
</tr>
<tr>
<td>with epinephrine 1:100,000</td>
<td>4%</td>
<td>P: 60-75 minutes/ S: 3-6 hours</td>
</tr>
<tr>
<td>Bupivicaine (Marcaine, Sensorcaine)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>with epinephrine</td>
<td>0.5%</td>
<td>P: 90-180 minutes/S: 4-9 hours</td>
</tr>
<tr>
<td>Etiodocaine (Duranest)</td>
<td></td>
<td>P: 90-180 minutes /S: 4- 9 hours</td>
</tr>
<tr>
<td>Lidocaine (Xylocaine)</td>
<td></td>
<td>P: 5-10 minutes/ S: 60-120 minutes</td>
</tr>
<tr>
<td>with epinephrine 1:50,000</td>
<td>2%</td>
<td>P: 60 minutes/ S: 3-5 hours</td>
</tr>
<tr>
<td>with epinephrine 1:100,000</td>
<td>2%</td>
<td>P: 60 minutes/ S: 3-5 hours</td>
</tr>
<tr>
<td>Mepivicaine (Carbocaine)</td>
<td></td>
<td>P: 20-40 minutes /S: 2-3 hours</td>
</tr>
<tr>
<td>with levonordefrin 1:20,000</td>
<td>3%</td>
<td>P: 60-90 minutes/S: 3-5 hours</td>
</tr>
<tr>
<td>Prilocaine (Citanest)</td>
<td></td>
<td>P: 10-60 minutes/S: 1.5 - 4 hours</td>
</tr>
<tr>
<td>with epinephrine 1:200,000</td>
<td>4%</td>
<td>P: 60-90 minutes/S: 3-8 hours</td>
</tr>
</tbody>
</table>
A Possible Alternative When All Else Fails – Diphenhydramine (Benadryl)

On rare occasions, when patients demonstrate sensitivity to both the ester and the amide collections of local anesthetics, anesthesia may be obtained by using diphenhydramine (Benadryl) injection. While diphenhydramine is classified as an antihistamine (see Chapter 18, Allergic Reactions and Other Emergency Situations), it has the capacity to induce local anesthesia. For this purpose, a 1% concentration is used, combined with a 1:100,000 dilution of epinephrine. At present, there is no commercially available product offering this combination. Specialty compounding pharmacies are capable of creating this injection using the raw materials and aseptic technique.

Natural Anesthesia – Eugenol (oil of cloves)

In the film Marathon Man, Dustin Hoffman is tortured by Sir Lawrence Olivier, not with prolonged readings from Shakespeare, but in character as an ex-Nazi dentist, bent on extracting teeth and information. Between sessions, the doctor demonstrates rare moments of beneficence by providing Mr. Hoffman with oil of cloves to apply to his oral wounds.

Topical application of clove oil depresses the function of sensory receptors by a powerful inhibition of prostaglandin biosynthesis (see discussion of prostaglandins as pain mediators in Chapter Eight, Analgesic Drugs). When applied topically, it causes local anesthesia and analgesia to the oral mucosa and in post-extraction alveolitis (dry socket).

Clove oil is a component of dental cements and fillings and is used as a flavoring in toothpaste, soaps, cosmetics, and perfumes. The concentration of eugenol in clove oil is anywhere from 60-90%. At these concentrations, eugenol can inhibit gram-positive and gram-negative bacteria, and demonstrate fungistatic and anthelminthic properties.

Repeated dental applications can result in oral tissue sensitivity, local tissue irritation, and damage to dental pulp or supporting periodontium. There is one report of permanent local facial anesthesia with subsequent inhibition of sweat glands after clove oil was spilled on a patient’s face.

