27 Local Anesthetics

J. David Haddox

DRUG LIST

The first clinical uses of a local anesthetic agent occurred in 1884, when cocaine was employed as a topical agent for eye surgery and to produce a nerve block. These events inaugurated a new era, that of regional anesthesia. New applications were developed, including spinal, epidural, and caudal anesthesia. The search for a better local anesthetic led to chemical synthesis of a number of other compounds that have more selective local anesthetic properties and few systemic side effects.

PROPERTIES OF LOCAL ANESTHETICS

An important property of the ideal local anesthetic is low systemic toxicity at an effective concentration. Onset of action should be quick, and duration of action should be sufficient to allow time for the surgical procedure. The local anesthetic should be soluble in water and stable in solution. It should not deteriorate by the heat of sterilization, and it should be effective both when injected into tissue and when applied topically to mucous membranes. Its effects should be completely reversible.

Although the characteristics of an ideal local anesthetic are easily identifiable, synthesis of a compound possessing all these properties has not been accomplished. The compounds discussed in the following sections fall short of the ideal in at least one aspect. However, the judicious choice of a particular agent for a particular need will permit the practitioner to employ local anesthesia effectively and safely.

Chemistry

The basic components in the structure of local anesthetics are the lipophilic aromatic portion (a benzene ring), an intermediate chain, and the hydrophilic amine portion (Fig. 27.1). The intermediate chain has either an ester linkage from the combination of an aromatic acid and an amino alcohol or an amide linkage from the combination of an aromatic amine and an amino acid. The commonly used local anesthetics can be classified as esters or amides based on the structure of this intermediate chain.

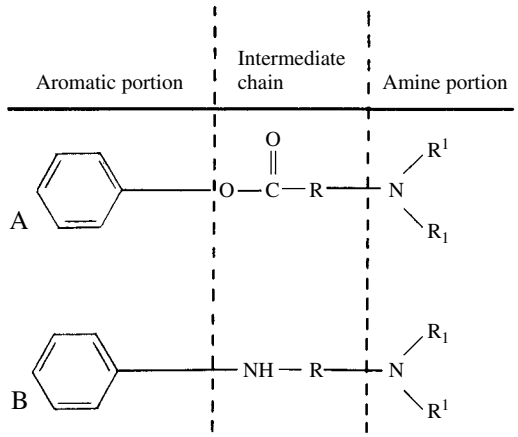

FIGURE 27.1
Model structure of local anesthetics showing aromatic portion, intermediate chain, and amine portion.

Mechanism of Action

The application of a local anesthetic to a nerve that is actively conducting impulses will inhibit the inward migration of Na^+. This elevates the threshold for electrical excitation, reduces the rate of rise of the action potential, slows the propagation of the impulse, and if the drug concentration is sufficiently high, completely blocks conduction. *The local anesthetics interfere with the process fundamental to the generation of the action potential, namely, the large, transient voltage-dependent rise in the permeability of the membrane to* Na^+.

While the physiological basis for the local anesthetic action is known, the precise molecular nature of the process is not completely clear. Almost all local anesthetics can exist as either the uncharged base or as a cation. The uncharged base is important for adequate penetration to the site of action, and the charged form of the molecule is required at the site of action. The cation forms of local anesthetics appear to be required for binding to specific sites in or near the Na^+ channels. The presence of the local anesthetic at these sites interferes with the normal passage of Na^+ through the cell membrane by stopping a conformational change in the subunits of the voltage-gated Na^+ channel.

Studies suggest that the receptor for the local anesthetic is near the inner (axoplasmic) surface of the cell membrane, because quaternary analogues of local anesthetics are quite effective when applied to the inside of the axonal membrane but are inactive when placed on the outside of the membrane. These permanently charged molecules cannot penetrate to the receptor sites.

Nerves that are rapidly depolarizing are inherently particularly susceptible to the effects of local anesthetics. This is termed *frequency-dependent blockade* and is thought to occur because the local anesthetics get to their receptor sites only when the Na^+ channel is open (depolarizing).

