Section 1 Chapter 1

Introduction

Pharmacology: local anesthetics and additives

Introduction

An understanding of basic local anesthetic pharmacology is essential prior to safe and effective placement of any regional block. Numerous pharmacology texts and literature sources are available describing similarities and differences with regard to onset time, duration, selective motor and/or sensory blockade, tissue penetration, and toxic profile. The goal of this chapter is to provide a brief overview of the more common local anesthetics used in performing peripheral nerve blocks.

To introduce the mechanism of local anesthetic action, the chapter begins with a brief review of nerve electrophysiology. A short discussion on local anesthetic structure is then covered followed by key points regarding pharmacologic properties of individual agents commonly used in peripheral nerve blocks. Local anesthetic toxicity and its management are reviewed, and the chapter concludes with a discussion of local anesthetic additives for peripheral nerve blocks.

Nerve electrophysiology

One of the basic ways peripheral nerve fibers can be grouped is based on the presence or absence of a myelin sheath surrounding the nerve axon (Figure 1.1). Myelin, composed mostly of lipid, provides a layer of insulation around the nerve axon when present. Most nerves within the peripheral nervous system are myelinated (except C-fibers, which are un-myelinated) with variations in size and function. The largest myelinated nerves (A-alpha) are 12 to 20 micrometers thick and are involved with motor and proprioceptive functioning. In comparison, the smallest myelinated (A-delta) and un-myelinated (C-fibers) are around 1 to 2 micrometers or less in diameter and play a role in transmission of pain and temperature sensation.

Impulses travel along the un-myelinated portions of nerves in waves of electrical activity called action potentials. Nerves without myelin propagate action potentials in a continuous wave of electrical activity along the nerve's axon.

Action potentials are spread a bit differently, and faster, in myelinated nerves. Nerves containing myelin have small un-myelinated sections along the nerve's axon called nodes of Ranvier (Figure 1.1). Instead of traveling continuously down the axon, impulses jump from one node of Ranvier to the next, a concept known as saltatory conduction. Saltatory conduction allows action potentials to spread faster in myelinated nerves.

Nerve cells maintain a resting potential gradient with extracellular fluid of approximately −70 mV to −90 mV. This resting gradient exists as positively charged sodium ions (Na^+) are actively pumped out of the cell in exchange for potassium ions (K^+) across transmembrane proteins via a Na/K ATPase. In addition to the active transfer of Na^+ out, K^+ flows out passively from the cell's inner cytoplasm to the extracellular space. This net flow of positively charged ions out of the cell's interior at rest leads to a consistent negative resting potential gradient across the nerve cell axonal membrane.

Action potentials are formed as a result of positive fluctuations in this resting potential gradient. These fluctuations occur with changes in Na^+ concentration and direction of flow across the nerve cell membrane. Stimulation of the nerve leads to activation of Na^+ channels spanning the nerve cell's membrane, allowing Na^+ to now flow *into* the cell's interior. As Na^+ enters the cell, the negative transmembrane potential difference becomes more positive. At a cellular threshold of approximately −60 mV, additional Na^+ channels are activated, leading to rapid depolarization of the nerve cell followed by action potential formation. The nerve cell membrane depolarizes and

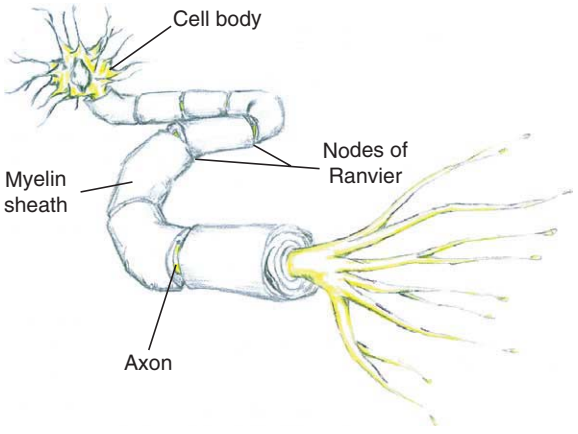

Figure 1.1 Nodes of Ranvier on a myelinated nerve fiber.

