Local Anesthetics in Dentistry: Then and Now

Local anesthetics have been in use in dental practice for more than 100 years. The advent of local anesthetics with the development of nerve blockade injection techniques heralded a new era of patient comfort while permitting more extensive and invasive dental procedures. A brief history and summary of the current local anesthetics available in the United States is provided, and some of the newest techniques for delivering local anesthetics are reviewed. General guidelines for addressing difficulties encountered in anesthetizing patients are also discussed.

The first local anesthetic agent to be widely used in dentistry was cocaine. Centuries before European exploration of the New World, Peruvian Indians had found that chewing leaves of the coca plant produced exhilaration and relief from fatigue and hunger. Following the import of coca leaves to Europe, much research was conducted to elucidate the properties of the coca leaf extract. In 1859, Albert Niemann refined the coca extract to the pure alkaloid form and named this new drug “cocaine.” Niemann recognized the anesthetic effect of cocaine when he noted that “it benumbs the nerves of the tongue, depriving it of feeling and taste.” In the summer of 1884, Carl Koller, a junior resident in the University of Vienna Ophthalmological Clinic, conducted experiments to test the topical anesthetic properties of cocaine on the corneas of various lab animals and on himself (self-administration being common in medical research at that time). He found that the drug rendered the corneas insensitive to pain. In September of that year, Koller performed the world’s first operation using local anesthesia induced by topical cocaine on a patient undergoing glaucoma correction. The noted American surgeon William Halsted was the first person to inject cocaine for nerve conduction blockade, performing infraorbital and inferior alveolar nerve blocks for dental procedures in November 1884. Halsted subsequently developed numerous other regional nerve block injection techniques, many of which are still fundamental to dental practice.

Despite its promise for pain management during surgery, cocaine had major drawbacks, such as a high propensity for addiction and a short duration of action. The latter factor necessitated injection of large doses of the drug, increasing the potential for severe systemic toxicity. One technique developed to counteract this short duration/high dose problem was to apply a tourniquet near the operative site. In addition to the risk of local tissue damage, this approach had limited success in many regions of the body and was impractical for anesthesia of the oral cavity. In 1903, Heinrich Braun reported that epinephrine could be used as a “chemical tourniquet” when added to a solution of cocaine by producing localized vasoconstriction to slow the rate of vascular uptake, and thus reducing the required dose of cocaine.

However, the drawbacks of cocaine were still significant, and research to find a synthetic substitute was widely undertaken. In 1905, Alfred Einhorn and his associates in Munich reported their discovery of procaine, an ester-based synthetic local anesthetic. Procaine was immediately accepted as a safe substitute for cocaine. Some historians consider the discovery of procaine to mark the beginning of the modern era of regional anesthesia. Several other ester-type local anesthetics were subsequently developed and remained in wide use in the United States throughout most of the 20th century.

In 1943, Nils Löfgren, a Swedish chemist, synthesized a new amide-based local anesthetic agent, derived from xylidine, and named it “lidocaine.” Lidocaine was more potent and less allergenic than procaine and the other ester-based anesthetics. Since Löfgren’s discovery of lidocaine, several other amide anesthetics have been developed for use in dental procedures: mepivacaine, prilocaine, bupivacaine, etidocaine, and articaine. The advantages of the amide-based anesthetic agents, particularly their very low rate of allergenicity as compared to the ester-type anesthetics, led to their gradual and complete replacement of the ester-based anesthetics in dental use. The last ester anesthetics packaged in a dental syringe cartridge were discontinued in the mid-1990s.
Current Dental Anesthetic Agents

Today’s availability of a variety of local anesthetic agents enables dentists to select an anesthetic that possesses specific properties such as time of onset and duration, hemostatic control, and degree of cardiac side effects that are appropriate for each individual patient and for each specific dental procedure. Table 1 lists the anesthetic agents available for dental use in the United States and briefly summarizes their properties. It should be noted that these properties, particularly duration and depth of anesthesia, are only approximations and are variable due to a number of factors:7

* Individual variation in response to the drug administered;
* Accuracy in administration of the drug;
* Status of the tissues at the site of drug deposition (vascularity, pH);
* Anatomical variation; and
* Type of injection administered (supraperiosteal ["infiltration"] or nerve block).