Differential Blockade

Peripheral nerve functions are not affected equally by local anesthetics. Loss of sympathetic function usually is followed by loss of temperature sensation; sensation to pinprick, touch, and deep pressure; and last, motor function. This phenomenon is called *differential blockade.* Differential blockade is the result of a number of factors, including the size of the nerve, the presence and amount of myelin, and the location of particular fibers within a nerve bundle. For conduction to be effectively blocked, the local anesthetic must exert its effects over the distance between several nodes of Ranvier. Since the smallest nerves (C fibers) have no myelin, they can be most easily blocked; thus, sympathetic functions often are blocked soon after a local anesthetic is applied to a particular nerve bundle. Small myelinated nerves have correspondingly short distances between nodes of Ranvier and therefore are often blocked next. These nerves subserve temperature and sharp pain sensation. Larger nerves then become blocked, accounting for the loss of function up to and including motor innervation.

Pharmacokinetic Properties

Absorption and Distribution

The rate of absorption of a local anesthetic into the bloodstream is affected by the dose administered, the vascularity at the site of injection, and the specific physicochemical properties of the drug itself. Local anesthetics gain entrance into the bloodstream by absorption from the injection site, direct intravenous injection, or absorption across the mucous membranes after topical application. Direct intravascular injection occurs accidentally when the needle used for infiltration of the local anesthetic lies within a blood vessel, or it occurs intentionally when lidocaine is used for the control of cardiac arrhythmias.

All tissues will be exposed to local anesthetics after absorption, but concentrations will vary among the organs. Although the highest concentrations appear to occur in the more highly perfused organs (i.e., brain, kidney, and lung), factors such as degree of protein binding and lipid solubility also affect drug distribution. The lung can absorb as much as 90% of a local anesthetic during the first pass. Consequently, the lungs can act as a buffer to prevent higher and therefore more toxic concentrations.

Placental transfer of local anesthetics is known to occur rapidly, fetal blood concentrations generally reflecting those found in the mother. However, the quantity of drug crossing to the fetus is also related to the

time of exposure, that is, from the time of injection to delivery. Subtle neurobehavioral changes in the neonate are detectable for as long as 8 hours after mepivacaine administration to the mother but are absent following the use of bupivacaine, lidocaine, and chloroprocaine. In general, minimal amounts of chloroprocaine reach the fetus because of its rapid hydrolysis by serum cholinesterase; this feature is its principal advantage in obstetrics.

Metabolism

The metabolic degradation of local anesthetics depends on whether the compound has an ester or an amide linkage. Esters are extensively and rapidly metabolized in plasma by pseudocholinesterase, whereas the amide linkage is resistant to hydrolysis. The rate of local anesthetic hydrolysis is important, since slow biotransformation may lead to drug accumulation and toxicity. In patients with atypical plasma cholinesterase, the use of ester-linked compounds, such as chloroprocaine, procaine and tetracaine, has an increased potential for toxicity. The hydrolysis of all ester-linked local anesthetics leads to the formation of paraaminobenzoic acid (PABA), which is known to be allergenic. Therefore, some people have allergic reactions to the ester class of local anesthetics.

Local anesthetics with an amide linkage (and one ester-lined anesthetic, cocaine) are almost completely metabolized by the liver before excretion. However, the total dose administered and the degree of drug accumulation resulting from the initial and subsequent doses are still a concern.

Clinical Uses

Local anesthetics are extremely useful in a wide range of procedures, varying from intravenous catheter insertion to extensive surgery under regional block. For minor surgery, the patients can remain awake; this is an advantage in emergency surgery, because protective airway reflexes remain intact. Many operative procedures in the oral cavity are facilitated by regional block of specific nerves. If surgery permits, the patient can return home, because he or she is less sedated than would be the case after general anesthesia.

