An Update on Local Anesthetics in Dentistry

• Daniel A. Haas, BSc, DDS, BScD, PhD, FRCD(C) •

Abstract

Local anesthetics are the most commonly used drugs in dentistry. This article provides a brief update on the pharmacology, adverse effects and clinical applications of these drugs, as well as the role of vasoconstrictors.

MeSH Key Words: *anesthesia, dental; anesthetics, local/adverse effects; pharmacology; vasoconstrictor agents*

© J Can Dent Assoc 2002; 68(9):546-51
This article has been peer reviewed.

Intraoperative pain control by means of local anesthesia is an intrinsic part of clinical practice in dentistry. Each dentist in Canada injects approximately 1,800 cartridges of local anesthetic yearly,[1] and it has been estimated that more than 300 million cartridges are administered by dentists in the United States every year.[2] Therefore, all dentists should have expertise in local anesthesia. This article provides a brief overview of local anesthetics to reinforce dentists' knowledge of these agents.

Pharmacology

What follows here is a brief synopsis of the pharmacology of local anesthetics. Dentists should be familiar with sources that provide more detailed information on this topic.[2-5]

Local anesthesia is induced when propagation of action potentials is prevented, such that sensation cannot be transmitted from the source of stimulation, such as a tooth or the periodontium, to the brain. Local anesthetics work by blocking the entry of sodium ions into their channels, thereby preventing the transient increase in permeability of the nerve membrane to sodium that is required for an action potential to occur.

Structurally, local anesthetics have specific fundamental features in common. These include a lipophilic group, joined by an amide or ester linkage to a carbon chain which, in turn, is joined to a hydrophilic group. Local anesthetics are classified by these amide or ester linkages. All local anesthetics available in dental cartridges in Canada today, namely articaine, bupivacaine, lidocaine, mepivacaine and prilocaine, belong to the amide class. The prototype for the ester group is procaine (Novocain, Abbot), which is no longer available in dental cartridge form. The topical anesthetic benzocaine is an ester.

The onset and duration of action of local anesthetics are influenced by several factors, as summarized in Table 1.

The most important factors affecting onset are pH of the tissue and pKa of the drug. The pH may drop in sites of infection, which causes onset to be delayed or even prevented. Clinically, there are no significant differences in pKa among the amides, with the exception of bupivacaine, which has a slightly higher pKa and hence a slower onset of action. Proximity of the deposition of local anesthetic to the nerve can also be a factor, which is why infiltration is associated with rapid onset whereas the Gow-Gates block is relatively slow. Nerve morphology is a factor, in that the relatively thin pain fibres are usually anesthetized readily. Within limits, higher concentration and greater lipid solubility improve onset to a small degree.

The duration of action depends on the length of time that the drug can stay in the nerve to block the sodium channels. Local anesthetics cause vasodilatation, which leads to rapid diffusion away from the site of action and results in a very short duration of action intraorally when these drugs are administered alone. This diffusion can be reduced by the addition of a vasoconstrictor, usually epinephrine. Bupivacaine is unique in that it provides long-duration anesthesia for soft tissue in both the arches and pulp of mandibular teeth. The duration of action of local anesthetics is summarized in Table 2.[3,4,6] In general, blocks last longer than infiltrations, and soft-tissue anesthesia lasts longer than pulpal anesthesia.

Biotransformation of amides occurs primarily in the liver. Prilocaine is also metabolized in the plasma and kidney, and one of its metabolites may lead to methemoglobinemia, as

discussed below. Esters are biotransformed by plasma cholinesterase, also known as pseudocholinesterase. Patients with the genetic disorder pseudocholinesterase deficiency can be expected to metabolize procaine at a much slower rate. However, little clinical effect would be expected unless the dose was very high.

From a practical viewpoint, the dentist should be concerned about alterations in biotransformation only in patients with severe liver dysfunction. Reduced hepatic function predisposes the patient to toxic effects but, unlike the situation for systemically administered drugs, should not significantly increase the duration of action of locally administered anesthetics. In this context, it must be remembered that hepatic function does not affect the duration of action of local anesthesia, which is determined by redistribution and not biotransformation. Therefore, a patient with liver disease needs the standard amount of local anesthetic at each site. However, the total dose is a concern. Therefore, when treating a patient with significant liver disease, it is prudent to treat one quadrant at a time, thereby minimizing total dose. Use of an ester may not offer any advantage, because pseudocholinesterase is also synthesized in the liver.