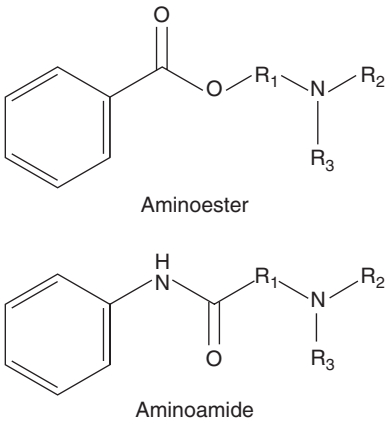

Figure 1.2 Local anesthetic structure.

rises to a potential difference of +20 mV before the transmembrane Na^+ channels become inactivated. The resting membrane potential difference is ultimately restored by the active Na/K ATPase and passive leakage of K^+ back out of the cell.

Additional considerations

Local anesthetics exert their effect at the inner portion of transmembrane Na^+ channel proteins. By reversibly binding these channels, depolarization of the nerve axon is prevented.

Local anesthetic pharmacology

Local anesthetic structure and classification

Local anesthetics are composed of lipophilic and hydrophilic ends connected by an intermediate chain.

The "head" of the molecule is an aromatic ring structure and the most lipophilic portion of the molecule, while the "tail" portion is a tertiary (neutral) or quaternary (charged) amine derivative. The intermediate carbon chain, which forms the body of the molecule, is connected to the amine portion typically by an amide or ester linkage (Figure 1.2). It is this association that is used to classify the commonly used local anesthetic agents as either an ester or an amide.

Local anesthetic pharmacodynamics

Local anesthetic ionization and pKA

Local anesthetics are weak bases and, by definition, poorly soluble and only partially ionized in aqueous solution. For stability, preparations of local anesthetics are stored as hydrochloride salts with an acidic pH ranging from 3 to 6.

It has long been felt an agent's pKa correlates closely to the speed of onset for a particular local anesthetic. There are, however, a number of factors that may be associated with onset time for these agents, especially when used in peripheral nerve blocks. Such factors include lipid solubility of the anesthetic, the type of block and proximity of anesthetic injection to the nerve, the type and size of nerve fibers blocked, and the degree of local anesthetic ionization.

It is the relationship between the agent's pKa and surrounding pH that relates to the degree of ionization for the drug (Table 1.1). The pKa is the pH at which the agent exists as a 50:50 mixture of ionized and free base (non-ionized) molecules. In other words, these agents exist in a continuum of ionized and neutral form in solution with the balance point at the agent's pKa. At physiologic pH, the balance favors the ionized form since those clinically relevant local anesthetics used in peripheral nerve blocks have a pKa in excess of the pH of extracellular fluid. But the lower a drug's pKa in physiologic solution, the more drug is available in the neutral form.

It is the neutral form of the drug that passes into and through the nerve cell membrane. The greater the amount of drug in the neutral form available to pass into the nerve cell, one might surmise, the faster the onset. While this theory is commonly accepted, it is not without exception, as is the case with chloroprocaine (pKa 8.7). Among the amide local anesthetics, however, this relationship seems to hold true.