Topical Anesthesia

Local anesthetics are used extensively on the mucous membranes in the nose, mouth, tracheobronchial tree, and urethra. The vasoconstriction produced by some local anesthetics, cocaine especially, adds a very important advantage to their use in the nose by preventing bleeding and inducing tissue shrinkage. Topical anesthesia permits many diagnostic procedures in the awake patient, and when it is combined with infiltration techniques, excellent anesthesia may be obtained for many surgical procedures in the eye and nose. The practitioner should be cautious when higher volumes are required, since overdosage may cause systemic reactions. Additionally, when the tracheobronchial tree and larynx are anesthetized, normal protective reflexes, which prevent pulmonary aspiration of oral or gastric fluids and contents, are lost.

Infiltration

Infiltration (i.e., the injection of local anesthetics under the skin) of the surgical site provides adequate anesthesia if contiguous structures are not stimulated. Since the onset of local anesthesia is rapid, the surgical procedures can proceed with little delay. Minimally effective concentrations should be used, especially in extensive procedures, to avoid toxicity from overdosage.

Regional Block

Regional block, a form of anesthesia that includes spinal and epidural anesthesia, involves injection near a nerve or nerve plexus proximal to the surgical site. It provides excellent anesthesia for a variety of procedures. Brachial plexus block is commonly used for the upper extremity. Individual blocks of the sciatic, femoral, and obturator nerves can be used for the lower extremity. An amount that is close to the maximally tolerated dose is required to produce blockade of a major extremity.

Spinal Anesthesia

Spinal anesthesia (subarachnoid block) produces extensive and profound anesthesia with a minimum amount of drug. The local anesthetic solution is introduced directly into the spinal fluid, where the nerves are not protected by a perineurium. This produces, in effect, a temporary cord transection such that no impulses are transmitted beyond the level that is anesthetized. The onset is rapid, and with proper drug selection, the anesthesia may last 1 to 4 hours. With careful technique, neurological complications are extremely rare. Procedures as high as upper-abdominal surgery can be performed under spinal anesthesia. Arterial hypotension produced by the local anesthetic is proportional to the degree of interruption of sympathetic tone, and it can produce pooling of blood in the lower extremities, which leads to decreased cardiac filling pressures. Knowing this allows blood pressure to be easily controlled, and hypotension is not usually a deterrent to spinal anesthesia. The sites of action of spinal anesthesia are the spinal nerve roots, spinal ganglia, and (perhaps) the spinal cord.

Lumbar Epidural Anesthesia

Lumbar epidural anesthesia affects the same area of the body as does spinal anesthesia. As the name implies, the

drug is deposited outside the dura. In contrast to spinal anesthesia, this method requires a much larger amount of drug. This procedure makes segmental anesthesia possible, whereby the anesthetized area is bordered caudally and cephalad by unaffected dermatomes and myotomes.

The concentration and volume of the local anesthetic solution will affect the extent of the cephalad and caudad spread of the block. The anesthesia can be made continuous by maintaining a small catheter in the epidural space; prolonged effects are obtained by periodically injecting supplemental doses through the catheter or by attaching it to a computer pump. The site of anesthetic action is on the nerves as they leave the intervertebral foramina. However, effective drug concentrations may be found in the spinal fluid, probably gaining entrance through the arachnoid villi. Arterial hypotension occurs by the same mechanism and is managed as in spinal anesthesia.

Epidural anesthesia is especially useful in obstetrics. Excellent analgesia occurs and the patient remains awake. Analgesia by the epidural route can be provided for labor and delivery or for cesarean section. Bupivacaine in lower concentrations has the advantage of providing excellent analgesia while minimally reducing motor strength.

Caudal Anesthesia

In the caudal form of extradural anesthesia, the agent is introduced through the sacral hiatus above the coccyx. It is particularly applicable to perineal and rectal procedures. Anesthetization of higher anatomical levels is not easily obtained, because the required injection volume can be excessive. Although caudal anesthesia has been used extensively in obstetrics, lumbar epidural blockade is now more commonly used because of the lower dose of drug required; in addition, the sacral segments are spared until their anesthesia is required for the delivery.

