Minor surgery is surgery performed on someone else…whenever it’s you it’s not so minor…

Plastic and Hand Surgical Associates is an academic private practice that performs between 3500 and 4500 surgical procedures each year. About 95% of patients give our practice the highest rating possible on our surveys. I am convinced that one of the main factors in meeting or exceeding patient expectations in surgery is our practitioners’ expert and liberal use of local anesthetics (LAs). Indeed, I would say that, other than an alcohol swab, LAs are the most frequently used medications in our practice.

Surgeons are asked to do more and larger procedures as outpatient procedures as the economics of medicine evolve. Indeed, we all carry out procedures on an outpatient basis that only a short time ago we would consider only on an inpatient basis. Further, procedures that had previously been performed under a general anesthetic are now being performed under local anesthesia. A good working knowledge of LAs will better enable the surgeon to meet those demands and to do so in a way that will enhance the patient’s safety, experience, and comfort. Although the focus of this issue of Clinics is minor surgery, any meaningful discussion of LAs has to go a little further than a 3-mL syringe and a small amount of lidocaine.

HISTORY

Erythroxylon coca, or the coca shrub, has been used by Andean natives for centuries. The stimulatory effect of chewing coca leaves was investigated in the mid nineteenth century, leading to the isolation of cocaine in 1860 by Albert Niemann. An enthusiastic Sigmund Freud investigated cocaine’s effect on mood and behavior, only to see the harmful and addictive effects it had on its users. Carl Koller was the first to use the numbing properties of cocaine in 1884, employing it as the first LA in ophthalmic surgery. As the toxicities of cocaine became better known, a search for other less toxic LAs was undertaken. In 1892, Einhorn synthesized procaine and the modern era of
LAs was born. The most commonly used LAs in our practice are lidocaine, bupivacaine, and prilocaine.

PHARMACOLOGY OF LOCAL ANESTHETICS

LAs are agents that reversibly block action potentials at the level of the sodium channels, thereby interrupting axonal conduction. LAs’ actions are nonspecific: they work on any nerve with a functioning sodium channel. Knowledge of the structural components of LAs will aid in better understanding how these interesting compounds work and perhaps why, sometimes, they do not.

LAs are composed of a lipophilic/hydrophobic group (an aromatic ring) connected by an amide or ester intermediate chain to a hydrophilic or ionizable group (a secondary or tertiary amine). Those compounds with highly lipophilic/hydrophobic moieties are more potent, more long lasting, and more toxic. This appears to be related to the site of action on the nerve cell membrane.

The sodium pore channel is a complex entity. Its anatomy and function are not reviewed here. Suffice it to say that there is a hydrophobic entity in the sodium channel pore that has a binding affinity for the lipophilic/hydrophobic group of the LA. Binding can only occur with the sodium gate or pore in an open or stimulated position; LAs need access to get to their binding site. Once there, the LA stabilizes the channel in its inactive state and the nerve cannot repolarize. Only a critical length of nerve need be affected to stop conduction. The channel eventually recovers but at a speed 10 to 10,000 times slower than normal. The stronger the bond between the hydrophobic groups, the longer the effect. The strength and duration of this bond affect the therapeutic window, making it smaller, and hence influence toxicity.

Amide linkages are less prone to hydrolysis than ester linkages and therefore influence the duration of effect. The hydrophilic group influences the onset of effect.

Metabolism of LAs relates to their duration of effect and to their toxicity. The more free LA there is in plasma, the more toxic it is. Ester-linked LAs are generally much shorter acting. They are rapidly inactivated by plasma cholinesterase. Amide-linked LAs are metabolized in the liver by the cytochrome P450 enzyme system. More than 50% of amide-linked LAs are bound to Alpha1 acid glycoprotein (AAG), a substance found in the plasma. Fluctuation in the levels of this important compound greatly influence metabolism.

pH plays a very important role in LA function. LAs are for the most part poorly soluble amines. LAs are found on the surgeon’s shelf as slightly acidic hydrochloride water-soluble salts. When injected into normal tissue, there is rapid equilibration of the pH, allowing the unprotonated compound to diffuse across the cell membrane. The cationic form of the LA binds with the sodium pore: ionization must occur after passage through the membrane in order for the LA to take effect. The charged form of the LA will not diffuse through the membrane; therefore, anything that alters the pH of the local milieu will affect the LA’s ability to get through the cell membrane. The most obvious offender in this regard is local infection; here the environment is acidic, the LA is charged, and it cannot pass through the cell membrane to exert its effect.