Once inside the nerve cell, it is the ionized form of the local anesthetic that attaches to the

Table 1.1 Pharmacokinetic and pharmacodynamic differences between common ester and amide local anesthetics used in peripheral nerve blocks

Agent	Type	Pot	pKa	%PB	Dur	Met
2-Chloroprocaine (Nesacaine®)	E	Low	8.7	–	S	Pl esterase
Lidocaine (Xylocaine®)	A	Int	7.9	64.3	Int	Hepatic
Mepivacaine (Carbocaine®)	A	Low	7.6	77.5	Int	Hepatic
Bupivacaine (Marcaine®/Sensorcaine®)	A	High	8.1	95.6	L	Hepatic
Levobupivacaine	A	High	8.1	>97	L	Hepatic
Ropivacaine (Naropin®)	A	Int	8.1	94	L	Hepatic

Notes: A = amide type; E = ester type; Pot = potency; %PB = percentage protein binding; Dur = approximate duration in peripheral nerve blockade; S = short; Int = intermediate; L = long; Met = metabolism; Pl esterase = plasma esterase.

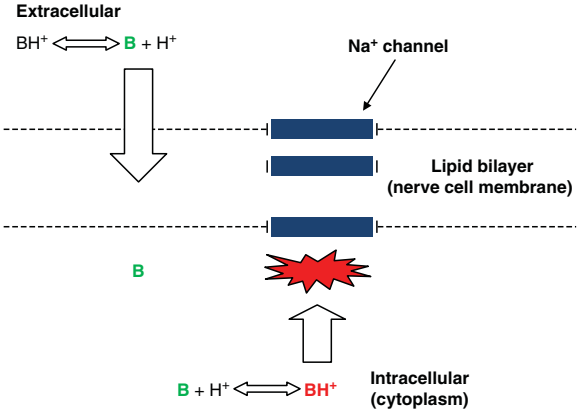

Figure 1.3 Non-ionized local anesthetic crossing the nerve cell membrane to affect intracellular portion of sodium channel as ionized drug.

internal portion of the Na^+ channel to exert the drug's effect (Figure 1.3).

Potency/lipophilicity

Lipid solubility of local anesthetic agents is a major determinant of drug potency. Lipid solubility is often quantified by use of a partition coefficient. The partition coefficient for a particular agent is a ratio of the un-ionized concentration of the drug between two solvents: an aqueous (ionized) solvent (e.g., water) and some non-ionized, hydrophobic solvent (e.g., hexane). In general, as the partition coefficient increases, so too does the agent's lipid solubility. Ultimately, the more lipid soluble an agent, the greater it's potency (Table 1.1).

Protein binding

Plasma proteins avidly bind to local anesthetics in circulation, essentially inactivating the drug. It is the free, unbound form of the drug that is active. Serum alpha 1-acid glycoprotein binds local anesthetics with high affinity along with serum albumin. As the drug is absorbed from the site of administration, serum proteins bind to the free drug in circulation until serum protein stores are saturated.

The affinity of local anesthetic agents for protein molecules has been correlated with the duration of anesthetic effect, though a number of other pharmacologic and physiologic factors are ultimately involved (Table 1.1).

Drug effect

Local anesthetics are capable of blocking nerve action potentials by reversibly binding to the intracellular portion of sodium channel proteins within nerve cell membranes.

To exert this effect, the un-ionized, neutral form of the anesthetic crosses into and through the nerve cell membrane (Figure 1.3). Once inside the cell, the anesthetic is ionized and binds to the inner portion of transmembrane sodium channels. By attatching to the sodium channels within the nerve cell membrane, local anesthetics prevent depolarization of the nerve cell, reducing action potential formation.

Local anesthetic metabolism

Amide local anesthetics are predominantly broken down by the liver. The rate of metabolism depends primarily on liver blood flow and the particular agent

used, as some variability does exist. In general, lidocaine and mepivacaine tend to be more rapidly metabolized than ropivacaine and bupivacaine.

Ester local anesthetics are rapidly metabolized by plasma pseudo-cholinesterase. As such, their metabolism may be prolonged in patients with severe liver dysfunction, pseudo-cholinesterase deficiency, or atypical pseudo-cholinesterase. While the metabolites of ester local anesthetics are inactive, they can rarely be allergenic as para-aminobenzoic acid (PABA) has been implicated in allergic reactions to ester agents.