With regard to efficacy, no studies have shown any significant differences among the agents. Therefore it is appropriate to assume that each of the 5 amides is equally efficacious.[7-10]

Adverse Reactions

Local anesthetics should be considered relatively safe, but with the high number of injections given yearly, adverse reactions are seen (Table 3).

Table 1 **Factors affecting onset and duration of action of local anesthetics**

pH of tissue
pKa of drug
Time of diffusion from needle tip to nerve
Time of diffusion away from nerve
Nerve morphology
Concentration of drug
Lipid solubility of drug

Psychogenic Reactions

Anxiety-induced events are by far the most common adverse reaction associated with local anesthetics in dentistry. These may manifest in numerous ways, the most common of which is syncope. In addition, they may present with a wide variety of symptoms, including hyperventilation, nausea, vomiting and alterations in heart rate or blood pressure. Psychogenic reactions are often misdiagnosed as allergic reactions and may also mimic them, with signs such as urticaria, edema and bronchospasm.

Allergic Reactions

Patient reports of allergic reactions to local anesthetics are fairly common, but investigation shows that most of these are of psychogenic origin.[11,12] True allergy to an amide is exceedingly rare, whereas the ester procaine is somewhat more allergenic. An allergy to one ester rules out use of another ester, as the allergenic component is the breakdown product para-aminobenzoic acid, and metabolism of all esters yields this compound. In contrast, an allergy to one amide does not rule out use of another amide. Allergy to epinephrine is impossible.

A patient may be allergic to other compounds in the anesthetic cartridge. For example, methylparabens are preservatives necessary for multidose vials and were present in dental cartridges in the past. They are no longer included as dental cartridges are single-use items. Allergy to para-aminobenzoic acid would rule out use of esters and methylparabens. It may be best to avoid a vasoconstrictor if there is a true documented allergy to sulfites, as metabisulfite is added as an antioxidant whenever vasoconstrictor is present. Vasoconstrictor can be used in patients with an allergy to the sulfonamide antibacterials, commonly called sulfa, as there is no cross-allergenicity with sulfites.

Toxicity

The toxicity of local anesthetics is a function of systemic absorption. High blood levels of the drug may be due to repeated injections or could result from a single inadvertant intravascular administration. This is one reason why

Table 2 **Expected duration of action of local anesthetics[a]**

	Duration of action (min)			
	Maxillary infiltration		Inferior alveolar block	
Formulation	Pulp	Soft tissue	Pulp	Soft tissue
Articaine 4% with epinephrine 1:100,000 or 1:200,000	60	190	90	230
Bupivacaine 0.5% with epinephrine 1:200,000	40	340	240	440
Lidocaine 2% with epinephrine 1:50,000 or 1:100,000	60	170	85	190
Mepivacaine 2% with levonordefrin 1:20,000	50	130	75	185
Mepivacaine 3% plain	25	90	40	165
Prilocaine 4% with epinephrine 1:200,000	40	140	60	220
Prilocaine 4% plain	20	105	55	190

[a]*Approximations only. Adapted primarily from Yagiela[3,4] and Haas.[6]*

Table 3 Adverse reactions of commonly used local anesthetics

Psychogenic
Syncope (most common)
Hyperventilation
Nausea, vomiting
Alterations in heart rate or blood pressure
Mimicking of an allergic reaction
Allergic (potential allergens)
Esters (true amide allergy is very rare)
Metabisulfite (present with epinephrine and with levonordefrin)
Methylparaben (no longer added to dental cartridges)
Toxic effects
Primarily neurologic signs
May initially manifest as sedation, lightheadedness, slurred speech, mood alteration, diplopia, sensory disturbances, disorientation, muscle twitching
Higher blood levels may result in tremors, respiratory depression, tonic–clonic seizures
If severe, may result in coma, respiratory arrest, cardiovascular collapse
Methemoglobinemia
Associated with prilocaine, articaine, benzocaine
Paresthesia
Apparently more common with articaine and prilocaine

Table 4 Recommended maximum doses of local anesthetics with vasoconstrictor

Drug	Maximum dose	Maximum no. of cartridges
Articaine	7 mg/kg (up to 500 mg) 5 mg/kg in children	7
Bupivacaine	2 mg/kg (up to 200 mg)	10
Lidocaine	7 mg/kg (up to 500 mg)	13
Mepivacaine	6.6 mg/kg (up to 400 mg)	11 (or 7 if plain[a])
Prilocaine	8 mg/kg (up to 500 mg)	8