Lidocaine

Lidocaine is considered the prototypical amide anesthetic agent. At its introduction in 1948, it was roughly twice as potent and twice as toxic as procaine, producing a greater depth of anesthesia with a longer duration over a larger area than a comparable volume of procaine. Consequently, lidocaine quickly became the most popular local anesthetic in dentistry. It is available in the United States in three formulations: 2 percent without vasoconstrictor (plain), 2 percent with 1:100,000 epinephrine vasoconstrictor, and 2 percent with 1:50,000 epinephrine. Lidocaine without vasoconstrictor has a soft-tissue anesthetic duration of one to two hours, but a pulpal duration of only five to 10 minutes and is therefore of limited use for most dental procedures. Both formulations with the epinephrine vasoconstrictor have a pulpal duration of one to 1.5 hours and a soft-tissue range of three to five hours. The 1:50,000 epinephrine concentration may be advantageous for hemostasis in surgical sites but has no significant advantage for duration of pulpal anesthesia.

Mepivacaine

Introduced in 1960, a 2 percent solution of mepivacaine has potency and toxicity ratings roughly equivalent to a 2 percent solution of lidocaine. The greatest advantage of mepivacaine is that it has less vasodilating activity than lidocaine (all anesthetic agents without an added vasoconstrictor are vasodilators to some degree) and can therefore be used reliably as a nonvasoconstrictor-containing solution for procedures of short duration.7 Mepivacaine is available on the U.S. market as either a 3 percent plain solution or a 2 percent solution with 1:20,000 levonordefrin. The plain solution has a pulpal anesthetic duration of 20 to 40 minutes with a soft-tissue duration of two to three hours. The vasoconstrictor-containing solution has a pulpal duration equivalent to that of lidocaine with vasoconstrictor, that is, pulpal anesthesia for one to 1.5 hours and soft-tissue duration of three to five hours. It should be noted that although the levonordefrin vasoconstrictor in mepivacaine is less likely to produce cardiac side effects, such as palpitations, than is epinephrine, it is more likely to increase blood pressure and does have a higher potential for interaction with tricyclic antidepressants such as amitriptyline hydrochloride.8-10 At the time of this writing, levonordefrin production has been discontinued in the United States and existing supplies of mepivacaine with levonordefrin are expected to be exhausted by early to mid-2003. However, a potential new producer of levonordefrin is currently running production tests and may have mepivacaine with levonordefrin back on the U.S. market by mid to late 2003.11

Prilocaine

Prilocaine, also introduced in 1960, is slightly less potent and considerably less toxic than lidocaine as a local anesthetic agent. Like mepivacaine, prilocaine produces less tissue vasodilation than lidocaine and can be used reliably in plain solution form for short-duration procedures. Prilocaine is available as a 4 percent plain solution or as a 4 percent solution with 1:200,000 epinephrine. The plain solution has a pulpal duration of 40 to 60 minutes with soft-tissue anesthesia for two to three hours. It is worth noting
that the duration of anesthesia with plain prilocaine is more dependent upon the type of injection given than are other anesthetics. Infiltration injections of prilocaine plain may only provide five to 10 minutes of pulpal anesthesia while regional block injections typically show the commonly described 40- to 60-minute durations. The vasoconstrictor-containing solution provides pulpal anesthesia for one to 1.5 hours like lidocaine and mepivacaine with a potentially longer soft-tissue duration of three to eight hours. Anecdotally, prilocaine has been said to have greater efficacy in patients who are difficult to anesthetize, for example, patients with a past or present history of substance abuse. An additional advantage is the decrease in cardiac side effects due to the lower vasoconstrictor concentration. Relative contraindications for the use of prilocaine include a patient history of methemoglobinemia, anemia, or cardiac or respiratory failure due to hypoxia.