Intravenous Extremity Block

Excellent and rapid anesthetization of an extremity can be obtained easily. Following insertion of an intravenous catheter in the limb of interest, a rubber bandage is used to force blood out of the limb, and a tourniquet is applied to prevent the blood from reentering; a dilute solution of local anesthetic, most commonly lidocaine, is then injected intravenously. This technique fills the limb's vasculature and carries the anesthetic solution to the nerve by means of the blood supply. Because of the pain produced by a tourniquet after some time, this procedure usually is limited to less than 1 hour. The systemic blood levels of drug achieved after tourniquet release generally remain below toxic levels.

Although it is more easily and therefore more commonly used on the upper extremity, intravenous extremity anesthesia can be used on the leg and thigh.

Sympathetic Block

Blockade of the sympathetic nervous system can be more selectively accomplished than that which occurs during spinal or epidural anesthesia. Cell bodies for preganglionic sympathetic nerves originate in the intermediolateral cell column of the spinal cord, from the first thoracic to the second lumbar segments. The myelinated axons of these cells travel as white communicating rami before joining the sympathetic chain and synapsing in the ganglia. The best location for a sympathetic block is at the sympathetic ganglia, since a block at this level will affect only the sympathetic nerves. For example, local anesthetic blockade of the stellate ganglion (which includes T1) blocks sympathetic innervation to all of the upper extremity and head on the injected side. A block of the sympathetic chain at L2 affects all of the lower extremity. This form of local anesthesia is particularly useful during treatment of a variety of vasospastic diseases of the extremities and for some pain syndromes.

Control of Cardiac Arrhythmias

Procainamide and lidocaine are two of the primary drugs for treating cardiac arrhythmias. Since lidocaine has a short duration of action, it is common to administer it by continuous infusion. Procainamide, because of its amide linkage, has longer action than does its precursor, procaine. Orally active analogues of local anesthetics (e.g., mexiletine) also are used as antiarrhythmics (see Chapter 16).

Use of Vasoconstrictors

The most commonly used vasoconstrictors, the sympathomimetic drugs, are often added to local anesthetics to delay absorption of the anesthetic from its injection site. By slowing absorption, these drugs reduce the anesthetic's systemic toxicity and keep it in contact with nerve fibers longer, thereby increasing the drug's duration of action. Administration of lidocaine 1% with epinephrine results in the same degree of blockade as that produced by lidocaine 2% without the vasoconstrictor.

Many vasoconstrictors are available, but epinephrine is by far the most commonly employed. Because epinephrine can have systemic α- and β-adrenergic effects, precaution is needed when local anesthetics containing this amine are given to a patient with hypertension or an irritable myocardium. Sensitivity to epinephrine may be incorrectly diagnosed as an allergy to local anesthetics. Epinephrine-containing solutions should be used cautiously in persons taking tricyclic antidepressants or monoamine oxidase (MAO) inhibitors, since those drugs may enhance the systemic pressor effects of sympathomimetic amines.

Levonordefrin (*Neo-Cobefrin*) is an active optical isomer of nordefrin that has α_1-adrenergic activity and

possesses little or no β-agonist properties. It is used exclusively in some dental anesthetic cartridges as a vasoconstrictor. Its theoretical advantage is that it causes less hypertension and tachycardia than does epinephrine.

Phenylephrine hydrochloride (*Neo-Synephrine*) is a pure α-agonist that is occasionally used for subarachnoid block and is marketed with procaine for use in dentistry. It has little direct cardiac effect.

Adverse Effects

The central nervous and cardiopulmonary systems are most commonly affected by high plasma levels of local anesthetics. Local anesthetics given in initially high doses produce central nervous system (CNS) stimulation characterized by restlessness, disorientation, tremors, and at times clonic convulsions. Continued exposure to high concentrations results in general CNS depression; death occurs from respiratory failure secondary to medullary depression. Treatment requires ventilatory assistance and drugs to control the seizures. The ultra–short-acting barbiturates and the benzodiazepine derivatives, such as diazepam, are effective in controlling these seizures. Respiratory stimulants are not effective. CNS manifestations generally occur before cardiopulmonary collapse.

Cardiac toxicity is generally the result of drug-induced depression of cardiac conduction (e.g., atrioventricular block, intraventricular conduction block) and systemic vasodilation. These effects may progress to severe hypotension and cardiac arrest.