Commonly used local anesthetics for peripheral nerve blocks

2-Chloroprocaine

2-Chloroprocaine (Nesacaine®) is an amino-ester local anesthetic that was first marketed in the 1950s. The drug has a rapid onset and short duration when used for peripheral nerve blockade, and is a popular choice for cases of short duration where postoperative analgesia is not a concern. The agent is available in 1%, 2% (preservative-free), and 3% (preservative-free) concentrations. Use of 3% 2-chloroprocaine in volumes of 20 to 30 ml may yield 1.5 to 3 hours of surgical anesthesia with a very low toxicity profile relative to commonly used amide local anesthetics due to its extremely rapid metabolism in the plasma.

Lidocaine

Lidocaine (Xylocaine®) was the first synthetic amino-amide local anesthetic developed (1940s) and remains one of the most popular agents available today. Used in peripheral nerve blocks, the drug's onset, duration, and degree of muscle relaxation are related to the total dose used. Lidocaine is typically characterized as an agent of intermediate onset and duration. Upper or lower extremity nerve blocks typically require the use of 1% to 2% concentrations with volumes ranging from 15 to 40 ml yielding approximately 1 to 3 hours of surgical anesthesia. The maximum recommended dose of this agent can be increased with the addition of a vasoconstictor such as epinephrine (Table 1.2).

Mepivacaine

Mepivacaine (Carbocaine®) is another commonly used amino-amide local anesthetic characterized by its intermediate onset and duration. The drug is available in 1%, 1.5%, and 2% concentrations for peripheral nerve blockade. Upper or lower extremity nerve blocks placed using 1.5% or 2% mepivicaine will provide approximately 3 to 6 hours of surgical anesthesia. The dose and duration of mepivacaine can be increased with adjunctive use of a vasoconstrictor, such as epinephrine (Table 1.2). Mepivicaine is usually a good choice for procedures requiring surgical anesthesia without the need for prolonged postoperative analgesia.

Table 1.2 Maximum recommended local anesthetic doses commonly used for peripheral nerve blocks[1]

	Without epinephrine	With epinephrine
2-Chloroprocaine	11 mg/kg (up to 800 mg)	14 mg/kg (up to 1,000 mg)
Lidocaine	5 mg/kg	7 mg/kg
Mepivacaine	5 mg/kg	7–9 mg/kg
Bupivacaine	3 mg/kg	3 mg/kg
Levobupivacaine	3 mg/kg	3 mg/kg
Ropivacaine	3 mg/kg	3 mg/kg

Note: [1]Toxicity data based on intravenous infusion in animals.

Bupivacaine

Bupivacaine (Marcaine®, Sensorcaine®) is characterized as a long-acting amino-amide local anesthetic. Introduced in the 1960s, the drug remains popular today despite the development of newer agents with safer toxicity profiles. Bupivacaine is highly lipid soluble and thus very potent relative to other local anesthetics. The drug's high pKa and strong protein binding affinity correlate with a relatively slower onset when used for peripheral nerve blockade in concentrations between 0.25% and 0.5%. Sensory blockade is usually profound, while motor blockade may be only partial or inadequate for cases where complete muscle relaxation is necessary. Postoperative sensory analgesia is prolonged after bupivacaine use and may last 12 to 24 hours following block placement.

Levobupivacaine

Levobupivacaine (Chirocaine®) is the S-enantiomer of bupivacaine. The drug was developed and

marketed in the late 1990s as an alternative to racemic bupivacaine with a safer cardiac toxicity profile. The agent's pharmacologic effect is very similar to bupivacaine, having a relatively slow onset and long duration. The drug is typically used in 0.25% and 0.5% concentrations for peripheral nerve blockade providing 6 to 8 hours of surgical anesthesia.