An additional precaution is raised by reports of a significantly increased risk of nerve paresthesia with the use of prilocaine and articaine, particularly for inferior alveolar and lingual nerve block injections. Haas, the lead author of a number of these studies, has speculated that chemical toxicity may be the cause of these increased paresthesias since the only common feature of prilocaine and articaine is that they are both 4 percent concentration anesthetic agents. His hypothesis is supported by reports of neurologic deficits with 4 percent lidocaine in animal studies and in human studies using 5 percent lidocaine for spinal anesthesia. This suggests that reduction of dosage to the absolute minimum amount required for effective anesthesia and the use of a slow, atraumatic injection technique with repeated aspirations are wise precautions if either of these anesthetic agents is selected for use with inferior alveolar and lingual nerve block injection techniques at all.

**Bupivacaine**

Bupivacaine is an analogue of mepivacaine that exhibits a fourfold increase in potency and toxicity and a remarkable increase in the duration of anesthesia. Released in the United States in 1983 and available only as a 0.5 percent solution with 1:200,000 epinephrine, bupivacaine may exhibit a slightly slower time of onset in some patients, approximately six to 10 minutes compared with two to seven minutes for lidocaine and mepivacaine. The longer duration of anesthesia for which bupivacaine is known is achieved primarily via regional nerve block injection techniques with mandibular blocks frequently having greater duration than maxillary blocks. As a block, pulpal durations of 1.5 to seven hours are common with soft-tissue anesthesia of five to 12 hours. When administered via infiltration technique, bupivacaine provides anesthetic depth and duration comparable to other local anesthetic agents.

**Etidocaine**

This long-acting amide anesthetic has been discontinued in the North American market.

**Articaine**

Articaine is an analogue of prilocaine in which the benzene ring moiety found in all other amide local anesthetics has been replaced with a thiophene ring. Although not released in the United States until April 2000, articaine has been available in Germany since 1976 and in Canada since 1983 in a number of formulations. To date, only one formulation has been approved in the United States, a 4 percent solution with 1:100,000 epinephrine. With a higher per-cartridge unit cost and a pulpal anesthesia duration of approximately one hour with soft-tissue anesthesia for two to four hours, it would initially appear that articaine is a less attractive agent for dental applications. However, with a slightly faster onset of action (1.4 to 3.6 minutes), reports of a longer and perhaps more profound level of anesthesia, and most notably frequent practitioner anecdotes of a greater ability to diffuse through tissues, articaine has become a very widely used anesthetic in the European and Canadian markets. The tissue diffusion characteristics of articaine are not well-understood; however, in a variable percentage of patients, a maxillary infiltration injection in the buccal vestibule will result in adequate palatal anesthesia for tooth extraction. Similar results have been claimed for the mandibular anterior and premolar teeth with buccal infiltrations. As discussed with prilocaine, reports of a significantly increased risk of nerve paresthesia with the use of articaine and prilocaine, particularly for inferior alveolar and lingual nerve block injections, warrants practitioner caution in the use of these anesthetic agents.
The Difficult-to-Anesthetize Patient

Many factors may affect the success of local anesthesia, some within the practitioner’s control and some clearly not. While no single technique will be successful for every patient, guidelines exist that can help reduce the incidence of failure. For this discussion, a failure will be defined as inadequate depth and/or duration of anesthesia to begin or to continue a dental procedure. Due to a number of factors, such as thicker cortical plates; a denser trabecular pattern; larger, more myelin(lipid)-rich nerve bundles; and more variable innervation pathways,22-29 more problems of inadequate anesthesia occur in the mandibular arch than in the maxillary. Although failures are more common in the mandibular arch, maxillary failures do occur and can be equally frustrating.

The Maxilla

Most problems with maxillary anesthesia can be attributed to individual variances of normal anatomical nerve pathways through the maxillary bone (Table 2).30 While the pulpal sensory fibers of the maxillary teeth are primarily carried in the anterior, middle, and posterior superior alveolar nerves, which also supply the buccal soft tissues, accessory pulpal innervation fibers may be found in the palatal innervation supplied by the nasopalatine and greater palatine nerves.30 By careful application of topical anesthetics, distraction techniques (application of pressure and/or vibration), and slow delivery of the anesthetic agent, palatal injections can be given with very little to no patient discomfort. With the availability of articaine hydrochloride 4 percent with epinephrine in the United States, many practitioners are finding that palatal injections may not be necessary when it is injected into the maxillary buccal vestibule.20 Additionally, new computer-controlled anesthetic delivery systems are particularly adept at eliminating, or at least minimizing, the discomfort of palatal injections.31-33 Such systems are discussed in greater detail under New Delivery Systems and Techniques.