[a]*3% solution without vasoconstrictor*

Table 5 Example calculations of maximum local anesthetic doses for a 15-kg (33-lb) child

Articaine
5 mg/kg maximum dose × 15 kg = 75 mg
4% articaine = 40 mg/mL
75 mg/(40 mg/mL) = 1.88 mL
1 cartridge = 1.8 mL
Therefore, 1 cartridge is the maximum.
Lidocaine
7 mg/kg × 15 kg = 105 mg
2% lidocaine = 20 mg/mL
105 mg/(20 mg/mL) = 5.25 mL
1 cartridge = 1.8 mL
Therefore, 2.9 cartridges is the maximum.
Mepivacaine
6.6 mg/kg × 15 kg = 99 mg
3% mepivacaine = 30 mg/mL
99 mg/(30 mg/mL) = 3.3 mL
1 cartridge = 1.8 mL
Therefore, 1.8 cartridges is the maximum.
Prilocaine
8 mg/kg × 15 kg = 120 mg
4% prilocaine = 40 mg/mL
120 mg/(40 mg/mL) = 3 mL
1 cartridge = 1.8 mL
Therefore, 1.67 cartridges is the maximum.

aspiration before every injection is so important. The signs and symptoms of toxicity are summarized in Table 3.

The maximum recommended doses of local anesthetics are shown in Table 4,[4,6,13] although predisposition to toxic effects in any given patient depends on several factors, such as site of administration, speed of injection and presence of vasoconstrictor. Maximum doses are much more relevant in the pediatric patient, and it is important to note how little anesthetic should be given to a child.[14] Examples of dose calculations for a young child are included in Table 5. The high-concentration solutions, namely prilocaine and articaine, will reach toxic levels with fewer injections than is the case for the other drugs.

Methemoglobinemia

This uncommon adverse reaction is associated most notably with prilocaine but may also occur with articaine or the topical anesthetic benzocaine. Methemoglobinemia is induced by an excess of the metabolites of these drugs and manifests as a cyanotic appearance that does not respond to the administration of 100% oxygen. Cyanosis becomes apparent when methemoglobin levels are low, but symptoms of nausea, sedation, seizures and even coma may result when levels are very high.[15] Prilocaine, articaine and benzocaine are best avoided in patients with congenital methemoglobinemia.

Paresthesia

Prolonged anesthesia or paresthesia of the tongue or lip are known risks of surgical procedures such as extractions but may also occur following nonsurgical dentistry. Most of these reactions are transient and resolve within 8 weeks, but they may become permanent. Articaine and prilocaine were reported as more likely than other anesthetics to be associated with paresthesia, a difference that was statistically significant when their distribution of use was taken into account.[16] Such reactions have most commonly affected the lingual nerve. So far, the reasons for these findings are speculative only.

Malignant Hyperthermia

Malignant hyperthermia can occur when patients with genetic susceptibility to this condition are exposed to inhalational general anesthetics or succinylcholine, but not to local anesthetics. Previous recommendations, now known to be wrong, precluded the use of specific local anesthetics in these patients. Today it is well accepted that all local anesthetics are safe for patients who are susceptible to malignant hyperthermia.[17]

Interactions

Unlike the vasoconstrictors in dental cartridges, local anesthetics have very few clinically significant interactions on their own.[14,18] When they are combined with an opioid and an antihistamine, there may be a predisposition to seizure activity, particularly in children. This concern can be minimized by use of low doses and careful monitoring, consistent with the standard of care for oral sedation.

Vasoconstrictors

Vasoconstrictors are invaluable to local anesthesia in dentistry. There are clear indications for their use, of which improving the depth and duration of anesthesia are the most important. Without them, local anesthetics have a very short duration of action intraorally. Vasoconstriction is more important for infiltration techniques in vascular sites than it is for mandibular blocks. The presence of a vasoconstrictor may also reduce systemic toxic effects and can provide hemostasis. The most common agent for this purpose is epinephrine, which is available in formulations of 1:50,000, 1:100,000 and 1:200,000.