Nerve fibers have differing susceptibilities to the effects of LAs. These differences are most likely due to differences in fiber diameter and myelination. The small-diameter unmeylenated fibers, such as type C pain fibers, are the most sensitive to LA-blocking effects. Heavily myelinated, thicker fibers such as type A motor fibers are less so. Any fiber that requires an action potential to function, however, can potentially be blocked by the effects of LAs (Table 1).
Aside from these characteristics, the single most influential component of LAs in practical use is the addition of epinephrine (EPI).

LOCAL ANESTHETICS AND VASOCONSTRICTORS

Vasoconstrictors in conjunction with LAs have been used to treat patients almost from their inception. Confusion and controversy regarding the use of vasoconstrictors with LAs may stem from a lack of understanding of how these drugs work and how they work together.

Two main catecholamines have been used in LA formulations over the years: EPI and norepinephrine (NE). EPI is by far more widely used. NE has fallen out of favor for good reason. These two compounds differ in the effect they have on the adrenergic system and on the effectiveness and toxicities of the LAs themselves.

The main areas of activity for the catecholamines are the alpha and beta receptors found throughout the body. Beta1 receptors increase heart rate and contractility. Beta2 receptors cause vasodilatation in pulmonary and skeletal muscle vascular beds. Alpha receptors increase vasoconstriction in peripheral vascular beds. EPI has both Beta1 and Beta2 effects, whereas NE has mostly Beta1 effects. EPI has a four-fold greater alpha effect than that of NE. EPI tends to improve ventricular diastolic function. Mean arterial pressure (MAP) in patients injected with LA/EPI tends to remain stable. EPI alpha effects prolong the effects of LAs by delaying their uptake by the local vascular bed and diminishing potential toxicity as well by slowing the rate of rise of LA serum levels. Local blood loss is decreased. EPI has a serum half-life of less than 1 minute. It is rapidly metabolized by catechol-O-methyl transferase in blood, lung, liver, and elsewhere. Those injected with LA/NE have impaired ventricular diastolic function. Patients become hypertensive with an elevation of MAP because of a lack of Beta2 effect. A compensatory vagal reflex results in rebound bradycardia. NE has no local alpha benefit; therefore, EPI is the better choice.\textsuperscript{4,11}

TOXICITIES OF LOCAL ANESTHETICS

In a 2003 study evaluating adverse events during oral and maxillofacial surgery in the state of Massachusetts, the most common adverse event associated with the use of

<table>
<thead>
<tr>
<th>Fiber Type</th>
<th>Function</th>
<th>Diameter (µm)</th>
<th>Myelination</th>
<th>Conduction Velocity (m/a)</th>
<th>Sensitivity to Block</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type A</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alpha</td>
<td>Proprioception, motor</td>
<td>12–20</td>
<td>Heavy</td>
<td>70–120</td>
<td>+</td>
</tr>
<tr>
<td>Beta</td>
<td>Touch, pressure</td>
<td>5–12</td>
<td>Heavy</td>
<td>30–70</td>
<td>+ +</td>
</tr>
<tr>
<td>Gamma</td>
<td>Muscle spindles</td>
<td>3–6</td>
<td>Heavy</td>
<td>15–30</td>
<td>+ +</td>
</tr>
<tr>
<td>Delta</td>
<td>Pain, temperature</td>
<td>2–5</td>
<td>Heavy</td>
<td>12–30</td>
<td>+ + +</td>
</tr>
<tr>
<td>Type B</td>
<td>Preganglionic autonomic</td>
<td>&lt; 3</td>
<td>Light</td>
<td>3–15</td>
<td>+ + + +</td>
</tr>
<tr>
<td>Type C</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dorsal root</td>
<td>Pain</td>
<td>0.4–1.2</td>
<td>None</td>
<td>0.5–2.3</td>
<td>+ + +</td>
</tr>
<tr>
<td>Sympathetic</td>
<td>Postganglionic</td>
<td>0.3–1.3</td>
<td>None</td>
<td>0.7–2.3</td>
<td>+ + +</td>
</tr>
</tbody>
</table>