The Mandible

Problems with mandibular anesthesia are most common in the molar region but are by no means limited to these teeth.23-29,34 As in the maxilla, most anesthesia problems encountered in the mandible are due to individual variations in the nerve pathways, in other words, accessory innervation (Table 2).34,35 The first, and simplest, guideline relates to the extent of anesthesia achieved. If, for example, a patient reports profound anesthesia of his or her lower lip and tongue after receiving an inferior alveolar and lingual nerve block injection, but the tooth in question is still sensitive, it is probable that those two nerves have been successfully anesthetized and that the tooth sensitivity is very likely due to accessory innervation. This conclusion is based upon nerve morphology. Fibers near the periphery of a nerve bundle tend to innervate the most proximal structures, i.e., molars in the case of the inferior alveolar nerve; while fibers in the center of the nerve bundle tend to innervate the most distal structures, i.e., the incisors in this example.7 If a patient reports that his or her lower lip and tongue are anesthetized, structures that are innervated by the most central fibers of the inferior alveolar and lingual nerve bundles respectively, than it seems reasonable to conclude that these two nerves are indeed anesthetized and that accessory innervation to the sensitive tooth likely exists in this patient.

For mandibular molars, a common, and therefore important, accessory pathway to be considered is the long buccal nerve.27,36-38 This nerve branches from the anterior division of the mandibular portion of the trigeminal nerve high within the infratemporal fossa and crosses the anterior border of the mandibular ramus above the retromolar pad to enter and innervate the mucosa and overlying skin of the cheek, including the mandibular buccal attached gingiva. Due to the possible branching of this nerve as it descends along the medial surface of the mandibular ramus, a high injection site along the long buccal nerve pathway may offer a greater likelihood of successfully anesthetizing more of these accessory branches.26 Such a site for blocking the long buccal nerve is to inject into the soft tissue just medial to the anterior border of the ramus at or above the same level above the mandibular occlusal plane as the inferior alveolar block injection is given, i.e., using the depth of the coronoid notch anteriorly as the landmark for the horizontal level of the injection.4 An added benefit of this site is improved patient comfort by injecting medial to the anterior border of the mandible rather than into
the lateral tissue.

An additional source of accessory innervation to any mandibular tooth is the mylohyoid nerve.23-25,28,39 This nerve arises from the inferior alveolar nerve at a variable level above the mandibular foramen and may not be consistently anesthetized with a conventional inferior alveolar block injection.40 Although it is anatomically described as a motor nerve innervating both the mylohyoid and the anterior belly of the digastric muscles, the mylohyoid nerve has been clearly shown to carry sensory fibers to mandibular teeth.28,39 A mylohyoid nerve block may be delivered by injecting into the floor of the mouth between the medial surface of the mandible and the sublingual fold formed by the sublingual salivary gland. The injection should be given just distal to the sensitive tooth, and the depth of the injection should approximate the root apices.41 An alternative technique to anesthetize the mylohyoid nerve is to administer a second inferior alveolar nerve block at a higher and/or deeper site.34 This may better approximate the origin of the mylohyoid nerve as it branches from the inferior alveolar nerve, but this technique does carry an increased risk of intravascular injection and possible hematoma.35,42

A potentially more efficient method for dealing with accessory innervations in the mandible is to use a more complete mandibular block technique such as the Gow-Gates43 or Vazirani-Akinosi44 techniques (Table 3). These injections, first described in the early 1970s, are given at higher sites on the mandibular ramus (Figure 1) and are aligned relative to the maxillary occlusal plane rather than the mandibular. Properly performed, these techniques have a very high success rate coupled with a very low risk of positive vascular aspiration.45 It should be noted, however, that even a high mandibular division nerve block technique, such as the Gow-Gates, may not have a 100 percent success rate in anesthetizing all possible nerve branches to mandibular tooth pulpal tissues.46,47 For this reason, the best advice is to be proficient with a variety of mandibular injection techniques as described in detail in the dental literature.