It is beyond the scope of this article to cover the pharmacology of epinephrine, but the cardiovascular actions of this drug should be noted. Vasoconstriction is due to epinephrine's stimulation of α_1 receptors in mucous membranes. However, it also stimulates the $ß_1$ receptor in the heart, increasing heart rate, strength of contraction and myocardial oxygen consumption, and the $ß_2$ receptors, vasodilating blood vessels in the skeletal muscle. These actions form the basis for potential interactions with other drugs that affect the same receptors (Table 6). Contrary to the information in certain drug monographs, epinephrine can be given to patients receiving monoamine oxidase inhibitors.[19]

A second vasoconstrictor is levonordefrin, which is available as a 1:20,000 solution and should be considered equivalent to 1:100,000 epinephrine. Levonordefrin is contraindicated for patients receiving tricyclic antidepressants.

Epinephrine dosage should sometimes be minimized, for example, for patients with significant cardiovascular disease, in particular ischemic heart disease. In these situations, or when the patient is taking one of the drugs listed in Table 6, certain precautions, outlined in Table 7, should be followed. The recommendation to keep doses below

Table 6 Drug interactions with epinephrine and levonordefrin

Nonselective ß-blockers
Examples: nadolol (Corgard[a]), oxprenolol (Trasicor), pindolol (Visken), propranolol (Inderal), sotalol (Sotacor), timolol (Blocadren, Timoptic)
Interaction may result in increased blood pressure
Reduced use of vasoconstrictor is warranted
Tricyclic antidepressants
Examples: imipramine (Tofranil), amitriptyline (Elavil), desipramine (Norpramin), nortriptyline (Aventyl), doxepin (Sinequan), protriptyline (Vivactil)
Interaction may result in increased blood pressure
Levonordefrin is contraindicated
Reduced dose of epinephrine is warranted
General anesthetic (halothane [Fluothane])
Interaction may result in serious cardiac dysrhythmia
Anesthetist should be advised as to whether epinephrine is needed in local anesthetic; epinephrine should be limited to 1 µg/kg if thiopental is used and 2 µg/kg otherwise
Cocaine
Interaction may result in increased blood pressure and cardiac dysrhythmias

[a]*Brand names are included only as examples and not to promote any one product. The manufacturers are as follows: Corgard, Squibb; Trasicor, Novartis Pharmaceuticals; Visken, Novartis Pharmaceuticals; Inderal, Wyeth-Ayerst; Sotacor, Bristol; Blocadren, MSD; Timoptic, Merck Frosst; Tofranil, Novartis Pharmaceuticals; Elavil, Merck Frosst; Norpramin, Aventis Pharma; Aventyl, Lilly; Sinequan, Pfizer; Vivactil, Merck and Company; Fluothane, Wyeth-Ayerst.*

Table 7 Treatment modifications to consider if there are concerns regarding vasoconstrictors

Monitor blood pressure and heart rate preoperatively
Minimize administration of epinephrine or levonordefrin
Monitor blood pressure and heart rate 5 min after injection
May re-administer epinephrine or levonordefrin if blood pressure and heart rate are stable
Continue to monitor as required
Consider limiting epinephrine to 0.04 mg, levonordefrin to 0.2 mg
Avoid epinephrine 1:50,000
Never use epinephrine-impregnated retraction cord

Table 8 Examples of calculations of doses of vasoconstrictors

Ratio concentrations represent grams per millilitre
1:100,000 = 0.01 mg/mL or 10 µg/mL
1:200,000 = 0.005 mg/mL or 5 µg/mL
1:50,000 = 0.02 mg/mL or 20 µg/mL
1 cartridge of epinephrine 1:200,000 = 9 µg
1 cartridge of epinephrine 1:100,000 = 18 µg
1 cartridge of epinephrine 1:50,000 = 36 µg
1 cartridge of levonordefrin 1:20,000 = 90 µg

Table 9 **Use of local anesthetics during pregnancy[13,21]**

Drug	FDA category
Local anesthetics (injectable)	
Articaine	C
Bupivacaine	C
Lidocaine	B
Mepivacaine	C
Prilocaine	B
Vasoconstrictors	
Epinephrine 1:200,000 or 1:100,000	C (higher doses)
Levonordefrin 1:20,000	Not ranked
Local anesthetics (topical)	
Benzocaine	C
Lidocaine	B

FDA = U.S. Food and Drug Administration

0.04 mg is arbitrary but can act as a guide (see Table 8).[2,6] Systemic epinephrine has a brief duration of action (approximately 10 minutes), so if more is required, injections can be repeated. If multiple quadrants are being treated, the timing of the injections should be spread out. Minimizing the likelihood of systemic effects of vasoconstrictors is another reason why aspiration before every injection is so important.