Allergic reactions, such as red and itchy eczematoid dermatitis or vesiculation, are a concern with the ester-type local anesthetics. True allergic manifestations have been reported with procaine. *The amides are essentially free of allergic properties,* but suspected allergic phenomena may be caused by methylparaben, a parahydroxybenzoic acid derivative used as an antibacterial preservative in multiple-dose vials and some dental cartridges. Esters probably should be avoided in favor of an amide when the patient has a history of allergy to a PABA-containing preparation such as certain cosmetics or sunscreens.

ESTERS

Cocaine

Cocaine hydrochloride remains useful primarily because of the vasoconstriction it provides with topical use. Toxicity prohibits its use for other than topical anesthesia.

Cocaine has a rapid onset of action (1 minute) and a duration of up to 2 hours, depending on the dose or concentration. Lower concentrations are used for the eye, while the higher ones are used on the nasal and pharyngeal mucosa. Epinephrine plus cocaine, although still used occasionally, is hazardous because the catecholamine potentiates the cardiovascular toxicity (e.g., arrhythmia, ventricular fibrillation) of cocaine.

Cardiovascular effects are related to both central and peripheral sympathetic stimulation. Initial bradycardia appears to be related to vagal stimulation; this is followed by tachycardia and hypertension. Larger doses are directly depressant to the myocardium, and death results from cardiac failure.

Cocaine is readily absorbed from mucous membranes, so the potential for systemic toxicity is great. The CNS is stimulated, and euphoria and cortical stimulation (e.g., restlessness, excitement) frequently result. Overdosage leads to convulsions followed by CNS depression. The cortical stimulation it produces is responsible for the drug's abuse (see Chapter 35).

Benzocaine

Benzocaine is a PABA derivative used primarily for topical application to skin and mucous membranes. Its low aqueous solubility allows it to stay at the site of application for long periods. Its minimal rate of absorption after topical administration is associated with a low incidence of systemic toxicity. Benzocaine is contraindicated in patients with known sensitivity to ester-linked anesthetics or PABA-containing compounds.

Chloroprocaine

Chloroprocaine hydrochloride (*Nesacaine*) is obtained from addition of a chlorine atom to procaine, which results in a compound of greater potency and less toxicity than procaine itself. This local anesthetic is hydrolyzed very rapidly by cholinesterase and therefore has a short plasma half-life. Because it is broken down rapidly, chloroprocaine is commonly used in obstetrics. It is believed that the small amount that might get to the fetus continues to be rapidly hydrolyzed, so there may be no residual effects on the neonate.

Procaine

Procaine hydrochloride (*Novocain*) is readily hydrolyzed by plasma cholinesterase, although hepatic metabolism also occurs. It is not effective topically but is employed for infiltration, nerve block, and spinal anesthesia. It has a relatively slow onset and short (1 hour) duration of action. All concentrations can be combined with epinephrine. It is available in dental cartridges with phenylephrine as the vasoconstrictor.

Tetracaine

Tetracaine hydrochloride (*Pontocaine*) is an ester of PABA that is an effective topical local anesthetic agent

and also is quite commonly used for spinal (subarachnoid) anesthesia. Epinephrine is frequently added to prolong the anesthesia. Tetracaine is considerably more potent and more toxic than procaine and cocaine. It has approximately a 5-minute onset and 2 to 3 hours of action.

AMIDES

Lidocaine hydrochloride (*Xylocaine*) is the most commonly used local anesthetic. It is well tolerated, and in addition to its use in infiltration and regional nerve blocks, it is commonly used for spinal and topical anesthesia and as an antiarrhythmic agent (see Chapter 16). Lidocaine has a more rapidly occurring, more intense, and more prolonged duration of action than does procaine.