LAs was syncope, occurring in approximately 1 in 160 patients. Nonetheless, 17 of approximately 180,000 patients suffered a seizure, and 12 had some sort of cardiac side effect. These statistics are in line with what is known about LAs: the most common toxicities are neurologic and cardiac. Deaths have occurred from inappropriate use of LAs. A recent report details a death from LA overdose. I encourage all to read it.\textsuperscript{12–14}

Neurologic toxicity is frequently manifested as agitation, restlessness, and tremor. These effects are presumably produced by LA depression of central cortical inhibitory pathways, leaving the excitatory pathways uninhibited. Seizures can follow. Higher levels of LAs can lead to central nervous system depression, respiratory failure, and death. In high concentrations, LAs can be injurious to nerve tissue itself, causing sensory and or motor impairment.

Cardiac toxicity results from a two-fold mechanism, direct to the cardiac muscle and from dysfunction of the autonomic ganglia. Myocardial contractility is greatly impaired due to the conduction-blocking effects of LAs. This effect can be used to great advantage, however, as many patients have been saved from malignant dysrhythmia by the timely use of lidocaine. True ventricular dysrythmias from LA overdose are rare, with the exception of bupivacaine, which can cause ventricular tachycardia and fibrillation. Cardiac side effects are usually seen with very high serum concentrations and most often follow neurologic manifestations.\textsuperscript{4,5,7,12–15}

TREATMENT OF LOCAL ANESTHETIC TOXICITIES

Drug treatment of LA toxicities has undergone an evolution over the past decade. The most important part of treating LA toxicity, however, is recognizing it. Remember, the first sign may be simple agitation. Inadvertent intravascular injection of LAs is the fastest way to elevate serum LA levels and precipitate a reaction. Under such circumstances, injection or infusion should be stopped immediately. Adding medications such as hyaluronidase may actually worsen the situation by further elevating plasma LA levels. Supportive measures, such as supplemental oxygen, positional change, oxygen saturation, and blood pressure monitoring, are all appropriate. Until recently, benzodiazepines were the drug of choice for the treatment of neurologic side effects. Diazepam 0.1 mg to 0.2 mg.kg can be given intravenous (IV), intramuscular (IM), or per rectum.

Twenty percent lipid emulsion has been shown to reverse the toxic effects of LAs, both neurologic and cardiac, quickly and effectively. Several cases have been documented in the literature reporting patients saved from bupivacaine toxicity by timely infusion of 1 mg to 2 mg/kg of 20% lipid emulsion. The mechanism of action is not clear; however, it has be postulated that the lipid acts as kind of a LA sink, scouring the blood for LA and binding it, quickly decreasing the serum level, perhaps mimicking AAG. Allergies to LAs are quite rare. Nonetheless, true IgE allergic reactions can occur. A thorough history should be taken, and, if a full-blown allergy is suspected, then the patient should be referred to an allergy/immunology specialist for evaluation. Ester-linked LAs are most often linked to true anaphylaxis. Sulfites used to stabilize vasoconstrictors and methylparaben, a bacteriostatic agent similar to an ester linkage found in some LA, can cause non–IgE-mediated allergic reactions.\textsuperscript{4,8,13,16}

There have been reports of prilocaine causing methemoglobinemia. Hydrolysis of prilocaine initially leads to the formation of o-toluidine products that can bind to hemoglobin and cause methemoglobinemia.\textsuperscript{8,13,17}

Most reactions not related to LA toxicity can be classified into psychosomatic responses and idiosyncratic reactions. Hyperventilation, tachycardia, or vagal episodes may well be due to anxiety. They are treated supportively. Idiosyncratic reactions can occur with the use of prilocaine as previously stated. Methemoglobinemia
causes cyanosis and is treated with 100% oxygen and IV methylene blue (which acts as an electron receptor and reduces the formation of methemoglobin). Newborns, patients with hemoglobinopathies, and those with glucose-6-phosphate dehydrogenase deficiency are at greatest risk.13,16