Another concern is the situation where anesthesia of all apparent nerve pathways is achieved, but the duration is short and/or the depth of anesthesia is poor. Giving a second injection into the same site as the first injection may prove adequate simply due to the increased volume of anesthetic solution. However, using a different anesthetic agent for the second injection may increase the likelihood of successful duration. This difference may be explained by individual variances in tissue pH conditions and differing characteristics of each anesthetic agent, such as dissociation characteristics, lipid solubilities, and receptor site protein-binding affinities. No contraindication exists for using any of the amide anesthetic agents in combination with one another; however, care must be taken to limit the total dosage of anesthetic given to the maximum amount allowable for the agent with the lowest permissible dosage. For all injections given, the precise amount of each agent injected and the specific site of each injection should be recorded in the patient’s treatment record. It is particularly helpful to note if one agent appears to have worked better than another. In these cases, this “better” agent should be used for the first injection at the next appointment.

The “Hot” Tooth

Anesthetizing the “hot” tooth, a condition generally indicating an irreversible pulpitis, can be one of the most frustrating problems for any dental practitioner. Whenever possible, prescribing antibiotic therapy to reduce inflammation and allowing the site to settle down may constitute the best course of action. When such a course is not an option, the first step in working through this situation is to deliver an appropriate nerve block injection as far back as possible along the innervation pathway of the hypersensitive tooth. If all of the surrounding soft tissues are numb, but the tooth itself is still sensitive, use of an intraosseous technique, which has a highly predictable success rate, is recommended.48-50 Less predictable, but also potentially effective, is a periodontal ligament injection technique.51-53 A last resort is to quickly access a pulp horn, creating a hole just large enough to insert a needle, and injecting anesthetic directly into the pulp chamber of the tooth. The major limitation of all three of these injection techniques is the inability to anesthetize multiple teeth with a single needle penetration and the relatively short duration of anesthesia achieved.53,54
New Delivery Systems and Techniques

In the past decade, two delivery systems have been developed that utilize computer technology in the administration of local anesthetics to patients. The Wand (Milestone Scientific) and the Comfort Control Syringe (Dentsply) both recognize that the more slowly an injection is given, the less traumatic it is to the tissues of the injection site and therefore the more comfortable the injection is to the patient. The Wand precisely controls the flow rate and modulates fluid pressure by use of a computer microprocessor and an electronically controlled motor to deliver the anesthetic solution at a slow rate regardless of tissue resistance.55 This allows the operator to deliver the anesthetic solution into any injection site, including the palate, at a rate that is potentially below the threshold of pain. An additional advantage is the smaller diameter of the syringe/handpiece itself, which permits the operator to use a more comfortable and stable pen grip on the syringe, allowing for more natural use of finger rests while injecting. The smaller size of the syringe may also be less intimidating to patients, a significant consideration when working with a dental-phobic patient.33,56-58 Disadvantages of the Wand system include the initial cost of the unit, approximately $1,400; the cost of the disposable syringe/handpiece assembly per patient, approximately $1; the longer/slower injection time; and, due to the volume of the tubing connecting the motor unit to the handpiece, only 1.4 ml of anesthetic solution can actually be delivered from each anesthetic cartridge.57 Additionally, the system does require some time to get accustomed to: The system is operated by a foot-pedal control, and the anesthetic cartridge is not directly visible in the operator’s hand. This latter factor is addressed by a series of audible sounds that inform the operator of how much anesthetic solution has been delivered. Introduction of the Wand delivery system has renewed interest in the palatal approach to anesthesia of the anterior and middle superior alveolar nerves.58,59 Using the palatal approach, anesthesia of the pulpal tissues of the maxillary incisor and premolar teeth, as well as anesthesia of the buccal and palatal gingival tissues, may be accomplished without the side effect of facial anesthesia found with the infraorbital nerve approach. Preservation of normal facial sensation and movement is an advantage for mid-procedure smile line assessment of maxillary anterior cosmetic procedures, and patient acceptance is an additional advantage. On a precautionary note, it is imperative that this injection be administered very slowly with constant visual monitoring by the operator to avoid excessive tissue blanching. The recommended injected volume is 0.6 to 0.9 ml administered over a 60- to 90-second, or longer, interval. If excessive tissue blanching is observed during the injection, a momentary pause to allow return of normal blood supply, indicated by return of pink coloration to the tissue, is recommended. A risk of palatal tissue ulceration must be recognized if marked ischemia occurs.58,59