Bupivacaine hydrochloride (*Marcaine, Sensorcaine*) has particularly long action, and some nerve blocks last more than 24 hours; this is often an advantage for postoperative analgesia. Its use for epidural anesthesia in obstetrics has attracted interest because it can relieve the pain of labor at concentrations as low as 0.125% while permitting some motor activity of abdominal muscles to aid in expelling the fetus. The lower concentration minimizes the possibility of cardiac toxicity. Fetal drug concentrations remain low, and drug-induced neurobehavioral changes are not observed in the newborn. Bupivacaine also is approved for spinal anesthesia and is approximately four times more potent and more toxic than mepivacaine and lidocaine. It can be used with or without epinephrine.

Levobupivacaine hydrochloride (*Chirocaine*) is the S-enantiomer of bupivacaine. It too has long action. Animal studies show that it has less CNS and cardiac toxicity than does bupivacaine. It also is slightly more motor sparing than is bupivacaine.

Ropivacaine (*Naropin*) is a recently developed long-acting amide-linked local anesthetic. Its duration of action is similar to that of bupivacaine, but it is slightly less potent and requires higher concentrations to achieve the same degree of block. Its primary advantage over bupivacaine is its lesser degree of cardiotoxicity.

Etidocaine hydrochloride (*Duranest*), although chemically similar to lidocaine, has a more prolonged action. It is used for regional blocks, including epidural anesthesia. It exhibits a preference for motor rather than sensory block; therefore, its use in obstetrics is limited, although fetal drug concentrations remain low. It can be used with or without epinephrine.

Mepivacaine hydrochloride (*Carbocaine*) is longer acting than lidocaine and has a more rapid onset of action (3–5 minutes). Topical application is not effective. It has been widely used in obstetrics, but its use has declined recently because of the early transient neurobehavioral effects it produces. Adverse reactions associated with mepivacaine are generally similar to those produced by other local anesthetics. It can be used with epinephrine or levonordefrin (dental use only).

Prilocaine hydrochloride (*Citanest*) is an amide anesthetic whose onset of action is slightly longer than that of lidocaine; its duration of action is comparable. Prilocaine is 40% less toxic acutely than lidocaine, making it especially suitable for regional anesthetic techniques. It is metabolized by the liver to orthotoluidine, which when it accumulates, can cause conversion of hemoglobin (HB^{++}) to methemoglobin (HB^{+++}). Oxygen transport is impaired in the presence of methemoglobinemia. Treatment involves the use of reducing agents, such as methylene blue, given intravenously, to reconvert methemoglobin to hemoglobin.

TOPICAL AGENTS

EMLA cream (lidocaine 2.5% and prilocaine 2.5%) consists of a *e*utectic *m*ixture of *l*ocal *a*nesthetics. It is used to provide topical anesthetic to intact skin. Other topical preparations are effective only on mucosal surfaces. EMLA has been shown to reduce pain on venipuncture and provide substantial anesthesia for skin graft donor sites. No significant local or systemic toxicity has been demonstrated.

TAC (tetracaine, adrenalin [epinephrine], and cocaine) is a combination topical anesthetic frequently used in pediatric emergency departments for repair of minor lacerations. The usual mixture is tetracaine 0.5%, epinephrine 1:2,000, and cocaine 11.8%. Because of potential complications (seizures), lower concentrations of cocaine and epinephrine in a tetracaine 1% solution have been suggested (TAC III).

Study Questions

1. Local anesthetics interfere with the movement of which ion as a fundamental basis for their action?
   (A) Calcium
   (B) Sodium
   (C) Potassium
   (D) Hydrogen
   (E) Oxygen
2. Sympathetic block is one use of local anesthetics. What is the best location to apply the local anesthetic?
   (A) Nerve cell ending
   (B) Neuromuscular junction
   (C) Sympathetic ganglia
   (D) Spinal cord
3. Frequently vasoconstrictors are combined with local anesthetics to delay absorption of the anesthetic from its injection site. What is the most widely employed agent?
   (A) Dopamine
   (B) Phenylephrine
   (C) Levonordefrin
   (D) Epinephrine
   (E) Cocaine
4. What is the most commonly used local anesthetic?
   (A) Bupivacaine
   (B) Procaine
   (C) Lidocaine
   (D) Etidocaine
5. A 25-year old-woman visits your office with red and itchy eczematoid dermatitis. She had a dental procedure earlier in the day, and the dentist administered a local anesthetic. There were no other findings, although she indicated that she had a history of allergic reactions. Which of the following drugs is most likely involved?
   (A) Cocaine
   (B) Procaine
   (C) Lidocaine
   (D) Bupivacaine
   (E) Etidocaine