Generalized Duration of Action Comparison

<table>
<thead>
<tr>
<th>Duration</th>
<th>Anesthetic (pulpal)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short (30 mins)</td>
<td>Chlorprocaine</td>
</tr>
<tr>
<td></td>
<td>Lidocaine (Xylocaine)</td>
</tr>
<tr>
<td></td>
<td>Mepivacaine (Carbocaine)</td>
</tr>
<tr>
<td></td>
<td>Prilocaine (Citanest)</td>
</tr>
<tr>
<td></td>
<td>Procaine (Novocain)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>Articaine (Septocaine) with epinephrine</td>
</tr>
<tr>
<td></td>
<td>Lidocaine (Xylocaine) with epinephrine</td>
</tr>
<tr>
<td></td>
<td>Mepivacaine (Carbocaine) with epinephrine or levonordefrin</td>
</tr>
<tr>
<td></td>
<td>Prilocaine (Citanest) with epinephrine</td>
</tr>
<tr>
<td>Long (90 mins)</td>
<td>Bupivacaine (Marcaine) with epinephrine</td>
</tr>
<tr>
<td></td>
<td>Etidocaine (Duranest) with epinephrine</td>
</tr>
<tr>
<td></td>
<td>Tetracaine (Pontocaine) -- topical use only</td>
</tr>
</tbody>
</table>
Topical Use of Local Anesthetics

Most of the previous discussion of ester and amide classes of local anesthetics have concentrated on their uses as injections. Non-invasive, topical application of anesthetics have their value in dentistry and other outpatient procedures, however:

- applied to tissues before an infiltration or nerve block injection to reduce the pain of the injection
- reduce pain and sensitivity of oral wounds or ulcers
- reduce pain from suture removal, scaling or probing

Lidocaine, benzocaine, and dyclonine are less toxic on abraded tissue. The concern with abrasions is that, if generously applied, topical administration of anesthetics can result in some systemic absorption and potential sensitization to the agents.

When used to reduce the pain and sensitivity of oral wounds or ulcers, care should be taken to prevent blocking the “gag reflex.” If lidocaine is gargled, for example, the body’s natural reflex to prevent inhaling, or aspirating, fluids and mucous into the lungs can be hindered.

Concerns with Toxicity

The newer agents for local anesthesia are noteworthy for their low frequency of toxic reactions. However, (there is always a however), toxicity is possible if high blood concentrations somehow occur, and the symptoms that emerge as levels accumulate include:

- anxiety, apprehension, and restlessness
- disorientation and confusion
- blurred vision and miosis
- twitching and tremors
- tinnitus (ringing in the ears)
- nausea
- seizures

When levels go higher still, the symptoms move from CNS excitation to depression:

- drowsiness
- unconsciousness
- respiratory arrest

There is no specific “cure” for toxic reactions to local anesthetic drugs. Treatments are symptomatic and supportive, meaning that therapy involves correcting the emerging symptoms and maintaining essential functions.

Storage Considerations

With the proliferation of single-use cartridges, storage considerations for local anesthetic agents are less of a problem than in the past. These agents are all stable at room temperature and will generally not degrade if kept out of direct sunlight. Epinephrine, if exposed to excesses of heat and sunlight, will launch upon a series of degrading chemical changes that will turn the solution from pink to brown. Of course, it is always important to pay attention to the expiration date provided by

Ch. 6 Pg. 15
the manufacturer.

In those rare cases where a multiple-dose vial is being used, an office policy should be in place to (1) note the date of first entry into the bottle, (2) note the number of times the vial has been used, and (3) a time limit on using the multiple-dose vial (six to nine months is often used as a guide).

Local Anesthesia Use Considerations – Diseases and Drug Interactions

Some specific cases have already been presented in this chapter of possible disease and drug-based interactions when dealing with local anesthetics. Here is a general overview of potentials for concern with certain patient populations:

• *Hypertension* (high blood pressure) – Generally the presence of epinephrine is only a concern among those patients whose blood pressure is very poorly controlled. In those cases, and when a non-specific beta-blocker drug is part of therapy (see Chapter 14, Cardiovascular Conditions) using a half-cartridge of epinephrine or levonordefrin containing local anesthetic is considered an appropriate starting point, with a maximum of 0.04mg of epinephrine (two cartridges) or 0.2mg of levonordefrin (also two cartridges).