The Comfort Control Syringe is a newer entry in the electronic, computer-controlled anesthetic delivery system market. This preprogrammed unit controls the delivery rate of anesthetic solution for a selection of injection techniques (block, infiltration, palate, PDL, intraosseous) preselected by the operator. Although bulkier than the Wand syringe/handpiece, the Comfort Control Syringe also enables the operator to use a pen grip while injecting. The Comfort Control Syringe houses the anesthetic cartridge directly behind the needle, just as in a traditional syringe; and the injection controls are fingertip accessible on the syringe rather than via foot pedal. The initial unit cost is approximately $900 with disposable supplies costing approximately 55 cents per patient.58-61

Although the technique of delivering local anesthetics directly into alveolar bone in close proximity to root apices is not new, recent technology has greatly improved the convenience of intraosseous injections. Systems marketed by Stabident, X-tip, and Intraflow have been incorporated into many dental practices. The intraosseous technique is quite reliable for pulpal anesthesia for one or two teeth and is particularly useful for anesthetizing the “hot tooth.” Primary pulpal anesthesia using an intraosseous technique is effective in 45 percent to 93 percent of cases with short duration of approximately 30 minutes.54

When used as a supplement to an inadequate conventional infiltration or nerve block injection, the intraosseous technique is effective in 80 percent to 90 percent of cases with profound anesthesia of moderate duration (60 to 90 minutes).54
Intraosseous injections require a system for penetrating the cortical plate of bone so that the anesthetic agent may be injected into the cancellous tissue space from where it then diffuses to the desired root apices. The Stabident System (Fairfax Dental) is a two-part system with a separate perforator needle that mounts to a low-speed handpiece. The anesthetic injection needle is then passed through the perforation into the cancellous bone. One cause of difficulty with this system is the necessity of aligning the injection needle precisely with the perforation channel to gain access to the cancellous space. This problem has been addressed in the Stabident System by adding a funnel-shaped needle guide that is inserted into the perforation channel.

The X-Tip System (X-Tip Technologies) has also addressed this problem in its system design. The X-Tip is also a two-part system, similar to the Stabident, with the exception that removal of the perforator needle leaves a cannular guide for insertion of the anesthetic injection needle into the cancellous bone.

The Intraflow System (IntraVantage) is based upon a special low-speed handpiece with a clutch and foot-pedal control system that permits perforation and injection with the handpiece in place, thus removing the need to switch from handpiece to syringe. The Intraflow handpiece system is about $900; the cost of disposable supplies is similar for all three systems, ranging from $1.50 to $2. Because intraosseous injections are into the highly vascular cancellous bone tissue space, use of vasoconstrictor-containing anesthetic agents is generally not advised due to the rapid uptake of the agent into the circulatory system with a subsequent increase in patient heart rate. In a number of studies, from 2 percent to 15 percent of patients reported moderate to severe pain during perforation, needle insertion, or injection of the anesthetic solution; and equal numbers of patients reported postoperative pain, swelling, or bruising at the injection site.

A variety of electronic anesthesia systems have come and gone from the dental marketplace. Although these systems had their clinical successes, most practitioners found them frustrating to use in routine practice. The increased time for patient education about use of the system and the large variance in predictable anesthesia from one patient to the next, and even between different sites on the same patient, have ultimately led to their discontinued use. In general, the systems were only useful for relatively non-invasive procedures on a small percentage of patients.

Summary

What might be next on the front for dental anesthesia? As dental lasers continue to evolve and become increasingly refined, they may yet reach their early promise of providing “painless dentistry without the needle or the drill.” Such an event will surely usher in a new era of patient comfort, potentially decreasing the number of dental-phobic patients. The prospect is truly exciting.

References

58. Friedman MJ, Hochman MN, A 21st century computerized injection system