ANSWERS

1. **B.** Inhibition of inward migration of Na^+ can result in complete block of conduction and therefore abolition of pain transmission. This block of conduction is not a feature of alteration of any of the other ions.
2. **C.** A block at this level will affect only the sympathetic nerves, not parasympathetic activity. Application to the nerve cell ending would result only in topical anesthesia, and blockade of the neuromuscular junction could produce respiratory failure. Administration to the spinal cord is too general an answer. The injection must be near a nerve or nerve plexus proximal to the surgical site.
3. **D.** Epinephrine is by far the most commonly employed vasoconstrictor. Phenylephrine is occasionally used with procaine for dental procedures. Levonordefrin is also used rarely in dental procedures. Dopamine has no vasoconstrictor activity. Cocaine is itself a local anesthetic with some vasoconstrictor properties. However, cocaine, because of its abuse potential and toxicity, is seldom used. Its only use is topical.
4. **C.** Lidocaine is well tolerated and has a rapid onset and an adequate duration of action for most procedures. Bupivacaine has a particularly long duration of action. This may be advantageous in certain procedures, but not in most. Procaine has a relatively slow onset of action as well as a short duration of action. Etidocaine shows a preference for motor rather than sensory block; this limits its effectiveness in obstetrics.
5. **B.** Allergic reactions occur only to the ester type of local anesthetics. This is because the metabolism of all ester-linked local anesthetics leads to the formation of PABA, which is known to be allergenic to some individuals. Both cocaine and procaine are esters. However, cocaine is not employed in dental procedures. Therefore, the best choice is procaine.

SUPPLEMENTAL READING

Denson DD and Mazoit JX. Physiology, pharmacology and toxicity of local anesthetics: Adult and pediatric considerations. In P Prithvi Raj P (ed.). Clinical Practice of Regional Anesthesia. New York: Churchill Livingstone, 1991.

McLeod GA, Burke D. Levobupivacaine. Anaesthesia. 2001;56:331.

Tucker CT and Mather LE. Properties, absorption, and disposition of local anesthetic agents. In Cousins MJ and Bridenbaugh PO (eds.). Neural Blockade in Clinical Anesthesia and Management of Pain (2nd ed.). Philadelphia: Lippincott, 1988.

Vercauteren MP et al. Levobupivacaine combined with sufentanil and epinephrine for intrathecal labor analgesia: A comparison with racemic bupivacaine. Anesth Analg 2001;93:996–1000.

CASE Study A Fatality Due to Local Anesthesia

A college athlete is scheduled to undergo open repair of two fractured fingers. She is otherwise healthy, takes no medications, and has no family history of difficulties with anesthesia. The anesthetic management is to be brachial plexus anesthesia with bupivacaine. During injection of the anesthetic, the patient abruptly becomes uncommunicative and loses consciousness. The electrocardiograph deteriorates rapidly, and no blood pressure is obtainable. The trachea is intubated, cardiopulmonary resuscitation is started and advanced life support follows. Despite aggressive treatment, the resuscitation is unsuccessful. What is a possible reason for this outcome in light of the type of anesthesia being used ?

ANSWER: Bupivacaine use for local anesthesia of this type is very safe and commonly done. However, SOMETIMES inadvertent vascular injection results in a large amount of anesthetic in the systemic circulation. Because the heart is beating, the excitable tissue in the heart is being depolarized repetitively. Local anesthetics bind to rapidly depolarizing tissues more than tissues at rest (frequency-dependent block). Also, bupivacaine has a long duration of action because of its long residence time at receptors (sodium channel). Thus, this combination of factors contributed to the catastrophic outcome of this case. Had the same case involved lidocaine, the resuscitation would have likely been successful.