• *Recent heart attack (myocardial infarction), angina, or stroke* – Epinephrine should be avoided within six months of a heart attack or stroke, or within three months of coronary bypass surgery or in the presence of unstable (or non-exertional) angina.

• *Diabetes Mellitus* – Epinephrine can counteract the hypoglycemic effects of insulin. Among poorly controlled diabetic patients (see Chapter 13, Diabetes) using high doses of insulin, this may result in an elevation in blood glucose levels.

• *Pheochromocytoma* – A tumor of the adrenal gland, pheochromocytoma results in elevated levels of norepinephrine in afflicted patients; further vasoconstriction with epinephrine is a contraindication.

• *Thyroid Disease* – Additional epinephrine is only a concern with severe thyroid disease (as in thyrotoxicosis); patients stabilized on oral therapy for thyroid deficiency generally need no adjustment during dental procedures.

• *Blood Disorders* – Presence of methemoglobinemia, a disease of the red blood cells, contraindicates the use of prilocaine

• *Asthma* – Some patients with asthma react to the preservatives present in local anesthetic injections, specifically sulfites and parabens.

• *Cocaine use* – While not a standard in medical practice, cocaine is a recreational reality. Patients who have used cocaine within 24 hours of exposure to a vasoconstrictor such as epinephrine risk potentially dangerous cardiac arrhythmia.

• *Tricyclic Antidepressant and Antipsychotic use* – Patients taking tricyclic antidepressants such as amitriptyline (Elavil) may have higher baseline levels of norepinephrine, as can those using antipsychotic drugs such as clozapine (Clozaril) and onlanzepine (Zyprexa). Minimizing the use of vasoconstrictive agents among these patients is warranted. The effect is not noted among those using the selective serotonin-reuptake inhibitor (SSRI) class of antidepressants such as fluoxetine (Prozac).

Conclusion

The history of local anesthesia began with the discovery of the coca plant and the isolation of cocaine. Other ester and PABA-related compounds followed, and the past century of development...
has resulted in compounds with increasing effectiveness with fewer side effects.

The quest for enhanced duration of activity resulted in long-acting amides, along with the co-administration of epinephrine as a local vasoconstrictive agent. These newer agents are noteworthy for their high degree of effectiveness, nearly non-existent cases of allergy, and wide range of dosage forms and applications.

**Study Guide Questions for Local Anesthetic Agents**

1. What are the five general routes for the application of local anesthetic agents?
2. What is the mechanism of action for local anesthetics? Which electrolyte is involved?
3. What is the numeric value of physiological pH? Is it basic, acidic or neutral?
4. Why is a local anesthetic less effective in the presence of inflammation?
5. What is the purpose of adding epinephrine to a local anesthetic?
6. Which local anesthetic causes vasoconstriction without the addition of epinephrine? What is its historical significance?
7. Which patient population is most prone to problems when sulfites are used as preservatives?
8. Which patient population is more likely to have excessive capillary constriction and tissue damage when epinephrine is used?
9. How many milligrams of epinephrine are contained in a 1.8ml cartridge when the stated dilution of epinephrine is 1:200,000?
10. How many milligrams of lidocaine are contained in a 1.8ml cartridge when the stated concentration is 2%?
11. What are the two general categories of local anesthetics? Do cross-over allergies between these categories exist? Which category is more prone to allergic reactions?
12. Which category is based on PABA? How are local anesthetics in this category metabolized?
13. The sulfonamide class of antibiotics can have a drug interaction with which category of local anesthetics?
14. A red flag should fly up when a patient states he is allergic “to novocaine.” Why?
15. Lidocaine is a prototype drug in which local anesthetic category?
16. What drug allergy is a specific contraindication to the use of articaine?
17. What is the name of a “natural” analgesic and anesthetic?
18. What is the name of an alternative anesthetic when a patient is allergic to drugs in the primary two categories?
19. Which reflex may be blocked by the use of lidocaine as a topical anesthetic? Why is this a concern?
20. What is the best way to store local anesthetic agents?