Topical Anesthetics

Topical anesthetics may be indicated to minimize the sensation of needle insertion or for very brief relief from painful mucosal lesions. Their effectiveness in preventing pain due to injection is equivocal,[20] but they may be of value for many patients. For this purpose benzocaine is available in concentrations up to 20%, and lidocaine is available as a solution or ointment in concentrations up to 5% or as a spray at a concentration of 10%. Dentists should be aware that excessive doses may lead to toxic effects, particularly in children.

Special Patient Populations

Pregnant and Lactating Women

The local anesthetics and vasoconstrictors used in dentistry can be safely administered to the pregnant or nursing patient (Table 9).[21] However, aspiration must always be carried out to minimize the likelihood of intravascular injection. Use of these agents enables definitive treatment, which may in turn allow the avoidance of prolonged use of systemic analgesics and antibiotics.

Lidocaine and prilocaine have the best Food and Drug Administration ranking (Table 9). Lidocaine may be preferable because it has a low-concentration formulation, which makes it easier to minimize the total dose. For topical preparations, lidocaine also has the safest rating.

Although high-dose vasoconstrictors used to manage significant hypotension may be a concern for pregnant patients, the doses of epinephrine used in local anesthetic formulations for dentistry are so low that they are unlikely to significantly affect uterine blood flow. The benefits of epinephrine or levonordefrin at the concentrations found in dental anesthetic cartridges justify their use.

Children

The main concern in pediatrics is the relative ease of inducing an overdose. Before administering local anesthetic to a child, the dentist should determine the child's weight and calculate the maximum dose, to help prevent inadvertent overdose. The calculations shown in Table 5 indicate the ease with which a young child can be overdosed.

Given the concerns regarding toxicity, selection of a low-concentration solution appears prudent. Thus, 2% lidocaine with epinephrine 1:100,000 may be the ideal local anesthetic for a child. Bupivacaine is best avoided in children because of its long duration of soft-tissue anesthesia. There should be no concerns regarding prolonged duration of action due to vasoconstrictor, as it has been shown that soft-tissue anesthesia does not differ significantly between 2% lidocaine with epinephrine 1:100,000 and 3% mepivacaine plain or 4% prilocaine plain.[22]

Elderly Patients

There are no significant differences in the response to local anesthetics between younger and older adults. Therefore, the doses required for each block are the same regardless of patient age. Nonetheless, it is prudent to stay well below the maximum recommended doses, as elderly patients often have some compromise in liver function. Responses to vasoconstrictors should not be considered significantly different in elderly patients, but some degree of cardiovascular compromise can be expected, even without an overt history of heart disease. Therefore, reducing the dose of epinephrine may be prudent.

Conclusions

All local anesthetics used in dentistry are efficacious. The decision regarding which drug to select should be based on the estimated duration of action required, the patient's medical history and potential drug interactions. Solutions without vasoconstrictor, namely mepivacaine and prilocaine plain, may be selected for short procedures, particularly those involving mandibular block, where vasoconstriction is less important. These drugs may also be used when epinephrine must be avoided, as in patients with severe ischemic heart disease or recent myocardial infarction. Bupivacaine can be selected when long duration of action is desired, particularly in the mandible. Lidocaine with epinephrine may be preferred for treatment of children and pregnant patients. Any one of articaine, lidocaine, mepivacaine or prilocaine may be considered for routine dental

procedures. Use of epinephrine can be justified for most dental procedures, but it may be necessary to minimize the dose for patients receiving specific medications and those with cardiovascular disease. ◆

Dr. Haas is a professor and associate dean at the University of Toronto's faculty of dentistry, where he holds the Chapman Chair in Clinical Sciences, and is head of the discipline of dental anesthesia. He is also a professor with the department of pharmacology at the faculty of medicine and active staff with the department of dentistry, Sunnybrook and Women's College Health Sciences Centre, Toronto, Ontario.

Correspondence to: Dr. Daniel A. Haas, Faculty of Dentistry, University of Toronto, 124 Edward St., Toronto, ON M5G 1G6. E-mail: daniel.haas@utoronto.ca.