Ropivacaine

Ropivacaine (Naropin®) is another long-acting amide local anesthetic first marketed in the 1990s. Found to have less cardiac toxicity than bupivacaine in animal models, the drug has grown in popularity as a safer alternative for peripheral nerve blockade where large volumes of anesthetic are required. Ropivacaine is distributed as the isolated S-enantiomer of the drug with a pKa and onset similar to bupivacaine, but slightly less lipid solubility. Sensory blockade when using ropivacaine is typically very strong, with motor blockade being variable, affected by the concentration and total dose of drug administered. Motor blockade may be less than that seen with equal concentrations and volumes of bupivacaine or levobupivacaine (McGlade *et al.* 1998; Beaulieu *et al.* 2006). Ropivacaine is available in 0.2%, 0.5%, 0.75%, and 1% concentrations for peripheral nerve blockade. While surgical anesthesia time may be limited to 6 to 8 hours following peripheral nerve blockade, the analgesic effects provided by ropivacaine may extend beyond 12 to 24 hours depending on the concentration used.

Local anesthetic toxicity

Systemic toxicity

Local anesthetic toxicity is a relatively rare, though potentially devastating, complication of regional anesthesia (Table 1.3). Systemic toxicity from local anesthetics can occur as a result of intra-arterial, intravenous, or peripheral tissue injection. Toxic blood and tissue levels will typically manifest as a spectrum of neurological symptoms (ringing in the ears, circumoral numbness and tingling) and signs (muscle twitching, grand mal seizure). If systemic levels of the anesthetic are high enough, respiratory and cardiac involvement with eventual cardiovascular collapse will result. This occurs as local anesthetic molecules avidly bind to voltage-gated sodium channels in cardiac tissue. As it turns out, bupivacaine does this more readily and with greater intensity than other types of local anesthetics, hence the greater concern for its pro-arrhythmic potential. Ropivacaine and levobupivacaine also share this concern but have a larger therapeutic window: reportedly 40% and 35% respective reductions in cardio-toxic risk as compared with bupivacaine (Table 1.4) (Rathmell *et al.* 2004).

Recall that signs and symptoms of local anesthetic toxicity can manifest within seconds to hours following injection depending on a number of factors including the amount, site, and route of injection (Tables 1.5 and 1.6). For example, a seizure may occur within seconds of a relatively small intra-arterial injection during an interscalene brachial plexus block, or require many minutes to manifest following placement of an intercostal nerve block with a large volume of concentrated local anesthetic (Table 1.5).

Table 1.3 Rates of systemic toxic reactions related to local anesthetic use in peripheral nerve blocks by study (without use of ultrasound)

	N	#STR	Rate (frequency/10,000)
1	7,532	15	20
2	21,278	16	7.5
3	9,396	0	0
4	521	1	20

Notes: 1 = Brown *et al.* 1995; 2 = Auroy *et al.* 1997; 3 = Giaufre *et al.* 1996 (pediatric cases only); 4 Borgeat *et al.* 2001. Revised chart from: Mulroy M (2002) Systemic toxicity and cardio-toxicity from local anesthetics: incidence and preventative measures. *Regional Anesthesia and Pain Medicine.* **27**(6):556–61.
#STR = frequency of systemic toxic reactions.

Table 1.4 Relative risk of cardio-toxicity among equivalent doses of amide local anesthetics commonly used for peripheral nerve blockade (greatest to least)

Bupivacaine
Levobupivacaine
Ropivacaine
Mepivacaine
Lidocaine

Additional considerations

According to three separate studies, the incidence of systemic toxicity during brachial plexus blockade in

Table 1.5 Factors increasing systemic toxicity of local anesthetics

Local anesthetic choice
Local anesthetic dose
Block location
Decreased protein binding of local anesthetic (low protein states: malnutrition, chronic illness, liver failure, renal failure, etc.)
Acidosis
Peripheral vasoconstriction
Hyperdynamic circulation (this may occur with use of epinephrine)

Table 1.6 Systemic absorption of local anesthetic by site of injection (greatest to least)

Intercostal
Caudal
Paracervical
Epidural
Brachial plexus
Sciatic

adults has been reported from 7.5 to 20 per 10,000 peripheral nerve blocks.