**DOsing AND ADMINISTRATION TECHNIQUE**

Dosing guidelines for LAs are vague. In fact, the recommended doses for the same LAs differ from country to country. Manufactures have issued dosing guidelines for LAs that are more empirically based rather than evidence based. The reason for this may be the companies’ attempt to ensure a very generous margin of safety for these widely used medications; some of it may be out of liability concerns. To be fair, dosing of LAs is not straightforward. Comorbidities, anatomic location, and surface area to be treated as well as concentration of the LA, the addition of EPI, and rapidity of the infusion all factor into safe dosing guidelines (Table 2).7,10–12,18,19

**PATIENT FACTORS IN DOSING**

Much of what is contained within this section is in greater part derived from an excellent article by Rosenberg and colleagues.7 The authors take a critical look at all of the factors involved in LA dosing.

Before injecting patients with an LA, it is important to consider their age, comorbidities, and medications, as all of these are factors in dosing decisions. Some of the recommendations that are noted below do not have any direct relevance in the minor procedure in the office setting. Nonetheless, they are important to mention as an aid in understanding these medications, thereby conveying informed caution.

The extremes of age are for the most part the most important factor to consider. Infants younger than 4 months of age have been shown to have higher plasma concentrations of LAs when given the adult equivalent dose. The reason postulated for this is the lower concentration of AAG found in plasma. Lower AAG puts this age group at risk for toxic effects at lower doses. Further, infants younger than 4 months of age appear to be more sensitive to bupivacaine. As a result, recommendation for lowering the dose of LAs by 15% is given to infants, especially those undergoing regional anesthetics.

The elderly, those older than 70 years, also deserve special dosing considerations. Diminished blood flow to those organs responsible for metabolism of LAs leads to decreased plasma clearance of LAs in those affected. Loss of fatty tissue and diminution in axonal function mean that the elderly are more sensitive to blockade of nerve function. Although there has been a report of an elderly patient who suffered the effects of LA toxicity at a lower serum concentration than had previously been reported,13 plasma concentrations of LAs are similar to those found in younger age groups. The recommendation is for decreasing LA dose by 20% in those patients older than 70 years.

Renal impairment patients deserve special consideration. Lidocaine and bupivacaine have very different profiles in the patients.

Lidocaine appears to be very well tolerated. Lidocaine is metabolized by a hepatic route.5 Plasma clearance of lidocaine is unchanged in the renal patient. Dosing guidelines are unchanged.

Bupivacaine has a lower plasma clearance rate in the renal impaired. In hyperdynamic uremia patients, bupivacaine shows a rapid rise in plasma concentration. Fortunately, AAG levels appear to be higher in this population. Increased AAG may act as a kind of safety mechanism or buffer, ameliorating some of the effects of renal
Table 2
Officially recommended highest doses of LAs in various countries