The author has no declared financial interests in any company manufacturing the types of products mentioned in this article.

References

1. Haas DA, Lennon D. Local anesthetic use by dentists in Ontario. *J Can Dent Assoc* 1995; 61(4):297-304.

2. Malamed SF. Handbook of local anesthesia. 4th ed. St. Louis: Mosby; 1997.

3. Yagiela JA. Local anesthetics. In: Yagiela JA, Neidle EA, Dowd FJ, editors. Pharmacology and therapeutics for dentistry. 4th ed. St. Louis: Mosby; 1998. p. 217-34.

4. Yagiela JA. Local anesthetics. In: Dionne RA, Phero JC, Becker DE, editors. Pain and anxiety control in dentistry. Philadelphia: W.B. Saunders; 2002. p. 78-96.

5. Haas DA, Carmichael FJ. Local anesthetics. 6th ed. In: Roschlau WHE, Kalant H, editors. Principles of medical pharmacology. New York: Oxford; 1998. p. 293-302.

6. Haas DA. Drugs in dentistry. In: Compendium of pharmaceuticals and specialties (CPS). 37th ed. Canadian Pharmaceutical Association; 2002. p. L26-L29.

7. Donaldson D, James-Perdok L, Craig BJ, Derkson GD, Richardson AS. A comparison of Ultracaine DS (articaine HCl) and Citanest forte (prilocaine HCl) in maxillary infiltration and mandibular nerve block. *J Can Dent Assoc* 1987; 53(1):38-42.

8. Haas DA, Harper DG, Saso MA, Young E. Comparison of articaine and prilocaine anesthesia by infiltration in maxillary and mandibular arches. *Anesth Prog* 1990; 37(5):230-7.

9. Haas DA, Harper DG, Saso MA, Young ER. Lack of differential effect by Ultracaine (articaine) and Citanest (prilocaine) in infiltration anesthesia. *J Can Dent Assoc* 1991; 57(3):217-23.

10. Malamed SF, Gagnon S, Leblanc D. Efficacy of articaine: a new amide local anesthetic. *J Am Dent Assoc* 2000; 131(5):635-42.

11. Gall H, Kaufmann R, Kalveram CM. Adverse reactions to local anesthetics: analysis of 197 cases. *J Allergy Clin Immunol* 1996; 97(4):933-7.

12. Rood JP. Adverse reaction to dental local anaesthetic injection — 'allergy' is not the cause. *Br Dent J* 2000; 189(7):380-4.

13. United States Pharmacopeial Drug Information Index. 22nd ed. Greenwood Village (Colorado): Micromedex; 2002.

14. Moore PA. Adverse drug reactions associated with local anesthesia. In: Bennett JD, Rosenberg MB, editors. Medical emergencies in dentistry. Philadelphia: Saunders; 2002. p. 447-59.

15. Wilburn-Goo D, Lloyd LM. When patients become cyanotic: acquired methemoglobinemia. *J Am Dent Assoc* 1999; 130(6):826-81.

16. Haas DA, Lennon D. A 21 year retrospective study of reports of paresthesia following local anesthetic administration. *J Can Dent Assoc* 1995; 61(4):319-20, 323-6, 329-30.

17. Malignant Hyperthermia Association of the United States. Malignant hyperthermia: a concern in dentistry and oral & maxillofacial surgery. Available from: URL: http://www.mhaus.org/dentoral.html.

18. Moore PA. Adverse drug interactions in dental practice: interactions associated with local anesthetics, sedatives and anxiolytics. Part IV of a series. *J Am Dent Assoc* 1999; 130(4):541-54.

19. Yagiela JA. Adverse drug interactions in dental practice: interactions associated with vasoconstrictors. *J Am Dent Assoc* 1999; 130(5):701-9.

20. Meechan JG. Intra-oral topical anaesthetics: a review. *J Dent* 2000; 28(1):3-14.

21. Haas DA, Pynn BR, Sands TD. Drug use for the pregnant or lactating patient. *Gen Dent* 2000; 48(1):54-60.

22. Hersh EV, Hermann DG, Lamp CJ, Johnson PD, MacAfee KA. Assessing the duration of mandibular soft tissue anesthesia. *J Am Dent Assoc* 1995; 126(11):1531-6.