Patient safety is probably improved with some simple safety checks and considerations when bolusing with large volumes of local anesthetic for peripheral nerve blockade: use of less cardio-toxic long-acting agents (ropivacaine and levobupivacaine), incremental aspirations prior to injections, and limiting the total dose of anesthetic administered.

Management of systemic local anesthetic toxicity

In a patient where local anesthetic toxicity is suspected, treatment and supportive care by the anesthesiologist should be undertaken without delay. Emergency airway and resuscitation equipment as well as medications should always be immediately available wherever regional anesthetics are being performed. The airway should be made secure and oxygen provided. If symptoms of central nervous system (CNS) toxicity progress to seizures, medication should be given to abort the seizure activity. Sodium pentothal 50 to 100 mg or midazolam 2 to 5 mg will often suffice. For cases of complete cardiovascular collapse, advanced cardiac life support (ACLS) protocol should be undertaken. The morbidity and mortality in cases of ventricular fibrillation due to bupivacaine overdose is high, and it is often recommended to consider cardiopulmonary bypass in refractory cases.

Since the late 1990s, increased research has been undertaken regarding the use of lipid emulsion therapy in local anesthetic induced cardio-toxicity. Several laboratory and clinical case reports have now been published reporting successful resuscitative efforts using lipid infusions to counter local anesthetic induced cardio-toxicity. Bolus doses ranging from 1 to 3 ml/kg of 20% lipid emulsion in cases of local anesthetic overdose are typical.

There are theories as to the biologic plausibility of lipid therapy in cases of local anesthetic toxicity. One such theory involves lipid partitioning of the anesthetic away from receptors in tissue ("lipid sink"), thereby alleviating or preventing signs of cardio-toxicity (Weinberg 2008). As more data have become available, it now seems prudent to consider early use of this medication in suspected overdose cases.

Additional considerations

Dosing regimen for lipid emulsion therapy: For suspected local anesthetic toxicity, administer 20% lipid solution 1 ml/kg bolus every 5 minutes up to 3 ml/kg followed by 20% lipid infusion 0.25 ml/kg/min for 3 hours.

Information on lipid emulsion therapy for local anesthetic overdose, including case reports and current research, may be found at LipidRescue™ (www.lipidrescue.org)

Neurotoxicity

Toxicity to nerves during regional anesthetic blockade can occur as a result of local anesthetics themselves or from additives and preservatives within the anesthetic. Local anesthetics do have some neurotoxic effect when applied directly to isolated nerve fibers, though this effect is largely concentration dependent. Lidocaine has specifically been studied for its toxic effect in high concentrations with prolonged exposure to nerve axons (Lambert *et al.* 1994; Kanai *et al.* 2000). This toxic effect is likely

multifactorial involving disruption of the nerve's normal homeostatic environment and perhaps changes in intrinsic neural blood blow. Despite findings of some neurotoxic potential, however, the clinical use of local anesthetics in currently recommended concentrations for peripheral nerve blockade is considered safe.

Additives to local anesthetics for peripheral nerve blocks

Additives to local anesthetics for peripheral nerve blockade will have variable effects on block onset time, anesthetic duration, and postoperative analgesia. When deciding on whether or not to use such medications, practitioners should always be aware of the additive drug's pharmacology, effects, and systemic side-effects profile. Integration of this information with the type of local anesthetic to be used, as well as surgical and patient specific factors, may influence the decision to use a particular adjuvant agent.

Epinephrine

Epinephrine is a commonly used additive to local anesthetics when performing peripheral nerve blocks for a number of reasons. Epinephrine has been shown to increase block intensity as well as duration of anesthesia and analgesia with intermediate-acting local anesthetics such as lidocaine and mepivacaine. As a vasoconstrictor with strong alpha-1 effects, epinephrine decreases systemic absorption of the local anesthetic limiting peak plasma levels and prolonging block time. The drug also provides a marker for intravascular injection in dilute concentrations due to its beta-1 effects.