<table>
<thead>
<tr>
<th></th>
<th>Finland</th>
<th>Germany</th>
<th>Japan</th>
<th>Sweden</th>
<th>United States</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Chloroprocaine</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>800 mg</td>
</tr>
<tr>
<td>With epinephrine</td>
<td>—</td>
<td>—</td>
<td>1000 mg</td>
<td>—</td>
<td>1000 mg</td>
</tr>
<tr>
<td>Procaine</td>
<td>—</td>
<td>500 mg</td>
<td>600 mg (epidural)</td>
<td>—</td>
<td>500 mg</td>
</tr>
<tr>
<td>With epinephrine</td>
<td>—</td>
<td>600 mg</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Articaine</td>
<td>7 mg/kg</td>
<td>4 mg/kg</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>With epinephrine</td>
<td>7 mg/kg</td>
<td>4 mg/kg</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Bupivacaine</td>
<td>175 mg (200 mg&lt;sup&gt;a&lt;/sup&gt;) (400 mg/24 h)</td>
<td>150 mg</td>
<td>100 mg (epidural)</td>
<td>150 mg</td>
<td>175 mg</td>
</tr>
<tr>
<td>With epinephrine</td>
<td>175 mg</td>
<td>150 mg</td>
<td>—</td>
<td>150 mg</td>
<td>225 mg</td>
</tr>
<tr>
<td>Levobupivacaine</td>
<td>150 mg (400 mg/24 h)</td>
<td>150 mg</td>
<td>—</td>
<td>150 mg</td>
<td>150 mg</td>
</tr>
<tr>
<td>With epinephrine</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Lidocaine</td>
<td>200 mg</td>
<td>200 mg</td>
<td>200 mg</td>
<td>200 mg</td>
<td>300 mg</td>
</tr>
<tr>
<td>With epinephrine</td>
<td>500 mg</td>
<td>500 mg</td>
<td>—</td>
<td>500 mg</td>
<td>500 mg</td>
</tr>
<tr>
<td>Mepivacaine</td>
<td>—</td>
<td>300 mg</td>
<td>400 mg (epidural)</td>
<td>350 mg</td>
<td>400 mg</td>
</tr>
<tr>
<td>With epinephrine</td>
<td>—</td>
<td>500 mg</td>
<td>—</td>
<td>350 mg</td>
<td>550 mg</td>
</tr>
<tr>
<td>Prilocatine</td>
<td>400 mg</td>
<td>—</td>
<td>—</td>
<td>400 mg</td>
<td>—</td>
</tr>
<tr>
<td>With epinephrine</td>
<td>600 mg</td>
<td>—</td>
<td>—</td>
<td>600 mg</td>
<td>—</td>
</tr>
<tr>
<td>Ropivacaine</td>
<td>225 mg (300 mg&lt;sup&gt;a&lt;/sup&gt;) (800 mg/24 h)</td>
<td>No mention</td>
<td>200 mg (epidural) 300 mg (infiltr)</td>
<td>225 mg</td>
<td>225 mg (300 mg&lt;sup&gt;a&lt;/sup&gt;)</td>
</tr>
<tr>
<td>With epinephrine</td>
<td>225 mg</td>
<td>No mention</td>
<td>—</td>
<td>225 mg</td>
<td>225 mg (300 mg&lt;sup&gt;a&lt;/sup&gt;)</td>
</tr>
</tbody>
</table>

<sup>a</sup> For brachial plexus block in adults.

impairment on bupivacaine metabolism. A decrease of 10 to 20% in those patients getting larger doses (regional blocks, continuous infusions via pump) of bupivacaine is recommended.

Hepatic dysfunction is an important consideration. Hepatic insufficiency rarely occurs alone. Other organ systems, renal, pulmonary, and so forth, are frequently involved, making dosing decisions in these patients even more complex. Amide LAs are mainly metabolized via the liver, so it would seem that hepatic dysfunction would greatly alter plasma concentrations of LAs. As expected, patients with end-stage liver disease have a 60% decrease in plasma clearance rates of LAs. Interestingly, those with mild impairment (alcoholics) have little change in their clearance rates. AAG may again play a role here, but it has been poorly studied. It does appear that even in end-stage liver disease, AAG continues to be made. Great care and due consideration need to be given to these patients when administering amide LAs. Although up to a 50% reduction in dosing of LAs has been recommended for higher-dose repeat regional blocks, under normal office minor procedure circumstances, no reduction in dosing is recommended for isolated mild hepatic impairment.

Cardiac disease needs to be considered. A spectrum of patients from those with mild hypertension to those with significant heart failure needs to be treated differently. This relates to the degree of impairment of blood flow to lung, liver, and kidneys and its effect on plasma clearance of LAs. For patients with well-controlled disease, no dosage adjustment is required. For patients with more severe disease, a reduction of as much as 20% for repeat regional block has been recommended.7,11

The bigger concern for practitioners with regard to use of LAs in patients with cardiac disease most likely has nothing to do with the LA itself, but rather the EPI is frequently the greater cause for concern. The best data on the outpatient experience comes from the maxillofacial literature, “Epinephrine and Local Anesthesia revisited” by Brown and Rhodus11 All are encouraged to read it.