Adjuvant use of epinephrine will have systemic effects, including tachycardia and increased cardiac inotropy, and therefore its use in patients with a significant cardiac history should be carefully considered. The drug should probably be avoided when performing a block to an area receiving diminished or absent anastomotic blood flow. Due to concerns about ischemic neurotoxicity, doses administered in concentrations of 1:400,000 (2.5 mcg/ml) or less may be prudent. Epinephrine administered perineurally decreases extrinsic blood supply when administered in higher concentrations, though there is no evidence this effect is detrimental to humans.

Clonidine

Clonidine is an alpha-2 adrenergic agonist, which has been shown to improve anesthesia and analgesia of peripheral nerve blocks, especially in conjunction with intermediate-acting local anesthetics such as lidocaine and mepivacaine. Use of the drug causes dose-dependent side effects (hypotension, bradycardia, and sedation). By keeping the total dose to <150 mcg, these side effects can be minimized or avoided altogether (Rathmell *et al.* 2004).

Sodium bicarbonate

The addition of sodium bicarbonate to intermediate-acting local anesthetics is often used in an effort to speed onset during peripheral nerve blockade by raising the local anesthetic's pH closer to physiologic pH. In theory, the greater the proportion of the drug in the base (non-ionized) form, the more rapid its passage across the nerve cell membrane to the site where it will have an effect.

In the case of plain mepivacaine or lidocaine, 1 mEq $NaHCO_3$ per 10 ml of local anesthetic is mixed and purported to help speed onset, though this effect is largely unsupported in the literature (Neal *et al.* 2008). There is some evidence of decreased onset time when bicarbonate is added to anesthetics commercially prepared with epinephrine (these preparations tend to be more acidic in nature than plain preparations). The addition of sodium bicarbonate, however, can destabilize local anesthetics. In the case of concentrated preparations of bupivacaine or ropivacaine, the anesthetic will precipitate in solution when mixed with sodium bicarbonate.

Opioids

The use of opioids as an adjuvant for peripheral nerve blocks has largely been shown to be equivocal. One drug, however, has shown some benefit when used in conjunction with local anesthetics for peripheral blocks. Buprenorphine is an opioid agonist-antagonist. Controlling for a systemic effect of the drug, one study has been published showing a prolonged analgesic effect from buprenorphine when administered perineurally with mepivacaine and tetracaine (Candido 2001). Patients administered a dose of 0.3 mg with local anesthetic for axillary brachial plexus block demonstrated an average analgesic duration of 22.3 hours, compared with 12.5 hours for the group receiving local

anesthetic with intramuscular (IM) buprenorphine. Nausea, vomiting, and sedation are potential side effects of concern with the use of buprenorphine.

Dexamethasone

The use of the synthetic glucocorticoid dexamethasone as an adjunct to local anesthetics for peripheral nerve blocks is receiving increasing interest. The drug clinically appears to lengthen the sensory, motor, and analgesic time of peripheral nerve blocks when added to both intermediate and longer-acting local anesthetics. The mechanism by which this effect occurs has yet to be determined.

At the time of writing, a number of studies have been published showing a beneficial effect of dexamethasone as an adjunct to local anesthetics in regional anesthesia and pain medicine procedures (see "Suggested reading"). Dexamethasone use in epidural steroid injections is increasingly popular among pain practitioners because of the medication's pharmacologic profile in comparison with other corticosteroids: dexamethasone is non-particulate and void of neurotoxic preservatives (Benzon *et al.* 2007). It should be noted, however, that current studies assessing the effect of dexamethasone added to plain local anesthetics for peripheral nerve blockade have generally been critiqued as being non-standardized and/or under-powered to achieve statistically significant results (Williams *et al.* 2009).

Concern over ischemic neurotoxicity has been raised due to the drug's effect, like epinephrine, of decreasing normal nerve tissue blood flow as demonstrated by topical application of 0.4% dexamethasone to the exposed sciatic nerve in rats. As when using epinephrine, it would seem prudent to properly select candidates for adjunctive use of dexamethasone excluding patients at greatest risk for ischemic nerve injury (e.g., poorly controlled diabetes, preexisting nerve injury, or demyelinating disorder).

At the time of publication, there are clinical studies under way looking to further assess the effect of dexamethasone added to local anesthetics for peripheral nerve blocks. Many of these studies are being conducted using 8 mg of dexamethasone or less diluted in a 20- to 40-cc local anesthetic mixture. It has been suggested that additional studies are still needed to further assess the side-effects profile and safety of perineural dexamethasone, in addition to an optimal adjuvant dose, before its use becomes more mainstream (Williams *et al.* 2009).

Suggested reading

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Chapter 2

Introduction to ultrasound

Introduction

The use of ultrasound guidance in regional anesthesia is an ever-evolving field with changing technology. This chapter provides a brief overview of the physics involved in two-dimensional ultrasound image generation, ultrasound probe types and machine control features, basic tissue imaging characteristics, and imaging artifacts commonly seen during performance of a regional ultrasound-guided procedure.

Image generation

Ultrasound waves are generated by piezoelectric crystals in the handheld probe. Piezoelectric crystals generate an electrical current when a mechanical stress is applied to them. Therefore, the generation of an electrical current when a mechanical stress is applied is called the *piezoelectric effect.* The reverse can also occur via the *converse piezoelectric effect*, so that an electrical current applied to piezoelectric crystals can induce mechanical stress and deformation. Ultrasound waves are generated via the converse piezoelectric effect. Application of an electrical current to the piezoelectric crystals in the handheld probe causes cyclical deformation of the crystals, which leads to generation of ultrasound waves.

The ultrasound probe acts as both a transmitter and receiver (Figure 2.1). The probe cycles between generating ultrasound waves 1% of the time and "listening" for the return of ultrasound waves or "echoes" 99% of the time. Using the piezoelectric effect, the piezoelectric crystals in the handheld probe convert the mechanical energy of the returning echoes into an electrical current, which is processed by the machine to produce a two-dimensional grayscale image that is seen on the screen. The image on the screen can range from black to white. The greater the energy from the returning echoes from an area, the whiter the image will appear.

- **Hyperechoic** areas have a great amount of energy from returning echoes and are seen as white.
- **Hypoechoic** areas have less energy from returning echoes and are seen as gray.
- **Anechoic** areas without returning echoes are seen as black (Table 2.1).

Generation of images requires reflection of ultrasound waves back to the probe to be processed, this reflection occurs at the boundary or interface of different types of tissue. *Acoustic impedance* is the resistance to the passage of ultrasound waves, the greater the acoustic impedance, the more resistant that tissue is to the passage of ultrasound waves. The greatest reflection of echoes back to the probe comes from interfaces of tissues with the greatest difference in acoustic impedance (Table 2.2). From Table 2.2 we can see that there is a large difference between the acoustic impedance of air and soft tissue, which is why any interface between air and soft tissue will give a hyperechoic image. There is also a large difference between the acoustic impedance of bone and soft tissue, therefore, bone and soft tissue interfaces will also give a hyperechoic image. The difference in acoustic impedance between various types of soft tissue, such as blood, muscle, and fat, are very small and result in hypoechoic images.

Other imaging technologies used in medicine, such as X-rays or computed tomography (CT) scans can show density directly. However, ultrasound imaging is based on the differences in acoustic impedance at tissue interfaces. A hyperechoic image on ultrasound should not be interpreted as more dense and a hypoechoic image as less dense. Recall that both bone and air bubbles can give hyperechoic images, yet they have very different densities.