In short, EPI given to patients with well-controlled cardiac disease in conjunction with LAs in the office setting is safe and requires little in the way of dose modification. Addition of EPI to LAs slows their uptake and helps to diminish their potential for toxicity, a huge benefit. As previously noted, the Massachusetts study showed that 12 of 180,000 patients had some sort of cardiac side effect. I would postulate that at least a portion of those patients have side effects from endogenous NE released in response to pain from inadequate LA effect, an important fact to remember when trying to evaluate a hypertensive person in the minor surgery room.

A thorough review of a patient’s medication should be undertaken before injecting any LA. Several medications influence the metabolism of LAs.

Amide LAs are metabolized by the cytochrome P450 enzyme system. Anything that inhibits a portion of that system impairs LA metabolism. In addition, some of these medications impair hepatic blood flow, further slowing LA clearance. Bupivacaine appears to be more greatly affected by these drugs than lidocaine. Propranolol and cimetidine are two such drugs and can impair bupivacaine clearance by up to 35%. The antifungal Itraconazole also affects the metabolism of bupivacaine similarly. Significant dose reduction in patients receiving repeat blocks is recommended.7,16

Epinephrine itself has been implicated as interacting with antidepressant drugs such as tricyclic antidepressants, monoamine oxidase inhibitors, and selective serotonin reuptake inhibitors causing hypertension. Change in beta-adrenergic receptors, specifically downregulation, has been postulated as the mechanism of interaction. A review of relevant literature does not support this conclusion; no case report has been published describing a link between LAs with EPI and TCA antidepressants. In the minor procedure office setting, LAs with EPI can be safely used in these patients.16
AAG levels are also affected by a variety of factors. Trauma, smoking, uremia, and surgery increase AAG levels in plasma. Oral contraceptives decrease levels.4

TUMESCENT SOLUTION AND LOCAL ANESTHETIC DOSING

LAs commonly used in the United States are 1% and 2% lidocaine with EPI 1:100,000 or 1:200,000 and bupivacaine 0.25% and 0.5% with similar EPI dilutions. Clinicians have modified these medications postmanufacture by mixing them, diluting them, and by adding bicarbonate to achieve their own particular cocktail. Plastic surgeons have taken this idea and created highly dilute solutions of LAs, EPI, and buffer. They are called tumescent solutions. A brief discussion of tumescent solutions will aid in further understanding the dynamic of dosing and toxicity.

Shortly after the first published reports of suction lipectomy by Illouz in 1977, surgeons began to look for ways to minimize blood loss, ease and enhance removal of fatty tissue, and improve patient comfort. First, a “wet” technique of infusing a large volume of fluid containing dilute hyaluronidase was used. To this were added low-dose EPI and dilute LA. In 1987, Klein coined the phrase “tumescent technique” and so it has been ever since. Though formulations of tumescent solution vary, a typical mixture would contain 0.1% lidocaine, sodium bicarbonate 12mEq/L, and EPI 1:1,000,000. The solution is usually warmed to approximately 37°C.15,18,20,21

As previously noted, the recommended dose of lidocaine in an otherwise healthy adult has been set at 7 mg/kg. Using tumescent solution, doses as high as 50 mg/kg have been administered without toxicity (although 35 mg/kg or lower is considered a safer dose); how can this be?14,15,18 Suppositions that most of the LA has been suctioned out have not been validated. The explanation lies in the solution itself and where it is injected. Tumescent solution is injected into the subcutaneous space. When compared with plasma levels with IM or IV injections, subcutaneous levels are much lower. This is presumed to be due to the decreased vascularity of the compartment, leading to slower absorption. Diluting the LA and adding EPI with its powerful local alpha effects slows absorption even further. Add to these factors a relatively slow rate of injection and we go a long way in explaining why a 5-fold increase in the standard lidocaine dose is well tolerated.7,8,11,19

Not all areas of the body are created equal. In 2005 Rubin and colleagues18 published an excellent study of plasma levels of lidocaine after infusion of a standard tumescent solution above the clavicles and then in the lower extremities. The plasma lidocaine concentration curves were similar in duration, meaning that by 14 hours postinfusion plasma levels of lidocaine were trending sharply downward. However, the average peak concentration from the neck infusion was 16% higher than that of the lower extremity. Further peak concentrations from the neck infusion were reached much earlier (5.8 hours) than those from the lower-extremity infusion (12.8 hours). Studies have shown that lidocaine toxicity occurs at approximately 4 mcg/mL. In studies using tumescent solutions with as much as 55 mg/kg of lidocaine, plasma levels never rose more than 3.6 mcg/ml.14,15,18,22

In summary, the risk of toxicity from LA use can be minimized by the following:

1) Using the lowest concentration of LA required; diluting is allowed.
2) Avoiding direct injection into the intravascular space.
3) Using EPI to slow absorption of LAs into the blood stream and to prolong anesthetic effect as well as minimize blood loss.
4) Modify the dose of LA/EPI for those patients with risk factors for toxicity.
5) Using enough LA to adequately anesthetize the area of interest.
TOPICAL LOCAL ANESTHETICS

Topical use of LAs has been employed since their discovery. More and more topical anesthetics are being used alone or in conjunction with injectable LAs. The absorption of topical anesthetics is related to the concentration of the LA employed, the amount of surface area covered, and the type of surface to which it has been applied. Systemic toxicity has been reported with the use of these compounds. A 22-year-old woman died in 2001 after application of 10% lidocaine/10% tetracaine cream from waist to feet for a laser hair removal procedure. Lidocaine applied to a mucosal surface can lead to plasma levels approaching that of parenteral administration. Care must be taken in the use of these compounds.10,23,24

Many surgeons are familiar with the combinations of topical compounds such as TAC and LET, which have been used in emergency departments for many years to anesthetize small lacerations. TAC is no longer in wide use as it has been largely replaced by LET, which has been shown to be just as efficacious, without the risks posed by combining cocaine and EPI (Table 3).

EMLA cream (AstraZeneca LP, Wilmington, Delaware) is currently in wide use. It is just one of a number of topical LA creams, but it is perhaps the best known. EMLA is a cream that contains 2.5% lidocaine and 2.5% prilocaine. It delivers maximal benefit after being in place for 30 to 60 minutes with an occlusive dressing. Systemic absorption of even large amounts of EMLA on large surface areas has been shown to be far below toxic levels. EMLA works very well in anesthetizing the skin before minor vascular access procedures and in superficial laser skin treatments. Though I was unable to find any report in the literature of methemoglobinemia from EMLA use, age-related guidelines have been issued to minimize the risk of this complication. EMLA is used on intact skin (Table 4).10,25

Special mention should be made with regard to compounding. Compounding pharmacies were until recently allowed to create or compound LA creams. High-dose creams, such as those involved in the death of the 22-year-old woman mentioned above, were made to order. The Food and Drug Administration put a stop to this practice in 2006 saying that these medications were not properly reviewed and that the pharmacies could no longer act like drug manufacturers.26

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Product descriptions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product</td>
<td>Composition</td>
</tr>
<tr>
<td>TAC</td>
<td>0.5% tetracaine, 1:2000 epinephrine, and 11.8% cocaine</td>
</tr>
<tr>
<td>LET</td>
<td>0.5% tetracaine, 1:2000 epinephrine, and 4% lidocaine</td>
</tr>
<tr>
<td>Topicaine</td>
<td>4% lidocaine</td>
</tr>
<tr>
<td>EMLA</td>
<td>2.5% lidocaine and 25% prilocaine</td>
</tr>
<tr>
<td>LMX 4/5</td>
<td>4% or 5% liposomal lidocaine</td>
</tr>
<tr>
<td>BLT</td>
<td>20% benzocaine, 6% lidocaine, and 4% tetracaine</td>
</tr>
</tbody>
</table>

I am often asked by students and practitioners alike if it is okay to inject EPI-containing LAs into various body parts, most often in the digits. The answer is yes, it is okay. When used to effect a digital block, EPI-containing LAs are quite safe and provide intraoperative hemostasis and postprocedure pain relief. As always, good judgment needs to be used: an insulin-dependent diabetic vasculopathic patient with a finger laceration might not be the best candidate for EPI injection in the finger.\textsuperscript{27,28}

### TECHNIQUE OF ADMINISTRATION

Delivering a good LA can be called an art form in and of itself. I have witnessed patients (other surgeons’, not mine) writhing in pain, struggling to hold still while the surgeon, with beads of sweat collecting on his or her brow, attempts to deliver a small amount of LA. More often than not, this need not be the rule for administering LAs for minor procedures in the office setting.

A good LA begins with a good discussion. Make every effort to inform the patient of what to expect and tell the truth; telling the patient it will not hurt at all will only hurt your credibility with the patient. Every patient who elects to undergo a procedure under LA expects some discomfort. Be as specific as you can in telling the patient what will happen: where the surgery will take place, if they will need to change out of their clothes, what position they will be in, how long the procedure will take, and what monitoring precautions you may choose to employ. Tell them about the LA administration, how long it will last, and what to expect for discomfort. In cases of extreme anxiety, a topical LA can be placed approximately 1 hour before the procedure to alleviate the pinprick sensation of dermal penetration. If necessary, low-dose benzodiazepines can be prescribed to be taken 30 minutes before surgery.

The pain of injection of LAs is related to the site of injection, size of the needle, and the rapidity of the injection. The pH of the LA also plays a role in pain with injection. Injecting an area with a high concentration of sensory fibers, the tip of the nose, a fingertip, is much more painful than an area with lesser sensory representation, the thigh, the back. Small-caliber needles, 27 to 30 gauge, should be used to minimize the pain of dermal penetration. Inject slowly making sure that you avoid intravascular injection. This can occasionally be manifested by a sudden increase in pain as well as acute blanching in a vascular pattern. Adding a buffer to the LA has been said to decrease the pain of injection. Add sodium bicarbonate to the LA if desired. A 1 mL sodium bicarbonate to 9 mL LA ratio has been reported to work best. Do your best to be calm and reassuring but not patronizing.\textsuperscript{29–31}

<table>
<thead>
<tr>
<th>Age and Body Weight Requirement</th>
<th>Maximum Total Dose of EMLA (g)</th>
<th>Maximum Application Area (cm²)</th>
<th>Maximum Application Time (h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–3 mo or &lt;5 kg</td>
<td>1</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>3–12 mo and &gt;5 kg</td>
<td>2</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>1–6 y and &gt;10 kg</td>
<td>10</td>
<td>100</td>
<td>4</td>
</tr>
<tr>
<td>7–12 y and &gt;20 kg</td>
<td>20</td>
<td>200</td>
<td>4</td>
</tr>
</tbody>
</table>


**EPINEPHRINE IN DIGITS**

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It has been said that dogs and children can smell fear. In our experience working with the latter, being calm and assertive is very important (this has also been said of working with the former). Maintain control of the room. Tell parent and child what will happen and do it. Do not wait for the child to give you permission; you may never get it. All you need is his or her understanding. Have everything you will need ready. Do not fumble around and draw up a 10-mL syringe of local with a 2-in long 18-gauge needle in front of a 9-year-old child and his or her mother. Try to transmit competence and inspire confidence.

Zilinsky and colleagues sum up all of these thoughts in a paper published in 2005 entitled, “Ten Commandments for Minimal Pain during Administration of Local Anesthetics.” I encourage you to read it. 29

The minor procedure room should have adequate lighting and a comfortable multi-position table capable of Trendelenberg positioning. Instruments, suture, and specimen containers should all be within arm’s reach. Your preference for LAs should be present in abundance. Blood pressure monitoring equipment and an oxygen saturation monitor are essential. Supplemental oxygen should be readily accessible. Assistance should be close by.

SUMMARY

LAs are compounds unparalleled in their ability to alleviate pain. Surgeons with a good understanding of the actions and toxicities of these medications as well as the skill to deliver them will find that the minor procedure room is an enjoyable place for them and a comfortable and safe place for their patients.

REFERENCES